The health and care of children with Down Syndrome

MD(Res) thesis

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I, Caoimhe McKenna 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.

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ABSTRACT

Down Syndrome (DS) affects ~10,500 children in the UK. Individuals with DS continue to have poorer health outcomes compared with the general population, and other forms of intellectual disability.

By systematically mapping two decades of paediatric DS literature, I found a general decline in the number of publications, since 2014. The majority of publications utilised observational methodologies, with few interventional (5.6%) or qualitative/mixed-method studies (4.3%). Most publications focused on development & cognition, oncology and neurology; relatively few looked at the prevalence of morbidities and health surveillance.

Using a large electronic health record dataset I determined the prevalence of morbidities among individuals with DS (N=4,648, age range 0-75 years), and compared with matched controls. The most prevalent morbidities in the DS cohort were hypothyroidism (30.4%), congenital cardiac disease (27.8%), epilepsy (21.9%) and hearing impairment (19.2%). We also found an increased risk of autism (aOR 7.7), chronic kidney disease (aOR 2.3), inflammatory bowel disease (aOR 2.4), non-accidental injury (aOR 1.9), sleep disordered breathing (SDB) (aOR 6.6) and vitamin-D deficiency (aOR 3.1).

Finally, I explored current practice with regard to the routine health surveillance of children with DS, in paediatric departments across the UK. Sixty four departments returned a copy of their local health surveillance protocol. Practice was compared across departments, and with three national guidelines. For congenital cardiac disease, hypothyroidism and hearing/visual impairment, practice appeared to be consistent and compliant with national guidelines. However, in other areas (echocardiogram at transition, SBD, vitamin-D deficiency & renal/liver function), practice was patchy and inconsistent.

The findings highlight a need for ongoing research in the field of paediatric DS, targeted at areas of greatest need, and those morbidities which are prevalent in the DS cohort. Furthermore, our findings highlight a need a single, evidence based guideline for the health surveillance of children with DS, to promote high quality, consistent care.

IMPACT STATEMENT

The findings of this thesis are important for the DS community, health professionals involved in their care and researchers working in this field.

In the context of limited resources and funding, targeted research is vital. Our unique mapping exercise, of two decades of paediatric DS literature, illustrates what research has already been undertaken in the field and areas of relative paucity. These findings are useful to researchers, by highlighting areas where evidence is currently lacking, and to justify academic investment in these areas.

In determining the prevalence of morbidities and cancers in a large cohort of individuals with DS, this research provides some of the most reliable existing estimates of disease prevalence in this population. An appreciation of disease prevalence is important for health professionals caring for individuals with DS, informing them about which conditions their patients may develop, and empowering them to target health surveillance and therapies accordingly. These figures are also important to inform parents/carers about what may lie ahead in the health of child with DS; arming them with knowledge, but also potentially allaying some fears.

Finally the exploration of health surveillance practice, in paediatric departments across the UK, provides a unique insight to practice "on the frontline". In many areas this research highlights inconsistencies in practice which have the potential to increase health inequalities and contribute to missed opportunities to reduce mortality and morbidity. Our findings provide support for the development of a single national guideline for the health surveillance of children with DS, in order to achieve optimal and consistent care across the UK.

The findings of this thesis will be disseminated in a number of ways. Manuscripts, based on the findings of each project, will be submitted for peer reviewed publication. Any subsequent publications will be shared directly with key stakeholders in DS healthcare (e.g. the Down Syndrome Medical Interest Group (DSMIG), the Royal College of Paediatrics and Child Health (RCPCH), the British Association of Community Child Health (BACCH) and the Royal College of General Practitioners (RCGP). A report of the findings will also be shared with third sector organisations such as the Down Syndrome Association (DSA) and the Down Syndrome Research Foundation (DSRF). These organisations have the ability to translate these

findings into widely used clinical practice guidelines and/or to share this material with their members, for the purpose of education and raising awareness.

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ABBREVIATIONS

A&E	Accident and Emergency
AAP	American Association of Paediatrics
ADHD	Attention Deficit Hyperactivity Disorder
AGREE-11	Appraisal of Guidelines for Research & Evaluation
ALL	Acute lymphoblastic leukaemia
aOR	Adjusted Odds Ratio
ASD	Autistic spectrum disorder
BACCH	British Association of Community Child Health
BACE	β-Secretases
BMI	Body Mass Index
CALIBER	Cardiovascular disease research using Linked Bespoke studies and Electronic health Records
CI	Confidence Interval
CNS	Central Nervous System
CPRD	Clinical Practice Research Datalink
C-spine	Cervical spine
CXR	Chest X-Ray
DELBI	German instrument for methodological Guideline Appraisal
DM	Diabetes Mellitus
DMARD	Disease-modifying anti-rheumatic drugs
DoH	Department of Health
DHSC	Department of Health and Social Care
DS	Down Syndrome
DSA	Down Syndrome Association
DSMIG	Down Syndrome Medical Interest Group
DSS	Down Syndrome Scotland
ECG	Electrocardiogram
Echo	Echocardiogram
EDSA	European Down Syndrome Association
EEG	Electroencephalogram
ENT	Ear Nose and Throat
FBC	Full Blood Count
GORD	Gastroesophageal Reflux Disease
GP	General Practitioner
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HbA1c	Glycated haemoglobin
HES	Hospital Episode Statistics
iCAHE	International Centre for Allied Health Evidence
ICD	International Classification Of Disease
LLR	Leicester, Leicestershire & Rutland
LOMEDS	Late onset myoclonic epilepsy in DS
Mb	Megabase
MiChe	Mini-Checklist
NCRAS	National Cancer Registration and Analysis Service
NDSCR	National Down Syndrome Cytogenic Register
NHS	National Health Service
NIHR	National Institute for Health Research
NIPT	Non-Invasive Prenatal Testing
ONS	Office for National Statistics
OPCS	Office of Population Census and Surveys

OR	Odds Ratio
PbR	Payments by Result
PET	positron emission tomography
PHE	Public Health England
RCPCH	Royal College of Paediatrics and Child Health
RR	Risk Ratio
Rx	Treatment
SDB	Sleep Disordered Breathing
SES	Socioeconomic Status
TFT	Thyroid Function Test
TIA	Transient ischaemic attack
U&E	Urea and Electrolytes
UK	United Kingdom
USA	United States of America
UTS	Up To date Standard
yrs	Years

BACKGROUND

Down Syndrome

Down syndrome (DS) is the most prevalent chromosomal disorder worldwide and the most common genetic cause of intellectual disability, with an estimated incidence of 1 per 1000 live births in the UK[1-3]. Approximately two children with DS are born every day in the UK[1]. A recent population study estimated that there are 10,500 children with DS living in the UK[2].

The condition was described by its eponym, Dr John Langdon Down, in 1866[4]. DS is associated with trisomy of part, or all, of chromosome 21, in some (mosaicism), or all, of the cells. Chromosome 21 is the smallest autosomal chromosome, representing 1.5% of the human genome, it is comprised of approximately 400 genes. It is hypothesised that a trisomic dose of these genes is responsible for the DS phenotype[5 6]. In particular a 16Mb region on the long arm of chromosome 21 has been implicated in explaining the cardinal features of DS[6].

Chromosomal trisomies are usually caused by an error in cell division ("non-disjunction"), however a small proportion (3-4%) are associated with chromosomal translocations. The incidence of DS increases with maternal age, due to an increased occurrence of nondisjunction in aging oocytes[7]. As average maternal age in the UK has increased, the prenatal incidence of DS has also increased, however the live birth rate has remained relatively constant due to a high uptake of terminations[8].

Antenatal screening for DS has been available on the NHS since 1989. At present, serum and ultrasound screening for DS is available for pregnant women between 10 and 14 weeks gestation, followed by invasive screening as required (amniocentesis and chorionic villus sampling). In recent years there have been significant scientific advancements in prenatal screening for DS, through the detection of free foetal DNA in the blood of pregnant women[9]. In those UK centres, where non-invasive prenatal testing (NIPT) is available, the uptake has been high[10]. The introduction of NIPT has been met with controversy from some members of the DS community[11].

Due to its common nature and associated morbidities, clinicians from various disciplines are likely to encounter individuals with DS throughout their career. This thesis aims to add to the evidence base which supports clinicians in providing optimal care for individuals with DS.

Down Syndrome Associated Morbidity

DS is characterised by intellectual disability and the development of multiple health problems throughout the life-course[12]. These include congenital heart defects[13], leukaemia[14], disorders of the thyroid[15], impairment of vision[16] and hearing[17], disorders of the gastrointestinal tract[18], immune deficiency[19], respiratory tract infections[20], sleep disordered breathing[21], instability of the c-spine[22], dementia[23] and various malignancies[24].

In this thesis, health conditions which are considered to occur more commonly in individuals with DS, compared to the general population, will be referred to as 'DS associated morbidity'. Specific DS associated morbidities are explored in more detail below.

There is limited existing literature on the prevalence of DS associated morbidity among individuals with DS, and within the literature the reported prevalence of these morbidities varies dramatically (

Table 1). Most of the studies rely on retrospective chart reviews and have small sample sizes. Furthermore, the majority of existing publications focus on the adult population and do not provide a comparison with a reference group[12 25-27 28].

Table 1: Existing literature estimating the prevalence of multiple DS associated morbidities in individuals with Down Syndrome, showing wide variance in the reported figures.

	Henderson et al. (2007)a. [25]		**Van Allen et al. (1999)b.** [26]		**Prasher et al. (1994)c.** [27]		**Kerins et al. (2008)d.** [28]	
Methodology	Retrospective chart review		Retrospective chart review		Retrospective chart review		Retrospective chart review	
Age of participants (Mean/range)	43.8 / 18-61yrs		47.9 / 30-68yrs		42.2 / 16-76yrs		51.0 / 30-65yrs	
Number of DS participants	89		38		201		141	
Congenital heart disease	14%		15.8%		-		18%	
Disorders of the ear	Hearing deficit	33%	Hearing deficit	25%	Severe hearing deficit	12%	-	
Disorders of the eye	36%		Cataract	50%	Cataract	24%	Cataract	14%
			Keratoconus	15.8 %	Nystagmus	11%		
Epilepsy / Seizures	28%		36.8%		8%		21%	
Behavioural problems	Childhood conduct disorder	50%	50%		-		-	
Dementia	Alzheimer's	16%	Alzheimer's	75%	-		70%	
Gastrointestinal disorders	Coeliac disease	11%	-		Gastro surgery	4%	Gastroesophageal reflux	14%
Diabetes Mellitus (DM)	Type 1 DM	5%	-		3%		-	
Hypothyroidism	23%		28.9%		-		40%	
Depression	19%		-		-		18%	
Skin pathology	Eczema	23%	-		Eczema	10%	26%	
Musculoskeletal disorders	Osteoarthritis	14%	Atlantoaxial instability	7.9%	Arthritis	<1%	Arthritis	13%
Respiratory problems	-		Pulmonary hypertension	7.8%	-			
			Chronic interstitial disease	30%				
Acquired cardiovascular disease	-		15.8%		Hypertension	<1%	Hypertension	3%

Genitourinary disorders	-	31.6%	Undescended testis	15%	Incontinence	18%

a) Prevalence of DS associated morbidities among adults with DS (mean age 43.8yrs), attending intellectual disabilities services in North East England. Prevalence based on retrospective chart review. No comparison group.

b) Prevalence of DS associated morbidities among adults with DS (mean age 47.9yrs) residing in a provincial residential centre in North America. Prevalence based on retrospective chart review. No comparison group.

c) Prevalence of DS associated morbidities among adults and adolescents with DS (mean age 42.2yrs), residing in community or in small residential units, in Birmingham, UK. Prevalence based on retrospective chart review and patient/carer recall. No comparison group.

d) Prevalence of DS associated morbidities among adults with DS (mean age 51.0yrs), attending a teaching hospital in a metropolitan area of the United States. Prevalence based on retrospective chart review. No comparison group.

In this thesis I will focus on those DS associated morbidities which tend to be chronic in nature, as opposed to acute illnesses, such as infection. While infections, and respiratory infections in particular, are a significant cause of mortality and morbidity in individuals with DS[29], research has recently been published exploring this from within our own research group[20 30]. Furthermore, chronic and multi-morbidity arguably contribute a larger burden to the health and well-being of individuals with DS throughout the life-course, and constitute the majority of interactions with health care services[31 32]. Chronic health disorders are also the more common focus of DS health surveillance programmes. As I will explore below, health surveillance is a key component of DS healthcare.

Although the primary focus of this MD thesis is children, I also explore the occurrence of DS associated morbidities across the life-course (see Project 2). Health in childhood shapes that in adulthood. Understanding the burden of specific DS associated morbidities in the adult population also informs the care of younger patients, for example by identifying conditions which are amenable to early detection through screening, and potential targets for preventative therapies. An appreciation of disease burden in adulthood is particularly relevant in the context of an aging population of individuals with DS.

In recent decades the life expectancy of individuals with DS has increased dramatically, from 12 years in the 1940s, to 60 years in present-day[29 33]. This has inevitably led to a shift in the burden of disease. An aging population of individuals with DS presents clinicians with new challenges, with regard to management. Adults with DS display features of premature aging, with an increased occurrence of multiple DS associated morbidities, compared to the general population. The early recognition, treatment and ideally the prevention of disease in childhood will set children with DS on a trajectory for better health in adulthood.

DS associated morbidity in the context of this thesis

In this section I explore a number of DS associated morbidities which relate specifically to this thesis, in more detail. As mentioned above, these DS associated morbidities tend to be more chronic in nature and some are core component of DS health surveillance. The conditions explored in detail below also mirror those morbidities whose prevalence will be explored in Project 2.

As a general structure, for each DS associated morbidity I aim to summarise the current estimated prevalence of these conditions in the DS population (where available), the importance of these morbidities in this cohort (e.g. contribution to mortality), their relevance to DS health surveillance and the unique challenges of diagnosing and managing these morbidities in individuals with DS.

Cardio- And Cerebrovascular Disease in Down Syndrome

Individuals with DS are at risk of both congenital and acquired cardiac disease. The prevalence of congenital heart disease is estimated between 40 to 60%[13 34-36], compared with 0.8% in the general population[37].

In newborns with DS, physical examination alone may fail to identify the most commonly occurring congenital heart defects[38]. Consequently, additional investigations such an echocardiogram (echo), chest X-ray (CXR), pre and post-ductal saturation measurements and electrocardiograms (ECG) are required. The most commonly occurring defects in the DS population are atrioventricular, ventricular and secundum atrial septal defects[13 35]. The majority of these require surgical correction in early childhood[39]. After surgical correction, patients may still develop valvular dysfunction, arrhythmias and/or require reoperation[39]. Despite significant advancements in management, congenital heart disease remains a significant cause of mortality among individuals with DS[40].

From adolescence onwards, even those individuals with a "normal" heart at birth, are at risk of developing mitral valve prolapse and aortic regurgitation[41-46]. Clauss et al. undertook echocardiograms on 149 young people (aged 10-20years) with DS, who had no previous cardiac diagnosis and were asymptomatic. They found a new cardiac diagnosis in 9 patients

(6%), including left ventricular hypertrophy, valve abnormalities and arrhythmia[47]. In later life, respiratory disease may also lead to pulmonary vascular disease and right heart failure[48].

There is limited existing evidence on the prevalence of adult onset cardiac disease in individuals with DS, however several studies have suggested lower rates of atherosclerosis, coronary artery disease and hypertension, compared to the general population[49-51]. It is hypothesised that overexpression of 'atherosclerotic protective genes' on chromosome 21 may explain this reduction in risk[52-54].

Despite this, individuals with DS have higher rates of stroke and transient ischaemic attacks (TIAs), compared with non-DS[55]. The association between DS and ischaemic stroke may be explained by cardio-embolic risk, secondary to congenital heart disease or acquired valvular defects[55 56]. Moyamoya disease, a chronic vascular occlusive disorder of the internal carotid artery which predisposes to ischaemic stroke, is also increasingly recognised in the DS population[57-59]. Individuals with DS are more likely to have a stroke at a younger age and to have multiple events, compared with the general population[55].

In this thesis I aim to determine the prevalence of congenital and acquired (ischaemic heart disease and stroke) cardiovascular disease in children and adults with DS. I will also explore local practices, with regard to cardiac health surveillance, in paediatric departments across the UK. The literature mapping exercise will determine what proportion of the existing paediatric DS literature focuses on cardiovascular disorders.

Dementia in Down Syndrome

Dementia is used an umbrella term for the multiple subtypes of neuropathology (e.g. Alzheimer's disease, vascular dementia, frontotemporal dementia), which result in a chronic, irreversible decline in cognitive function.

Although the primary focus of this thesis is children, and dementia is classically considered a disorder of old age, this condition is still relevant in the context of this thesis: Not only because it appears to be a common condition in DS, looming on the horizon for many of our paediatric patients and their families, with onset at an early age compared to the general population, but also because it has been suggested that dementia in DS has its aetiological origins long before disease onset, possibly in childhood[60 61].

The estimated prevalence of dementia in individuals with DS varies widely, reportedly between 4-55% in those ages over 50 years[62-65], with a mean onset of ~54years[66]. Other studies have reported that almost all individuals with DS, over the age of 35years, demonstrate "neuropathology of Alzheimer's disease"[67 68].

It is postulated that a "trisomic dose" of the *APP* gene on chromosome 21 results in the overproduction of beta-amyloid protein, leading to the development of senile amyloid plaques in the brain: The "amyloid cascade" is considered to be the central pathogenesis of Alzheimer's disease[69]. Both an exponential rise in the biochemical levels of beta-amyloid protein and the prevalence of neuropathology has been demonstrated in individuals with DS, after the age of 40 years[67 70]. Furthermore, many of the conditions which are generally considered more common in DS, such as obesity[71], diabetes[72] and sleep apnoea[73], are also associated with an increased risk of the other subtypes of dementia[74].

Even at a younger age, a decline in cognitive function, distinct from a diagnosis of dementia, is described among individuals with DS. Severe cognitive deterioration, including acquired apraxia (difficulty planning and performing motor tasks) and agnosia (difficulty interpreting sensations), have been reported in up to one third of individuals with DS at the age of 30 years, with a rising prevalence in subsequent years[75 76]. Individuals with DS also show a more rapid decline in verbal ability and performance skills throughout the aging process, both compared to the general population and other adults with non-DS related intellectual disability[77].

Dementia is a significant contributor to the mortality of individuals with DS. Coppus et al. demonstrated, over a 3 year period of follow-up, that the mortality of individuals with DS and dementia was more than twice that of those with DS who not suffering from dementia[62]. In another longitudinal study of over 200 adults with DS, dementia was reported as the proximate cause of death in 70% of cases, and crude mortality rates were reported as five times higher in individuals with dementia, compared to those without[78].

While dementia appears to be common in elderly individuals with DS, it is not universal. As the early neuropathological abnormalities, which predispose to the development of dementia, are postulated to develop decades before the onset of symptoms, it is argued that effective efforts will have to focus on preventative therapies and biomarkers to predict disease onset.

Rafii et al. have investigated multiple biomarkers for the early detection of dementia in individuals with DS. They found some correlation with cognitive and functional measures and regional glucose metabolism on PET neuroimaging[79]. If early detection is possible, early intervention and treatment, even in childhood, may be possible. It is also plausible that simply the optimal management of DS associated morbidities (e.g. obesity, sleep apnoea) in childhood would have the potential to reduce the risk of dementia in later life.

In this thesis I aim to determine the prevalence of dementia in individuals with DS. The literature mapping exercise will also determine what proportion of the existing paediatric DS literature focuses on neurological disease and cognition.

Seizures and Epilepsy in Down Syndrome

As with many DS associated morbidities, the reported prevalence of seizures disorders in this population varies widely (1.4-46%)[80-83]. Even in the absence of seizures, a high prevalence of EEG abnormalities (~25%) are reported in the DS population[84]. It is postulated that inherent structural brain anomalies in DS, "due to decreased neuronal density with frontal and temporal hypoplasia, persistence of dendrites, abnormal neuronal lamination, fewer inhibitory interneurons, and other metabolic adaptations related to genetic overexpression" may account for this[85].

A triphasic pattern of epilepsy among individuals with DS is described: Infantile onset (before 1 year of age), early adulthood onset and late onset epilepsy, including late myoclonic epilepsy in DS (LOMEDS)[81]. Overall, the prevalence of epilepsy among individuals with DS increases with age[80].

Among those with DS and seizures, the largest proportion will present in their first year of life with infantile spasms and/or tonic-clonic seizures. In the non-DS population, it is well documented that infantile spasms are associated with poor developmental outcomes and high mortality rates[86]. Within the DS population, Eiserman et al. demonstrated a significant correlation between treatment lag and the persistence of spasms, lower developmental quotient and a higher score of autistic features[87]. These findings highlight the importance of prompt recognition and adequate therapy for infantile spasms in children with DS. A small number of studies have suggested that children with DS have a different therapeutic response to the

commonly prescribed medications, compared with non-DS children[85 88 89]. However, there is limited existing literature to support clinicians in choosing the optimal therapeutic regime for those with DS[85].

In middle and late childhood, seizures are more typically tonic-clonic in nature, however reflex-seizures and Lennox-Gastaux syndrome have also been described at this age[80 81]. In adulthood, the most common seizure types are simple or complex partial seizures, as well as tonic-clonic seizures[80].

Over the age of 50 years, late myoclonic epilepsy in DS (LOMEDS) is described[90 91]. Among individuals with DS and dementia, seizures appear to be associated with a rapid decline in cognitive function[92]. The early recognition and appropriate management of seizures in adults with DS may ameliorate the progression of cognitive decline. Only a small number of studies have explored DS specific therapies in this group[93 94].

In this thesis I aim to determine the prevalence of epilepsy in children and adults with DS. The literature mapping exercise will determine what proportion of the existing paediatric DS literature focuses on neurological disorders, such as epilepsy[80 81 95].

Sleep Disordered Breathing in Down Syndrome

Sleep disordered breathing (SDB) is an umbrella term for several conditions which result in decreased oxygenation during sleep. These conditions include central sleep apnoea (decreased neurological drive to breathe), hypoventilation (inadequate respiratory effort) and obstructive sleep apnoea (the complete or partial, mechanical obstruction of the upper airway during sleep). Obstructive sleep apnoea (OSA) appears to be the most common subtype of SDB in individuals with DS[96].

During sleep, OSA may present with loud snoring, gasping, snorting or choking noises, gaps in breathing or frequent waking. However, there may not be any observable signs. During the day, OSA may manifest as fatigue, poor concentration, mood and behaviour changes and headache[97]. If untreated, OSA can cause hypertension, premature heart disease and contribute to neurocognitive disease[97].

Individuals with DS tend to have several features which predispose to the development of OSA, including underdevelopment of the midface and jaw, relative enlargement of the tongue, obesity and hypotonia. They are also more likely to suffer with upper respiratory tract infections, increased nasal secretions and gastroesophageal reflux[98].

Typical therapies for OSA include adenotonsillectomy, lingual tonsillectomy, positive airway pressure ventilation while asleep and lifestyle measures (e.g. weight loss). Studies have demonstrated that, among children with DS, OSA may persist even after tonsillectomy[96 99].

SDB is particularly common among children with DS, with reported prevalence of up to 43-66%[96 100-102]. In children, SDB has been associated with brain changes in areas which regulate cognition, mood and behaviour[103]. In a large parental survey, sleep disturbance in children with DS was negatively associated with personal care, recreation, education, mobility, mealtimes, fitness, relationships and homelife[104].

SDB is most reliably diagnosed via an overnight polysomnographic study. The procedure is often poorly tolerated, particularly among children with intellectual disability[105]. Some studies have shown that homebased cardiorespiratory polygraphy may be more acceptable to parents[101] and shows high diagnostic sensitivity[106], specifically in children with DS. While proxy diagnostic markers of SDB (e.g. urinary concentration of neurotransmitters) show some utility in non-DS populations, these findings have not been replicated in the DS cohort[107].

Active screening for SDB in individuals with DS is included in only a minority of DS health surveillance guidelines[105]. Consequently testing for SDB tends to be prompted by patient symptoms or parent report of symptoms. Multiple studies have shown that parental report is insufficient to identify all those with evidence of SDB on polysomnography[108 109]. Furthermore studies have failed to accurately predict SDB based on obesity, tonsillar size or age[101 102 110]. This reinforces the importance of active screening for SDB among individuals with DS.

In this thesis I aim to determine the prevalence of SDB in children and adults with DS. I will also explore local practices, with regard to surveillance for SDB, in paediatric departments across the UK. The literature mapping exercise will determine what proportion of the existing paediatric DS literature focuses on disorders of the Ear, Nose and Throat (ENT), such as SDB.

Thyroid Dysfunction in Down Syndrome

It is well established that individuals with DS are at an increased risk of thyroid disorders throughout the life-course[15 111]. This spectrum includes congenital hypothyroidism, acquired hypothyroidism (immune and non-immune related), subclinical hypothyroidism and hyperthyroidism[112].

Hypothyroidism is generally considered more common among individuals with DS, than the other forms of thyroid dysfunction, with reported prevalence ranging from 13-63%[113-117]. Among 500 children with DS, Pierce et al. estimated that 50% developed thyroid disease (predominantly hypothyroidism) by late adolescence, with 20% of hypothyroidism diagnosed before the age of 6 months[112].

It is hypothesised that dysregulation of the immune system underlies the development of thyroid disorders in individuals with DS[118]. It is estimated that thyroid autoantibodies are found in 13-34% of individuals with DS[118-121].

The signs and symptoms of hypothyroidism can be subtle and insidious. Children with hypothyroidism may present with fatigue, weight gain, constipation, failure to thrive and developmental delay. Particularly among adults with DS, hypothyroidism is an important differential for dementia and depression.

If diagnosed, hypothyroidism is easily treated with thyroxine supplementation. Untreated, hypothyroidism can have lasting effects of cognition, growth and general health[122]. It has been demonstrated that every month without thyroid hormone supplementation worsens developmental outcomes at school age[123 124].

A study of over 600 individuals with DS, found that active screening for thyroid disease resulted in a significant increase in diagnostic rate, suggesting that relying on self-report of symptoms alone is insufficient to identify disease[125]. Thyroid function tests and testing for thyroid antibodies are a common component of DS health surveillance guidelines.

In this thesis I aim to determine the prevalence of both hypo- and hyperthyroidism in children and adults with DS. I will also explore local practices, with regard to thyroid health surveillance, in paediatric departments across the UK. The literature mapping exercise will determine what proportion of the existing paediatric DS literature focuses on endocrine disorders, such as thyroid dysfunction.

Mental Health in Down Syndrome

Psychiatric disorders in general are more common among individuals with intellectual disability[126], however some specific psychiatric illnesses are considered to be more prevalent in the DS population.

In childhood, the prevalence of attention deficit hyperactivity disorder (ADHD) has been estimated between 34 and 44% in DS[127 128]. ADHD is characterized by inattentiveness, hyperactivity and impulsivity. It can negatively impact a children's ability to learn, and ADHD associated behaviours can be challenging for care givers. ADHD is commonly treated with stimulant medications, however caution must be used when prescribing such treatments to non-typically developing children with intellectual disability, as their use has been associated with increased side effects, such as sleep disturbance, agitation and irritiability[129 130]. Few studies have explored the safety and efficacy of treatments for ADHD in individuals with DS[131 132].

The reported prevalence of autistic spectrum disorder (ASD) among individuals with DS is highly variable with figures quoted between 7 and 42%[128 133 134]. This may reflect challenges in diagnosing ASD in those with intellectual disability and developmental delay, as many of the diagnostic tools have not been adapted for use in this subgroup of patients[135]. Capone et al. cautioned against "over reliance upon standardized rating scales to make the diagnosis of ASD" specifically in children with DS, and made a number of recommendations to alter the diagnostic criteria when assessing individuals with DS, including taking into account inherent delay in speech and language abilities[136].

In a study comparing the symptom profiles of children with ASD, children with DS and children with both, Godfrey et al. reported that children with DS and ASD present with "less severe social-communication impairments than peers with ASD alone, particularly when controlling for verbal cognitive abilities[137]. The diagnosis of ASD in individuals with DS is further complicated by the co-occurrence of numerous DS associated morbidities which may contribute to the development of ASD (e.g. hypoxic brain injury following cardiac surgery, infantile spasms and congenital hypothyroidism)[138].

Autism may manifest as a delay in the development of speech and language, repetitive behaviours, difficulties with social interaction and rigidity of routine. As a parent of a child

with DS once described during a consultation at a community paediatric clinic *"there are children with DS who are 'easy work', and there are those that are 'hard work'. The ones that are 'hard work' have autism"*. Similar views have been reported in a number of qualitative studies of parenting experience of children with DS and autism, highlighting the challenges of behavioural management in this group of patients [139-141].

Some parents also report feeling that behavioural disorders, such as autism and ADHD, are underdiagnosed and undertreated in children with DS, because the signs and symptoms are dismissed as simply being "part of DS". This phenomenon is known as "diagnostic overshadowing", whereby clinicians minimise the significance of emotional disorders in individuals with intellectual disability due to inherent bias about the "normal spectrum" of emotional and psychiatric behaviours in this cohort[142 143].

Rasmussen et al. report a significant delay in the age of diagnosis of ASD among children with DS, ranging between 4 and 33 years, with a mean age of diagnosis being 14.4years[138], compared with an average age of diagnosis in the non-DS population of around 4 and a half years[144]. Early intervention for ASD is key for both children and families, and a delay in diagnosis of ASD among children may result in suboptimal outcomes[145-147].

Treatments for ASD include behavioural management, family therapy, education and school-based interventions, social skills training, cognitive behavioural therapy and occupational therapy. A delay, or failure to diagnose ASD, may result in a missed opportunity for treatment. As a mother of a child with DS and ASD describes "*this delayed diagnosis [of ASD] creates many problems. Clearly, children with a dual diagnosis are at a real disadvantage in their development and education, even relative to children with only one of the disabilities. Even more problematic are the faulty expectations that may be placed on the child where the autism has gone undetected*"[148].

There is limited existing literature exploring mental health in adolescents with DS. While Dykens et al. did not find any significant difference in the prevalence of anxiety and depressive disorders among young adults with DS, compared to those with other forms of intellectual disability, they did report higher rates of psychosis and depression with psychotic features[149]. Interestingly, they also reported lower rates of bipolar disorder in the adolescents with DS[149].

In a 8 year cohort study of almost 200 young people with DS, looking at changes in mental health over time, Foley et al. reported that, while behavioural difficulties in young adults with DS tend to improve over time, depressive symptoms do not. Consequently they recommended "screening for potential depressive symptoms [among adolescents with DS] and increased awareness among families, carers, and service providers", in order to identify and treat symptoms earlier[150].

Several studies have also described a cognitive regression in adolescents with DS[151-154], sometimes referred to as "Young Adults with Disintegrative Syndrome" (YADS)[155]. This is characterized by cognitive decline, regression in speech and language, loss of adaptive and social skills and behavioural changes. In addition, these adolescents may also experience anxiety and mood disorders, worsening of repetitive thoughts and behaviours, aggression, psychosis and in some cases catanonia[151-154]. Significant life events or emotional stressors have been suggested as a trigger for this regression[156].

The limited existing literature on mental health in adolescents DS extends to literature on appropriate therapies in this cohort. In a small case series, Fujino et al. describe a psychosocial treatment programme for young adults with emotional and behaviour problems[157]. Another case series reported the successful use of medications (donepezil and serotonin reuptake inhibitors) to treat acute regressions in adolescents with DS[158].

In adulthood, the prevalence of depression among individuals with DS has been reported between 2 and 11%[159-161], with an average age of onset estimated around 29 years[162]. There are several factors which are postulated to predispose individuals with DS to the development of depression including "smaller hippocampal volumes, changes in neurotransmitter systems, deficits in language and working memory, attachment behaviours and frequently occurring somatic disorders"[161]. Thyroid dysfunction, dementia and SDB, which are also common among individuals with DS, are important organic differentials for depression or altered mood in patients with DS.

The presentation of depression in adults with DS may differ to from that in the general population. For example, biological features (e.g. psychomotor retardation, disturbed sleep, loss of appetite) and adaptive skills (e.g. dressing, feeding, washing) may be more frequent presentations that cognitive features (e.g. loss of concentration, suicidal ideation)[163 164]. This

can present diagnostic challenges, particularly for clinicians who are not experienced in diagnosing mood disorders in patients with co-existing intellectual disability. Modified guidelines for the diagnosis of depression in adults with intellectual disability have been developed[165 166], but these are not specific to DS.

The morbidity and mortality associated with depression in adults with DS can be significant. Myers et al. reported attempted suicide in 27% of a small group of adults with DS and major depression[167]. Over a mean follow-up for 7 years, Collacott et al. also found that individuals with DS and depression showed significantly more impairment in adaptive behaviour (e.g. independent functioning, economic activity, language development, socialisation) than those without depression, even after the resolution of depressive symptoms[168]. Meins et al. reported an increase in depressive symptoms over time, among adults with DS, compared to reduction in symptoms in individuals with other forms of intellectual disability[169].

The prevalence and natural history of schizophrenia is less well explored in the DS cohort. Collacott et al. reported a prevalence of schizophrenia and/or 'paranoid state' in 1.6% of a DS cohort cohort[170]. In a case series of individuals with DS and schizophrenia, Cooper et al described the most common features as "a marked change from premorbid functioning, with decline in functioning and social performance, marked abnormal (psychotic) beliefs and/or experiences and bizarre behaviours". The mean age of onset was 37.4 years[171]. Unlike Collacott et al.[168] they did not find the same decline in adaptive behaviours, after symptom resolution[171].

Despite a significant burden of disease, mental health and behavioural disorders are not commonly included in health surveillance guidelines for individuals with DS. As described above, this may in part be due to a lack of diagnostic tools adapted specifically for use in DS or, as described above, "diagnostic overshadowing".

In this thesis I aim to determine the prevalence of several mental health disorders (i.e. ADHD, autism, anxiety and depression, and schizophrenia) in children and adults with DS. I will also explore local practices, with regard to ASD surveillance (e.g. developmental assessments), in paediatric departments across the UK. The literature mapping exercise will determine what proportion of the existing paediatric DS literature focuses on mental health and behaviour.

Hearing and Visual Impairment in Down Syndrome

Hearing and visual impairments are common across the life-course of individuals with DS. Early detection and intervention is vital to prevent such sensory impairments impacting on development (e.g. language, behaviour and social functioning), cognition and executive function.

It is estimated almost all individuals with DS will experience hearing loss at some point throughout their life[172-174]. This may be sensorineural, conductive or mixed in nature and may be either temporary or permanent.

In childhood, the most common cause of hearing impairment is otitis media with effusion ("glue ear")[172 175]. In a cohort of 290 children with DS, Schrijver et al estimated the prevalence of glue ear around 40% and of sensorineural hearing loss around 4.5%[176]. However, the reported prevalence of glue ear among children with DS has been reported as high as 93% in 1 year olds, dropping to 68% by 5 years[172]. Furthermore the ear canals of individuals with DS tend to be narrow, predisposing to the accumulation of wax, which can contribute to conductive hearing loss[177].

Hearing impairment in childhood in particular can contribute to the delayed development of speech and language and social skills. Specifically in children with DS, Laws et al. demonstrated a significant adverse impact of hearing loss on the acquisition of language, compared to those without hearing loss[178].

In children with DS, conductive hearing loss can be managed similarly to that in typically developing children, for example with hearing aids or ventilation tubes (grommets)[17 179 180]. However the latter may be technically challenging to perform, less effective and more prone to complications in children with DS, compared with typically developing children[179].

Lau et al. demonstrated that relying on parental report alone was insufficient to identify all children with DS who had evidence of hearing loss on testing[181]. Again, this emphasises the importance of regular routine screening. Screening for hearing impairment in children is a common component of DS health surveillance guidelines.

Among adults with DS, age-related sensorineural hearing loss (presbyacusis) is more common than conductive hearing loss. This tends to develop at an earlier age, both compared with the general population and other forms of intellectual disability[182]. There are few studies examining the prevalence of hearing loss in adults with DS, with current estimates between 51 and 74%[183].

Particularly in adulthood, hearing loss has the potential to impact an individual's ability to live and function independently, and to increase social isolation. Hearing loss may also exacerbate co-existing DS associated morbidities such as dementia.

Ocular disorders are also considered common among children with DS[184 185]. These include cataracts, infantile glaucoma, strabismus, nystagmus, blepharitis and refractive errors. As with hearing loss, visual impairment can have an adverse impact on wider development. Sauer et al. found an association between visual impairment and challenging behaviour in children with developmental delay, including DS[186].

The prevalence of ocular disorders increases with age[187]. It is estimated that visual impairment is present in almost half of individuals with DS aged 50 to 59 years, compared to 13% of individuals of the same age with other forms of intellectual disability[188 189]. Over the age of 60 years, the prevalence has been reported as high as 85%. Senile cataracts also develop earlier in adults with DS, compared to the general population, with a high proportion requiring surgery[190]. Visual assessments are a core component of DS health surveillance and are commonly included in guidelines.

In this thesis I aim to determine the prevalence of hearing impairment and a number of ocular disorders (e.g. cataract, glaucoma) in children and adults with DS. I will also explore local practices, with regard to surveillance for hearing and visual impairment, in paediatric departments across the UK. The literature mapping exercise will determine what proportion of the existing paediatric DS literature focuses on ENT and neurological disorders (such as visual and hearing impairment).

Gastroenterological and Renal Disease in Down Syndrome

Gastrointestinal disorders are common among individuals with DS and can have a significant impact on quality of life. Spaphis et al. reported that 77% of neonates with DS had some form

of gastrointestinal disorder[191]. Among children with DS, gastrointestinal diseases and feeding difficulties are estimated to account for 19% of all hospital admissions[192].

A wide range of gastrointestinal disorders have been associated with DS. In general these are can be grouped into three main categories: anatomical abnormalities, immunological anomalies and functional disorders[193].

Duodenal atresia and stenosis are the most common anatomical gastrointestinal abnormalities reported in individuals with DS, affecting approximately 4% of infants[194]. Duodenal atresia or stenosis may be detected antenatally[195] but a number of cases, particularly those with the less severe 'congenital duodenal membrane', may not be detected until adolescence or adulthood[196].

Hirschsprung's disease is also a congenital anatomical gastrointestinal disorder, estimated to affect 2.8% of individuals with DS[197]. Hirschsprung's disease refers to the absence of a particular subset of nerve cells in the bowel, which results in ineffective or absent peristalsis. Consequently patients may have symptoms ranging from constipation to acute bowel obstruction. There is limited existing literature suggesting that additional anatomical abnormalities, such as anorectal malformations, oesophageal atresia, pyloric stenosis and malrotation of the small intestine are also more common in individuals with DS[193].

Coeliac disease is the most common immunological gastrointestinal anomaly associated with DS, with estimates of prevalence ranging from 4 to 19%[25 27 198 199]. Coeliac disease is an autoimmune disorder associated with a reaction to gliadins and glutens, commonly found in wheat and similar grains. In children with DS the most common symptoms are constipation, growth failure, anaemia, intermittent diarrhoea and vomiting[200]. However the presentation of coeliac disease in DS can be atypical and insidious. It has been reported that up to one third of patients with DS and coeliac disease have no gastrointestinal symptoms at all[201]. Furthermore individuals with intellectual disability may find it difficult to describe their symptoms in a way which is understood.

Coeliac disease can be effectively treated with dietary modification. Delayed diagnosis and treatment of coeliac disease has been associated with increased risks of gastrointestinal cancer and lymphoma[202]. Active screening for coeliac disease in included in a number of DS health surveillance guidelines, however its inclusion is not universal.

Inflammatory bowel disease (IBD) is also an immunological disorder of the gastrointestinal tract. There have been numerous case series and reports of inflammatory bowel disease among individuals with DS[203-206], but there are no reliable estimates of prevalence within the DS population. In a small cohort, Wallace et al. reported the presence of IBD in 2% of adult patients with DS[207]. It is postulated that such an association between DS and IBD may be explained by "immune dysregulation"[19 203 208].

IBD typically presents with intermittent abdominal discomfort, diarrhoea and rectal bleeding. However the existing case reports often describe a delay in diagnosis, which suggests that IBD may present atypically in patients with DS, or that patients may find it difficult to express their symptoms and/or to access healthcare[203-206]. Untreated, IBD can be life threatening during acute flare ups and predispose to the development of bowel cancers[209]. IBD is usually diagnosed via endoscopy, colonoscopy and histological sampling. Screening for IBD is not a common component of DS health surveillance.

Gastrooesophageal reflux disease (GORD) is a common functional gastrointestinal disorder estimated to affect up to 40% of children[210], and 9-14% of adults[28 207] with DS. This may be explained by a generalised reduction in tone and less time spent in the sitting position in infancy. Studies have also described a reduction in the number of neurons in the oesophageal plexus ganglia in individuals with DS, compared to controls[211].

GORD may present with vomiting, epigastric discomfort or feeding difficulties. However in individuals with intellectual disability the symptoms are often atypical (e.g. presenting with rumination and hematemesis)[212].

Untreated, GORD can exacerbate obstructive sleep apnoea, contribute to recurrent respiratory tract infections, cause severe peptic oesophagitis, with or without stricture, and rarely oesophageal adenocarcinoma[193 213]. Hillemeier et al reported that up 43% of infants and children with DS and GORD developed a "serious complication", including recurrent pneumonia and oesophageal stricture[214]. Treatment of GORD in individuals with DS is based on standard protocols for the general population. However, individuals with DS are more likely to require surgical treatment (e.g. fundoplication)[215].

Given its frequency and associated complications, screening for GORD among children with DS has been recommended by some[193 215], however it is not a common component of DS health surveillance guidelines. Diagnosis is often based on symptomatology, but the gold standard for diagnosis remains 24-hour pH-metry[216 217].

A broad range of kidney disorders have also described in the DS population. In a large cohort of children with DS, Kupferman et al. reported renal and urinary tract anomalies in 3.2% of children, compared with 0.7% of the general population. These included anterior urethral obstruction, cystic dysplastic kidney, hydronephrosis, posterior urethral valves and renal agenesis[218]. A number of case series, mostly describing findings from autopsy in individuals with DS, have also described disorders affecting the glomeruli (e.g. glomerulonephritis, minimal change disease and focal segmental glomeruloscelorsis)[219-222]. All of these conditions have the potential to result in chronic kidney disease and renal failure.

As described below, renal failure is a major contributor to mortality across the life-course of individuals with DS[29]. In a small cross-sectional study of 69 children and young adults with DS, Malaga et al. actively screened individuals with DS for renal disease and found evidence of chronic renal failure in 4.5%, none of whom had a prior diagnosis[223]. This may suggest that active monitoring for renal disease, as opposed to relying on self-report of symptoms, is required. Routine screening for renal disease is not a common component of DS health surveillance guidelines.

In this thesis I aim to determine the prevalence of a number of gastrointestinal and renal disorders (e.g. congenital gastrointestinal disease, gastro-oesophageal reflux, inflammatory bowel disease and chronic kidney disease) in children and adults with DS. I will also explore local practices, with regard to surveillance for a number of some of these conditions (e.g. coeliac disease and renal function), in paediatric departments across the UK. The literature mapping exercise will determine what proportion of the existing paediatric DS literature focuses on gastrointestinal and genitourinary disorders.

Obesity and Diabetes Mellitus in Down Syndrome

Overweight and obesity is considered to be significantly more common among individuals with DS, however the reported prevalence figures are highly variable, ranging from 20-95% among

adults[78 224-227] and 12-70% among children[228-231]. This may reflect the variable methods of measuring overweight and obesity. Some of these methods, such as Bergman's body adiposity index and bio-impedance analysis, lack validity in individuals with DS[232-234]. Monitoring of weight status is a common component of routine DS health surveillance.

A number of factors have been suggested to contribute to the increased risk of overweight and obesity among individuals with DS, compared to the general population. These include lower physical activity levels[230 235-238], unfavourable diets[230 236 239 240], co-morbidities including hypothyroidism[230 241], reduced resting energy expenditure[230 242 243], increased serum leptin levels[230 244 245], a high prevalence of sleep disordered breathing[230 235], reduced opportunities for friendship and social opportunities[246] and parental feeding practices[247].

A number of studies have suggested that higher rates of overweight and obesity tend to occur in children with DS, from the age of 2 years[228 248-250]. Given that weight status tends to persist throughout childhood and into adulthood, this suggests that early infancy may be a key window for intervention in DS. A number of trials have used various combinations of exercise training, education, nutritional interventions and family based therapies to tackle overweight and obesity in children in DS, with either no impact or only modest effects[251-256].

The negative impact of overweight and obesity on health and well-being is well established in the general population[257]. In a large DS cohort, obesity was associated with a significantly increased risk of mortality, compared to those with DS who were not obese[258]. Also within the DS population, overweight and obesity have been associated with the development of obstructive sleep apnoea[259-261], dyslipidaemia[262], gait abnormalities,[263 264], reduced cardiorespiratory fitness[265] and hyperinsulinemia[266 267].

A number of studies have suggested that type 1 diabetes mellitus is more common in individuals with DS, compared to the general population[268-270]. However, an association with type 2 diabetes is less well established[12 266 269].

Rohrer et al. reported a younger age of onset of type 1 in patients with DS, versus non-DS, with 19% being diagnosed in the first 3 years of life. However, the DS patients appeared to require less insulin and showed better glycaemic control. It was postulated that this may be due to a "less complex lifestyle"[271]. Anwar et al. also reported that individuals with DS and type 1

diabetes mellitus tended to require "simpler" insulin regimens to achieve adequate glycaemic control, compared with non-DS patients[269].

Diabetes (type 1 and 2) has been shown to cause the same complications in patients with DS, as are reported in the general population, including diabetic retinopathy, peripheral neuropathy and nephropathy[269]. Despite this, active screening for diabetes mellitus is not a common component of DS health surveillance guidelines.

In this thesis I aim to provide estimates of average BMI in a large population of individuals with DS, compared to controls, and to determine prevalence of type 1 diabetes mellitus and type 2 diabetes mellitus. I will also explore local practices, with regard to surveillance for diabetes, in paediatric departments across the UK. The literature mapping exercise will determine what proportion of the existing paediatric DS literature focuses on endocrine, nutritional and metabolic disorders (such as obesity and diabetes mellitus).

Musculoskeletal Disease in Down Syndrome

Arthritis is an umbrella term incorporating a large number of conditions which ultimately cause pain and inflammation of the joints.

Very few studies have examined the prevalence of arthritis in the DS population. In actively screening 503 children with DS for signs of musculoskeletal disease, Foley et al. reported a prevalence of arthritis in 2%, with the majority having a 'polyarticular rheumatoid factor negative arthritis', predominantly affecting the small joints of the hands and wrists. Other studies have suggested the prevalence is much lower in children with DS, although these did not involve active screening by musculoskeletal specialists[272]. The literature on the prevalence of arthritis among adults with DS is also limited. In a group of 64 adults with DS, with an average age of 43.8 years, Henderson et al. reported that 14% had osteoarthritis[273]. Osteoarthritis is a form of arthritis characterised by 'wear and tear' of the joint cartilage and bone.

It has been suggested that arthritis is underdiagnosed in the DS population[272 274], and that when made, the diagnosis tends to be delayed[272 275-277]. In a retrospective review of electronic health records of children with DS and arthritis, Juj et al. reported that the average time between symptom onset and diagnosis was 2 years[272]. In a smaller case series, Olsen et al. reported a

mean time to diagnosis of 3.3 years[276]. This is compared with 0.25 years in children without DS[278].

Juvenile idiopathic arthritis is the most common form of arthritis in children and adolescents in the general population. It is characterised by joint pain or inflammation in one or more joints, with the potential to cause irreversible joint damage. In a group of almost 50 children with DS and juvenile idiopathic arthritis, Jones et al. reported that almost 30% had erosive bone damage at diagnosis and the majority required an escalation to 'combination therapy' including steroids and disease-modifying antirheumatic drugs (DMARDs). Of those started on DMARDs, 72% had to be discontinued due to intolerance or medication side-effects[275]. There are no existing guidelines specifically for the management of arthritis in children or adults with DS.

Untreated, arthritis has the potential to adversely affect the development of gross motor skills and limit mobility in a group which are already at a higher risk of developmental delay, a sedentary lifestyle, obesity and social isolation. Active screening for musculoskeletal conditions is not a common component of DS health surveillance guidelines.

Atlantoaxial instability is another musculoskeletal condition, affecting the cervical spine, which occurs more commonly in individuals with DS, compared with the general population. However the reported prevalence varies significantly, with existing studies suggesting a prevalence of between 2-27% among individuals with DS[22 279-283].

Atlantoaxial instability is characterised by instability between the 1st and 2nd vertebrae of the spine. As a result, the odontoid on the 2nd vertebrae is at risk of becoming displaced and impinging on the spinal cord. Impingement of the spinal cord can manifest as neck discomfort, an abnormal gait, incontinence, paralysis or decreased respiratory drive and death.

Atlantoaxial instability can be visualised on lateral neck X-rays in the neutral and flexed position, demonstrating an increase in the anterior atlano-odontoid distance[284]. Even with a normal appearance on X-ray, displacement of the odontoid can be precipitated by neck trauma, injury, intubation or surgery to the head and neck[22].

Providing education and raising awareness about atlantoaxial instability, among individuals with DS and parents/carers, is a common component of routine clinical review. Typically this

advice includes avoiding sports which are associated with a higher risk of neck injury (e.g. trampolining and rugby), and red flag symptoms such as neck pain, abnormal head posture, reduced neck movement, a change in gait or frequency of falls, increasing fatigue on walking and a deterioration in fine motor skills[285].

In this thesis I aim to determine the prevalence of arthritis and atlantoaxial instability in children and adults with DS. I will also explore local practices, with regard to the provision of 'c-spine advice' during routine clinical review, in paediatric departments across the UK. The literature mapping exercise will determine what proportion of the existing paediatric DS literature focuses on musculoskeletal disorders, such as arthritis and atlantoaxial instability

Dermatological Disorders in Down Syndrome

While there are a large number of case reports documenting skin conditions[286-293] among individuals with DS, there are few observational studies examining the breadth and prevalence of dermatological disease in this population.

Eczema (atopic dermatitis) is the most common inflammatory condition of the skin. It is typically a chronic condition, associated with dry, itching and cracked skin. Eczema has the potential to significantly impact quality of life, for both the patient and the family[294-296], as well as predisposing to superimposed infections[297 298]. Through clinical examination of 200 children and adults with DS, Schepis et al. found evidence of eczema in 4.9%[299]. However, other studies have reported prevalence as high as 56.5%[300-302], possibly due to different diagnostic definitions.

As explored above, DS is associated with a number of autoimmune conditions such as hypothyroidism, type 1 diabetes mellitus and coeliac disease[208 303]. A number of studies have also reported an increased prevalence of autoimmune skin conditions, among individuals with DS, compared to the general population. These include relatively common disorders, associated with scaling and skin plaques, such as psoriasis and seborrheic dermatitis[304-306], as well as rarer blistering skin conditions such as pemphigoid and pemphigus[307]. An increased prevalence of pigment altering conditions, such as vitiligo, has also been reported[300 304 306].

In this thesis I aim to determine the prevalence of eczema, and a combined category of other dermatological conditions (i.e. psoriasis, lichen planus, pemphigoid, pemphigus, vitiligo, and

seborrheic dermatitis) in children and adults with DS. The literature mapping exercise will also determine what proportion of the existing paediatric DS literature focuses on dermatological disorders.

Non-Accidental Injury and Maltreatment in Children with Down Syndrome

A large number of observational studies have demonstrated that children with disabilities are significantly more likely to suffer maltreatment and neglect, compared to children without disability[308-312]. In a meta-analysis, Jones et al. reported that children with disability had a 3 times increased risk of suffering physical violence[313], compared to those without.

Very few studies have examined the issue of child maltreatment specifically within in the DS population. In a population based study of substantiated childhood maltreatment in Texas, Van Horne et al. found that while children with birth defects had a higher risk of maltreatment in general, the risk in a subgroup of children with DS was not significantly greater, compared with controls[314]. In a Western Australian cohort, McClean et al. also reported that while children with disabilities had a significantly increased risk of maltreatment, children with DS had the same risk as the general population after adjusting for ethnicity, socioeconomic status, maternal age and parental mental health and substance abuse[315].

In this thesis I aim to determine the prevalence of non-accidental injury and maltreatment among children with DS. The literature mapping exercise will also determine what proportion of the existing paediatric DS literature focuses on child protection.

Vitamin D and Iron Deficiency in Down Syndrome

Vitamin D deficiency is common in the UK general population[316 317], but there is limited existing literature which explores the prevalence of vitamin D deficiency and its consequences, specifically in the DS population.

In a longitudinal study of 31 children and adolescents with DS, Stagi et al. reported reduced levels of vitamin D in those with DS, compared to matched controls. They postulated that this difference may be accounted for by reduced exposure to sunlight, as individuals with DS reported ‘less time spent outside’ and ‘less time being physically active’. They also found that vitamin D levels were particularly low among individuals with DS who also had co-existing

obesity or an autoimmune disease[318]. In a cohort of over 400 children with DS, Bokhari et al. estimated the prevalence of vitamin D deficiency to be 66%[319].

The association between Vitamin D, decreased bone mass density and a propensity to fractures is well established[320]. However recent studies, in the non-DS population, have also suggested an association between vitamin D deficiency and propensity to infection[321], respiratory disorders such as asthma[322], insulin resistance[323 324], cardiovascular disease[325-327], Alzheimer's disease[328], autism[329-331], ADHD[332 333], a multitude of cancers[334-336], dental caries[337] and reduced functional ability in the elderly[338], . Many of these conditions are already considered more common in DS population.

It may be that patients with DS would benefit from active screening and treatment of vitamin D deficiency, however this is not commonly included in DS health surveillance guidelines.

The beneficial impact of vitamin D supplementation has already been demonstrated in the DS population, with regard to biochemical markers related to phosphor-calcium metabolism and bone remodelling and bone density[338 339]. However there is limited evidence on specific treatment regimens for this population. Stagi et al. reported that standard doses of vitamin D did not appear sufficient to significantly increase vitamin D levels, particularly among those were obese or had a history of autoimmune disease. They recommended supplementing all children with DS, particularly those in high risk groups, with a higher dose of vitamin D than is recommended for the general paediatric population[318]. However, it should be noted that vitamin D supplementation is not without risks and adverse events have been described[340-342]. Specifically in the DS population, tissue calcification has been reported among children receiving vitamin D[343]. Consequently it would be valuable to determine whether the benefits of supplementation with vitamin D outweigh the risks in all patients with DS, or certain subgroups, and the optimal therapeutic dose.

The prevalence of iron deficiency among individuals with DS is not well characterised. In a cross-sectional study of over 100 children with DS, Dixon et al. reported iron deficiency in 10%, and iron deficiency anaemia in 3%[344].

In the general paediatric population, iron deficiency has been associated with neurocognitive impairment[345 346], stroke[347], behavioural disturbance and ADHD[348-351] and sleep disturbance[352-354]. Again, conditions which are already considered to be more common in DS population.

Checking for anaemia, in the form of a full blood count, is included in a number of DS health surveillance guidelines, however anaemia has been demonstrated as a poor predictor of iron deficiency[355], and additional testing, such an iron studies (transferrin saturation, iron and ferritin) levels, may be required to identify all those with the potential to benefit from iron supplementation.

In this thesis I aim to determine the prevalence of vitamin D and iron deficiency in children and adults with DS. I will also explore local practices, with regard to health surveillance for vitamin D and iron deficiency, in paediatric departments across the UK. The literature mapping exercise will determine what proportion of the existing paediatric DS literature focuses on endocrine, nutritional and metabolic disorders, such as vitamin D and iron deficiency.

Down Syndrome And Cancer

Cancer remains a significant cause of mortality and morbidity in those with DS[29 356-358]. Bittles et al. estimated that cancers accounted for 3.4-7.7.% of the reported causes of death among individuals with DS, across the life-course[29].

The risk of leukaemia among children with DS is high, compared with the general population. Hasle et al. reported that leukaemia constitutes 60% of cancers overall in individuals with DS and 97% of cancer in children[359]. This is compared with around 35% of cancers among non-DS children[360]. The cumulative risk of leukaemia among individuals with DS is estimated to be 2.1% by 5 years of age, and 2.7% by 30 years[359]. The increased risk of leukaemia among individuals with DS seems to dissipate after the age of 30[359 361].

It has been suggested that the 'extra dose' of several genes on chromosome 21 may explain the predisposition to leukaemia in individuals with DS[362]. Lane et al. reported that the overexpression of a nucleosome remodelling protein which in encoded on chromosome 21 (HMGN1), promotes B cell proliferation and the development of B-lineage acute lymphoblastic leukaemia (ALL)[363].

Approximately 10% of newborns with DS develop a variant of acute megakaryocytic leukaemia, termed transient myeloproliferative disorder[364-366]. Although this condition may resolve spontaneously, in a significant number of cases it requires active management and/or supportive therapy[364]. Consequently screening for transient myeloproliferative disorder, in the form of a full blood count taken soon after birth, is a common component of health surveillance guidelines.

While the increased risks of leukaemia among individuals with DS are well established[367], there is ongoing debate about the risks of solid tumours in individuals with DS.

A number of studies have suggested that solid tumours are under-represented in the DS population[40 258 368-371]. In a European cohort of individuals with DS, Hasle et al found lower than expected rates of almost all solid tumours. They reported a significantly lower risk of solid tumours in both men and women with DS, over the age of 40 years, and among older age groups the cancer incidence was ~25% of that found in the general population[361].

Several mechanisms have been proposed to explain a reduced risk of certain cancers among individuals with DS. In a mouse model of DS, Reynolds et al. found that melanoma and lung cancer cells grew at a much slow rate and had fewer blood vessels, compared to a matched control. They hypothesised that this protective restriction of blood vessel growth is secondary to an extra copy of four genes on chromosome 21[372]. It has also been suggested that bioactive adipokines, produced by an excessive number of fat cells in individuals with DS, may also provide a protective effect against solid tumours, while increasing the risk of childhood leukaemia[373]. Some of the reduction in risk may also be explained by lifestyle factors, with individuals with DS being less like to smoke and consume alcohol, compared with the general population[374].

In contrast, a number of studies have reported higher than expected rates of testicular cancer among men with DS[258 358 375]. Hasle et al. reported that testicular tumours occurred three times more often than expected in men with DS[361]. It has been postulated that the increased risk of testicular cancer in males with DS may be explained by increased rates of hypogonadism, undescended testis and higher follicular stimulating hormone concentrations in this population[375-377].

A number of cohort studies have also suggested increased rates of liver[358], gastric[378] and ovarian cancer[361], retinoblastoma[360 361] and lymphoma[360] among individuals with DS, but with only some of these findings reaching statistical significance, and with contradictory findings existing in other studies.

At present, it is recommended that adults with DS avail of standard national cancer screening programmes, such as those for colorectal, breast and cervical cancer[185]. However, if solid tumours such as breast and colorectal cancer are indeed less common among individuals with DS it may be that such screening is unnecessary, and that the risks of screening may outweigh the benefits. Furthermore, if additional cancers (e.g. testicular) are indeed more common among individuals with DS it may be that they would benefit from supplementary screening.

Following a systematic review of cancer screening opportunities, Rethore et al. recommended that adults with DS should participate in colon cancer screening but that breast cancer screening for women was not recommended, and instead should be replaced with annual 'clinical monitoring'. Also for women, they suggested screening for cervical cancer only in those women with DS who were over the age of 25 years and sexually active. For men they recommended annual surveillance for testicular cancer by palpation by a health professional, between the ages of 15 and 45years[379].

The ongoing lack of clarity about the risks of some tumour types in DS reflects a relative paucity of observational studies using large datasets to explore the occurrence of multiple tumour types among those with DS. None of the existing studies have used linked primary, secondary and Cancer Registry healthcare data.

In this thesis I aim to determine the prevalence of multiple cancer types in children and adults with DS using a large linked electronic health record dataset. I will also explore local practices, with regard to cancer surveillance (leukaemia), in paediatric departments across the UK. The literature mapping exercise will determine what proportion of the existing paediatric DS literature focuses on oncological disorders.

Mortality in Individuals with Down Syndrome

It has been reported that 75% of adults with DS survive to 50 years of age and 25% live beyond 60 years of age[380] . While the life expectancy of individuals with the DS has increased

dramatically over recent decades[29 33], they continue to die at a younger age and from different conditions, compared with the general population. After age 35, mortality rates double every 6.4 years in those with DS, as compared to every 9.6 years for those in the general population[381].

In a meta-analysis, O'Leary et al. estimated that individuals with DS die approximately 28 years younger than matched controls. Death at an earlier age was associated with congenital heart disease, multi-morbidity, more severe intellectual disability, low birth weight, maternal age, parental level of education and Black and minority ethnicity. Over time the most significant improvements in life expectancy had been among those with congenital heart disease, likely due advancements in early diagnosis and surgical management[40].

In a large Australian cohort, Bittles et al. examined the causes of mortality in individuals with DS. Across the life-course, they reported that pneumonia, and other types of respiratory infection, were the most common cause of death in individuals with DS, ranging from 23% of deaths in adulthood (19 – 40 years) to almost 40% of deaths in 'senescence' (>40 years). Respiratory infections were also the most common causes of death in childhood (0 – 18years) accounting for 33% of deaths, followed by congenital heart defects (12.8%), cardiac, renal and respiratory failure (11.5%), and cancers (3.4%). In adulthood, congenital heart defects and respiratory infections accounted for the same proportion of deaths (23.1%), also followed by cardiac, renal and respiratory failure (10.2%), and cancers (7.7%). In 'senescence' respiratory infections was followed by coronary artery disease (9.9%), cardiac, renal and respiratory failure (9.0%) and cerebrovascular accidents (6.3%)[29]. These figures reflect the persistent contribution of respiratory infections to mortality in individuals with DS throughout the life-course, with a general shift away from mortality related to congenital heart disease in early life, and towards cancers and cardiovascular diseases in later life.

In this thesis I am to determine the prevalence of major contributors to mortality (e.g. congenital heart disease, acquired heart disease, renal disease, cancer and stroke) in children and adults with DS. I will also explore local practices, with regard to health surveillance for some of these conditions (e.g. congenital heart disease, renal disease), in paediatric departments across the UK. The literature mapping exercise will determine what proportion of the existing paediatric DS literature focuses on mortality.

Healthcare For Individuals With Down Syndrome

The Royal College of Paediatric and Child Health (RCPCH) provides a paediatric service specification for healthcare services for children and young people with DS in the UK[382]. Their essential service standards are summarised in Figure 1. These include a core recommendation that, from diagnosis to transition, all children with DS should be under the care and regular review of a paediatrician with expertise in DS. There are different models for this provision: For example, children with DS may be reviewed regularly at Child Development Clinics in the community setting, with general paediatricians in a hospital setting, or less commonly, at specialist DS clinics led by paediatricians[382]. These clinicians will have different approaches to managing the health of children with DS and in some settings local 'care pathways' have been developed.

Care pathways describe a systematic approach to the health management of patients. They "detail essential steps in the care of patients with a specific clinical problem and describe the patient's expected clinical course"[383]. The aim of a care pathway is to ensure that patient-care is safe, effective, planned and consistent. The ideal care pathway incorporates evidence based best practice, specific guidance on what should be done, when and by whom, an appreciation of local resources and addresses the priorities of patients and carers[384]. Given the complex health needs of individuals with DS, which continue throughout the life-course, care pathways have a valuable role.

Leicester, Leicestershire & Rutland (LRR)[385] and Hull CGG[386] provide examples of local care pathways for children and adults with DS, which incorporate the RCPCH service standards[387]. Both recommend regular follow-up with a community paediatrician from birth to 19 years, with input from specialist paediatric services, allied therapies and education.

Figure 2 provides a summary example of a local paediatric DS care pathway.

Children with DS would be expected to transition from paediatric to adult health services in their adolescence. For example, the LRR and Hull DS care pathways describe transition around 19 years, with planning from 14 years. Following transition, care is largely taken over by General Practitioners (GPs), with input from adult specialist services where necessary (e.g. endocrinology, cardiology).

Transition can be a risky time for adolescents with chronic diseases in general[388]. In a survey of the parents of 151 children with DS and almost 17,000 non-DS children with 'special healthcare needs' who were undergoing transition from paediatric to adult health services, Nugent et al. reported significantly worse outcomes among children with DS, compared to those without, in all of the outcome measures. These included 'successful shift to an adult provider', 'the meeting of adult healthcare needs', 'maintaining health insurance cover' and 'increasing personal responsibility for self-care'[389].

1. From diagnosis to transition, all children with Down's syndrome (DS) must be under the care and regular review of a paediatrician with expertise in DS (who may be a community paediatrician, a paediatrician specialising in neurodisabilities, or a general paediatrician).

2. Children with DS are reviewed by the paediatrician regularly in the first year of life. (A frequency of every 3 months is common practice), and subsequently a minimum of once a year.

3. Specialist services to support the lead paediatrician must be commissioned for *all* children with DS, namely:
   - Speech & Language Therapy
   - Paediatric cardiology (echocardiography and clinical review) in the neonatal period
   - Paediatric ophthalmology
   - Paediatric audiology

4. In addition, the following professionals must be commissioned to perform assessment & management of complications of DS, if found necessary after review by the DS specialist:
   - Physiotherapy
   - Medical specialists (as required and depending on local arrangements) including, but not limited to:
     - Paediatric cardiology
     - Paediatric endocrinology
     - Paediatric surgery
     - ENT surgery
     - Dermatology
     - Paediatric gastroenterology
     - Paediatric orthopaedic/spinal surgery
     - Paediatric respiratory specialists / sleep disordered breathing service
     - Paediatric neurology
     - Sexual health service
     - Occupational Therapy
     - Special needs dentistry
     - Child and Adolescent Mental Health services

5. The lead paediatrician and local education authority must work in close collaboration to ensure specialist education provision is provided as required for children with DS, including early educational interventions such as portage, and educational psychology.

6. The service must have sufficient clerical and administrative support to facilitate early and sustained communication between clinical specialists, and with children/young people with DS and their families, as well as to capability for audit, governance and service improvement to maximise quality of care.

Figure 1. Adapted from RCPCH (2015) Paediatric Service Specification, Service for Children and Young People With Down Syndrome, Core/Essential care pathway service standards.

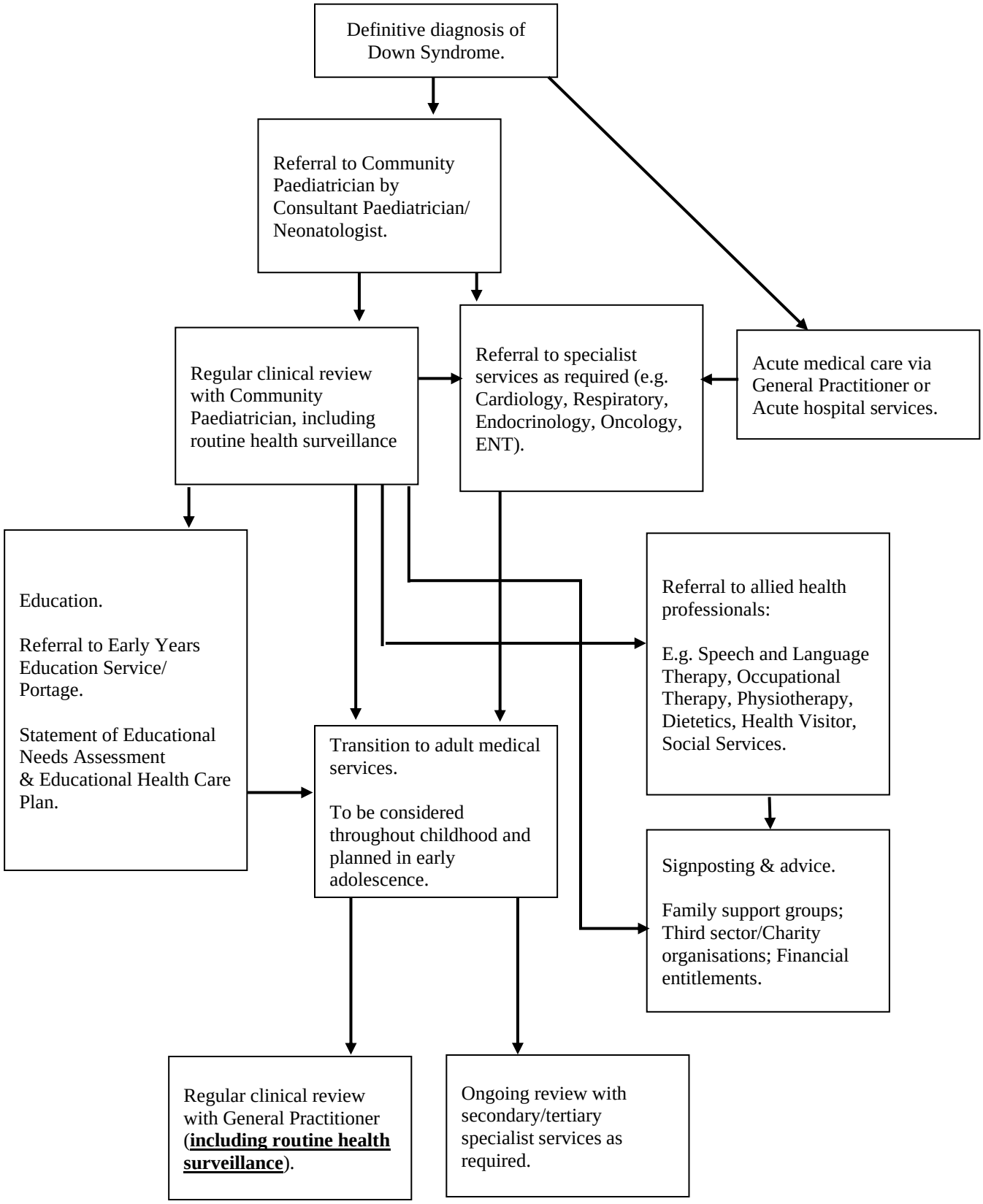

Figure 2: Example Care Pathway for children with Down Syndrome; Adapted from the Leicester, Leicestershire & Rutland (LRR)[385] and Hull CGG[386] Down Syndrome Pathways.

A key component of any paediatric DS care pathway is a regular routine clinical review with a General or Community Paediatrician. In this role, the clinician is well placed to oversee the "bigger picture" of the child's health, often acting as a coordinator of care and a patient advocate. The frequency of clinical review will vary according to local practice, but commonly children with DS are reviewed in an outpatient clinic at frequent intervals under 1 year of age (e.g. 3 – 6 monthly) and less frequently thereafter (e.g. annually).

Appendix 1 provides an example clinic proforma used in the routine clinical review of children with DS in a Community Paediatric department.

During the clinic appointment, the paediatrician will review the medical history and examine the patient in order to identify any underlying ill-health. This may be accompanied by blood tests or additional investigations (e.g. blood pressure, radiological imaging). The paediatrician can prescribe treatments or refer onto specialist centres, where necessary. Ideally clinicians should also provide parents/carers with information and education on important aspects of DS health; for example recognising the signs and symptoms of cervical spine instability and maintaining a healthy lifestyle. Clinicians may also use these appointments to address some of the social determinants of health; for example by signposting to information on financial entitlements, education, housing and family support organisations.

The routine clinical review also provides an opportunity to ensure that key aspects of the child's health needs are being addressed (e.g. compliance with the DS immunisation schedule) and to screen for the development of DS associated morbidity (i.e. health surveillance).

Health Surveillance for Individuals With DS

The objective of health surveillance is to identify disease in its early stages, thus enabling prompt medical intervention, in order to prevent, or reduce, morbidity and mortality. According to the Wilson and Junger criteria[390], to satisfy the suitability of a condition for health surveillance, it should be considered clinically important, there should be a recognisable latent or early symptomatic stage, an appropriate diagnostic test and treatment should be available, the test should be acceptable to the population and the natural history of the condition should be adequately understood. Health surveillance also requires an appreciation of disease prevalence in the target population. As described above there is a paucity of literature regarding

the occurrence of some DS associated morbidities in the DS population, with wide variance in reported prevalence and contradicting figures.

The terms health surveillance and health screening are often used interchangeably. However, there are important distinctions between these terms which may be summarised according to the application population, the diagnostic implications of testing, timing, frequency and remit. In general screening is applied to populations who are presumed to be healthy, but at risk of developing disease (e.g. 3 yearly mammograms for breast cancer in all women aged over 50 years), while health surveillance can be applied to patients who are either healthy or not (e.g. ongoing monitoring of thyroid function in a child with Down Syndrome and hypothyroidism). Screening tests also tend to stratify groups into high and low risk for a disease, with a requirement for further diagnostic follow-up, while health surveillance often uses diagnostic tests at the outset (e.g. polysomnography for sleep disordered breathing). Related to this, the outcome of screening tests are often binary (i.e. 'high risk' and requires further testing, or not), whereas health surveillance tends to be a more longitudinal process during which the progress of a disease can be tracked over time. Furthermore, screening usually occurs at set time points (e.g. 2 yearly occult blood testing for bowel cancer), while the frequency and timing of health surveillance is more likely to vary from patient to patient. Finally screening tests should satisfy the Wilson Junger criteria, as described above. Strict criteria such as this is necessary when delivering a safe and cost-effective screening programme to a large population. However, there are many conditions which are still highly "clinically important" but where diagnostic tests and treatments are less clear cut (e.g. autism, mood disorders, dementia).

In the UK there are a number of ongoing screening programs which are available to the general population (the newborn blood spot & the newborn hearing screening programmes) or to specific at risk subgroups (the cervical cancer, abdominal aortic aneurysm, breast cancer, diabetic retinopathy and bowel cancer screening programmes)[391]. Individuals with DS avail of national screening however, due to the risks of DS associated morbidity, it is recommended that they undergo additional, routine health surveillance.

Existing literature suggests that some DS associated morbidities are under-diagnosed among individuals with DS. For example, Pasher at al. (1994) found that patient/carer reported of existing morbidities in their child under-represented the true burden of disease[27]. Ng at al.

(2006) found that obstructive sleep apnoea, diagnosed via polysomnography, was highly prevalent among children who had no apparent parent reported symptoms[108]. Lau et al. found that parent report of hearing impairment, among children with DS, showed poor agreement with diagnostic tests[181]. These discrepancies highlight the importance of a regular, robust programme of health surveillance, to identify morbidities among individuals with DS (i.e. it is insufficient to rely on self or parent/carer report alone).

Down Syndrome Health Surveillance Guidelines

Guidelines for the routine health surveillance of children and adults with DS in the UK are provided by the Down Syndrome Medical Interest Group (DSMIG) [392], the Royal College of Paediatrics and Child Health (RCPCH) [387] and the Department of Health and Social Care (DHSC), formerly referred to as the Department of Health (DoH) [393]. Appendix 2 includes a copy of the three UK guidelines. International guidelines are provided by the European Down Syndrome Association (EDSA)[394] and the American Association of Pediatrics (AAP)[395].

The DSMIG is network of professionals involved in the healthcare of children with DS. Their steering committee consists of clinical and academic experts in the field of paediatric DS. As well as providing health surveillance guidelines they also provide educational materials and leaflets relevant to DS health, support DS research and hold regular scientific meetings.

The RCPCH is a professional body for paediatricians in the UK. It is responsible for the postgraduate training of paediatricians and is involved in developing clinical guidelines and standards for various aspects of child health in the UK.

The DHSC is a ministerial department who support the Government in shaping and delivering health policy. The department in led by the Secretary of State for Health and Social Care. The DHSC introduced annual health checks for adults and young people aged 14 or over with learning disability in 2010. These health checks are accessed via the individual's General Practitioner.

The EDSA is a non-profit organisation which aims to support and represent people with DS across Europe. Similarly to the DSMIG they provide educational materials for clinicians and families, support DS related research and develop healthcare guidelines.

The AAP is the American professional association of paediatricians. The AAP includes approximately 30 subcommittees which develop AAP policies and programs. The AAP Committee on Genetics produced their clinical guidelines for the routine health surveillance of children with DS.

Table 2 summarises these existing guidelines. Table 3 outlines the clinical indication and the testing modalities for the various components of DS health surveillance.

All of these guidelines include recommendations related to five key DS associated morbidities: Cardiac, haematological and thyroid disease, as well as vision and hearing impairment. However, within these disease areas there are differences in the recommended timing and frequency of surveillance. Other disease areas are covered by only one of the five guidelines (e.g. coeliac disease, renal and liver function, diabetes mellitus, immunological defects and dental health) or none (e.g. sleep disordered breathing).

Table 2: Summarising national (UK) and international guidelines for the routine health surveillance of children with Down Syndrome.

	DSMIG[a]	**RCPCH[b]**	**The Department of Health[c]**	**EDSA[d]**	**AAP[e]**
Cardiac (Echo)	Echo <6 weeks & once in adulthood	Echo < 6 weeks	Single echo in adulthood	Echo at birth	Echo <4 weeks
Haematological (FBC & film)	Birth	Birth	≥ 14 years - annual	Birth 12 months – FBC 1-18 years – annual FBC	Birth 1-18 years - annual
Thyroid (TFTs & thyroid antibodies)	Birth & 2 yearly from age 1 year.	Birth & 2 yearly thereafter.	≥ 14 years - TFTs annual	12 months 1-18 years – annual TFTs	Birth 1-18 years – annual TFTs
Vision / ophthalmology	Birth – screen for cataract < 18 months- formal vision assessment 4 years – formal vision assessment > 5 years – 2 yearly	Birth – screen for cataract <2 years – formal vision assessment 4 years – formal vision assessment > 5 years – 2 yearly	≥ 14 years - 2 yearly	Birth – screen for cataract 6 & 12 months 3 years 6 years 7-18 years - annual	Birth – screen for cataract < 6 months – formal vision assessment 1-4 years – annual 5-12 years – 2yearly 13-18 years – 3yearly
Hearing	Birth- universal hearing screening test < 10 months - audiology assessment > 5 years – 2 yearly hearing check	Birth- universal hearing screening test 1 – 4yrs – annual audiology assessment > 5 years – 2 yearly audiology assessment	≥ 14 years - 2 yearly	Birth- brainstem auditory evoked response or otoacoustic emission 6 & 12 months 3 years 6 years 7-18 years - annual	Birth- brainstem auditory evoked response or otoacoustic emission 6 months – 18 years - annual
Coeliac disease (Anti-transglutaminase antibodies)	-	-	-	12 months 1-18 years – annual	-
Renal and liver function (U&E, LFTS)	-	-	≥ 14 years - annual	-	-
Diabetes Mellitus (Glucose, HbA1c)	-	-	≥ 14 years - annual	-	-
Vitamin D deficiency	-	-	≥ 14 years - annual	-	-
Immunological defects	-	-	-	12 months 7-18 years - annual	-
Dental health	-	-	-	1-18 years - annual	-
Sleep disordered breathing	-	-	-	-	-

a) Down Syndrome Medical Interest Group guidance for essential medical surveillance [392].
b) Royal College of Paediatrics and Child Health service specification for services for children and young people with Down Syndrome [387].
c) Department of Health, annual health check for individuals with DS aged 14 and over [393].
d) European Down Syndrome Association, healthcare guidelines for people with Down Syndrome [394].
e) American Academy of Paediatrics, health supervision for children with Down Syndrome [395].
Full blood count (FBC), Thyroid function test (TFT), Urea & electrolytes (U&E), Liver function test (LFT), Glycated haemoglobin (HbA1c).

Table 3: Health surveillance: Clinical indication for testing and methodology

	Clinical indication(s)*	Testing modalities
Cardiac	Structural heart disease (congenital and adult onset). Heart failure secondary to respiratory disease.	Echocardiogram, ECG, CXR, pre/post ductal oxygen saturations.
FBC & film	Transient neonatal leukaemia. Acute lymphoblastic and myeloid leukaemia. Anaemia.	Serum blood sample.
TFTs & thyroid antibodies	Hypo/hyperthyroidism.	Serum blood sample.
Vision / ophthalmology	Visual impairment (refractive error, squint, astigmatism, cataract, nystagmus).	Red reflex, fundus examination, ocular motility, refractive assessment, evoked potential testing.
Hearing	Hearing impairment (conductive and sensorineural hearing loss, glue-ear, recurrent otitis media, hearing adjuncts).	Visual reinforcement audiometry, play audiometry, pure tone audiometry, bone conduction test, tympanometry.
Coeliac screen	Coeliac disease.	Serum blood sample.
U&E, LFTS	Renal failure. Liver disease (fatty liver disease, biliary obstruction, autoimmune hepatitis).	Serum blood sample.
Glucose, HbA1c	Diabetes Mellitus, type 1 & 2.	Fasting serum blood sample.
Vitamin D	Vitamin D deficiency.	Serum blood sample.
Immunological defects	Immune deficiency (reduced lymphocyte and complement counts, suboptimal response to vaccination).	Serum blood sample.
Dental check	Dental caries, delayed eruption of teeth, periodontal disease, malocclusion.	Examination with a registered dentist.
Sleep disordered breathing	Sleep disordered breathing/ sleep apnoea.	Polysomnography.

**DS associated morbidities. ECG electrocardiogram, CXR chest X-ray.*

Clinical Practice Guidelines

Clinical practice guidelines are defined by the Institute of Medicine as "systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances"[396]. The aim of clinical practice guidelines are to improve the quality of care received by patients and health outcomes. They should incorporate the best available evidence, synthesized into an accessible format, for routine use in clinical practice.

Existing evidence suggests that, when guidelines have been rigorously developed, they have the power to translate complex scientific research findings into achievable improvements in healthcare[397-399]. For clinicians, guidelines "offer explicit recommendations, where there is uncertainty about how to proceed, overturn the beliefs of doctors accustomed to outdated practices, improve the consistency of care, and provide authoritative recommendations that

reassure practitioners about the appropriateness of their treatment policies"[400]. For patients, guidelines should promote consistency of care across doctors, specialties and geographical areas. Patient accessible guidelines may also empower patients to advocate for evidence-based healthcare and in some cases, to make informed choices.

However, clinical guidelines have various limitations. In some instances guidelines may be based on scientific evidence which is insufficient, misleading or misinterpreted. As described by Woolf et al. "Guideline development groups often lack the time, resources, and skills to gather and scrutinise every last piece of evidence. Even when the data are certain, recommendations for or against interventions will involve subjective value judgments when the benefits are weighed against the harms. The value judgment made by a guideline development group may be the wrong choice for individual patients"[400]. The promotion of flawed guidelines may reinforce or institutionalize practices which are in fact detrimental to health outcomes. Other limitations include conflicting recommendations[401-403], insufficient consideration of patient factors (e.g. multimorbidity, ethnicity, individual preferences)[404 405], external barriers (e.g. geographical regions, resources, organisational and economic factors)[406 407], failure to manage potential conflicts of interest (e.g. a recommendation which would result in financial gain for a member of the guideline development committee)[408 409] and a lack of transparency in the methodology of guideline development[410 411].

Various tools have been developed to assist in evaluating the methodological quality and validity of clinical guidelines. The most commonly utilised tools internationally include AGREE-II[412], DELBI[413] and GRADE[414]. These tools assess clinical guidelines across common domains: Internal validity (i.e. minimisation of biases affecting the recommendations; including mode of evidence collection, assessment and utilisation); external validity (i.e. the guidelines actually lead to the intended improvement in patient care); and applicability of the guideline (e.g. stakeholder input, pilot testing, pre-implementation review)[415]. Accurately applying these tools can be time consuming and require expert skill and experience. Consequently several rapid-assessment instruments have been developed, to complement the more complex tools, and to make such assessments more accessible. Rapid assessment instrument include, AGREE GRS[416], MiChe[417] and iCAHE[418] .

The AGREE GRS (AGREE Global Rating Scale) is a four-item rapid assessment tool which was developed as an alternative to the AGREE II checklist. The four elements prompt the user to rate guidelines on a 7-point scale based on: methodology, presentation, the recommendations themselves and the completeness of reporting. Brouwers et al. demonstrated a high degree of agreement between AGREE II and AGREE GRS, however the latter was "*less sensitive to picking up differences in guidelines quality as a function of the type of user*"[416].

The MiChe rapid assessment tool uses a 3 point scale across 8 elements. There is overlap with AGREE GRS checklist but with the addition of criteria that relate to the target audience, the background and objectives, conflicts of interest and discussion of the risks and benefits of treatments[419]. Given that MiChe contains more assessment criteria, Siebenhofer et al. postulated that it would take longer to complete than AGREE GRS, but has not been formally tested[419].

The iCAHE checklist is a also validated clinical guideline rapid assessment tool, developed by the International Centre for Allied Health Evidence, at the University of South Australia, in 2009[418]. It contains 14 items across 4 domains. In comparison with AGREE GRS and MiChe, the iCAHE includes additional assessment criteria (e.g. criteria based on availability and dating). An iCAHE score of ≥10 is typically used as a cut-off for acceptable level of quality[420] [421].

Studies have demonstrated a high level of agreement between these three rapid assessment tools[419] [422].

Table 4 demonstrates use of the iCAHE criteria to compare the three UK guidelines for the health surveillance of children with DS. The iCAHE rapid assessment tool was chosen as I felt it struck a balance between brevity, depth and ease of use; furthermore the incorporation of a score makes it easier to compare more than one guideline.

All three of the UK guidelines score below the iCAHE cut off for an acceptable level of quality, with none scoring points in the 'Underlying Evidence' domain. This may reflect a paucity of high quality research to inform health surveillance practice, or a lack of transparency in the methodology of guideline development.

Table 4: iCAHE Guideline Quality Check List: Assessment of DSMIG, DHSC and RCPCH guidelines for the routine surveillance of children with DS according using the iCAHE rapid-assessment tool[418].

	Criteria	DSMIG[392]	RCPCH[387]	DHSC[393]
Availability	Is the guideline readily available in full text?	1	1	1
	Does the guideline provide a complete reference list?	1	0	0
	Does the guideline provide a summary of its recommendations?	0	1	0
Dates	Is there a date of completion available?	1	1	1
	Does the guideline provide an anticipated review date?	1	1	1
	Does the guideline provide dates for when literature was included?	1	1	1
Underlying Evidence	Does the guideline provide an outline of the strategy they used to find underlying evidence?	0	0	0
	Does the guideline use a hierarchy to rank the quality of the underlying evidence?	0	0	0
	Does the guideline appraise the quality of the evidence which underpins its recommendations?	0	0	0
	Does the guideline link the hierarchy and quality of underlying evidence to each recommendation?	0	0	0
Guideline developers	Are the developers of the guideline clearly stated?	1	1	1
	Does the qualifications and expertise of the guideline developer(s) link with the purpose of the guideline and its end users?	1	1	1

Guideline purpose and users	Are the purpose and target users of the guideline stated?	1	1	1
Ease of use	Is the guideline readable and easy to navigate?	0	1	1
TOTAL score /14		8	9	8

Down Syndrome Medical Interest Group (DSMIG), Department of Health and Social Care (DHSC), Royal College of Paediatrics and Child Health (RCPCH) International Centre for Allied Health Evidence (iCAHE).

There are various reasons why clinical guidelines, even those of high quality and validity, are not followed in practice. Baiardidn et al.[407] summarise the factors that influence guideline compliance according to four key domains: guidelines specific factors (e.g. credibility of the authors, the evidence based strategy, transparency and guideline complexity); contextual factors (e.g. organisational characteristics, social and clinical norms and habits); implementation factors (e.g. communication strategies, the use of incentives); and doctor related factors.

Doctors may not follow clinical guidelines for a multitude of reasons. They may not be aware that guidelines exist or may be unfamiliar with using them. They may disagree with the content of the guidelines, either due to personal professional experience, or a perceived a lack of credibility among the authors. They may also feel that the guidelines are unrealistic or unachievable in their clinical context, or that the guideline is too rigid to allow for flexibility.

Given that there are no gold standard national or international guidelines for the routine health surveillance of children with DS it is possible that practice tends to vary according to local policy[423 424]. Variation in practice may lead to patchy, inconsistent care and widen health inequalities. I am not aware of any existing studies which look at current practice, with regard to DS health surveillance in the UK, or comparisons with national recommendations.

In this thesis I aim to determine local practice, with regard to DS health surveillance, in paediatric departments across the UK and to compare this with existing national guidelines.

Down Syndrome Evidence Base

Early intervention, and the research which supports these interventions, has resulted in significant improvements in the health and wellbeing of individuals with DS[258 357]. Despite improvements, individuals with DS continue to have a greater mortality and morbidity at any

age compared with individuals of the same age from the general population, and those with other forms of intellectual disability[425]. Therefore, there is a continued need for ongoing research to improve the quality and duration of life for those with DS.

An existing review of the DS literature suggests that there has been a shift in focus, away from childhood, and towards prenatal diagnostic studies[426]. This shift in focus may be at the detriment of academic progress in improving the health and wellbeing of children and adults with DS. It is arguable that academic focus should reflect the burden of disease, the priorities of the patients and carers, and address gaps in the literature. I am are not aware of any studies which map the current landscape of the paediatric DS evidence base and make recommendations for areas of future research.

It has been almost 30 years since evidence based medicine (EBM) was declared the "new paradigm for medical practice"[427]. EBM is defined as "the conscientious, explicit, judicious and reasonable use of current best evidence in making decisions about the care of individual patients"[428]. "The principle of EBM emphasizes, above all, that the foundation of any medical decisions regarding the optimal diagnostic or therapy procedure are scientific evidences from clinical research, and clinical experience and intuition are of great help, but not the main basis in decision-making"[428]. The ultimate aim of EBM is to use scientific evidence to ensure that medical care is safe, effective, consistent and cost-effective.

There are multiple examples of the use of EBM to improve patient care and to end dangerous or ineffective practices[429]. Specifically within the field of Down Syndrome, EBM has contributed to a significant reduction in mortality and morbidity through early surgical intervention for congenital heart disease[39 430], the development of a supplemented vaccination schedule[431] and the use of DS specific therapeutic regimens for leukaemia[432-434] and infantile spasms [85 435].

Clinical practice guidelines, as described above, are a means of translating EBM into everyday practice. As described by Djulbegovic et al., "A decade of efforts to teach EBM to medical trainees had revealed that few clinicians would ever have the skills - and those with the skills would seldom have time - to conduct sophisticated assessment of the evidentiary basis for their practice. This realisation led to a refocusing of EBM efforts, directing clinicians to processed

sources of evidence, and aiding decision making by advancing the science of trustworthy clinical practice guidelines that would be available to clinicians at the point of care delivery"[436].

Not only should clinical guidelines incorporate the best available evidence, but the strength of guidance should reflect the strength of the available evidence. As described above, a preliminary assessment of existing guidelines for the health surveillance of children with DS, suggests that the underlying evidence for these recommendations appears to be lacking. I am not aware of any existing studies which attempt to quantify this existing evidence base.

The Voice Of Patients with Down Syndrome and Their Carers

The importance of the voice of patients and parents/carers, both in research and healthcare, has been increasingly recognised over the past decade[437]. Patient and public involvement (PPI) engagement in research refers to "the practice of patients, members of the public and researchers working together to prioritise, plan, conduct and disseminate research"[438]. Demonstrating the involvement of patients and the public in the design and development of research projects is strongly encouraged as part of funding applications, and in some instances it is a compulsory component[439].

The purpose and intention of PPI is to produce research which is relevant, acceptable and considered a priority by the group which it intends to benefit. PPI has been shown to positively impact research at all stages, including "the development of user-focused research objectives, development of user-relevant research questions, development of user-friendly information, questionnaires and interview schedules, more appropriate recruitment strategies for studies, consumer-focused interpretation of data and enhanced implementation and dissemination of study results"[440].

There is limited existing literature which captures the voice and priorities of patients with DS and their parents/carers, with regard to research priorities and healthcare experiences. To explore the research priorities of parents/carers of children with DS, in the field of DS and otitis media, Fortnum et al. utilised a mixed methods approach to explore parent/carer views on research and to create recommendations for future research. They found that parents/carers were open to all study designs but that randomisation in clinical trials and studies involving surgery were perceived as significant barrier that might prevent them from consenting their child to a research study. One parent commented "*I think I said I was nervous about involving him in a randomised control trial because that could lead to him being randomly placed in a group where he gets a treatment option that I don't agree is right for him at that time*". Observational research, that would involve treatment actively allocated by a clinician, was perceived to be more acceptable. Parents/carers also prioritised improvement in speech and communication over outcomes focusing on measures of hearing. Fortnum et al. conclude "any proposed research study needs to respond the shared challenges of parenting a child with DS… and also needs to accommodate and negotiate the variety of highly personal perspectives and

experiences that families have demonstrated"[441]. The recommendations made in their report, to promote the feasibility and clinical value of future research, are conceivably relevant to the wider field of paediatric DS research.

Williams et al. also undertook structured interviews with health professionals and volunteers working with families experiencing DS, in order to explore factors which influence recruitment of infants with DS to cohort studies. They reported that these decisions were influenced by "the child's overall health, parent demographics, medical interactions that take place with the family and study logistics". Williams et al. concluded that research involving children with DS and their families ideally needs to utilise diverse recruitment methods and incorporate flexibility in research timings to meet the needs of the participants and the child's health status, and sensitivity of the variable responses elicited by families to a diagnosis of DS for their baby" [442].

There are several examples where individuals with DS or their parents/carers have been involved in the development of healthcare services.

The Leicester, Leicestershire & Rutland (LRR)[385] & Hull CCG[386] care pathways outlined above (Figure 2) were developed in collaboration with parents of children with DS, alongside a broad multidisciplinary team[443] [444]. One parent involved in the development of the Hull CGG pathway commented "*I am so proud to be part of this achievement. It is such a good example of all the local health, social care and voluntary organisations working together to make what I hope will be a massive difference to people living with Down Syndrome. The pathway makes it clear to families and healthcare professional which services are out there and when people with Down syndrome should be accessing them*"[444]. This illustrates that parents/carers are willing and eager to contribute to the development of services for children with DS.

Sayers et al. also included parents of infants and toddlers with DS in the design and delivery of a therapeutic strength intervention programme. The experiences and perceptions of the parents obtained through qualitative analysis were used to develop guidelines for future paediatric strength intervention progams[445]. This provides a further example of stakeholder involvement in DS service design and delivery.

There are a small number of studies which attempt to capture the experience patients with DS and parents/carers in coping with ill-health and in interacting with the healthcare system.

In a qualitative study of young people and adults with DS living in Australia, Haddad et al. found that "a lower quality of life was reported for those with a higher burden of illness compared to those with no impact". These effects persisted into adolescence and adulthood, "where in general the burden of medical comorbidities is much less than in childhood". Positive predictors of quality of life included friendships and employment[446]. These findings highlight the negative impact of ill health on the quality of life of individuals with DS.

Farkas et al. also performed a survey of over 400 parents of individuals with DS in the US. They attempted to capture parenting experience across a broad range of themes (e.g. education, social inclusion and health). They reported that the most prevalence theme in the "negative experience data" was related to "the experiences parents had due to their child's medical issues or direct experiences with medical professionals that were viewed as negative by the parents". They stated that "common responses from parents, ranged from describing medical professionals as being insensitive or uneducated on the topic of DS to refusing to acknowledge their child while receiving medical services"[447]. These findings suggest that negative healthcare experiences occur and have a significant impact on families.

Kaye et al. undertook interviews and questionnaires with parents and siblings of individuals with DS, to explore factors impacting on access and experience of dental care in this group. The main themes elicited from interviews, regarding what influenced their experiences of dental care, included the attitudes and skills of the dental health professionals, feelings of stigma and the information and support received[448]. Kreuger et al. also surveyed parents of children with DS, focusing on the strategies of parents in advocating for their children, across various settings. Healthcare was one of the most common settings where advocacy was required. They reported that the goals of parents tended to include inclusiveness, equality, and acceptance. Commonly reported reasons for advocacy were "discrimination" and "judgement"[449].

Common themes across these studies are the negative impact of ill-health on the quality of life of individuals with DS, the pressure on parents to advocate for their children in healthcare

settings and the importance of interpersonal interactions with health professionals (which are influenced by clinician's knowledge, attitude and inclusivity).

In 2017 Down Syndrome Scotland (DSS), a charitable foundation, published the results of a questionnaire completed by over 400 of their members, focusing on their experiences with healthcare services[450]. With regard to routine health reviews, the majority of parents caring for adults with DS were not accessing annual health checks via their GP and/or were not aware than an annual health checks were recommended or available. Furthermore, approximately one quarter of parents caring for a child with DS stated that they did not have an annual health review. Several respondents also expressed that they did not receive reminders about routine health reviews and therefore carried "the burden of gathering relevant information, remembering checks and chasing up appointments." There also appeared to be some inconsistency across regions and barriers to access with respondents commenting "*I have asked for this at my GP surgery on more than one occasion over the past couple of years but have been told they are still finalising the details*" and "'*Some health authorities do [health checks] every year and some two yearly, I found different areas do things differently no matter what the rules are*" and "*The thoroughness of the annual review is a bit hit or miss, dependant on the paediatrician*" [450].

It is unclear whether these responses are representative of the experience of patients and parents/carers across the UK, but they suggest possible deficiencies in the awareness of annual health reviews (among both clinicians and patients/carers), difficulties accessing this service and inconsistencies in provision. With regard to their experience of health services in general, the majority of respondents were positive.

Themes suggested that patients and parents/carers appreciated clinicians who were respectful, knowledgeable and flexible to meet the unique needs of individuals with DS, for example by allowing more time for consultations and attempting to address consultation related anxieties. Recurrent barriers to positive experiences included inconsistency of care, the use of poor terminology (e.g. referring to an infant as "a Downs baby" or dismissing health concerns as "normal for Downs"), perceived lack of knowledge about DS among health professionals and inflexible care (e.g. insufficient time for consultations and failures to adapt consultation style or procedures to the needs of the individual).

In the personal professional experience of myself, and members of the research team, encountering children with DS and their families in the clinic, we also recognise common concerns and priorities. Similar to the findings in the literature described above, we recognise that patients and parents/carers appreciate clinicians who are knowledgeable about DS, but also respectful of the lived expertise of the patient and family. Unfortunately, parents often report that concerns about their child's health have been dismissed as "a normal part of DS" or because the child's symptoms are considered to be at the "less severe end of the DS disease spectrum". Furthermore, parents/carers commonly report that it can be extremely difficult to balance the large number of appointments which their children are required to attend. Consequently they appreciate flexibility and efficiency in care (for example arranging visits in the same location on the same day and having routine blood tests taken at the same time as other investigations). They also expect routine clinical reviews to occur in a timely fashion (e.g. annually, as expected) and to be fundamentally consistent across different clinicians. Finally, our experience has also suggested that parents appreciate and value clinicians who are willing and capable of addressing some of the social determinants of health; for example by providing advice on financial entitlements, education and signposting to family support groups.

The aims of this thesis incorporate a number of the priorities of patients and parents/carers that I identified in the literature and in my professional experience. Specifically incorporating these, I explore the themes of quality and consistency of routine health surveillance and clinician awareness of the existing guidelines, expand the knowledge base which is available to clinicians caring for individuals with DS, including the prevalence of DS associated morbidities and cancers across the life-course, and identify potential gaps in the literature, which together with PPI collaboration, will have the potential to guide future research priorities.

The overall aims & objectives of the thesis

The MD thesis outlined herein consists of three inter-related studies. First, a systematic literature mapping exercise provides an overview of the existing paediatric DS literature. This assists in the identification of gaps in the literature and potential areas for future research.

Second, the analysis of a large linked dataset of routinely collected electronic health care data determines the prevalence of a multitude of DS associated morbidities and cancers in a large

cohort of individuals with DS, compared with matched controls. These findings contribute to the limited existing literature on the burden of disease in DS and also inform the development of health surveillance guidelines.

Third, the collation and comparison of local protocols for the routine health surveillance of children with DS, from paediatric departments across the UK, explores current practice, as well as areas of consensus and divergence in practice. The findings also provide insight into what health surveillance is being performed on the "front line" and inform the development of future health surveillance guidelines.

Together these projects document key aspects of the current health and care of children with DS in the UK, and provide evidence to inform its improvement.

PROJECT 1: MAPPING THE EXISTING PAEDIATRIC DOWN SYNDROME LITERATURE

Introduction

As explored in the Background, research has informed advancements in the treatment and care of individuals with DS, and thus contributed to a significant increase in life expectancy over recent decades[29 33]. However, individuals with DS continue to have a greater mortality and morbidity compared with both the general population, and also with individuals who have other forms of intellectual disability[425]. This demonstrates a need for ongoing research, to improve the quality and duration of life for those with DS.

Existing studies have suggested a general decline in the proportion of all academic publications focusing on DS, and a shift in focus away from childhood and towards prenatal diagnostic studies[426]. However, there are no existing studies which provide an overview of the existing paediatric DS literature.

Mapping of academic literature according to themes can be described as an 'epistemological approach'. As with traditional systematic reviews, it employs a standardised, repeatable approach to select, review and synthesise the literature, however its applications and outcomes differ. While traditional systematic reviews may address a more specific research question, a mapping exercise provides a broader overview.

A broader overview of the existing DS literature will assist in identifying gaps and areas of relative research paucity in this field. Such an understanding will help guide future DS research, and funding allocation, in order to direct resources to the areas which are potentially most in need of academic investment.

Aims & Objectives

By systemically mapping and summarising the existing paediatric DS literature, I aimed to determine:

1. The annual number of publications which have focused on children with DS, per year, since 2000.

2. The geographical distribution (as defined by the Institution of the primary author) of those publications.
3. The current distribution of research methodologies used in the paediatric DS literature.
4. The current distribution of 'primary health themes' in the paediatric DS literature.
5. The current distribution of 'subcategory research themes' in the paediatric DS literature.
6. Identify gaps in the evidence base, and thus guide future research.

Methods

Search strategy

Literature searches were performed using the online databases Pubmed, Embase.com, CINAHL-Plus and the Cochrane Library. The search terms for each database are included in Appendix 3. The search terms were developed in conjunction with UCL library services and through consultation with the wider research group. The titles and abstracts identified through the literature search were originally downloaded on August 8th 2016 and then updated on the 2nd January 2020.

Duplicate titles were removed using Endnote X7 duplication recognition software. The author and another member of the research team independently screened the titles and assessed their eligibility for inclusion. Only those with a unanimous decision to exclude were removed at this initial screening stage.

Based on the initial title screening, a list of phrases, tending to correspond with exclusion, were compiled (Appendix 4). All remaining titles were screened for these phrases using Endnote X7. Again, the author and another member of the research team independently reviewed the eligibility of these titles for inclusion and only those with a unanimous decision to exclude were removed.

Inclusion / Exclusion criteria

The inclusion and exclusion criteria was refined following an initial trial extraction of 100 articles (see *Data Extraction*).

Inclusion criteria for publications:

- Literature published between the 1st January 2000 and 1st January 2020.
- Observational or interventional studies which include children (aged ≤18 years) with DS (either as the focus or control / comparator group).
- Review articles which focus on DS in childhood, morbidities in children with DS, or reviews which are not specifically focused on DS but contain a relevant sub-focus on paediatric DS.
- Articles which had an available English language abstract.

Exclusion criteria for publications:

- Where participants, or the focus, is on adulthood only. However, such articles were included if children with DS constituted a subgroup or, for example, in a DS case report where a reasonable description of childhood was included. Review articles about adult-related or adult onset disease (e.g. dementia) were not included.
- Prenatal studies, including those which looked at risk factors for non-disjunction, or publications focusing on parental experience of being given a prenatal diagnosis of DS.
- Articles focusing on mosaic DS / partial translocations or trisomy 21 plus another aneuploidy.
- Where an abstract or English language abstract was not available.
- Publications which use animal models of DS or animal models of DS associated morbidity.
- Publications where DS is not the focus or a specific sub-focus of the article.
- Articles which do not describe research (e.g. a summary of a DS related seminar or presentation).

Primary outcomes

1. Annual number of publications in the field of paediatric DS, from January 2000 to January 2020.

2. The proportionate distribution of paediatric DS literature, published between January 2000 to January 2020, according to methodology, ‘primary health themes’ and ‘subcategory research themes’ (see definitions below).

Secondary outcomes

1. The change in the number of research publications, which focus on paediatric DS, over time.
2. The identification of gaps in the literature and areas for future research.

Variable definitions

Research methodology

The definitions of the research methodologies are outlined in

Table 5. These definitions are based upon those presented in the A Dictionary of Epidemiology[451], the (National Institute for Health Research) NIHR Glossary, Evaluation, Trials and Studies[452] and research group consensus. Research methodology definitions were refined following an initial trial extraction of 100 articles (see *Data Extraction*).

Table 5: Definitions of research methodologies.

Review - systematic	A systematic, standardised, and repeatable, approach to select, review and synthesise relevant studies on a particular topic. Defined as a 'systematic review' in the title or abstract or including details of those databases searched. This definition also includes publications which statistically synthesise data from separate but similar/comparable studies, leading to a quantifiable summary of the results (i.e. Meta-analysis). The review must focus on DS or include a specific sub-focus on DS. *For the purpose of the analysis, *Review – systematic & Review – unspecified* were combined into "*Review (combined)".*
Review - unspecified	A literature review where it is unclear if the approach was systematic or narrative. The review must focus on DS, or include a specific sub-focus on DS. (See *Inclusion/ Exclusion criteria*). *For the purpose of the analysis, *Review – systematic & Review – unspecified* were combined into "*Review (combined)".*
Interventional study/ trial	A study in which participants are assigned to a treatment/intervention group or a comparison/control group, and followed prospectively. It may also include "before and after" studies where there is no standard control group, i.e. the outcome is described in the participants before and after treatment. It may also constitute a retrospective comparison for one treatment group with another, however it must include measurements of the outcome before and after treatment, and/or the primary focus is the impact of the intervention. The aim of the study is usually to evaluate the effectiveness of a treatment/intervention compared with none, or the status quo.
Cohort study	An observational study in which a group of patients are followed over time with observations, in the same individuals, at >1 point in time. These may be prospective or retrospective.
Cross-sectional study	A study in which the participants are characterised/ measured at one point in time or multiple patients characterised/ measured within a set period of time. Note, the same patients characterised/ measured at multiple time points should be defined as *Cohort Study*.
Case control study	Retrospective comparisons between a DS group with an associated morbidity and a control group (DS without associated morbidity). The study retrospectively observes/measures/describes attributes or suspected risk factors in order to identify potential relationships/ associations.
Case series	A descriptive account of the presentation, management or prognosis of a group of patients with DS (>1 ≤20) with a full description of the clinical picture. If the articles includes multiple patients but only 1 with DS, record as *Case Report*.
Case report	A descriptive account of the presentation, management or prognosis of a single case. It usually includes a full description of the clinical picture. May include case series where only one patient described has DS.
Qualitative study	A study which aims to explore the experiences, opinions or motivations of patients, and/or related groups, through interviews, focus groups, reflective field notes and other non-quantitative approaches.
Mixed methods	A study which combines both quantitative and qualitative methodology.
Basic science / underpinning	Lab based studies with non-human participants but may include human cell lines. Note animal studies should be excluded.
Guideline	A clinical guideline/ protocol relating to DS. For the purpose of the analysis these articles were reclassified as "*Other*".
Opinion piece / letter to the editor	Expert opinion or editorial piece which reflects on DS or related topic. Does not include systematic or non-systematic literature reviews (*see above*). This definition includes 'letters to the Editor'. For the purpose of the analysis these articles were reclassified as "*Other*".

Primary health themes

The ‘primary health themes’ correspond to key areas of medical research, which in turn largely correspond to clinical specialties and body/ disease systems. Twenty two primary health themes categories were agreed by the research group: Behaviour/ Mental Health, Cardiac/ Circulatory, Child Protection, Dental, Dermatological, DS Prevalence Study, Development & Cognition, Endocrine, Nutrition & Metabolic, Ear, Nose and Throat (ENT), Gastrointestinal, Growth, Haematological, Infection and Immunology, Mortality, Musculoskeletal, Neurology, Non-specific/ General, Oncology, Other, Renal/ Genitourinary, Respiratory, and Surgical/ Anaesthetics. The list of ‘primary health themes’ was also refined following an initial trial extraction of 100 articles (see *Data Extraction*).

Subcategory research themes

The definitions for ‘subcategory research themes’ are outlined in

Table 6. These definitions reflect those presented in UK Clinical Research Collaboration, Health Research Classification System[453] and World Health Organisation, Basic Epidemiology[4] and research group consensus. Again, the definitions were refined following an initial trial extraction of 100 articles (see *Data Extraction*).

Table 6: Definitions of 'subcategory research themes'.

Aetiology / risk factors for DS associated morbidities	The study aims to identify factors which may be associated with the development of DS associated morbidity. This also includes studies where DS is a risk factor for a disease or a specific outcome.
Prevalence/ incidence of DS associated morbidities	The study aims to determine the number of individuals with a DS associated morbidity, or health event, in a defined population, within a specified period of time. Also includes studies where the prevalence of DS is described in a disease subgroup.
Prevalence/ incidence of DS	The study aims to determine the prevalence/ incidence of DS within a defined population (e.g. geographical). If the study determines the prevalence of DS in a disease subgroup this should be defined as *Prevalence/ incidence of DS associated morbidities.*
Diagnosis / health surveillance for DS associated morbidities	The study focuses on the diagnosis of/health surveillance for DS associated morbidities.
Diagnosis of DS (postnatal)	The study aims to determine the accuracy of diagnosis of DS in a post-natal population (e.g. comparing clinical diagnosis with molecular diagnosis).
Treatment (including Rx outcomes)/prevention	The study focuses on a treatment/intervention that aims to improve the health or well-being of a patient(s) with DS, or to prevent associated morbidities. It includes studies which look at outcomes of treatments/interventions. This definition does not include studies which look at the outcomes of health service interventions, i.e. interventions which target the way in which health care is organised or functions (see *Service delivery*).
Prognosis / Natural history of DS	The study aims to describe/inform/further the knowledge base on the natural course of DS, or a morbidity in the context of DS. This includes studies which aim to define 'normality' or normative values within the DS phenotype. This definition also includes studies which further the knowledge base on the development of the DS phenotype, but does *not* include studies which focus on the aetiology or risk factors for DS associated morbidities (see *Aetiology / risk factors for DS associated morbidities*). Where the focus is on prevalence (proportion, rate, count) of an associated morbidity, these should be classified as *Prevalence/ incidence of DS associated morbidities)*. (Note these are usually cross-sectional studies). This definition does *not* include studies which focus on the outcomes of treatments/interventions (*see Treatment (incl Rx outcomes)/prevention*).
Economic analysis	The study focuses on the economic evaluation (e.g. cost-benefit) of services, interventions or treatments.
Family impact	The study focuses on the impact of DS on any aspect of family life, including familial experiences and perceptions. However, those studies with a prenatal focus should *not* be included (see *Inclusion/ Exclusion criteria*).
Service delivery	The study focuses on the organisation, functioning, and performance of health services relevant to those with DS. Such research is usually concerned with relationships between needs, demand, supply, use, and outcomes of health services.
Ethical issues	The study primarily focus on ethics or 'moral principles'. This does not include publications which focus on the ethics of prenatal diagnosis or terminations, these studies should be excluded.
Outcome research	The study assesses the validity / reliability of specific outcome measures such as (generic or disease specific) quality of life instruments and the inter-reliability of diagnostic tests.
Full/ general picture	Typically case reports, case series or review articles which include multiple health and 'subcategory research themes'.
Other	Those studies not clearly covered by other definitions.

Data extraction

The definitions of research methodology, the list of 'primary health themes', the definitions of 'subcategory research themes' and the data extraction tool, were trialled by the author and two additional members of the research team, using 100 abstracts. Following feedback, the definitions and extraction table were refined and re-trialled, using a further 50 abstracts, by the author and another member of the research team, to optimise clarity and consistency. With >95% agreement between the two reviewers, during the second trial, it was agreed to proceed with the review and data extraction.

The final review and data extraction was performed in parallel by the author and one other member of the research team, using Excel 2016. Cell entries were conditionally formatted for each variable to ensure consistency in data recording between the two reviewers. The author and the second reviewer compared the outcomes of their review and extractions iteratively (upon the completion of one calendar year of abstracts). Discrepancies were resolved by consultation between the two reviewers and, if necessary, reviewing the full text of the papers and/or discussing with a third reviewer from the research team. If a consensus was not reached the wider research team was consulted.

Governance

Research Design approval was sought and obtained from the Joint Research and Development Office at the Great Ormond Street Institute of Child Health, UCL (R&D number 17PP09)

Results

Publications included/excluded

A total of 11,066 titles were downloaded from the literature databases, of which 5,800 were included in the final analysis (Figure 3).

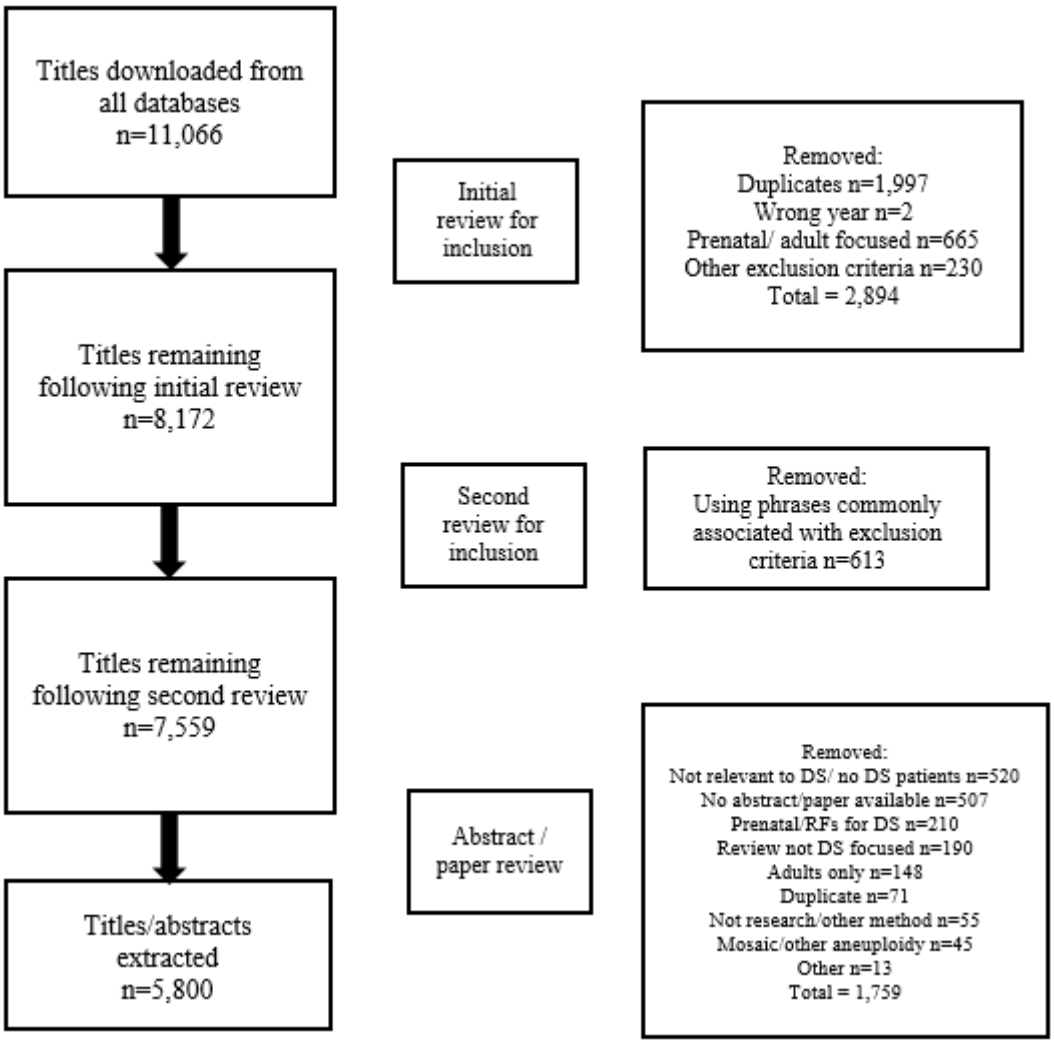

Figure 3: Flow chart illustrating the number of titles identified through literature searches (N=11,066) and the final number of publications which were included in the mapping exercise (n=5,800).

Number of Publications Per Year

Figure 4 summarises the number of publications per year, which were included in the final analysis. There was a general trend of an increase in the number of publications per year until 2014, and then a general trend of decline thereafter.

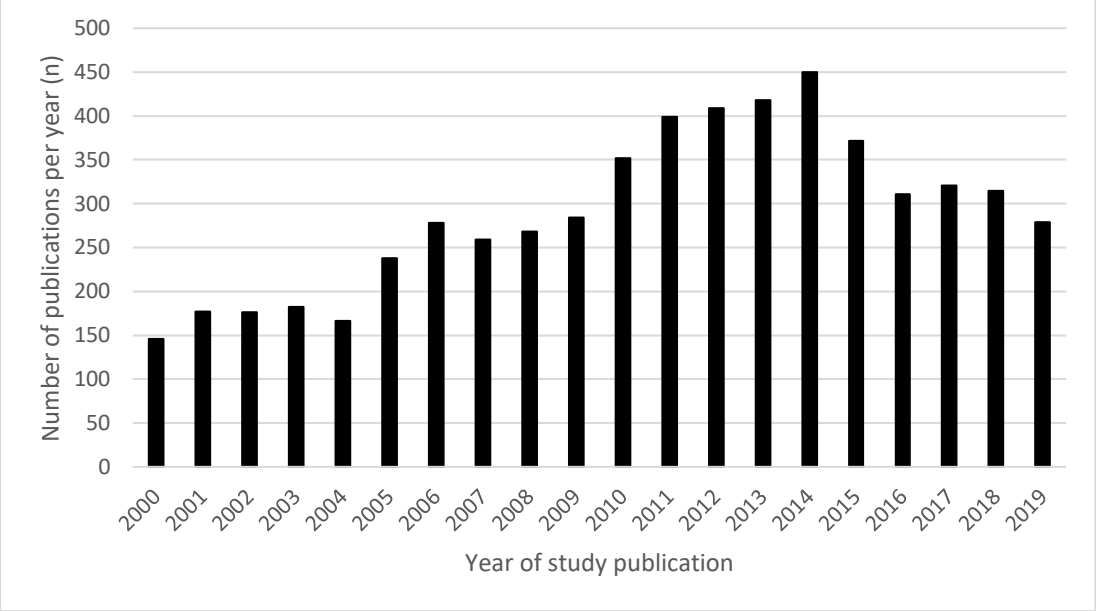

Figure 4: The number of paediatric DS publications per year, Jan 1st 2000-Jan 1st 2020 (n=5,800).

Country of First Author Publication

Publications originated from institutions in 101 different countries. For 5.2% (n=304) of publications it was not possible to identify the country of first author institution.

Table 7 summarises the number and proportion of publications according to country of first author institution, for those countries which contributed ≥1% of the total. The largest proportionate contributions were from the USA and UK.

Table 7: Paediatric DS publications according to country of first author institution, limited to those countries contributing ≥1% of the total (N=4,923).

Country of 1st author institution	**n=**	**%**
USA	1,535	26.5
UK	450	7.8
Italy	322	5.6
Unknown	304	5.2
Japan	295	5.1
Brazil	259	4.5
Spain	204	3.5
India	195	3.4
Canada	184	3.2
The Netherlands	169	2.9
Turkey	167	2.9
Australia	160	2.8
Germany	133	2.3
France	117	2.0
Israel	86	1.5
Saudi Arabia	77	1.3
Poland	75	1.3
Sweden	68	1.2
China	65	1.1
Ireland	58	1.0
Total (N=5,800)	4,923	84.9

Research Methodologies

Table 8 summaries the distribution of methodologies utilised in the existing paediatric DS literature.

Cross-sectional studies made up the largest portion of methodologies used (33.3%, n=1,933), followed by cohort studies (15.7%, n=913) and case reports (13.7%, n=792). There were relatively few interventional studies (5.6%, n=322), basic science studies (5.5%, n=321), qualitative studies (2.7%, n=158) and those utilising mixed methods (1.6%, n=94).

Table 8: Paediatric DS publications according to methodology (%) (N=5,800).

Methodology	**n=**	**%**
Cross-sectional study	1,933	33.3
Cohort study	913	15.7
Case report	792	13.7
Review (combined)*	512	8.8
Case control study	363	6.3
Case series	328	5.7
Interventional study / Trial	322	5.6
Basic science/ underpinning	321	5.5
Qualitative study	158	2.7
Mixed methods	94	1.6
Other*	64	1.1
Total=	5800	100

** Publications categorised as guidelines, opinion pieces and letters to the editor were combined as "Other". Systematic and 'unspecified' review articles were combined into one category (Review (combined)).*

Primary Health Themes

Table 9 summaries the distribution of 'primary health themes' in the existing paediatric DS literature.

Publications focusing on development & cognition (13.1%, n=757), neurology (9.9%, n=576) and oncology (9.8%, n=569) made up the largest proportions. Relatively few publications focused on renal and genitourinary (n=53), growth (n=50), mortality (n=50) and child protection (n=10).

Table 9: Paediatric DS publications according to 'primary health themes' (%) (N=5,800).

Primary health theme	**n=**	**%**
Development & Cognition	757	13.1
Neurology	576	9.9
Oncology	569	9.8
Other	518	8.9
Cardiac/ Circulatory	468	8.1
Endocrine, nutrition, metabolic	383	6.6
Musculoskeletal	366	6.3
Behaviour / Mental health	351	6.1
Ear, Nose & Throat (ENT)	303	5.2
Gastrointestinal	247	4.3
Dental	228	3.9
Infection & Immunology	204	3.5
Surgical/ anaesthetics	194	3.3
Respiratory	118	2.0
DS prevalence study	106	1.8
Dermatological	88	1.5
Haematological	82	1.4
Non-specific, general	79	1.4
Renal, genitourinary	53	0.9
Growth	50	0.9
Mortality	50	0.9
Child protection	10	0.2
Total =	5,800	100

Subcategory Research Themes

Table 10 summaries the distribution of 'subcategory research themes' in the existing paediatric DS literature. Publications focusing on prognosis and the natural history of DS made up the largest proportion (24.9%, n= 1,445), followed by those that focused on treatments and prevention (20.5%, n=1,191) and full or 'general picture' (14.3%, n=831). There were relatively few publications focusing on the postnatal diagnosis of DS (n=45), economic analysis (n=15) and ethics (n=6).

Table 10: Paediatric DS publications according to 'subcategory research theme' (%) (N=5,800)

Subcategory research theme	**n=**	**%**
Prognosis / natural history of DS	1,445	24.9
Treatment (including outcomes) / prevention	1,191	20.5
Full / general picture	831	14.3
Prevalence/ incidence of DS associated morbidities	592	10.2
Aetiology / risk factors for DS associated morbidities	561	9.7
Diagnosis / health surveillance for DS associated morbidities	301	5.2
Family impact / parent experience	228	3.9
Other	202	3.5
Service delivery	138	2.4
Outcome research	125	2.2
Prevalence/incidence of DS	120	2.1
Diagnosis of DS (postnatal)	45	0.8
Economic analysis	15	0.3
Ethical issues	6	0.1
Total=	5,800	100.0

Discussion

Statement of principal findings

This unique systematic literature mapping exercise of 5,800 paediatric DS publications, over two decades, provides a broad overview of the existing literature.

The findings demonstrate a general increase in the number of publications focusing on paediatric DS between 2000 and 2014, with a trending decline thereafter. The majority of

publications were affiliated with institutions based in the USA and UK. The majority of studies utilised a cross-sectional methodology, while relatively few studies were interventional, qualitative or mixed method. The distribution of 'primary health themes' in the paediatric DS literature was more spread. Overall, most publications focused on development & cognition, oncology and neurology, with fewer focusing on genitourinary health, growth, mortality and child protection. With regard to 'subcategory research themes', the majority of paediatric DS publications focused on prognosis and/or the natural history of DS and treatments.

Strengths and weaknesses of the study

The literature mapping exercise was performed using a systematic approach. Relevant titles were extracted from multiple medical literature databases. The search terms were highly inclusive, and developed in association with several experienced researchers. The definitions used for methodologies and 'themes' were based on those frequently utilised in research. These definitions were refined to optimise applicability to the paediatric DS literature and trialled by multiple researchers, reaching a high degree of consensus. The assessment for inclusion and exclusion of all titles, and subsequent data extraction for those publications, was performed by two independent reviewers and discrepancies were resolved by discussion with a third reviewer, or the wider research team where appropriate. This provided a 'sense check' and reduced the possibility of misclassification.

While this systematic approach reflects a high degree of academic rigor, it is possible that some titles may still have been misclassified (i.e. categorised as the incorrect methodology, 'primary health' or 'subcategory research theme'). However, given the large number of publications included in the mapping exercise infrequent misclassifications would not be expected to significantly impact the overall findings.

It should also be noted that some publications focused on more than one 'primary health' or 'subcategory research theme' (e.g. the 'primary health theme' of a study looking at the impact of congenital heart disease on neurodevelopmental outcomes could be classified as either 'Cardiac/circulatory' or 'Development & Cognition'). On these occasions the two reviewers chose the category which they felt was most appropriate. If the two reviewers had a tendency to repeatedly choose one theme over another this may lead to a bias towards, or against, certain

themes. However, publications with competing themes occurred rarely and thus this would not be expected to have a significant impact on the overall findings.

The mapping exercise focused on publications after the year 2000. Consequently it is not possible to comment on the characteristics of publications published before this date. There are many publications published before the year 2000 which contribute to the evidence based management of children with DS today. Similarly, publications which focused on the adult population were also excluded, and many of these will still be relevant to the health of paediatric population. However, in the context of this thesis, focusing primarily on modern paediatric DS literature was felt to be the most relevant and appropriate approach.

It should be noted that for the majority of publications, categorisation was based on the contents of the abstract only, as opposed to review of the full text publication. However, where the methodology or 'themes' were unclear, and in the case of reviewer discrepancy, the full-text was consulted. It is possible that in some cases the content of the abstract was a poor reflection of the study, thus leading to misclassification. An example of this was that it was often difficult to differentiate between a truly systematic review and a narrative review based on the abstract alone. In order to address this issue these two methodological categories were combined. Extracting data from the abstracts had the advantage of making it possible to include a larger number of publications, over a longer time period, than would have been practical if the full text article was consulted for every paper. Furthermore, in the vast majority of cases the abstract provided to contain sufficient information to categorise the publication according to the outcomes, and consulting the full text was unnecessary.

Comparison with other studies

I am not aware of any existing effort to map the paediatric DS literature. In fact, despite its value, this 'epistemological approach' is rarely employed in research in general, possibly due its laborious nature and the requirement to review a relatively large number of publications.

Venekamp et al (2017) employed this methodology to map 5 years of literature focusing on obstructive sleep apnoea in childhood. In this field they too found a predominance of publications focusing on treatment and prognosis, and few publications focusing on service delivery and health economics. Also reflecting the findings of this mapping exercise, the

majority of the studies utilised an observational methodology, with very few interventional or qualitative studies[454].

Implications for practice and research

The general trend of an increased number of publications focusing on paediatric DS per year, over the majority of the study period (2000-2014), is somewhat promising. However, the number of publications should be considered in the context of all research articles published over the same time period. As has previously been illustrated[426], while there may have been an increase in the number of DS research publications over time (not limited to paediatric DS), there has been a proportionate decline, relative to all academic publications. This suggests that DS is receiving relatively less academic focus and attention.

The trend of decline in the number of publications focusing on paediatric DS from 2014-2020 noted in this study may represent a shift in focus away from childhood studies and towards prenatal. This follows significant advancements in the prenatal diagnosis of DS via non-invasive techniques over recent years[9 426]. Research focusing on the prenatal diagnosis of DS does not inform improvements in the health and care of live-born children with DS. The findings of this study provide support for a "rebalancing" of focus in DS research, by increasing investment in studies which aim to improve the health and well-being of children with DS.

Academic institutions in the UK, and particularly the USA, appear to dominate paediatric DS publications. This may be a recurrent pattern in the wider field of research and academia. However, the over-representation of research from certain regions, where the population is predominantly White and 'high income', may limit the generalisability of findings in paediatric DS research. Therefore, these findings provide some support for investment in research which includes patient groups which are likely under-represented in the paediatric DS literature (e.g. low resource settings, non-white ethnicity).

The mapping exercise also demonstrates a predominance of observational studies (cross-sectional, cohort and case control studies, case reports and case series). In particular, there were a large number of case reports focusing on children with DS (13.7% of publications). While case reports make a valuable contribution to research literature they are considered further down the 'hierarchy of evidence'. Robust, large-scale interventional studies will be

required to advance the evidence-based healthcare of children with DS. These findings support increased investment in interventional studies aimed at children with DS.

The study findings also highlight a relative paucity of qualitative and/or mixed method studies. Improving healthcare for children with DS requires, not only a quantitative approach, but also an understanding of the experience of the child and family. Qualitative research is ideal to identify areas of health priority for patients and carers, and also to identify opportunities to optimise their interactions with the healthcare system. Furthermore, as explored by Fortnum et al[441], parent/carer engagement is vitally important to ensure the feasibility and acceptability of future research. In their mixed methods study looking at research related in otitis media in the DS population they conclude, "any proposed research study needs to respond the shared challenges of parenting a child with DS… and also needs to accommodate and negotiate the variety of highly personal perspectives and experiences that families have demonstrated"[441]. The findings of this study support increased investment in paediatric DS research utilising a qualitative and mixed methods approach.

Looking at 'primary health themes', the distribution of categories was more spread than that observed for the other outcomes. The 'primary health themes' which appeared to receive the greatest attention are not surprising and reflect important, well established areas of DS child health (i.e. development & cognition, neurology and oncology). However, it is notable that relatively few publications focus on respiratory health, infections and immunological disease, as these are recognised as significant causes of mortality and morbidity in children with DS[29] [455]. The findings of this study support investment in these areas of DS child health, as well growth, mortality and child protection, as these health themes appear to have received the least attention in the existing paediatric DS literature.

Finally with regard to 'subcategory research themes', the majority of publications described the natural history of children with DS (i.e. they aimed to define normality or normative values within the DS phenotype, or to further the knowledge base on the development of the DS phenotype over time). For example, studies determining the average lipid profiles among individuals with DS, the typical trajectory of speech and language development in children with DS or average activity levels among teenagers with DS. Notably this category did not include publications which describe the prevalence or incidence of disease in DS, these were

categorised separately. While it is valuable to understand normative health characteristics in the DS population the findings suggest that, more than 150 years since the condition was first described, the natural history of DS is relatively well documented. The findings of this study support investment in other areas of DS research which appear relatively under-represented e.g. the diagnosis of and screening for DS associated morbidities, service delivery and economic analyses.

Within the context of this thesis it is notable that relatively few studies focused on the prevalence and incidence of DS morbidities and the diagnosis/screening for DS associated morbidity, which includes publications looking at health surveillance.

Unanswered questions and future research

It was not within the remit of this study to map existing research which focuses on adults with DS. Much of this research will still be relevant to the health of children. Future research could attempt to repeat the methodology described here to map the adult DS literature and draw comparisons the findings from the paediatric literature. As described above, some of the patterns in the paediatric DS literature reflected those also found by Venekamp et al. in the obstructive sleep apnoea literature[454]. Future research could explore whether these patterns are repeated in wider paediatric literature and potential explanations for these patterns.

Furthermore, it was not within the remit of this study to determine whether the distribution of research themes presented here reflects the research priorities of DS patients and their parents/carers. As explored in the Background, it is vital that research incorporates the interests of the population that it intends to benefit. Future studies could explore the research priorities of patients with DS and their parents/carers, and compare these with the findings of this review.

The study identified a small proportion of interventional studies. Future research could explore these studies in more details. For example the characteristics of participants, details of the interventions, the outcomes measured and the methodologies (e.g. randomised control trial, pre-post study). It may be that certain health themes and patient cohorts are underrepresented in these studies.

Based on those areas of relative paucity within the paediatric DS literature, the findings suggest that future research should include interventional studies, qualitative studies and those which

utilise a mixed methodology; as well as studies which focus on respiratory health, immunology, mortality, growth and child protection; and those studies with a ‘subcategory research’ focus on the diagnosis and screening for DS associated morbidities, service delivery and economic analyses.

PROJECT 2: DISEASE PREVALENCE IN THE DOWN SYNDROME POPULATION

Introduction

As explored in the Background, DS is associated with the development of a multitude of health conditions throughout the life-course, affecting almost every body system. In this thesis I refer to these conditions as "DS associated morbidity". Also in the Background I explore how individuals with DS are considered at an increased risk of some cancers (e.g. leukaemia) but that there is ongoing debate regarding their risk of other malignancies, in particular solid tumours.

There is limited existing literature on the prevalence of DS associated morbidity and cancers in the DS population, and the reported figures tend to vary considerably. This variation is likely a reflection of the reality that the majority of existing studies are based on retrospective chart reviews and have small sample sizes. Furthermore, these studies tend to focus on the adult population, limiting their relevance for children. Also, very few of these studies include a comparator group of individuals who do not have DS, thus permitting a relative appreciation of risk.

Obtaining more precise estimates of the prevalence of morbidities and cancers is key to understanding the burden of disease in the DS population. This information provides clinicians with an awareness of which conditions their patients are likely, or indeed unlikely, to develop. Such an awareness also informs health surveillance practices: for example, active screening for conditions which are common in DS and amenable to this, or reduced screening for those conditions which are in fact rare. An appreciation of disease prevalence also informs the allocation of health resources, for example with the most prevalent conditions potentially requiring relatively more healthcare investment. Finally understanding the burden of disease in the DS population also informs future research, potentially highlighting health conditions which are relatively common in the DS population, and thus worthy of increased academic attention.

I therefore set out to determine the prevalence of DS associated morbidities and cancers in a large cohort of individuals with DS, and to compare this with the prevalence in a group of matched controls, who do not have DS. To do this I utilized a large linked dataset which

incorporates routinely collected electronic health record data from primary care (CPRD), secondary care (HES) and the Cancer Registry. The DS population included in this study represents one of the largest DS cohorts reported in the academic literature to date.

Aims & Objectives

By analysing a large cohort of individuals with DS, and their matched controls, using a linked electronic health record data set, I aimed to:

1. Determine the prevalence of a multitude of DS associated morbidities among children and adults with DS, compared to matched individuals who do not have DS.
2. Determine the prevalence of a multitude of cancers (as defined by site) among children and adults with DS, compared to matched individuals who do not have DS.

Methods

This matched retrospective cohort study utilises population-based electronic health record data in England. This data is provided by the Clinical Practice Research Datalink (CPRD), and is linked to Hospital Episode Statistics (HES), The National Cancer Registration and Analysis Service (NCRAS) and Office for National Statistics (ONS) datasets.

This study was carried out as part of the ClinicAl Disease Research Using LInked Bespoke Studies and Electronic Health Records (CALIBER©) programme (https://www.ucl.ac.uk/health-informatics/caliber). CALIBER is a research platform led from the UCL Institute of Health Informatics consisting of anonymised, coded variables extracted from linked electronic health records, methods and tools, specialised infrastructure, and training and support.

The database & data access

The database is comprised of patient's electronic records from primary care (CPRD) [456], linked to their records in secondary care (HES) [457], their records in the Cancer Registry (NCRAS) [458] and their mortality and deprivation data (ONS). Multiple and linked data sources provide complimentary and corroborating longitudinal information about a patient's medical history (Figure 5).

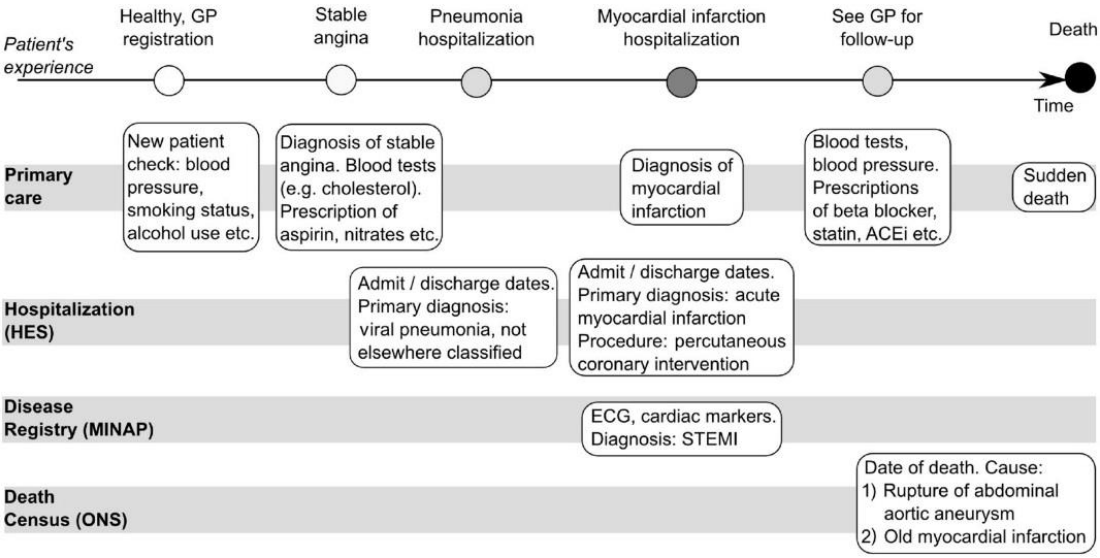

Figure 5: A graphical representation of a hypothetical patient's medical history in the CALIBER database[459].

The database was accessed via the UCL Data Safe Haven, whereby data is stored, processed and managed within the security of a 'walled garden' system. Aggregate data can be transferred out of the 'walled garden' through a secure transfer mechanism [460]. The database is pseudo-anonymised with unique patient identifiers and GP location at a crude level only (one of 10 regions). Identifiers such as date of birth, name and address, as well as NHS or hospital numbers, are removed.

Primary Care dataset: Clinical Practice Research Datalink (CPRD)

The CPRD dataset is a longitudinal primary care database of anonymised medical records, from general practitioners. In June 2018, it had coverage of approximately 15 million patients from 735 practices in the UK[461 462]. CPRD is a rich source of patient data providing information on demographics, symptoms, health behaviours, diagnoses, investigations, referrals, procedures, vaccinations and prescriptions[461].

Data in CPRD is recorded using Read codes, which map to Systematic Nomenclature of Medicine – Clinical Terms[463]. Read codes are a hierarchical clinical classification system containing more than 96,000 codes[464]. During a consultation, patient data is routinely entered via computer programme interfaces, or retrospectively from correspondence (e.g. secondary care clinic reports, discharge letters). More than one Read code can be entered for each consultation or clinical encounter.

CPRD uses data quality criteria to help identify patients, and periods of data recording, which are considered of an "acceptable standard" for research. The acceptability of patient-level data is based on registration status, consistent recording of events, and valid age and gender (Figure 6). An up to standard (UTS) time is also calculated for participating practices, reflecting the duration of gaps in their recorded data and the reported deaths, compared with that which would be expected based on the practice size[461]. Despite these criteria, research has shown variations in inter-practice recording of data[465]. Any practices considered to be submitting poor quality data are provided with feedback and if coding practices are not rectified the data from those practices is subsequently removed from CRPD[466].

Data entry is also enhanced by the Quality and Outcomes Framework[467] which provides incentive payments for GPs to record of key data items (e.g. smoking status) and the delivery of services to key patient groups. Following the introduction of the Quality and Outcomes Framework in 2004, completeness in recording of multiple variables showed subsequent improvement[461].

If any of the following conditions are met then the patient's data is labelled as "unacceptable", and is not recommended for use in research.

- An empty or invalid first registration date
- An empty or invalid current registration date
- Absence of a record for a year of birth
- A first registration date prior to their birth year
- A current registration date prior to their birth year
- A transferred out reason with no transferred out date
- A transferred out date with no transferred out reason
- A transferred out date prior to their first registration date
- A transferred out date prior to their current registration date
- A current registration date prior to their first registration date
- A gender other than Female/Male/Indeterminate
- An age of greater than 115 at end of follow up
- Recorded health care episodes in years prior to birth year
- All recorded health care episodes have empty or invalid event dates
- Registration status of temporary patients

Figure 6: 'Up to Standard' data: CPRD criteria to assess the acceptability of patient data for use in research[466].

Validation of CPRD data has shown high positive predictive value and comparable disease incidences with other UK data sources[468-472]. A systematic review of these CPRD validation studies also found that diagnoses were generally reliable[473]. Studies have also shown that CPRD patients are broadly representative of the UK population in terms of age, sex, ethnicity,

body mass index (BMI) and mortality[461] [474-477], and the dataset is used widely for epidemiological research[461].

A subset of primary care practices, all based in England, participate in a linkage scheme which links patient-level data to additional datasets such as Hospital Episode Statistics[478] (secondary care data), the Office for National Statistics (mortality data[479], Index of Multiple Deprivation and Townsend scores[480]), and disease registries including the Cancer Registry[480]. Data is linked through a trusted third party, NHS Digital[481]. The linkage utilised in this study (linkage 16) includes data from 405 practices, representing ~75% of the contributing English practices and ~57% of all UK CPRD practices.

Within the participating practices, 88% of research quality (acceptable) patients have the necessary data to allow linkage to Hospital Episode Statistics (HES), Cancer Registry, and the Office for National Statistics (ONS) Death Registration data. Within the participating practices, 97% of acceptable patients are eligible to be linked to data on the Index of Multiple Deprivation (IMD) and Townsend socioeconomic scores. Table 11 summarises the coverage periods for linked data sources in linkage 16.

Please note, Clinical Practice Research Datalink (CPRD) is both the name given to the primary care dataset and also the research service organisation which is the custodian of the linked dataset.

Table 11: Coverage periods for the linked data sources in linkage 16.

Dataset	**Coverage period**
HES Admitted Patient Care	April 1997 – December 2017
HES Outpatient	April 2003 – December 2017
HES Accident & Emergency	April 2007 – December 2017
ONS Death Registration	January 1998 – December 2017
Cancer Registration	1990 – 2017

Secondary care data: Hospital Episode Statistics (HES)

Hospital Episode Statistics data (HES) provides information on hospital admissions, outpatient appointments, procedures and A&E attendances for eligible patients in England. HES covers all NHS trusts in England, including mental health Trusts. Data is extracted for the purpose of hospital reimbursement under Payment by Results (PbR).

Diagnoses are coded using the hierarchical coding scheme, International Statistical Classification of Diseases and Health-Related Problems, 10th revision (ICD-10)[482]. The ICD-10 coding system includes codes for disease, signs, symptoms, abnormal findings, social circumstances and external causes of injury or disease.

Upon discharge from hospital, a discharge summary is produced for each patient by one of the treating clinicians. The discharge summary is then forwarded to the clinical coding department who enter the information on the local patient information database. Clinical coders undergo an accredited training programme and follow standardised rules for translating information into clinical codes[457 483 484]. Discharge letters, clinical letters and referral letters are ideally copied to the primary care physician and transcribed onto the primary care (CPRD) dataset, as described above. However, in practice, this is not always the case and the linkage of HES and CPRD therefore provides a more complete picture of patient journey. The HES dataset has been used extensively used for epidemiological research[485-487] and validated for several conditions [488-491].

Cancer Registry

Data from primary care (CPRD) and secondary care (HES) is linked to the Cancer Registry, provided by Public Health England (PHE), via the National Cancer Registration and Analysis Service (NCRAS). This dataset includes a record of all registerable tumours diagnosed or treated in England, of which NCRAS has been notified[480].

Cancers are coded using the International Classification of Diseases for Oncology, revision 3, 2011[492] and also 'back mapped' to the tenth revision of the International Classification of Diseases version 10 (ICD-10) [482]. Registrable conditions are broadly: all invasive tumours, all uncertain behaviour tumours, all in situ tumours and benign tumours within the brain or central nervous system[458].

Estimates of data completeness are high (estimate >99%), as the registry is population based and receives death certificates[458].

Office of National Statistics (ONS)

Office of National Statistics data, which is also linked to CPRD, provides information on the causes of mortality of all patients in England, and the official date of death. Cause-specific mortality data is extracted from death certifications, and coded using ICD-10.

The ONS also provides the Indices of Multiple Deprivation and Townsend Score[493 494], based on the patient and/or practice postcode. This information is poorly recorded elsewhere in the linked dataset and provides a measure of socio-economic status[480].

Study Population

The custodians of the linked dataset (CPRD) provided the required subset of data. This subset included the anonymised electronic health care data for individuals with DS and their matched controls. The custodians identified individuals with DS, in the wider linked dataset, using the ICD-10 and Read codes provided by myself (Appendix 5). Females with a first record of DS after pregnancy were excluded, as they are likely to represent the mothers of children with DS, as opposed to individuals with DS[25]. Individuals with DS were matched with up to 5 controls (minimum of 4) based on GP practice, practice level index of multiple deprivation, year of birth ± 1 year, sex and index date (the date at which a case is first labelled as having DS).

Participants' entry into the cohort (herein referred to as 'start of follow-up') was defined as the latest of the patient registration date, the practice UTS date (Figure 6), and 01/01/1998.

Participants' exit from the cohort (herein referred to as 'end of follow-up') was defined as the earliest of the patient transfer out date, the practice last collection date, date of death (defined as the ONS date of death, or where missing, the 'CPRD derived date of death') and 31/12/2017.

In the 'primary analysis', outcomes were determined for the entire study population (i.e. including children and adults), however given that that the focus of this thesis is children I have also presented a subgroup-analysis of the primary outcomes for children only, defined as only those participants who were aged ≤18 years at the end of follow-up. Note, there will still be some individuals who contributed data in their childhood years during the study period, but because they were aged over 18 years at the end of follow-up they were not included in the subgroup-analysis. A justification for splitting the analyses in this way (children and adults combined, and children only) is presented in the Discussion.

Outcomes: DS associated morbidities and cancers

The occurrence of a DS associated morbidity or cancer was defined as a positive record of that condition within the dataset, regardless of the date. The characterisation of each condition of interest (phenotyping) is described in detail below.

Table 12 summarises the 31 morbidities and 24 cancers which were investigated.

The selection of DS associated morbidities to be examined was based on both existing literature which suggests that these conditions are more common in the DS population, and also on clinical experience. Myself, and several members of the research team have first-hand experience of caring for children with DS in various healthcare settings. Consequently the analysis also includes a number of conditions where existing literature to suggest these conditions are more common among individuals with DS is scant or contradictory (e.g. inflammatory bowel disease[203], chronic kidney disease[223], non-accidental injury[314], vitamin D deficiency[319], type 1 diabetes mellitus[268], Duchenne muscular dystrophy[495]), but where our own clinical experience and professional consensus suggested that there conditions still warranted inclusion. In the subgroup-analysis focusing on children only, I did not include dementia or ischaemic heart disease as these are typically diseases of adulthood.

Cancers to be examined were defined according to body site and their categorisation reflects that used in existing epidemiological studies[257 359 375 378]. Unlike the "DS associated morbidities", only a minority of these cancers are considered to be more common in the DS population, compared to the general population. In the subgroup-analysis focusing on children only, I limited the analysis to classic cancers of childhood (i.e. leukaemia, lymphoma and neuroblastoma).

Table 12: The DS associated morbidities and cancers which were investigated in the dataset.

Cardiovascular	Congenital cardiac disease Ischaemic heart disease Stroke
Ear, Nose & Throat	Hearing impairment Sleep disordered breathing
Vision / Ophthalmic	Cataract Glaucoma
Neurological	Epilepsy
Psychiatric/ Behaviour	ADHD Anxiety & depression Autism Dementia Schizophrenia
Gastrointestinal / Renal	Chronic kidney disease Congenital gastrointestinal disorders Gastroesophageal reflux disease Inflammatory bowel disease
Endocrine / Autoimmune	Coeliac disease Hyperthyroidism Hypothyroidism Type 1 diabetes mellitus Type 2 diabetes mellitus Diabetes mellitus (combined)
Haematological	Iron deficiency
Musculoskeletal	Arthritis (combined) Duchene muscular dystrophy
Dermatological	Eczema Skin disorders, non-eczema (combined)
Other	Non-accidental injury / maltreatment Undescended testis Vitamin D deficiency
Cancers	Bladder Bone Brain/ CNS Breast Cervix Colorectal Gastro-oesophageal Leukaemia Liver / hepatobiliary Lung Lymphoma Melanoma Myeloma Neuroblastoma Ovarian Pancreas Prostate Renal Retinoblastoma

	Skin, non-melanomatous Testicular Thyroid & parathyroid Uterus Wilms'

Nb. Each health condition of interest is defined using a phenotyping code list. This process is described in the Methods. The list of codes used to define each condition is included in Appendix 5.

Code lists / phenotyping

Each morbidity and cancer of interest was defined according to a list of Read and ICD-10 codes (Appendix 5).

Researchers must interpret codes to determine whether or not the patient has the condition of interest. In some cases this interpretation is straightforward (e.g. Read code Eu90011: "Attention deficit hyperactivity disorder"), but in other circumstances it may be less clear (e.g. Read code 1P00.00: "Hyperactive behaviour"). Therefore it is necessary to make a judgement as to whether or not a patient in the dataset has the condition of interest. The use of linked datasets provides an inherent advantage in developing code lists as there are multiple sources of data, providing more extensive and/or corroborating information[496].

The phenotyping code lists were developed in a stepwise process: (1) Compiling code lists utilised and published in existing peer review research, examining the same conditions of interest; (2) Searching the Read and ICD-10 complete code database using relevant terms, and (3) reaching expert consensus on which codes should be included to define the condition of interest (Appendix 5).

In CALIBER, the creation of code lists is assisted by access to the CALIBER Data Portal, an online resource for researchers. The portal provides access to code lists which have been compiled and utilised by other researchers undertaking research on the CPRD and HES datasets. The CALIBER portal currently contains more than 300 variables with code lists (Read and ICD-10) agreed by both clinical and non-clinical researchers in a transparent and reproducible manner[460]. When a CALIBER researcher is examining a condition of interest, not currently included on the Data Portal, their final code list will be made available for use by future researchers, following peer review. In the context of this thesis, an appropriate

CALIBER ICD-10 and Read code phenotyping list existed for 10 of the 55 conditions examined. These lists were reviewed and amended before being incorporated into the phenotyping code lists utilised in this study, to ensure that they were appropriate for the analysis.

In this study, the final phenotyping code lists for each condition were compiled by myself and reviewed by two additional clinicians and two researchers with experience in the field of epidemiology and research utilising electronic health records. Disputes were resolved through discussion with the wider research team.

Statistical analysis

The statistical methodology, analysis plan, data interrogation and interpretation was designed, written and performed by myself, with support from Dr Arturo Gonzalez-Izquierdo (senior research associate in electronic health records, UCL Institute of Health Informatics) and the wider research team. All data was analysed using Stata v16 (StataCorp, Texas). The syntax written and used by myself is included in Appendix 6.

In this thesis the prevalence figures calculated may be further described as "study prevalence" since they refer to the occurrence of disease within a period of time (i.e. the study period), as opposed to at a single point in time. Study prevalence of DS associated morbidities and cancers was calculated as the number of individuals with any record of the condition of interest (as defined by the phenotyping code lists) during their period of follow-up in the dataset, over the total number of individuals in that population. For example, a prevalence of 30% for hypothyroidism in the DS population means that 30% of the individuals with DS in our study had any record of hypothyroidism during their period of follow-up.

Standard statistical approaches (chi-squared and Fisher's Exact test for normal and non-normal binary outcomes respectively: two sample t-tests and Mann Whitney U-test for numeric outcomes) were used to compare outcomes in those with DS and the matched controls. A p.value of <0.01 was considered significant and 95% confidence intervals were also calculated for all measures of average and proportions.

Odds ratios (OR) were calculated for the occurrence of DS associated morbidities and cancers in the those with DS verses controls using logistic regression[497]. Logistic regression is a

standard statistical approach to examine the association between binary exposures (i.e. DS or non-DS) and outcomes (i.e. disease occurrence). Adjusted odds ratios were also calculated, adjusting for the cofounding variables ethnicity and smoking status.

In the primary analysis (i.e. including both children and adults), the study prevalence, OR and aOR for ischaemic heart disease and dementia are presented both for the entire population and also limited to the population aged ≥40 years and 30 years at the beginning of follow-up, respectively. This was to reflect the adult onset nature of these conditions and existing literature on the age of disease onset[49-51 62-68].

Primary outcomes

1. The study prevalence of DS associated morbidities among children and adults with DS, and a comparison with matched individuals, who do not have DS.
2. The study prevalence of cancers among children and adults with DS, and a comparison with matched individuals, who do not have DS.

Secondary outcomes

3. Risk of occurrence of DS associated morbidities and cancers in individuals with DS, compared to matched controls, before and after adjustment for confounding factors.

Ethical approval

Approval for access to the dataset was granted by the MRHA (UK) Independent Scientific Advisory Committee (ISAC), under Section 251 (NHS Social Care Act 2006), in 2018 (protocol number: 17_009R). The ISAC is a non-statutory expert advisory body established in 2006 by the Secretary of State to provide advice on research related requests to access data provided by CPRD.

Access to the database was via the UCL Data Safe Haven, which requires data to be stored and analysed within a secure platform[460]. Data users are provided with pseudo-anonymised data only and are obliged to comply with confidentiality standards.

Governance

Research Design approval was sought and obtained from the Joint Research and Development Office at the Great Ormond Street Institute of Child Health, UCL (R&D number 17PP09)

Results

Demographics of the DS cohort and their matched controls

There were 4,648 individuals with DS and 23,238 matched controls in the dataset (including both children and adults). In the subgroup-analysis of children only, data was available for 1,340 individuals with DS and 6,711 matched controls, who were aged ≤18 years at the end of follow-up.

Table 13 summarises key demographic characteristics of the DS cohort and controls.

In the primary analysis (i.e. children and adults combined), individuals with DS contributed on average 5.7 years of follow-up and controls contributed 10.6 years. Individuals with DS were more likely to have a record of death during the study period, compared to controls (24.1% (95CI 22.8%-25.3%) v. 3.4% (95CI 3.2%-3.7%), p<0.001)).

The predominant recorded ethnicity of individuals in both the DS cohort and the controls was "White". The mean BMI of individuals with DS was significantly higher than that of controls (29.3kg/m^2 (95CI 29.0-29.5 kg/m^2) v. 26.3 kg/m^2 (95CI 26.3- 26.4 kg/m^2) respectively (p<0.001). Individuals with DS were significantly less likely to have any record of smoking (9.1% (95CI 8.2%-10.2%) v. 48.9% (95CI 48.1%-49.7%) of controls, <0.001). The prevalence of smoking is likely to be exaggerated compared to the wider UK population due to 'recording bias' as a positive history of smoking is much more likely to be recorded in the health record than 'no history'[498]. Both a raised BMI and lower rates of smoking are in keeping with what would be expected in the DS population, compared to the general population[230 235 374].

In the subgroup-analysis of children only, children with DS contributed on average 3.9 years of follow-up and controls contributed 6.1years. Children with DS were more likely to have a record of death during the study period, compared to controls (3.1% (95CI 2.3%-4.2%) v. 0.3% (95CI 0.2%-0.4%), p<0.001). These figures are in keeping with the reality that children with DS are more likely die in early childhood from causes such as congenital heart disease, infection and leukaemia, as is explored in the Background. Again, the predominant recorded

ethnicity of children in both the DS cohort and the controls was "White". The mean BMI of children with DS was significantly higher compared to controls, 27.1kg/m^2 (95CI 25.7-28.4 kg/m^2) v. 22.3 kg/m^2 (95CI 21.7-23.0 kg/m^2) ($p<0.001$) respectively.

The study prevalence and odds of DS associated morbidities in the DS cohort and controls

Table 14 presents the study prevalence of DS associated morbidities in the DS cohort and the matched controls (including both children and adults). The most prevalent morbidities among individuals with DS were hypothyroidism (30.4%), eczema (29.1%), congenital cardiac disease (27.8%), epilepsy (21.9%), hearing impairment (19.2%) and dementia (17.6%).

For 25 of the 33 morbidity outcomes examined, the study prevalence was significantly higher among individuals with DS, compared with controls. A further 3 morbidities were close to reaching statistical significance (iron deficiency anaemia, ischaemic heart disease, schizophrenia). Of all the morbidities examined there was only two where individuals with DS were significantly *less* likely to have a positive record: anxiety/depression, 14.1% (95CI 13.2%-15.2%) v. 21.4% (20.9%-21.9%), $p<0.001$) and ischaemic heart disease in those aged over 40 years at the start of follow-up (9.6% (95CI 8.26%-11.2%) v. 13.8% (95CI 13.0%-14.7%), $p<0.001$).

The biggest *differences* in the study prevalence of morbidities, when comparing the DS cohort and controls, were in dementia amongst those aged over 30 years at the start of follow-up (37.3% v. 1.5%), hypothyroidism (30.4% v. 3.2%), congenital cardiac disease (27.8% v. 0.9%), epilepsy (21.9% v. 2.6%), hearing impairment (19.2% v. 3.7%) and cataract (16.3% v. 2.6%).

Table 14 also presents the odds ratios (OR) and adjusted odds ratios (aOR) for the 32 morbidity outcomes examined in the DS cohort versus controls. As we would expect, the ORs mirror the differences in disease prevalence, with the majority of morbidities having a significantly increased OR. However, after adjusting for ethnicity and smoking status, the increased odds ratio for ADHD and ischaemia heart disease in individuals DS v. controls lost statistical significance. This may reflect small case numbers and missing data among the confounding variables, as the 95% confidence intervals widen in both analyses.

Subgroup-analysis, DS associated morbidities in children only

Table 16 presents the subgroup-analysis, looking at morbidities among children only. The most prevalent morbidities among children with DS were congenital heart disease (56.3%), eczema (24.1%), hearing impairment (23.5%), sleep disordered breathing (19.1%) and gastroesophageal reflux (19.0%).

Among the 29 morbidities examined in children, those with DS were significantly more likely to have a record of 25 of the conditions, compared to controls. However, they were significantly less likely to have a record of eczema (24.1% (95CI 21.9%-26.5%) v. 31.6% (95CI 30.5%-32.7%), p<0.001). The reduced study prevalence of anxiety/depression among children with DS versus controls was also close to reaching statistical significance (1.9% (95CI 1.3%-2.8%) v. 2.8% (95CI 2.5%-3.2%), p=0.048), but the absolute difference was small.

The biggest *differences* in the study prevalence of morbidities, when comparing children with DS and their controls, were in congenital cardiac disease (56.3% v. 1.1%, aOR 109.2), hearing impairment (23.5% v. 2.5%, aOR 12.3) sleep disordered breathing (19.1% v. 1.6%, aOR 13.8), hypothyroidism (15.8% v. 0.5%, aOR 33.4) and gastroesophageal reflux (19.0% v. 4.2%, aOR 4.8).

The study prevalence and odds of cancers in the DS cohort and controls

Table 15 presents and compares the study prevalence of cancers in the DS cohort and the matched controls (including children and adults); 217 individuals with DS (4.7% (95CI 4.1%-5.3%)) and 2,421 of the controls (10.4% (95CI 10.0%-10.8%)) had a record of any of the 24 cancers examined (p<0.001). The most prevalent cancers among individuals with DS were leukaemia (1.0%), non-melanomatous skin cancer (0.6%), colorectal (0.5%), testicular (0.4%), breast (0.3%) and uterine cancer (0.3%).

When comparing the study prevalence of cancers in the DS cohort and the controls, individuals with DS were significantly more likely to have a record of leukaemia (1.0% v. 0.2%) and testicular cancer (0.4% v. 0.1%). However, they were significantly less likely to have a record of breast (0.3% v. 1.3%), cervical (0.1% v 1.9%), colorectal (0.5% v. 1.8), lung (0.1% v. 0.5%) melanoma (0.1% v. 0.5%), non-melanomatous skin (0.6% v. 2.3%), prostate (0.1% v. 0.6%) and uterine cancer (0.3% v. 1.3%).

Table 15 also presents odds ratios and adjusted odds ratios for the 24 cancers examined in DS cases versus controls. The increased odds ratio of leukaemia and testicular cancers remain statistically significant, even after adjustment for confounding factors (i.e. ethnicity and smoking status). However, the decreased odds ratios of breast, colorectal, lung, ovarian, prostate and uterine cancer lose statistical significance after adjustment for confounders. This may reflect a reduction in statistical power following the inclusion of confounders in the model and/or that ethnicity and smoking status are a source of confounding bias in the association between DS and these cancers.

Subgroup-analysis, cancers in children only

Table 16 presents the subgroup-analysis, looking at the occurrence of leukaemia, lymphoma and neuroblastoma in children only. Leukaemia was the most prevalent cancer among children with DS (2.2% (95CI 1.5%-3.1%) and this was significantly higher when compared with controls (0.03% (95CI 0.001%-0.12%), $p<0.001$). The increased odds ratio of leukaemia remained statistically significant after adjusting for confounders. The study prevalence of lymphoma and neuroblastoma was not significantly different between children with DS and controls.

Table 13: Summarising and comparing the demographic characteristics of the Down Syndrome (DS) cohort and the control group, in the primary & subgroup-analysis.

	Primary analysis (i.e. adults & children)			Subgroup-analysis (i.e. ≤18yrs at end of follow-up)		
	DS COHORT N= 4,648 *n* (%)/average (95% CI)	**CONTROL GROUP N= 23,238** *n* (%)/average (95% CI)	**p.value*** (p<0.01)	**DS cohort, children only N=1,340** *n* (%)/average (95% CI)	**Control group, children only N=6,711** *n* (%)/average (95% CI)	**p.value*** (p<0.01)
PERSON YEARS						
Total years contributed:	32,919.8	236,883.0		6,889.9	45,464.3	
Median years contributed per person:	5.7yrs (5.4-6.0yrs)	10.6yrs (10.6-10.7yrs)	<0.001’	3.9yrs (3.6-4.2yrs)	6.1yrs (5.9-6.3yrs)	<0.001’
GENDER						
Male	2,551 (54.0%)	12,553 (54.0%)	0.996	698 (52.1%)	3,443 (51.3%)	0.599
Age						
Median age at start of follow-up (yrs):	26yrs (25-28) Range: 0-74yrs	25yrs (24-26) Range: 0-72yrs	0.022’	1yr (1-2yrs) Range: 0-18yrs	0yrs (0-0yrs) Range: 0-18yrs	<0.001’
Median age at end of follow-up (yrs):	35yrs (33-36) Range: 0-75yrs	33yrs (33-34) Range: 0-88yrs	0.090’	8yrs (8-9yrs) Range: 0-18yrs	9yrs (8-9yrs) Range: 0-18yrs	0.377‡
DATA ENTRY						
Age range at start of follow-up^						
0-5 years	1,013 (21.8%)	6,011 (25.9%)	<0.001	958 (71.5%)	5,593 (83.3%)	<0.001
6-10 years	352 (7.6%)	1,718 (7.4%)	0.669	229 (17.1%)	739 (11.0%)	<0.001
11-18 years	475 (10.2%)	2,319 (10.0%)	0.619	153 (5.7%)	379 (11.4%)	<0.001
19-30 years	686 (14.8%)	3,099 (13.3%)	0.010	-	-	-
31-60 years	1,931 (41.5%)	9,589 (41.3%)	0.723	-	-	-
>60 years	191 (4.1%)	502 (2.2%)	<0.001	-	-	-
Age range at end of follow-up^						
0-5 years	449 (9.7%)	2,241 (9.6%)	0.972	449 (33.5%)	2,241 (33.4%)	0.935
6-10 years	385 (8.3%)	1,895 (8.2%)	0.771	385 (28.7%)	1,895 (28.2%)	0.714
11-18 years	506 (10.9%)	2,575 (11.1%)	0.699	506 (37.8%)	2,575 (38.4%)	0.676
19-30 years	764 (16.4%)	4,173 (18.0%)	0.013	-	-	-
31-60 years	2,092 (45.0%)	8,906 (38.3%)	<0.001	-	-	-
>60 years	452 (9.7%)	3,448 (14.8%)	<0.001	-	-	-
Total person years contributed per age group (at start of follow-up)						
0-5 years	6,566.8 (19.9%)	47,505.4 (20.1%)	0.671	5,617.4 (81.5%)	40,215.9 (88.5%)	<0.001

6-10 years	2,804.6 (8.5%)	19,119.2 (8.1%)	0.005	926.8 (13.5%)	4,230.3 (9.3%)	<0.001
11-18 years	3,769.3 (11.5%)	24,228.4 (10.2%)	<0.001	345.7 (5.0%)	1,018.1 (2.2%)	<0.001
19-30 years	5,467.8 (16.6%)	27,870.7 (11.8%)	<0.001	-	-	-
31-60 years	13,811.0 (41.9%)	113,153.5 (47.8%)	<0.001	-	-	-
>60 years	500.3 (1.5%)	5,005.9 (2.11%)	<0.001	-	-	-
DATA EXIT						
Death during follow-up	1,119 (24.1%)	796 (3.4%)	<0.001	42 (3.1%)	17 (0.3%)	<0.001
ETHNICITY						
White	3,510 (85.7%)	14,440 (84.11%)	0.013	990 (77.8%)	4253 (77.2%)	0.652
Bangladeshi/Pakistani/Indian/Chinese/Asian other	138 (3.4%)	666 (3.9%)	0.124	84 (6.6%)	345 (6.3%)	0.656
Black African/Caribbean/Other	123 (3.0%)	413 (2.4%)	0.029	87 (6.8%)	218 (4.0%)	<0.001
Mixed/Other	326 (8.0%)	1,651 (9.6%)	0.001	111 (8.7%)	218 (4.0%)	<0.001
SOCIOECONOMIC STATUS *(Practice Level Index of Multiple Deprivation)*						
1 (highest)	596 (12.8%)	2,980 (12.8%)	0.998	181 (13.5%)	923 (13.8%)	0.811
2	849 (18.3%)	4,243 (18.3%)	0.991	246 (18.4%)	1,239(18.5%)	0.929
3	965 (20.8%)	4,825 (20.8%)	0.998	253 (18.9%)	1,293(19.3%)	0.743
4	1,096 (23.6%)	5,480 (23.6%)	0.998	329 (24.6%)	1,593(23.7%)	0.523
5 (lowest)	1,142 (24.6%)	5,710 (24.6%)	0.998	331 (24.7%)	1,663(24.8%)	0.951
AVERAGE BODY MASS INDEX (BMI) kg/m2						
Mean BMI (kg/m^2)	29.29 (29.0-29.5)	26.34 (26.3-26.4)	<0.001†	27.1 (25.7-28.4)	22.3 (21.7-23.0)	<0.001†
SMOKING STATUS						
Non-smoker	2,899 (90.9%)	8,097 (51.1%)	<0.001	-	-	-
Smoker (any history)	291 (9.1%)	7,752 (48.9%)	<0.001	-	-	-
GEOGRAPHICAL REGION						
1	81 (1.7%)	405 (1.7%)	0.999	20 (1.5%)	94 (1.4%)	0.795
2	695 (14.9%)	3,475 (14.9%)	0.998	174 (13.0%)	854 (12.7%)	0.795
3	173 (3.7%)	865 (3.7%)	0.999	65 (4.9%)	320 (4.8%)	0.897
4	145 (3.1%)	725 (3.1%)	0.999	40 (3.0%)	218 (3.3%)	0.617
5	490 (10.5%)	2,448 (10.5%)	0.988	139 (10.4%)	678 (10.1%)	0.765
6	433 (9.3%)	2,165 (9.3%)	0.999	121 (9.0%)	630 (9.4%)	0.681
7	684 (14.7%)	3,420 (14.7%)	0.998	182 (13.6%)	915 (13.6%)	0.959
8	585 (12.6%)	2,925 (12.6%)	0.998	164 (12.2%)	836 (12.5%)	0.825
9	794 (17.1%)	3,970 (17.1%)	0.998	281 (21.0%)	1379 (20.6%)	0.728
10	568 (12.2%)	2,840 (12.2%)	0.998	154 (11.5%)	787 (11.7%)	0.807

Nb. Cases (individuals with DS) are matched with at least 4 controls (non-DS individuals) based on GP practice, practice level index of multiple deprivation, year of birth ± 1 year, sex and index date.
**p Values calculated using χ2 (comparison of proportions)*
‡p Values calculated using Fisher's exact test (comparison of proportions, non-parametric)
†p Values calculated using t-test (comparison of normally distributed continuous variables)
'p Values calculated using Mann-Whitney U-test (comparison of non-normal continuous variables)
Missing data: Primary analysis: Gender=0, Ethnicity: DS=551, Control=6,068; SES:0; BMI DS=1,989, Control=10,285; Smoking status: DS=1,458 Controls=7,389; Geographical region=0; Subgroup-analysis: Gender=0, Ethnicity: DS=68, Control=1,205; SES:0; BMI DS=1,258, Control=6,487; Geographical region=0
^Start of follow-up is defined as the latest of the patient registration date, the practice UTS date, and 01/01/1998. End of follow-up is defined as the earliest of the patient transfer out date, the practice last collection date, date of death and 31/12/2017..
Yrs: Years

Table 14: Primary analysis (adults & children): Summarising and comparing the study prevalence, odds ratios (OR) and adjusted odds ratios (aOR) of DS associated morbidities in the DS cohort v. the control group.

Morbidity	DS COHORT N= 4,648		CONTROL GROUP N= 23,238		p.value * (p<0.01)	OR (CI) (95% CI </>1)	aOR (CI) (95% CI </>1)
	n	% (95CI)	n	% (95CI)			
ADHD	59	1.3% (1.0%-1.6%)	159	0.7% (0.6%-0.8%)	<0.001	1.9 (1.4 -2.5)	1.3 (0.8-2.1)
Anxiety/depression	657	14.1% (13.2%-15.2%)	4,969	21.4% (20.9%-21.9%)	<0.001	0.6 (0.6-0.7)	0.7 (0.6-0.8)
Arthritis (combined)	570	12.3% (11.4%-13.2%)	2,906	12.5% (12.1%-12.9%)	0.648	1.0 (0.9-1.1)	1.1 (0.9-1.5)
Atlantoaxial instability	39	0.8% (0.6%-1.2%)	26	0.1% (0.1%-0.2%)	<0.001	7.6 (4.6-12.4)	10.7 (5.1-22.5)
Autism	230	5.0% (4.4%-5.6%)	160	0.7% (0.6%-0.8%)	<0.001	7.5 (6.4-8.0)	7.7 (6.1-9.7)
Cataract	731	15.7% (14.7%-16.8%)	593	2.6% (2.4%-2.8%)	<0.001	7.1 (5.3-6.5)	6.2 (5.5-7.0)
Chronic kidney disease	300	6.5% (5.8%-7.2%)	645	2.8% (2.6%-3.0%)	<0.001	2.4 (2.1-2.8)	2.3 (1.7-3.2)
Coeliac disease	100	2.2% (1.8%-2.6%)	87	0.4% (0.3%-0.5%)	<0.001	5.9 (4.4-7.8)	9.6 (6.1-15.1)
Congenital cardiac disease	1,293	27.8% (26.6%-29.1%)	207	0.9% (0.8%-1.0%)	<0.001	42.9 (36.9-49.9)	55.0 (44.7-67.8)
Congenital gastrointestinal disease	106	2.3% (1.9%-2.8%)	57	0.3% (0.2%-0.3%)	<0.001	9.5 (6.9-13.1)	12.0 (7.5-19.0)
Dementia	816	17.6% (16.5% 18.7%)	168	0.7% (0.6%-0.8%)	<0.001	29.2 (24.7-34.6)	25.6 (19.1-34.2)
Dementia (≥30yrs at start of follow-up)"	807	37.3% (35.3%-39.4%)	158	1.5% (1.3%-1.8%)	<0.001	38.4 (32.1-45.9)	26.8 (19.3-37.2)
Diabetes Mellitus (combined)	375	8.1% (7.3%-8.9%)	1,394	6.0% (5.7%-6.3%)	<0.001	1.4 (1.2-1.6)	2.0 (1.6-2.6)
Diabetes Mellitus, Type 1^	56	1.2% (0.9%-1.6%)	101	0.4% (0.4%-0.5%)	<0.001	2.8 (2.0-3.9)	2.7 (1.5-5.2)
Diabetes Mellitus, Type 2^	145	3.1% (2.7%-3.7%)	784	3.4% (3.2%-3.6%)	0.378	0.9 (0.8-1.1)	1.3 (0.9-1.9)
Duchenne muscular dystrophy	4	0.1% (0.0%-0.2%)	18	0.1% (0.1%-0.1%)	0.849‡	1.1 (0.4-3.3)	2.6 (0.8-8.5)
Eczema	1,354	29.1% (27.8%-30.5%)	5,504	23.7% (23.1%-24.2%)	<0.001	1.3 (1.2-1.4)	0.9 (0.8-1.0)
Epilepsy	1,018	21.9% (20.7%-23.1%)	598	2.6% (2.4%-2.8%)	<0.001	10.6 (9.5-11.8)	8.2 (6.7-10.0)
Gastro-oesophageal reflux	576	12.4% (11.5%-13.4%)	2,154	9.3% (8.9%-9.7%)	<0.001	1.4 (1.3-1.5)	2.5 (2.2-3.0)
Glaucoma	38	0.8% (0.6%-1.1%)	254	1.1% (1.0%-1.2%)	0.092	0.8 (0.5-1.1)	1.4 (0.7-2.6)
Hearing impairment	890	19.2% (18.0%-20.3%)	856	3.7% (3.5%-3.9%)	<0.001	6.2 (5.6-6.8)	8.7 (7.4-10.3)
Hyperthyroidism	150	3.2% (2.8%-3.8%)	214	0.9% (0.8%-1.1%)	<0.001	3.6 (2.9-4.4)	4.1 (2.8-6.1)
Hypothyroidism	1,413	30.4% (29.1%-31.7%)	738	3.2% (3.0%-3.4%)	<0.001	13.3 (12.1-14.7)	14.1 (11.6-17.0)
Inflammatory bowel disease	371	8.0% (7.2%-8.8%)	772	3.3% (3.1%-3.6%)	<0.001	2.5 (2.2-2.8)	2.4 (1.9-2.9)
Iron deficiency anaemia	215	4.6% (4.1%-5.3%)	907	3.9% (3.7%-4.2%)	0.022	1.2 (1.0-1.4)	1.7 (1.2-2.2)
Ischaemic heart disease (IHD)	269	5.8% (5.2%-6.5%)	1,134	4.9% (4.6%-5.2%)	0.010	1.2 (1.0-1.4)	1.3 (0.9-1.9)
IHD (≥40yrs at start of follow-up)'	144	9.6% (8.2%-11.2%)	911	13.8% (13.0%-14.7%)	<0.001	0.7 (0.6-0.8)	0.4 (0.3-0.7)
Non-accidental injury/ maltreatment	108	2.3% (1.9%-2.8%)	284	1.2% (1.1%-1.4%)	<0.001	1.9 (1.5-2.4)	1.9 (1.6-2.4)

Schizophrenia	39	0.8% (0.6%-1.2%)	124	0.5% (0.5%-0.6%)	0.013	1.6 (1.1-2.3)	1.9 (1.0-3.6)
Skin disorders, non-eczema	756	16.3% (15.2%-17.4%)	1,742	7.5% (7.2%-7.8%)	<0.001	2.4 (2.2-2.6)	2.0 (1.6-2.4)
Sleep disordered breathing	402	8.7% (7.9%-9.5%)	537	2.3% (2.1%-2.5%)	<0.001	4.0 (3.5-4.6)	6.6 (5.4-7.9)
Stroke	173	3.7% (3.2%-4.3%)	443	1.9% (1.7%-2.1%)	<0.001	2.0 (1.7-2.4)	2.0 (1.4-2.9)
Undescended testis	146	3.1% (2.7%-3.7%)	169	0.7% (0.6%-0.9%)	<0.001	4.4 (3.5-5.5)	3.2 (2.4-4.5)
Vitamin D deficiency	73	1.6% (1.3%-2.0%)	181	0.8% (0.7%-0.9%)	<0.001	2.0 (1.6-2.7)	3.1 (1.9-5.1)

Nb. Cases (individuals with DS) are matched with at least 4 controls (non-DS individuals) based on GP practice, practice level index of multiple deprivation, year of birth ± 1 year, sex and index date.
ADHD: Attention Deficit Hyperactivity Disorder, IHD: Ischaemic heart disease, OR = odds ratio; aOR = adjusted odds ratio; CI = 95% confidence intervals
**p values calculated using χ2 (comparison of proportions)*
‡p value calculated using Fisher's exact test (comparison of proportions, non-parametric)
^The prevalence of type 1 and type 2 diabetes (separately) is based on CPRD data only.
"DS N=2,163, Controls N=10,346
'DS N=1,501, Controls N=6,596
Adjusted odds ratios have been adjusted for ethnicity and smoking status. Missing data: Ethnicity: DS=551, Control=6,068; Smoking status: DS=1,458 Controls=7,389
Start of follow-up is defined as the latest of the patient registration date, the practice UTS date, and 01/01/1998.

Table 15: Primary analysis (adults & children): Summarising and comparing the study prevalence, odds ratios (OR) and adjusted odds ratios (aOR) of cancers in the DS cohort v. the control group.

Cancer site	DS COHORT (N=4,648)		CONTROL GROUP (N=23,238)		p.value* (p<0.01)	OR (CI) (95% CI </>1)	aOR (CI) (95% CI </>1)
	n	%(95CI)	n	%(95CI)			
Bladder	9	0.2% (0.1%-0.4%)	64	0.3% (0.2%-0.4%)	0.319	0.7 (0.4-1.4)	0.6 (0.1-2.4)
Bone	4	0.1% (0.0%-0.2%)	18	0.1% (0.1%-0.1%)	0.849‡	1.1 (0.4-3.3)	2.1 (0.2-17.8)
Brain/Central Nervous System	15	0.3% (0.2%-0.5%)	79	0.3% (0.3%-0.4%)	0.853	1.0 (0.6-1.7)	1.9 (0.4-3.4)
Breast	16	0.3% (0.2%-0.6%)	311	1.3% (1.2%-1.5%)	<0.001	0.3 (0.2-0.4)	0.3 (0.1-1.1)
Cervix	5	0.1% (0.0%-0.3%)	429	1.9% (1.7%-2.0%)	<0.001‡	0.1 (0.1-0.2)	0.1 (0.0-0.5)
Colorectal	24	0.5% (0.4%-0.8%)	413	1.8% (1.6%-2.0%)	<0.001	0.3 (0.2-0.4)	0.5 (0.3-1.1)
Gastro-oesophageal	6	0.1% (0.1%-0.3%)	46	0.2% (0.2%-0.3%)	0.321	0.7 (0.3-1.5)	-
Leukaemia	45	1.0% (0.7%-1.3%)	38	0.2% (0.1%-0.2%)	<0.001	6.0 (3.9-9.2)	12.2 (6.1-24.4)
Liver/biliary	3	0.1% (0.0%-0.2%)	15	0.1% (0.0%-0.1%)	1.00‡	1.0 (0.3-3.5)	-
Lung	5	0.1% (0.0%-0.3%)	116	0.5% (0.4%-0.6%)	<0.001	0.2 (0.1-0.5)	0.2 (0.0-1.2)
Lymphoma	12	0.3% (0.2%-0.5%)	72	0.3% (0.3%-0.4%)	0.557	0.8 (0.5-1.5)	0.7 (0.2-2.8)
Melanoma	6	0.1% (0.1%-0.3%)	104	0.5% (0.4%-0.5%)	0.002	0.3 (0.1-0.7)	-
Skin, non-melanoma	27	0.6% (0.4%-0.9%)	539	2.3% (2.1%-2.5%)	<0.001	0.3 (0.2-0.4)	0.4 (0.2-1.0)
Myeloma	0	0.0% (0.0%-0.0%)	3	0.01% (0.0%-0.04%)	0.439‡	-	-
Neuroblastoma	0	0.0% (0.0%-0.0%)	3	0.01% (0.0%-0.04%)	0.439‡	-	-
Ovarian	6	0.1% (0.1%-0.3%)	84	0.34% (0.3%-0.5%)	0.011	0.4 (0.2-0.8)	1.45 (0.5-4.2)
Pancreas	6	0.1% (0.1%-0.3%)	24	0.1% (0.1%-0.2%)	0.624	1.3 (0.5-3.1)	2.2 (0.6-8.2)
Prostate	3	0.1% (0.0%-0.2%)	132	0.6% (0.5%-0.7%)	<0.001‡	0.1 (0.0-0.4)	0.6 (0.2-2.0)
Renal	3	0.1% (0.0%-0.2%)	33	0.1% (0.1%-0.2%)	0.179‡	0.5 (0.1-1.5)	0.6 (0.1-4.7)
Retinoblastoma	0	0.0% (0.0%-0.0%)	1	0.0% (0.0%-0.03%)	0.655‡	-	-
Testicular	20	0.4% (0.3%-0.7%)	20	0.1% (0.1%-0.7%)	<0.001	5.0 (2.7-9.3)	4.6 (1.5-14.3)
Thyroid/parathyroid	5	0.1% (0.0%-0.3%)	42	0.2% (0.1%-0.2%)	0.267‡	0.6 (0.2-1.5)	0.6 (0.1-4.3)
Uterus	16	0.3% (0.2%-0.6%)	308	1.3% (1.2%-1.5%)	<0.001	0.3 (0.2-0.4)	0.6 (0.2-1.4)
Wilms' tumour	2	0.04% (0.0%-0.2%)	30	0.1% (0.1%-0.2%)	0.114‡	0.3 (0.1-1.4)	0.6 (0.1-5.0)
Any of the cancers above	217	4.7% (4.1%-5.3%)	2,421	10.4% (10.0%-10.8%)	<0.001	0.4 (0.4-0.5)	0.8 (0.6-1.0)

Nb. Cases (individuals with DS) are matched with at least 4 controls (non-DS individuals) based on GP practice, practice level index of multiple deprivation, year of birth ± 1 year, sex and index date.
**p Values calculated using χ2 (comparison of proportions). ‡p value calculated Fisher's exact test (comparison of proportions, non-parametric)*
Adjusted odds ratios have been adjusted for ethnicity and smoking status. Missing data: Ethnicity: DS=551, Control=6,068; Smoking status: DS=1,458 Controls=7,389
- = unable to calculate odd ratios due to absence of cancer in cases and/or controls, including after the inclusion of confounders in the model.

Table 16: Subgroup-analysis (children only): Summarising and comparing the study prevalence, odds ratios (OR) and adjusted odds ratios (aOR) of DS associated morbidities and cancers in the DS cohort v. the control group.

Morbidity	**DS COHORT, CHILDREN ONLY N=1,340** *n* (%)/average (95% CI)		**CONTROL GROUP, CHILDREN ONLY N=6,711** *n* (%)/average (95% CI)		**p.value*** (p<0.01)	**OR (CI)** (95% CI </>1)	**aOR (CI)** (95% CI </>1)
	n	**% (95CI)**	**n**	**% (95CI)**			
ADHD	20	1.5% (1.0%-2.3%)	78	1.2% (0.9%-1.5%)	0.314	1.3 (0.8-2.1)	1.1 (0.7-1.9)
Anxiety/depression	25	1.9% (1.3%-2.8%)	189	2.8% (2.5%-3.2%)	0.048	0.7 (0.4-1.0)	0.6 (0.4-1.0)
Arthritis (combined)	12	0.9% (0.5%-1.6%)	26	0.4% (0.3%-0.6%)	0.013	2.3 (1.2-4.6)	2.2 (1.1-4.3)
Atlantoaxial instability	11	0.8% (0.5%-1.5%)	0	0.0% (0.0%-0.0%)	<0.001‡	-	-
Autism	85	6.3% (5.2%-7.8%)	89	1.3% (1.1%-1.6%)	<0.001	5.0 (3.7-6.8)	4.7 (3.5-6.4)
Cataract	28	2.1% (1.5%-3.0%)	6	0.1% (0.0%-0.2%)	<0.001	23.9 (9.9-57.7)	18.3 (7.5-44.6)
Chronic kidney disease	15	1.1% (0.7%-1.9%)	19	0.2% (0.2%-0.4%)	<0.001	4.0 (2.0-7.9)	3.5 (1.8-6.8)
Coeliac disease	38	2.8% (2.1%-3.9%)	17	0.3% (0.2%-0.4%)	<0.001	11.5 (6.5-20.4)	10.2 (5.7-18.4)
Congenital cardiac disease	754	56.3% (53.6%-58.9%)	72	1.1% (0.9%-1.4%)	<0.001	118.6 (91.8-153.3)	109.2 (84.0-141.9)
Congen. gastrointestinal disease	63	4.7% (3.7%-6.0%)	24	0.4% (0.2%-0.5%)	<0.001	13.8 (8.6-22.1)	12.9 (7.9-21.0)
Diabetes Mellitus (combined)	37	2.8% (2.0%-3.8%)	46	0.7% (0.5%-0.9%)	<0.001	4.1 (2.7-6.4)	3.6 (2.3-5.6)
Diabetes Mellitus, Type 1^	22	0.9% (0.4%-1.3%)	9	0.7% (0.1%-0.3%)	0.002	3.5 (1.5-8.2)	2.7 (1.1-6.4)
Duchenne muscular dystrophy	4	0.3% (0.1%-0.8%)	3	0.04% (0.01%-0.14%)	0.004‡	6.7 (1.5-30.0)	8.7 (1.6-47.5)
Eczema	323	24.1% (21.9%-26.5%)	2119	31.6% (30.5%-32.7%)	<0.001	0.7 (0.60-0.8)	0.7 (0.6-0.8)
Epilepsy	80	6.0% (4.8%-7.3%)	110	1.6% (1.4%-2.0%)	<0.001	3.8 (2.8-5.1)	3.4 (2.5-4.6)
Gastro-oesophageal reflux	254	19.0% (16.9%-21.%)	280	4.2% (3.7%-4.7%)	<0.001	5.4 (4.5-6.4)	4.8 (4.0-5.8)
Glaucoma	6	0.5% (0.2%-1.0%)	3	0.04% (0.01%-0.14%)	<0.001‡	10.1 (2.5-40.3)	12.9 (2.6-64.1)
Hearing impairment	315	23.5% (21.3%-25.9%)	165	2.5% (2.1%-2.9%)	<0.001	12.2 (10.0-14.9)	12.3 (10.0-15.2)
Hyperthyroidism	34	2.5% (1.8%-3.5%)	1	0.01% (0.00%-0.11%)	<0.001‡	-	-
Hypothyroidism	212	15.8% (14.0%-17.8%)	32	0.5% (0.3%-0.7%)	<0.001	39.2 (26.9-57.2)	33.4 (22.8-49.1)
Inflammatory bowel disease	113	8.4% (7.1%-10.1%)	172	2.6% (2.2%-3.0%)	<0.001	3.5 (2.7-4.5)	3.0 (2.4-3.9)
Iron deficiency anaemia	34	2.5% (1.8%-3.5%)	84	1.3% (1.0%-1.6%)	<0.001	2.1 (1.4-3.1)	2.0 (1.3-2.9)
NAI/Maltreatment	45	3.4% (2.5%-4.5%)	139	2.1% (1.8%-2.4%)	0.004	1.6 (1.2-2.3)	1.7 (1.2-2.4)
Schizophrenia	1	0.1% (0.01%-0.5%)	5	0.1% (0.0%-0.2%)	0.999‡	1.0 (0.1-8.6)	0.9 (0.1-7.4)
Skin disorders, non-eczema	60	4.5% (3.5%-5.7%)	171	2.6% (2.2%-3.0%)	<0.001	1.8 (1.3-2.4)	1.7 (1.3-2.4)
Sleep disordered breathing	256	19.1% (17.1%-21.3%)	104	1.6% (1.3%-1.9%)	<0.001	15.0 (11.8-19.0)	13.8 (10.9-17.6)
Stroke	14	1.0% (0.6%-1.8%)	5	0.1% (0.0%-0.2%)	<0.001‡	14.2 (5.1-39.4)	12.2 (4.4-34.1)

Undescended testis	72	5.4% (4.3%-6.7%)	102	1.5% (1.3%-1.8%)	<0.001	3.7 (2.7-5.0)	3.4 (2.5-4.7)
Vitamin D deficiency	20	1.5% (1.0%-2.3%)	78	0.6% (0.5%-0.8%)	0.001	2.5 (1.4-4.2)	2.8 (1.6-4.9)
Cancers							
Leukaemia	29	2.2% (1.5%-3.1%)	2	0.03% (0.01%-0.12%)	<0.001‡	74.2 (17.7-311.4)	59.2 (14.1-249.2)
Lymphoma	3	0.2% (0.1%-0.7%)	7	0.1% (0.1%-0.2%)	0.257‡	2.2 (0.6-8.3)	1.9 (0.5-7.2)
Neuroblastoma	0	0.0% (0.0%-0.0%)	2	0.03% (0.01%-0.12%)	0.527‡	-	-

Nb. Cases (individuals with DS) are matched with at least 4 controls (non-DS individuals) based on GP practice, practice level index of multiple deprivation, year of birth ± 1 year, sex and index date.
Children were defined as only those individuals who were aged ≤18 years at the end of follow-up.
End of follow-up is defined as the earliest of the patient transfer out date, the practice last collection date, date of death and 31/12/2017..
ADHD: Attention Deficit Hyperactivity Disorder, CI = 95% confidence intervals, NAI: Non-accidental injury, OR = odds ratio; aOR = adjusted odds ratio;
**p values calculated using χ2 (comparison of proportions).*
‡p value calculated Fisher's exact test (comparison of proportions, non-parametric)
^The prevalence of type 1 and type 2 diabetes (separately) is based on CPRD data only.
Adjusted odds ratios have been adjusted ethnicity. Missing data: Ethnicity: DS=68, Control=1,205.

Discussion

Statement of principal findings

Individuals with DS had a significantly increased risk of almost all of the morbidities examined, compared with controls. The most prevalent conditions among those with DS, and those with the largest difference in prevalence when comparing DS cases and controls, reflect those conditions which are frequently described in the DS literature (e.g. hypothyroidism, congenital heart disease, epilepsy, hearing impairment and dementia).

However, the findings presented here also highlight a significantly increased risk of a number of additional morbidities, which have been less well described in the existing literature. These include autism, chronic kidney disease, diabetes mellitus type 1, inflammatory bowel disease, non-accidental injury/ maltreatment and vitamin D deficiency.

Notably there were two DS associated morbidities which appeared to be significantly *less* common in the DS cohort versus controls; anxiety/depression and eczema (the latter after adjustment for confounders).

With regard to cancer, individuals with DS were more likely to have a diagnosis of leukaemia and testicular cancer, compared with controls, even after adjusting for confounders.

Individuals with DS appeared to have a significantly lower overall prevalence of the cancers combined and more specifically, a lower study prevalence of breast, cervical, colorectal, lung, melanoma, non-melanomatous skin cancer, ovarian, prostate, uterine cancer and Wilms' tumour. However, after adjustment for confounders only the significantly reduced risk of cervical and non-melanomatous skin cancer persisted. Both of these reduced risks could be explained by differences in life-style factors between cases and controls (e.g. sunlight exposure, human papillomavirus infection), which were not possible to adjust for in this analysis.

Strengths and Limitations

The size of the linked dataset

The key strength of the linked dataset utilised in this study is its size. The DS population included in this study represents one of the largest DS cohorts reported in the academic literature to date. This large dataset made it possible to study rare outcomes, including congenital abnormalities and cancers, and increased statistical power to detect differences between populations. Furthermore, our dataset includes both children and adults with DS, allowing us to gain a picture of disease burden across the life-course (i.e. not limited to one time period only, such as adulthood). In the existing literature, which examines the occurrence of morbidities in the DS population, small sample sizes, absence of a comparator group and a paucity of data on childhood are recurrent themes.

The study period

Participants contributed different amounts of follow-up during the study period. Their period of contribution was defined by 'biological factors' such as birth and death, as well as 'operational factors' such as leaving or joining a CPRD contributing practice and the time period during which CPRD data was collected and made available for this research.

Individuals with DS, on average, contributed fewer years of follow-up compared with controls. This difference may be due to the fact that individuals with DS were more likely to die during the period of follow-up. Consequently it is arguable that control participants had 'more time' during the study period to be diagnosed with a condition of interest. This could result in an underestimation of the associations between DS and the outcomes. However, it is also plausible that individuals with DS interact with health services more frequently than controls, and are more likely to be diagnosed with a condition of interest as a result of those interactions (e.g. through active health surveillance). We therefore chose not match the DS cases with controls based on the person years contributed. However, to explore this further, a sensitivity analysis was performed, including 'person years contributed' in the logistic regression model (Appendix 7). This illustrates no significant impact on the overall findings.

Diagnostic reliability

The linkage of primary care, secondary care and cancer registry datasets enabled access to much broader patient data. Therefore it is less likely that a diagnosis was "missed", compared with relying on one data source alone. However, the analysis was still reliant on the sensitivity

and specificity of coding within the dataset. The presence or absence a disease was defined as the presence or absence of a coded entry in the dataset.

Codes are entered by a large number of individuals, predominantly coding technicians and primary care physicians, some of whom have had no direct contact with the patient. Furthermore, coders may use different codes to define the same conditions. To address this, the phenotyping code lists used in the analysis were extensive, and reviewed by researchers with experience in the field of epidemiology and research utilising electronic health records. However, it is still possible that some diagnoses were not recorded in the dataset, and that some were misclassified. This could have led to over- or under estimates in disease prevalence.

Furthermore, if coding inaccuracies were more likely to occur in one group than the other (i.e. in DS v. controls) this could have led to spurious associations. However, the use of such a large dataset, with large participant numbers, is likely to reduce the impact of misclassification. Also, since the introduction of payment by results (PbR) in 2002, financial incentives have been introduced to enhance coding depth. This has resulted in "an increase in the number of diagnostic codes used and improvements in coding accuracy"[499].

Identification of DS cases and controls

The identification of DS "cases" in the wider linked dataset also relied on the presence of a code suggestive of DS in the patient record. It is possible that some patients with DS were missed, or indeed that some "non-cases" are misclassified and labelled as having DS in error. The possibility of this was somewhat reduced by removing mothers with a first record of DS after pregnancy, as they are likely to represent the mothers of children with DS, as opposed to individuals with DS themselves. However, if a large number of individuals with DS were not included in the study this could reduce the generalisability of our results and if a large number of non-cases were been misclassified as DS, this could have resulted in an underestimate of disease prevalence and associations.

The National Down Syndrome Cytogenic Register (NDSCR) is a collation of genetic reports of trisomy 21 from labs in England and Wales, from 1989 to date. Doidge et al. used probabilistic linkage of the National Down Syndrome to the HES dataset and reassuringly they demonstrated excellent agreement[500]. Linking our own dataset with the NDSCR may have

increased the capture of DS cases, but given that the register is incomplete it would not have been used it to remove cases from our DS cohort. Therefore additional linkage to the NDSCR is unlikely to have significantly changed our study populations. However, an additional advantage of linkage to the NDSCR would have been the ability to identify the small proportion of patients with DS who are in fact mosaic (i.e. with trisomy 21 in only some of their cells). These individuals tend to have a milder phenotype and a lower prevalence of DS associated morbidities, compared with "non-mosaics". However, given that only a small number of individuals with DS are mosaic, we would not expect the inclusion of "mosaics" in our DS cohort to have a substantial impact on disease prevalence.

The impact of differences in screening on disease prevalence

It must also be considered that individuals are more likely to be diagnosed with a condition where there is active screening. For example, if health professionals are following existing health surveillance guidelines, individuals with DS are more likely to have their thyroid function and hearing and vision checked, compared with the non-DS population. This may result in a relative underestimate of disease prevalence in the controls, and exaggerate the association between DS and the condition of interest. Similarly, for those conditions where screening is not yet common practice in the DS population (e.g. sleep disordered breathing, diabetes mellitus) the true disease prevalence may be underestimated.

The rationale behind the definition of study populations in the primary and subgroup-analysis

In the primary analysis, the study population included both children and adults. In the subgroup-analysis the population was limited to children aged ≤18 years at follow-up. The decision to split the analysis in this was way, as opposed to one analysis for adults and one for children, has three justifications.

First, in order to limit the data to only that which was contributed by patients during "adulthood", the population would have had to be defined as only individuals who were aged ≥18 years at the *start* of follow-up. This would have resulted in reduced statistical power, i.e. some individuals who did in fact contribute data in their adult years would have to be excluded because they were aged under 18 at the start of follow-up. For example, a DS participant who was aged 17 years at start of follow-up and 23 years at end-of follow-up would not have been

included in the "adult only" population. Such a participant would not be included in the "children only" population either as they are not aged ≤18 years at the *end* of follow-up. This would have meant that valuable data from these patients would have been lost from the analysis.

Second, although the majority of diagnostic codes have a date of application available, and in theory it would have been possible to look instead at which codes were applied to individuals between the ages of 0-18years and ≥19 years, the dating of codes is not always straightforward. For example, when a patient registers with a GP they may be coded as having a number of diagnoses on that date, simply reflective of their past medical history, as opposed to a new diagnosis. Consequently diagnoses could be misattributed to a certain age. Furthermore an individual may be coded as having a chronic, lifelong condition (e.g. coeliac disease) in childhood and then not be labelled with this again in adulthood. This may lead to an underestimate of disease burden in adulthood. For truly chronic, irreversible conditions, such as coeliac disease, it may have been possible to make some inferences about the persistence of this condition in adulthood, but for other morbidities it is less straightforward as they can be chronic, transient or reversible with treatment (e.g. hearing impairment, sleep disordered breathing, epilepsy, etc.).

Third, while the subgroup-analysis focusing on 'children only' is appropriate in the context of this thesis, it was felt that, even if it were possible to separate childhood and adulthood data entirely and reliably, that this separation is arbitrary and of less clinical value. As described above, the health of individuals does not end or begin at 18 years, it is a trajectory which begins in childhood. Understanding the full life-course picture is useful for the clinician working at either end of that life-course. In some circumstances, as explored below, it would indeed be useful to determine whether certain morbidities only develop during certain time periods e.g. to allow targeted health surveillance, however the aim of this thesis was to gain a broader over-view of DS health.

Consequently it was felt that splitting the study populations into a primary analysis of children and adults combined, and a subgroup-analysis of children only, achieved a balance which optimised use of the data available, clinical utility and relevance to this thesis.

Odd ratios v. risk ratios in the comparison of risk

Odds ratios (OR) were calculated for the occurrence of DS associated morbidities and cancers in the cases verses controls using logistic regression[497]. Logistic regression is a standard statistical approach to examine the association between binary exposures (i.e. DS or non-DS) and outcomes (i.e. disease occurrence).

OR is a commonly used measure of association in epidemiology. However caution must be employed when interpreting ORs in the context of common diseases (e.g. hypertension). In these scenarios, ORs may magnify or exaggerate associations, and another measure of association (relative risks, RR) may be more intuitive for the reader. There are various proposed methods to convert ORs to RRs but these are not without compromise[497]. For relatively rare conditions, such as those studied in this thesis, the magnitude of OR and RR are usually comparable. For this reason I presented ORs, as opposed to RRs.

Adjusted odds ratios and the selection of confounding variables

Odds ratios were adjusted for the confounding factors ethnicity and smoking status. As shown in Table 13, there were significant differences in the ethnicity and smoking status of individuals with DS and controls cohorts. Smoking and ethnicity are common confounding factors in epidemiological studies and are a plausible source of confounding bias for all of the morbidities and cancers examined.

Although the DS and control cohorts had significantly different BMIs, a decision was made not to adjust for BMI as increased BMI among individuals with DS may be a variable on the causal pathway between DS and the associated morbidities, as opposed to a confounder. Adjusting for variables on the causal pathway has the potential to mask associations.

Although there is a significant difference in the median years of follow-up, among individuals with DS and the controls, I did not include 'person years contributed' in the logistic regression model. As described above, a sensitivity analysis which does include adjustment for person years are available in Appendix 7.

Statistical correction

When making a large number of comparisons between an exposure and outcomes, some studies opt to include a statistical correction, such as the Bonferroni method. However, statistical

corrections are the subject of some controversy and they have the potential to reduce statistical power[501].

It is recommended that a statistical correction, such as the Bonferroni method, is most applicable when the study seeks to detect a universal null hypothesis (i.e. no association between the exposure and multiple outcomes), when it is imperative to avoid a type 1 errors and when a large number of tests of associations are carried out without a pre-formed hypothesis[501]. None of these scenarios apply in the context of this thesis. When comparing the study prevalence of outcomes in cases and controls I also chose to use a relatively stringent definition of statistical significance ($p<0.01$).

Generalisability of the findings

The linked dataset in known to be broadly representative of the UK population in terms of age, sex, ethnicity, BMI and mortality[461 474-477]. However, it is not established whether our DS cohort is broadly representative of individuals with DS in the UK, or further afield.

It is also possible for patients in general to 'opt-out' of having their records being included in the dataset. In 2014/15, 2.3% of patients had their data removed from the NHS Digital dataset, with substantial geographic variation in opt-out rates[457 502]. If the characteristics of those patients who opt out of the data-set are significantly different from patients who were included, this may limit the generalisability of results.

Missingness in the dataset

Within the linked dataset there is variation in the completeness of data across patients, with some variables being less complete than others. For example, in the HES dataset, information on age, sex and clinical characteristics are well reported but ethnicity is not[457]. In some cases, the degree of missingness is so substantial that valid research cannot be undertaken[503 504]. However the linkage of multiple datasets reduces the degree of missingness for some variables, for example combining CPRD and HES increases the completeness of the ethnicity variable from 78% to 97%[475]. Indeed, among participants in this study, missing data for the descriptive and confounding variables was minimal and the inclusion of confounding variables in the adjusted odd ratios did not have a significant impact on statistical power in the majority of analyses.

Linkage accuracy

The use of linked datasets relies on the quality of linkage, using patient identifiers. Within HES, linkage algorithms rely upon the accurate recording of NHS numbers. Hagger-Johnson et al. estimated a "patient identifier mismatch" of 4% in the HES dataset[505].

Errors in data linkage of electronic health records are known to result in significantly different conclusions about the association between exposures and outcomes[506]. However, the linkage methods used for the constituent datasets available through CALIBER have been used in multiple comparable projects and have demonstrated high quality matching[460].

Electronic health record research

Research utilising routinely collected healthcare data has been the subject of some criticism[507-510]. Data collected in this way was not designed to be used for research, but instead to inform financial remuneration. As described above, this has to be taken into account when interpreting results[510 511].

While research utilising electronic health records has its limitations, it also tends to have strengths in size and breadth data. This makes it possible to study rare outcomes and populations which are traditionally underrepresented in research. As explored in the Background, there are several reasons why individuals with DS may be underrepresented in research. Therefore, particularly in the context of DS, research utilising electronic health records can make a valuable contribution to the evidence base.

Comparison with other studies, DS associated morbidity

In general, the findings of this study are in-line with existing publications which explore the prevalence and risk of morbidities in individuals with DS, compared to controls. As expected, the "well-established" DS associated morbidities, such as hypothyroidism, congenital heart disease, epilepsy, hearing impairment and dementia were significantly more common in the DS cohort verses controls, and the figures overlap with existing reports of population prevalence.

However, for a small number of morbidities our findings differ from existing studies. These discrepancies tended to occur for the morbidities where existing evidence is scant, and where a relationship between DS and the morbidity is not well established.

For example, the study prevalence of ADHD among children with DS in this study (1.5%), is much lower than reported by Oxelgren et al.[128] (34.0%) and Ekstein et al.[127] (43.9%). This is also true for autism (6.3%), with existing reports of prevalence of up to 42%[128 133 134]. These large differences are likely explained by differences in diagnostic methodology. Those existing studies, which report a much higher prevalence of autism and ADHD, actively looked for these conditions in DS cohorts. Screening for ADHD and autism is not routinely included in existing DS health surveillance guidelines, which may contribute to under-diagnosis in our study population. As explored in the Background, several studies have suggested that behavioural disorders, such as autism and ADHD, are indeed underdiagnosed and undertreated among children with DS, due to a combination of atypical presentations and "diagnostic over-shadowing" [136 137 142 143].

Similarly, while some studies have reported a prevalence of sleep disordered breathing among individuals with DS ranging between 43-63%[96 100 102], the study prevalence of SDB in this study was much lower (8.7% in adults & children combined, 19.1% among children only). As explored in the Background, several studies have demonstrated that self or parental report of symptoms is insufficient to identify all cases of SDB and again, SDB is not routinely included in existing DS health surveillance guidelines. Thus, the relatively lower prevalence of SDB in our study population could again be secondary to under-diagnosis, as opposed to true absence of disease.

In contrast, the study prevalence of inflammatory bowel disease (IBD) in the DS population in this study (8.0%) was higher than existing reports in the literature of around 2%[207]. This suggests that IBD may be more common in the DS population than previously thought, and it may in fact affect a relatively large number of patients.

This study also identified a relatively high study prevalence of non-eczematous skin disorders (16.3%) in the DS cohort. This includes conditions such as psoriasis, lichen planus, pemphigoid, pemphigus and vitiligo. It is noteworthy that these conditions, and IBD, are believed to have an underlying autoimmune aetiology. Along with other immune mediated

conditions, such as coeliac disease, type 1 diabetes mellitus, hyperthyroidism and hypothyroidism, it appears that disorders of autoimmunity contribute a significant burden of disease in our DS cohort. This is in keeping with existing hypothesises regarding immune dysfunction in DS[19 118 203 208].

In both the primary and subgroup-analysis individuals with DS had a significantly increased study prevalence of non-accidental injury or maltreatment, compared with controls (Children only: 3.4% (95 CI 2.5%-4.5%) v. 2.1% (95CI 1.8%-2.4%), p=0.004). While there are a number of studies suggesting that the prevalence of maltreatment is higher among children with intellectual disability[308-312], literature specific to DS is scant. As explored in the Background, there are two existing studies which show either no increased risk of maltreatment among children with DS, compared to the general population[314], or no difference after adjustment for confounding factors[315]. The absolute difference in the prevalence of maltreatment between our DS cohort and controls may be small but it is significant, and adds to the limited existing evidence base on this topic.

As described above, in the primary analysis, there were only two morbidities which appeared to occur *less* commonly in the DS cohort, compared with controls (anxiety/depression and ischaemic heart disease (IHD) in older individuals).

As explored in the Background, several studies have already suggested lower rates of atherosclerosis, and coronary artery disease among individuals with DS[49-51]. In this study, the significant difference was only apparent when limiting the cohort to those aged over 40 years at start of follow-up. This likely reflects the fact that IHD tends to be a disease of older age. As the odds ratio of IHD among individuals with DS remains significantly reduced, even after adjusting for ethnicity and smoking status, it suggests that these confounding factors are insufficient to account for the entirety of the difference observed.

It is also noteworthy that individuals with DS were significantly less likely to have a record of depression or anxiety. Our reported prevalence of depression and anxiety in the DS cohort is similar to that reported in the existing literature[159-161]. However, as explored in the Background, mood disorders may present differently in individuals with DS, compared to the general population. It is uncertain whether this, combined with difficulties in accessing

healthcare or expressing symptoms, may have led to underdiagnoses of depression and anxiety in the DS cohort, as opposed to a truly reduced risk of mood disorders in this group.

By analysing a large population of individuals with DS, with outcome data drawn from multiple sources (primary care, secondary care, cancer registry, ONS), the inclusion of a matched comparator group and the ability to adjust for confounding factors, I assert that the findings presented here are a significant contribution to the existing literature which aims to determine the prevalence of disease in the DS population, and to make comparisons of risk with the general population. In particular our findings add to the scant literature on the association, or lack thereof, between DS and ADHD, autism, chronic kidney disease, diabetes mellitus, Duchenne muscular dystrophy, inflammatory bowel disease, non-accidental injury, vitamin D deficiency, and schizophrenia.

Comparison with other studies, Cancer

In general, the findings of this study complement existing publications describing the prevalence of cancers in individuals with DS. However, in particular our findings add the scant, and often contradictory, reports of "non-leukaemic cancers", among individuals with DS.

As explored in the Background, there is ongoing controversy about the prevalence and relative risk of solid tumours among individuals with DS. The findings of this study would support the hypothesis that individuals with DS have a lower prevalence of several solid tumours (i.e. breast, cervical, colorectal, lung, melanoma, non-melanomatous skin, ovarian, prostate, uterine and Wilms' tumour) however, it appears that some of this difference can be explained by the confounding factors, ethnicity and smoking status.

A significantly reduced prevalence of non-melanomatous skin cancer (e.g. basal cell and squamous cell carcinomas) was observed in the DS cohort, compared to controls. To the best of our knowledge this association has not previously been described in the literature. However, as described above, this difference may be explained by other confounding factors for which it was not possible to adjust (e.g. time spent outdoors, sunlight exposure).

The findings of this study would also support existing literature which suggest an increased prevalence of testicular cancer among males with DS, compared to the general population[258]

[358 361 375]. Furthermore the significantly increased odds of testicular cancer in the DS cohort persisted even after adjustment for smoking and ethnicity, suggesting these confounding factors are insufficient to account for the entirety of the difference observed.

As explored in the Background, a small number of studies have suggested increased risks of liver[358], gastric[378], ovarian cancer[361], retinoblastoma[360] and lymphoma[360], among individuals with DS. However, the findings of this study did not support these associations.

The study prevalence of leukaemia, in the primary analysis was lower than some existing reports, however when the population was limited to children only the findings were consistent with existing figures[359]. This reflects the fact that leukaemia is predominantly seen in children with DS, as opposed to adults, and that the increased risk appears to dissipate after 30 years[359 361].

Implications for practice and research

Our findings support many aspects of current practice in the health and care of individuals with DS in general, and more specifically in DS health surveillance. The morbidities which are core components of current DS health surveillance practice (congenital heart disease, leukaemia, thyroid dysfunction, and vision and hearing impairment) were all common in our DS cohort, and significantly more common compared to matched controls.

However, there were additional morbidities which occurred relatively commonly in our cohort, and that could be amenable to screening and therapy. These include disorders of skin, dementia, arthritis, sleep disordered breathing, diabetes mellitus (combined), inflammatory bowel disease, chronic kidney disease and ischaemia heart disease in older age groups, all occurring in >5% of individuals with DS. Furthermore the findings suggest an under-diagnosis of ADHD, autism and sleep disordered breathing, with a much lower study prevalence than would be expected, based on existing estimates where active screening was employed.

These findings provide some evidence to support the expansion of health surveillance protocols for both children and adults with DS to include established diagnostic tests (e.g. HbA1c, fasting glucose, renal function tests, polysomnography), targeted history taking and clinical examination (e.g. to identify signs and symptoms of inflammatory bowel disease, skin disease and arthritis) and cognitive or behavioural assessments (to detect ADHD, autism and the early

signs of dementia). Table 17 summarises these conditions and the potential modality of screening. However, it must also be acknowledged that screening for disease is not based on population prevalence alone. Additional evidence is needed to satisfy the Wilson and Junger criteria[390], as well as informing when and how best to test for these conditions.

Table 17: Additional DS associated morbidities with a study prevalence >5% in the DS cohort (children & adults) and which may be amenable to health surveillance, with potential testing modalities.

DS associated morbidity	Study prevalence (DS cohort) % (95CI)	Potential testing modality
	Adults & children	
Arthritis*	12.3% (11.4%-13.2%)	Targeted history taking Musculoskeletal examination
Dementia^	37.3% (35.3%-39.4%)	Targeted history taking Dementia screening questionnaires (e.g. DSDS, DMR, CAMDEX-DS)
Chronic kidney disease	6.5% (5.8%-7.2%)	Renal function tests (e.g. U&E)
Diabetes mellitus (T1 & T2 combined)	8.1% (7.3%-8.9%)	Fasting glucose HbA1c
Inflammatory bowel disease	8.0% (7.2%-8.8%)	Targeted history taking Faecal calprotectin
Ischaemia heart disease ^	9.6% (8.2%-11.2%)	Targeted history taking ECG Echocardiogram Clinical risk scores (e.g. QRISK, SCORE)
Skin disorders, non-eczema*	16.3% (15.2%-17.4%)	Clinical examination
Sleep disordered breathing	8.7% (7.9%-9.5%)	Polysomnography

**Arthritis includes ankylosing spondylitis, gout, osteoarthritis, inflammatory arthritidies, psoriatic arthritis, Still's disease and reactive arthropathy.*
**Skin disorders include psoriasis, lichen planus, pemphigoid, pemphigus, vitiligo, and seborrheic dermatitis*
^Ischaemic heart disease ≥40yrs, Dementia ≥30 years
95CI: 95% confidence interval; CAMDEX-DS: Cambridge Examination for Mental Disorders of the elderly, modified for DS; DMR: The Dementia Questionnaire for Individuals with Intellectual Disability; DSDS: Dementia Scale for Down Syndrome; ECG: Electrocardiogram; HbA1c: Glycated haemoglobin; QRISK: Cardiovascular disease risk score; SCORE: Systematic Coronary Risk Evaluation; U&E: Urea & electrolyte.

It is both noteworthy and concerning that the findings also suggest that children with DS are more likely to have a record of non-accidental injury or maltreatment, compared with controls. This is further evidence to support a high degree of vigilance among clinicians and other professionals caring for children with DS for the signs of child maltreatment.

As described in the Background, individuals with DS have access to standard national cancer screening programmes, which include surveillance for breast, colorectal and cervical cancer, in adulthood. Some existing publications suggest that, for some cancers, individuals with DS may not require any, or at least less frequent, screening[379]. The findings of this study provide

some support for amendments to the recommendations for cervical cancer screening among women with DS, to reflect their lower risk of disease. Conversely, our findings support the assertion that males with DS may benefit from *additional* screening, for testicular cancer[379]. However, our findings do not provide support for the reduction or cessation of screening for breast and colorectal cancers among individuals with DS[379]. It should be noted that the findings of this study cannot be used in isolation to make decisions about cancer health surveillance in the DS population, but they do contribute to the weight of available evidence.

Unanswered questions and future research

It was not within the remit of this study to examine changes in the prevalence or incidence of DS associated morbidities or cancers across the DS life-course. However, such evidence would be valuable to inform health surveillance guidelines, as it may be that screening for some conditions is only required during certain periods of life. This could reduce unnecessary screening for some, and increase the efficiency of resource allocation.

Furthermore, it was not within the remit of this study to determine which of the morbidities or cancers were diagnosed via health surveillance, and which were picked up through other means (e.g. symptomatic presentation). Such information could inform the efficacy of current health surveillance practices and inform their improvement. Such research would require a different dataset or methodological approach (e.g. a prospective observational study).

While I propose that the findings of this study support the expansion of DS health surveillance guidelines to include a wider range of morbidities it is not within the remit of this study to assess the acceptability, or reliability, of specific approaches to screening. As explored in the Background, some health surveillance practices (e.g. overnight polysomnography for the diagnosis of sleep disordered breathing) can be expensive, difficult to access and poorly tolerated. Future studies could explore the realities of delivering health surveillance protocols on the front line, in terms of access and acceptability.

Furthermore, while our findings may support a change to some aspects of routine cancer surveillance among individuals with DS, our findings cannot be used in isolation to revise guidelines. Future studies could explore the sensitivity and specificity of cancer screening,

particularly solid tumours, in the DS population and assess the impact on mortality and morbidity.

As discussed above, the average person years contributed to the analysis differed between the DS cohort and the controls. Although a sensitivity analysis was performed, adjusting for person years contributed, the potential impact of this difference on the results is difficult to predict. Therefore future analyses may wish to incorporate additional methods to control for this difference, for example matching patients on person years of data available.

Our study found a significantly increased mortality within the study period, in the DS cohort compared with controls. It was not within the remit of study to examine the causes of death in either group, but this data can be accessed within the larger linked dataset. Future research could explore the age and causes of death in this substantial DS cohort and compare with existing literature. It would also be valuable to explore what contribution multi-morbidity has to mortality among individuals with DS.

The linked dataset utilised in this study is a rich source of data for a large cohort of individuals with DS. With such data there is huge potential to undertake additional observational research, which would be difficult to achieve through other means. As described in the Background, the parents of children with DS are often keen to participate in trials, but hesitate to recruit their children to randomised control trials. As the CPRD and HES datasets also include data on procedures and prescriptions it may be possible to utilise these datasets to look at the impact of interventions or therapies in the DS population. Numerous existing studies have utilised the CPRD dataset in this manner in other patient populations[512-515].

Finally, while this study describes the study prevalence of morbidities among a large cohort of individuals with DS, it cannot capture the impact of these conditions on overall health and wellbeing. It may be that some morbidities, while less prevalent than others in the DS cohort (e.g., ADHD, coeliac disease, diabetes mellitus), do in fact have a very significant impact on the quality of life of patients and carers. Future research could employ a qualitative approach to explore the realities of living with these morbidities, and the health priorities of patients and carers.

PROJECT 3: ROUTINE HEALTH SURVEILLANCE OF CHILDREN WITH DOWN SYNDROME

Introduction

As explored in the Background and Project 2, individuals with DS are at an increased risk of a multitude of health conditions throughout the life-course. Existing literature suggests that some of these morbidities are likely under-diagnosed and that self/parent report is insufficient to identify all cases. This suggests that actively looking for these conditions, through health surveillance, is necessary. The aim of health surveillance is to identify disease in its early stages, thus enabling early intervention, in order to prevent or minimise morbidity and mortality. Consequently, routine health surveillance is a key component of DS healthcare.

As outlined in the Background, a number of Institutions provide guidelines for the routine health surveillance of children with DS; nationally, the Down Syndrome Medical Interest Group (DSMIG), the Royal College of Paediatrics and Child Health (RCPCH) and the Department of Health and Social Care (DHSC); and internationally, the European Down Syndrome Association (EDSA) and the American Academy of Paediatrics (AAP). However, these vary in their recommendations and there is no single accepted 'gold standard' guideline for paediatricians undertaking health surveillance for children with DS.

Between birth and 14 years there are two different UK guidelines for DS health surveillance which are applicable to this age range (DSMIG & RCPCH), and between the ages of 14 and 18 years there are three (DSMIG, RCPCH & DHSC). As summarised in Table 2, these guidelines vary in their recommendations. Consequently it is difficult to for paediatricians to know which of the guidelines to follow and it is likely that practice tends to vary according to local policy. Variation in practice may lead to patchy, inconsistent care and widen health inequalities.

For many aspects of healthcare, "local protocols" are developed to guide practice among health professionals working in the same department. Ideally the content of these local protocols are based on the best available evidence, which is likely to include relevant national and international guidelines. Local protocols are also influenced by regional access to resources, the experiences or preferences of clinicians working in that department, and other unique

factors. Therefore, while national guidelines for the routine health surveillance of children with DS exist, many paediatric departments will have developed their own local protocol for this practice. An example of such a protocol, developed by myself for use in a North East London community paediatric department, is presented in Appendix 1.

I are not aware of any existing studies which look at current practice, with regard to DS health surveillance, or make comparisons between current practice and the existing national and international guidelines. In collating and comparing local protocols for the routine health surveillance of children with DS, from paediatric departments across the UK, I aim to provide an insight into what health surveillance is being performed on the "front line". This will add to the existing limited evidence base, and inform the development of future health surveillance guidelines.

Aims & Objectives

By obtaining and reviewing local protocols on the routine health surveillance of children with DS, from paediatric departments across the UK, I aimed to:

1. Provide an overview of current practice, with regard to the routine health surveillance of children with DS.
2. Establish areas of consensus and divergence in current practice between paediatric departments, and assess compliance with existing national and international guidelines.

Methods

Obtaining local protocols for the health surveillance of children with DS

A list of all UK paediatric departments (N=458), and their contact details, was obtained from the Royal College of Paediatrics and Child Health (RCPCH).

Paediatric departments were contacted via post, addressed to the Clinical Lead for Paediatrics or Community Paediatrics. The enclosed letter provided a brief summary of the research project and requested a copy of local DS health surveillance protocol (Appendix 8).

A free postage self-addressed return-envelope was included, and these were coded to enable retrospective identification of the departments. A request for local guidelines was also

disseminated through the DSMIG and British Association of Community Child Health (BACCH) e-mailing lists.

A separate 'response slip' was provided with the letter (Appendix 9). The response slip was aimed at those departments which did *not* have a local protocol for the routine health surveillance of children with DS, and asked them to choose from a list of options: "Our department does not have a local protocol for the early recognition of association co-morbidities in children with Down Syndrome (e.g. practice varies according to clinician).", "Our department uses guidance directly from the RCPCH/ DHSC/the DSMIG/Other." or "Our department does not undertake routine health surveillance of children with Down Syndrome (e.g. this is undertaken by another department). A box was also included for free text explanation.

Inclusion / exclusion criteria

Inclusion criteria for protocols:

Local protocols which included guidance on health surveillance:

- of children with DS (≤18years). Where protocols included guidance on health surveillance beyond 18years, the data for health surveillance undertaken ≥19yrs was not extracted.
- for either a single DS associated morbidity (e.g. for thyroid disorders only) or for a multitude of DS associated morbidities.
- related to specific time periods only (e.g. neonatal, pre-school years), or those which provided guidance on health surveillance throughout childhood.

Exclusion criteria for protocols:

Local protocols which focused only on:

- the health surveillance of individuals with DS ≥19yrs.
- prenatal screening in order to diagnose DS.

Data extraction

All of the protocols returned via post and e-mail were initially reviewed for inclusion/ exclusion criteria by the author. Duplicate responses (e.g. where the same department had responded twice, for example both via post and e-mail) were removed. In a small number of cases different paediatric departments returned a copy of the same protocol, likely because the protocol had been developed in collaboration, or had been shared between neighbouring departments. In this case both protocols were still included, as they reflect practice in separate paediatric departments.

A draft extraction table (Excel 2016) was created and revised following a trial extraction of 10 protocols. Data was extracted from the local protocols according to the following 23 variables: Name of Institution, Community v. hospital based /tertiary care, Age range covered in protocol, Frequency of clinical review, Echocardiogram/cardiac assessment, Full blood count (FBC) & blood film, Thyroid function tests (TFTs), Thyroid antibodies, Vision/ophthalmology, Hearing/ audiology, Coeliac disease, Urea and electrolytes/Liver function tests (U&E/LFTs), Glucose/glycated haemoglobin (HbA1c), Vitamin D, Immunological, Dental, Sleep disordered breathing (SDB), Developmental assessment, Transition, Cervical spine (C-spine) advice, Immunisations, Parent support groups and Benefits/social services.

These variables are based on those aspects of DS child health which are included in existing national and international health surveillance guidelines. They were also informed by the clinical experience of myself, and other members of the research team, who have actively been involved in reviewing children with DS in the paediatric clinic, and organising their health surveillance. The variables were further informed by the trial extraction of 10 protocols.

For each variable the relevant data was recorded as a narrative entry, including age of surveillance (i.e. timing), frequency, surveillance method and/or whether the protocol included only a nonspecific prompt (e.g. “Children with DS should be assessed for thyroid disease”, with no specifics on testing, timing or frequency).

As described above, those departments who did not have a local protocol were asked to complete a ‘response slip’. The response slips were collated and separated into two categories: Departments which declared they neither had a local protocol, nor followed existing national guidelines; and Departments which did not have a local protocol but declared that they followed guidance directly from the RCPCH/ DHSC/the DSMIG/Other.

Data analysis

For the returned protocols, the narrative entries for each of the 23 variables were compared manually.

For most of the variables it was possible to create categories of common practice, and thus to determine the number and proportion of protocols which outlined practice fitting into those categories. For example: Age range covered in protocol: (neonatal only)/(infancy to >14 years)/ (<14yrs only)/ (unclear), FBC & blood film: (Any inclusion)/(Specify to be done at birth), Vision & ophthalmology: (Formal assessment <18 months)/(Formal assessment at 4 years)/ (Vision checks >5years (annual) v. (biennial)). For transition/ adolescence the mean age and range at which transition planning began, was also determined.

Local health surveillance practice was compared with guidance from the DSMIG (published 2007-2018), RCPCH (published 2011) and the DHSC (published 2017). The number and proportion of protocols which outlined practice in keeping with the existing guidelines was determined.

For the 'response slips', returned by departments who did not have a local protocol, the number and proportion of departments within the two categories (see *Data Extraction*) was determined.

Primary outcomes

According to practice outlined in local protocols for the health surveillance of children with DS:

1. The number and proportion of protocols which include any guidance relevant to each variable of interest (see *Data Extraction*).
2. The number and proportion of protocols which include specific guidance (categorised according to timing, frequency and methodology) for each variable of interest.

Secondary outcomes

1. Areas of consensus and divergence in practice, with regard to health surveillance, between paediatric departments across the UK, according to the variables listed in *Data Extraction*.

2. Overall compliance with existing national guidance from DSMIG, RCPCH and the DHSC, according to the variables listed in *Data Extraction*.
3. The number/proportion of responding paediatric departments who do not have a local guideline for the health surveillance of children with DS, but claim to follow existing national guidelines

Governance

Research Design approval was sought and obtained from the Joint Research and Development Office at the Great Ormond Street Institute of Child Health, UCL (R&D number 17PP09).

Results

Responses from paediatric departments.

In total 166 responses were received (response rate 36%) between September 2017 and September 2018, this includes protocols and 'response slips'. For 6 responses it was not possible to determine if they had come from community paediatrics or hospital-based/tertiary care as a different, non-coded envelope had been used. The majority of the responses were received via post (n=149/166, 90%). Seventy protocols were returned, 6 duplicates were removed, and 64 protocols were included in the final analysis.

Paediatric (community & hospital based/tertiary care) departments which have/do not have a local protocol, and/or follow existing national guidelines.

Sixty-nine (n=69/160 43%) of all responses received were from community paediatric departments. This included 32 local protocols. Thirty-one (n=31/69, 45%) of community paediatric respondents did not include a local protocol but stated in the "response slip" that they followed existing guidelines (DSMIG n=19, RCPCH n=9, DHSC n=1, Other n=2). Six of the community paediatric respondents stated that they neither had a local protocol nor followed existing guidance.

Ninety-one (n=91/160, 57%) of all responses received were from hospital based or tertiary paediatric care settings. This included 32 local protocols. Fifty-three (n=53/91, 58%) of

hospital based or tertiary care respondents did not include a local protocol but stated in the questionnaire that they followed existing guidelines (DSMIG n=35, RCPCH n=12, DHSC n=0, Other n=6). Six of the hospital based or tertiary care respondents stated that they neither had a local protocol, nor followed existing guidance.

Results for the following primary outcomes are summarised in Table 18.

Age range covered in protocols

The largest proportion of protocols received outlined practice guidance for children with DS from infancy to over the age of 14years (n=34/64, 53%). A smaller proportion of protocols were aimed at children under the age of 14 years only (<14yrs n=4, neonatal period only n=7). For 19 of the protocols, details of the applicable age range was unclear.

Frequency of clinical review

The DSMIG/RCPCH do not currently recommend a standard for minimum frequency of clinical review of children with DS.

Among the 32 protocols received from community paediatric departments, the frequency of review was discernible for 25. The mean number of reviews were as follows: 0 to 12 months: 2.3 reviews (range 1-4), 12 months – 5 years: 5.7 reviews (range 4-9), ≥6 years one review per year (range 0.5-1/ year).

Among the 32 protocols received from hospital based or tertiary paediatric care settings, the frequency of review was discernible for 18. The mean number of reviews were as follows: 0 to 12 months: 2.6 reviews (range 1-4), 12 months – 5 years: 5.4 reviews (range 5-9), ≥6 years: one review per year (range 0.5-1/ year).

Echocardiogram/cardiac

The DSMIG and RCPCH recommend that an echocardiogram should be undertaken in all infants with DS, under 6 weeks of age. The DSMIG and DHSC recommend that a repeat, routine echo should be performed at the time of transition (~18years).

Sixty-three of the received protocols included cardiac screening as part of local guidelines for the routine health surveillance of children with DS. Of these, 58 (n=58/63, 92%) specified the need for an echocardiogram, or referral to cardiology, under the age of 6 weeks. Three protocols additionally included pulse oximetry at birth and two included a chest x-ray at birth.

Fifty-seven of the protocols were applicable to adolescents, however of these only 11 (n=11/57, 19.3%) specified the need for an echocardiogram at transition.

FBC & blood film

The DSMIG and RCPCH recommend that a FBC and blood film should be performed at birth. The DHSC recommend that a FBC should be repeated annually over the age of 14 years.

Only thirty-three (n=33/64, 52%) of the received protocols included a recommendation to perform a FBC and/or blood film. Of these, 26 (n=26/33, 79%) specified the need for an FBC & film at birth. One specifically stated that a FBC & film should *not* routinely be performed at birth.

TFTs, Thyroid antibodies

The DSMIG and RCPCH recommend that TFTs and thyroid antibodies should be checked at birth and then biennially over the age of 1 year. The department of health recommends that TFTs should be checked annually over the age of 14 years.

Fifty-two (n=52/64, 81%) of the received protocols included TFTs in their practice recommendations. Over the age of one year, the majority of protocols (n=36/52, 69%), recommended two yearly (biennial) TFTs. Eleven (n=11/52, 21%) recommended annual TFTs, over the age of one year. Five protocols recommended a variable frequency in TFTs. Where stated, the majority of protocols recommended the first TFT be checked at age 12 months (n=35/45, 78%).

Forty (n=40/64, 63%) of the received protocols included thyroid antibodies in their practice recommendations. Of these, 37 provided specific guidance on the timing of thyroid antibodies; 33 (n=33/37, 89%) recommending biennial screening and two (n=2/37, 5%) recommending annual screening.

Vision / Ophthalmology

The DSMIG recommend a formal visual assessment under the age of 18 months, the RCPCH recommend the same, anytime under the age of 2 years. Both DSMIG and RCPCH recommend a repeat formal visual assessment at the age of 4 years, followed by biennial assessment over the age of 5 years. The DHSC recommend biennial assessment over the age of 14 years.

Fifty-six (n=56/64, 88%) of the received protocols referred to visual assessments. Where stated, 45 (n=45/50, 90%) recommended a formal visual assessment under the age of 18 months. Forty-three (n=43/44, 98%) recommended a formal vision assessment at the age of four years. Over the age of 5 years, the majority of protocols recommended biennial vision checks (n=36/50, 72%) and 14 (n=14/50, 28%) recommended annual visual checks

Hearing / Audiology

The DSMIG recommends a formal audiological assessment under the age of 10months. Both the DSMIG and RCPCH recommend annual hearing assessment between 1 – 4years. Over the age of five years, they recommend biennial assessment. The DHSC recommends biennial assessment over the age of 14 years.

All of the received protocols included hearing assessments as part of their practice guidelines. Where stated, the majority of protocols (n=45/57, 79%) recommended a formal audiological assessment under the age of 10 months. Between ages 1-4 years, the majority of protocols recommended biennial hearing assessment (n=36/47, 77%); 11 protocols (n=11/47, 23%) recommended annual hearing assessment. Over the age of five years, the majority of protocols (n=35/47, 75%) recommended biennial hearing assessment; 12 (n=12/47, 26%) recommended annual hearing assessment.

Coeliac disease

The DSMIG, RCPCH and DHSC do not provide any specific guidance on coeliac screening for children with DS. However, the European Down Syndrome Association (EDSA) recommends a coeliac screen (serum anti-transglutaminase antibodies) at 12 months and annually thereafter.

Twenty-six (n=26/64, 41%) of the received protocols included reference to screening for coeliac disease (via anti-transglutaminase antibody testing). Seven (n=7/26, 27%) of these provided specific ages for when coeliac screening should be routinely undertaken, regardless of symptoms (Six months n=3, One year =1, Two years n=1, Five years n=1, Biennially n=1).

U&E/LFTs, Glucose/HbA1c, Vitamin D

The DSMIG & RCPCH do not provide any specific guidance on performing U&E, LFTs, glucose, HbA1c or vitamin D screening in children with DS. The DHSC recommend annual assessment for these parameters from the age of 14 years.

Only one (n=1/64, 2%) of the received protocols included a U&E and LFTs as part of local practice guidelines. No specifics were included with regard to timing.

Twelve (n=12/64, 19%) of the received protocols included assessment of glucose or HbA1c. Again, no specifics were included with regard timing.

Only one (n=1/64, 2%) of the received protocols included a recommendation to check the vitamin D level. Again, no specifics were included with regard to timing.

Immunological

The DSMIG, RCPCH and DHSC do not provide any specific guidance on screening for immunological defects (e.g. response to vaccinations, complement and immunoglobulin counts) in children with DS. However, the EDSA recommend immunological assessment at 12 months and then annually between 7 – 18 years.

Eight (n=8/64, 13%) of the received protocols included screening for immunological deficiencies as part of local guidelines for the routine health surveillance of children with DS. Only one protocol provided specifics on what tests should be undertaken and when (i.e. “check immune function (immunoglobulins, functional antibodies, prevnar antibodies and lymphocyte subsets) 4 weeks after completion of primary immunisations”).

Dental

The DSMIG, RCPCH and DHSC do not provide any specific guidance on dental assessments in children with DS. However, the EDSA recommend annual checks from 1 – 18 years.

Eighteen (n=18/64, 28%) of the received protocols included dental check-ups as part of local guidelines for the routine health surveillance of children with DS. Nine (n=9/18, 50%) of these recommended dental check-ups at least annual between the age of 1-18 years.

Sleep disordered breathing

The DSMIG, RCPCH and DHSC do not provide any specific guidance on sleep disordered breathing screening (SDB) in children with DS. However, in a separate overview of SDB, the DSMIG concede "There is a growing evidence recommending that all children with Down Syndrome should be offered screening with an overnight pulse oximetry, once in infancy and thereafter yearly till aged 5 years and to have a low threshold for screening throughout the lifespan" [98].

Twenty-five (n=25/64, 39%) of the received protocols included SDB as part of local guidelines for the routine health surveillance of children with DS. Only four of these included specifics on the timing of SDB assessments (At one year n=1, Annually one-five years n=1, At one year and four years n=1, Annually one-three years n=1).

Developmental assessment

The DSMIG, RCPCH and DHSC do not provide any specific guidance on routine developmental assessment of children with DS.

Thirty-two (n=32/64, 50%) of the received protocols specified a developmental assessment, or a referral to a child development clinic, as part of local guidelines for the routine health surveillance of children with DS.

Transition/adolescence

The DSMIG, RCPCH and DHSC do not provide any specific guidance on the transition of children with DS.

Twenty-six (n=26/64, 41%) of the received protocols included some mention of transition as part of local guidelines for the routine health surveillance of children with DS. Twelve of these (n=12/26, 46%) included specific guidance around transition or reference to a care pathway. Where stated, the average (mean) age at which it was recommended that planning for transition began was 14.8 years (n=16, range 14-18 years).

C-spine advice

The DSMIG, RCPCH and DHSC do not provide any specific guidance on the provision of c-spine advice for children with DS.

Thirty-seven (n=37/64, 58%) of the received protocols included c-spine advice as part of local guidelines for the routine health surveillance of children with DS. One of the protocols specified performing a once off X-ray of the c-spine at 3-5years.

Immunisations

The DSMIG, RCPCH and DHSC do not provide any specific guidance on the immunisation of children with DS.

Twenty-three (n=23/64, 36%) of the received protocols included immunisations as part of local guidelines for the routine health surveillance of children with DS. Only six of these (n=6/23, 26%) provided any specifics regarding the type, or timing, of immunisations.

Parent support groups & Benefits/social services

The DSMIG, RCPCH and DHSC do not provide any specific guidance on the provision of information regarding parent support groups or financial entitlements, for children with DS.

Thirty-four (34/64, 53%) of the received protocols mentioned parent support groups as part of local guidelines for the routine health surveillance of children with DS. Nineteen (n=19/66, 30%) included references to available financial support or specified a referral to social services.

Table 18. Summarising practice, as outlined in local protocols, for the routine health surveillance of children with DS, from paediatric departments across the UK (N=64).

Please note, N=64 is the total number of protocols returned to the study.
In the table the 'N value' changes as not all protocols included a recommendation for all the primary outcomes.
***Text in bold** depicts 'categories of practice' within the outcome/variable of interest.*

Primary outcomes from paediatric DS health surveillance protocols	**Protocol recommendations on assessment N=64**				
Age range covered in protocol	**Infancy->14yrs**	**<14yrs only**		**Unclear**	
	34 (35%)	<14yrs	n=4 (6%)	n=19 (30%)	
		Neonatal	n=7 (11%)		
Frequency of routine clinical review	**Age range**	**Community (Mean number of reviews) N=32**		**Tertiary/ hospital based (Mean number of reviews) N=32**	
	0-12 months	2.3 (range 1-4)		2.6 (range 1-4)	
	12 months-5yrs	5.7 (range 4-9)		5.4 (range 5-9)	
	≥6 years	1 / year (range 0.5-1)		1 / year (range 0.5-1)	
	Unclear	n=7		n=14	
Echocardiogram / cardiac assessment	**<6 weeks (N=63)**	**Echo <6 weeks**		n=58 (92%)	
		Pulse oximetry		n=3 (5%)	
		CXR		n=2 (3%)	
	Adolescence (N=57)	**Echo at transition**		n=11 (19%)	
FBC & blood film	**Any inclusion (N=64)**	33 (52%)			
	Specify at birth (N=33)	26 (79%)			
TFTs & thyroid antibodies	**TFTs**		**Thyroid antibodies**		
	1st check at 12 months (N=45)	n=35 (78%)	**Specific guidance on timing (N=40)**	n=37 (89%)	
	>1 year (N=52)	Annual n=11 (21%)	**Frequency (N=37)**	Annual n=2 (5%)	
		Biennial n=36 (69%)		Biennial n=33 (89%)	
Vision / ophthalmology assessment	**Formal assessment <18 months (N=50)**	n=45 (90%)			
	Formal assessment 4yrs (N=44)	n=43 (98%)			
	Vision checks >5yrs (N=50)	Annual n=14 (28%)			
		Biennial n=36 (72%)			
Hearing/ audiology assessment	**Formal assessment <10m (N=57)**	n=45 (79%)			
	1 – 4 years (N=47)	Annual n=11 (23%)			
		Biennial n=36 (77%)			
	> 5 years (N=47)	Annual n=12 (26%)			

		Biennial n=35 (75%)
Coeliac disease	**Any inclusion (N=64)**	n=26 (41%)
	Specific guidance on timing (N=7)	6 months n=3
		1 year n=1
		2 years n=1
		5 years n=1
		Biennial n=1
U&E/LFTs, Glucose/HbA1c, Vitamin D	**Any inclusion (N=64)**	U&E/LFTs n=1 (2%)
		Glucose/HbA1c n=12 (19%)
		Vitamin D n=1 (2%)
Immunological assessment	**Any inclusion (N=64)**	n=8 (13%)
Dental	**Any inclusion (N=64)**	n=18 (28%)
	Annual checks (N=18)	n=9 (50%)
Sleep disordered breathing	**Any inclusion (N=64)**	n=25 (39%)
	Specific guidance on timing (N=4)	1 year n=1
		Annually 1-5yrs n=1
		1yr & 4yrs n=1
		Annually 1-3yrs n=1
Developmental assessment	**Any inclusion (N=64)**	n=32 (50%)
Transition / adolescence	**Any inclusion (N=64)**	n=26 (41%)
	Specific guidance on transition (N=26)	n=12 (46%)
	Mean age to begin transition planning (N=16)	14.8 years (range 14-18yrs)
C-spine advice	**Any inclusion (N=64)**	n=37 (58%)
Immunisations	**Any inclusion (N=64)**	n=23 (36%)
	Specific guidance on type or timing (N=23)	n=6 (26%)
Parent support groups & Benefits/social services	**Any inclusion (N=64)**	Parent support groups n=34 (53%)
		Financial support/ SS referral n=19 (30%)

C-spine: Cervical spine, CXR: Chest X-Ray, Echo: echocardiogram, FBC: Full Blood count, HbA1c: Gylcated haemoglobin, LFTs: Liver Function Tests; SS: social services; TFTs: Thyroid function tests,U&Es: urea & electrolytes, Yrs: Years

Discussion

Statement of principal findings

For key components of DS health surveillance, the majority of local protocols contained some form of practice recommendations relevant to those areas. These areas tended to correspond to health conditions which are well established as DS associated morbidities and commonly included in national/international health surveillance guidelines (i.e. congenital cardiac disease, hypothyroidism, leukaemia, hearing and visual impairment).

For these same health conditions, the protocols demonstrated reasonable consensus between different paediatric departments, in terms of timing, frequency and screening methodology (e.g. recommending echocardiogram to screen for congenital cardiac disease, as opposed to ECG or CXR). Also in these areas, there appeared to be reasonable compliance with the recommendations in national guidelines either from the DSMIG and RCPCH.

However, in the other aspects of DS child health, practice appeared to be patchy and inconsistent. The areas which were least well represented in the protocols included sleep disordered breathing, vitamin D deficiency and assessment of renal and liver function. When these areas were included in protocols, the specifics of timing, frequency and methodology were either absent, or highly variable between departments. Sleep disordered breathing, vitamin D deficiency and assessment of renal and liver function are *not* commonly included in national/international health surveillance guidelines. This may go some way to explain the apparent variability in practice.

However, there were other areas of DS child health which, although not typically included in existing national guidelines, were still incorporated into a large proportion of local protocols. These included recommendations to screen for coeliac disease, provide c-spine advice and signposting to parental groups and financial support services. This suggests that, despite an absence of national recommendations specific to these areas, paediatric departments recognise the importance of addressing these aspects of health when reviewing patients with DS.

Strengths and weakness of the study

The study aimed to be highly inclusive and attempts were made to contact all paediatric departments across the UK, both hospital and community based, through multiple channels (e.g. post, DSMIG and BACCH mailing lists). The use of DSMIG and BACCH mailing lists also provided access to paediatricians who are more likely to be involved in providing routine health surveillance for children with DS. To optimise participation, every attempt was made to minimise the burden of responding (e.g. minimal reading materials, a brief 'response slip', pre-paid return envelopes and the option to respond via e-mail).

The study received a moderate response rate (36%) and it is possible that re-contacting departments sometime after the initial letter would have increased participation. It must be

considered that if the practice differs significantly between the responding departments and non-responders, then the findings of this study would not be generalizable to all paediatric departments across the UK. Indeed our results may have been influenced by "responder bias", where those departments with more active health surveillance practices, and established protocols, were more motivated to respond to our request for information, and that those departments with no or limited health surveillance practices were less likely to respond. Consequently our results may overestimate health surveillance activity and compliance with national guidelines, in the UK.

The study reviewed a wide variety of potential health surveillance practices, ranging from highly clinical (e.g. cardiac screening) to factors that are more social (e.g. signposting to parent support groups and financial support services). This provides a rich picture of current practice. Furthermore having direct access to the local protocol, as opposed to relying on a questionnaire response, made it possible to gather data on the finer details of health surveillance practice (e.g. timing and modality). There were also recurrent themes, which only became apparent when reviewing the protocols, that may not have been identified if data had been gathered by limited questionnaire responses alone (e.g. the provision of c-spine and signposting advice). Furthermore, it is possible that the response rate to a questionnaire would have been lower, as this places more burden on the clinician.

In the vast majority of cases the recommendations made in protocols were clear and easy to interpret. However, it is possible that in some instances I may have misinterpreted the guidance, and thus local practice. Given that opportunities for misinterpretation were rare, I feel this is unlikely to have affected the overall findings. Furthermore, when uncertainty arose it will possible to consult the wider research team to aid interpretation.

Finally, while the study summarises practice as it is written in local protocols, it is not possible to substantiate whether paediatric departments are indeed compliant with their own protocols. It may be that the content of some protocols is not a true reflection of practice in that department.

It must also be noted that this study was not designed to detect the reasons for non-compliance with national guidelines, or variation in practice between departments. It may be that local

health surveillance practice is influenced by factors unique to each area (e.g. resources, expertise, geographical factors, and population characteristics), which were not captured.

Furthermore, as described in the Background, over the age of 14 years, some young people with DS will have health surveillance co-ordinated by their GP, as opposed to a paediatrician. It was not within the remit of this study to contact GPs across the UK to gather information on their health surveillance practices. GPs may be more likely to follow DHSC guidelines, which are specifically applicable to the over 14s, and thus GP practice may be more in line with DHSC recommendations, than the RCPCH or DSMIG recommendations.

Comparison with other studies

I am not aware of any existing studies collating and comparing health surveillance practice for individuals with DS. Several studies have attempted to summarise surveillance practice for specific conditions, in non-DS populations[516-519].

Some of these studies found differences in health surveillance practice according to location (e.g. rural, urban, affluent or deprived areas)[516-519]. It was not within the remit of this study to observe relationships between health surveillance practice and the demographic characteristics of the paediatric population.

Implications for practice and research

The findings of this study suggest that, if the protocols are indeed reflective of practice, health surveillance for key aspects of DS health is active, and largely compliant with national guidelines (i.e. congenital heart disease, leukaemia, hypothyroidism and hearing and visual impairment), among respondents. If practice among the respondents is reflective of wider practice in the UK this is highly reassuring, and suggests that for these conditions children with DS are likely to be diagnosed and treated where necessary.

However, given that the inclusion of other health conditions was patchy and inconsistent between respondents, it is possible that morbidities such as coeliac disease, renal or liver dysfunction, immune disorders and sleep disordered breathing are going undiagnosed. There are existing testing modalities which are readily available to clinicians and, with the exception of sleep disordered breathing, a blood test taken at the same time as that for thyroid function is

likely to suffice. Conditions which are undiagnosed and untreated have the potential to increase mortality and morbidity among individuals with DS.

Local practice and protocols are highly influenced by national guidelines. As described above there are numerous UK guidelines for the routine health surveillance of children with DS, each with different recommendations. To promote consistency in practice, paediatricians and patients would benefit from one unified guideline document, which is based on the best available evidence.

The findings of this study, and indeed the prevalence figures determined in Project 2, provide support to expand the conditions included in such a guideline (i.e. sleep disordered breathing, coeliac disease, renal or liver dysfunction and immune dysfunction). In order to optimise compliance and consistency, recommendations relating to these conditions should ideally be accompanied by specific guidance with regard to timing and frequency. From personal professional experience, recommendations which include a timeframe are much more likely to be implemented. Furthermore, as the findings of this study show, for those conditions where national guidelines *did* provide guidance around timing, the protocols suggested good compliance and inter-departmental agreement.

However, the expansion of national guidelines must be supported by additional evidence. As explored in the Background, health surveillance is not without the potential for harm, and where it is implemented the benefits must outweigh the risks and be acceptable to patients and clinicians. It is possible that guidelines do not currently include recommendations relating to these areas of DS health as there is deemed insufficient evidence to justify health surveillance, or to determine through what modality, or when, this screening is most appropriate. As such, the findings of this study support academic investment in these areas.

Unanswered questions and future research

While this study aims to collate and compare local protocols for the routine health surveillance of children with DS, it cannot explain the reasons for consensus or divergence in practice. Future research could explore whether these differences reflect professional preferences, resource availability and/or geographical population characteristics. Such research may

require a qualitative approach, for example interviewing clinicians and other stakeholders involved in the provision of DS health surveillance.

As explored in the Background, there are numerous reasons why clinicians do not follow guidelines, or integrate guidelines into their local protocols and practice. These include ‘guidelines specific factors’, ‘contextual factors’, ‘implementation factors’ and ‘doctor related factors’. Future research could explore how these factors influence compliance with national DS health surveillance guidelines among paediatricians, informing the development of future national guidelines which are both evidence based and acceptable to clinicians.

As described above the findings of this study highlight a need for a single, evidence-based and accessible guideline for the routine health surveillance of children with DS in the UK. While the findings of this thesis add to the existing evidence base which would inform the development of such a guideline, more research in needed to inform the specifics of such recommendations. For example, a cost-benefit analysis of screening for certain conditions, the most effective testing modalities and the timing and frequency of that screening.

THESIS SUMMARY AND CONCLUDING REMARKS

The MD thesis presented here consists of three interrelated projects with the common theme of exploring and adding to the existing evidence base, which aims to improve the health and care of children with Down Syndrome (DS).

DS is a common condition that professionals are likely to encounter in their career, in a multitude of settings. It is also a complex condition, affecting almost every organ system, and thus clinicians in all specialities are likely to be involved in the care of individuals with DS at some point. Not only does this mean that the health and care of DS is highly relevant to a large number of clinicians, it also means that there are a large number of opportunities to optimise care.

Individuals with DS continue to have an increased morbidity and mortality compared to the general population, and other groups with intellectual disability. As with the significant advancements which have already been achieved in the health and care of individuals with DS over the last number of decades, these improvements will be driven by research and evidenced based medicine. The findings of each project presented here add to this evidence base and I have identified keys areas for future academic investment.

The health surveillance of children with DS is a common theme across all three projects. Active health surveillance of this population is vital because children with DS are prone to developing a wide range of health disorders, their presentation may be atypical and research has shown that self or parent report is insufficient to identify all cases of disease. Health surveillance provides a valuable opportunity to identify disease early and to prevent mortality and morbidity. Addressing morbidity in childhood sets a trajectory for better health throughout the life-course. This is particularly relevant in an aging population of individuals with DS.

Table 19 compares and summaries key findings across the three projects which are particularly relevant to the health surveillance of children with DS. When comparing the study prevalence of morbidities in the paediatric DS cohort, with the proportionate distribution of primary health themes in the paediatric DS research literature, there are some conditions which appear to have received comparatively less academic attention (e.g. gastrointestinal disorders such as inflammatory bowel disease, non-eczematous skin disorders, iron deficiency anaemia, chronic

kidney disease and non-accidental injury/maltreatment). Furthermore, there are several morbidities which are relatively common in the DS paediatric population and would be amenable to health surveillance, but are not yet included in any of the existing UK guidelines (e.g. autism, sleep disordered breathing, inflammatory bowel disease, vitamin D and iron deficiency).

Table 19: The proportionate distribution of primary health themes in the paediatric DS literature (2000-2020) alongside the study prevalence of corresponding morbidities, the frequency of inclusion in UK DS health surveillance guidelines, and existing (or potential) health surveillance modalities.

Primary health theme (paediatric DS literature)	**% of paediatric DS literature (2000-2020)**	**DS associated morbidities**	**Study prevalence in the DS cohort (children only) %**	**Included UK paediatric DS health surveillance guidelines*** /3	**Existing/ potential modality of health surveillance**
Neurology (including vision)	9.9%	Epilepsy	6.0%	0	Targeted history taking EEG
		Cataract	2.1%	3	Red reflex at birth Vision check (e.g. optician)
		Glaucoma	0.5%	3	Vision check (e.g. optician)
Oncology	9.8%	Leukaemia	2.2%	3	FBC & blood film
Cardiac/ Circulatory	8.1%	Congenital cardiac disease	56.3%	3	Echocardiogram at birth
Endocrine, nutrition, metabolic	6.6%	Hyperthyroidism	2.5%	3	TFTs & thyroid antibodies
		Hypothyroidism	15.8%	3	TFTs & thyroid antibodies
		Type 1 diabetes mellitus	0.9%	1	Fasting glucose, HbA1c
		Diabetes mellitus (combined)	2.8%	1	Fasting glucose, HbA1c
		Vitamin D deficiency	1.5%	1	Vitamin D level
Musculoskeletal	6.3%	Arthritis	0.9%	0	Targeted history taking Musculoskeletal examination
Behaviour / Mental health	6.1%	ADHD	1.5%	0	Targeted history taking Developmental assessment
		Anxiety & depression	1.9%	0	Targeted history taking
		Autism	6.3%	0	Targeted history taking

					Developmental assessment
		Schizophrenia	0.1%	0	Targeted history taking
Ear, Nose & Throat (ENT)	5.2%	Hearing impairment	23.5%	3	Hearing check (e.g. audiology)
		Sleep disordered breathing	19.1%	0	Polysomnography
Gastrointestinal	4.3%	Coeliac disease	2.8%	1	Anti-transglutaminase antibodies
		Congenital gastrointestinal disorders	4.7%	0	Clinical examination Abdominal imaging (e.g. USS)
		Gastroesophageal reflux disease	19.0%	0	Targeted history taking 24-hour pH-metry
		Inflammatory bowel disease	8.4%	0	Targeted history taking Faecal calprotectin
Dermatological	1.5%	Eczema	24.1%	0	Clinical examination
		Skin disorders, non-eczema	4.5%	0	Clinical examination
Haematological	1.4%	Iron deficiency	2.5%	1	FBC & iron studies
Renal, genitourinary	0.9%	Chronic kidney disease	1.1%	1	U&E
		Undescended testis	5.4%	0	Clinical examination
Child protection	0.2%	Non-accidental injury / maltreatment	3.4%	0	Targeted history taking Clinical examination

**Existing UK guidelines include DSMIG, RCPCH and DHSC (see Background, Table 2).*
EEG: electroencephalogram, FBC: Full blood count, HbA1c: Glycated haemoglobin, TFTs,: Thyroid function tests, USS: ultrasound scan

The findings of this study provide some support for a revision of existing guidelines to include additional morbidities In some cases this inclusion could be relatively straight forward (e.g. checking serum vitamin D levels, HbA1c, renal function and iron studies, at the same time as blood is traditionally taken for thyroid function) or targeted history taking during routine reviews. However, for other conditions health surveillance could require additional appointments and service commissioning (e.g. polysomnography for sleep disordered breathing).

It must also be considered that the inclusion of additional morbidities in health surveillance practice, or indeed guidelines, cannot be based on prevalence figures alone. The benefits of any health surveillance practice must be weighed against the potential disadvantages (e.g. additional patient appointments, uncomfortable procedures, healthcare costs, and incidental findings). The extension of health surveillance guidelines to include a large number of conditions may also lead to guidelines which are considered onerous and unrealistic by the clinician, leading to poor uptake. Furthermore, the inclusion of additional morbidities must be supported by a sufficient evidence base which justifies the timing, frequency and modality of testing.

As highlighted in the mapping exercise, studies focusing on health surveillance are relatively under-represented in the existing literature. This was further compounded by relatively few studies looking at disease burden in the DS population (e.g. the prevalence of DS associated morbidities). This paucity of evidence, with regard to health surveillance and disease burden, appears to have translated into numerous national guidelines which vary in their recommendations and only cover a small number of morbidities, most commonly congenital heart disease, leukaemia, hypothyroidism and visual and hearing impairment. A lack of inclusion of other conditions, either because their true prevalence has been unrecognised, or because the evidence base in insufficient to inform guidelines, appears to have translated into patchy and inconsistent care in screening for those conditions on the front line.

I contend that these findings, taken together, highlight the need for a single national guideline for the health surveillance of children with DS, and an investment in the research required to ensure that these guidelines are evidence based.

There are several advantages and disadvantages to having a single, 'gold standard' national guideline. The existence of more than one clinical practice guideline may reflect the reality that the same evidence base can be interpreted in different, and equally valid ways, by different authors. There are also several examples where multiple national guidelines, with different recommendations, exist successfully alongside each other (e.g. the Scottish Intercollegiate Guidelines Network (SIGN) and the National Institute for Health and Care Excellence (NICE) guidelines for the management of asthma and epilepsy). Where a single guideline exists there is a risk that poor practice becomes embedded and goes unchallenged. Multiple guidelines

may also provide clinicians with more choice and flexibility in their practice. However, there is a risk that this flexibility, and contradictions between guidelines, can translate into inconsistent care for patients. As described in the Background, consistent, reliable care is a priority expressed by patients with DS and their parents/carers. Differences in practice between clinicians, departments and UK regions may widen health inequalities. A single national guideline would promote consistency of care, which is of value to both clinicians and patients. Furthermore, the creation of a single guideline allows pooling of resources (academic and clinical) in deciphering and translating the evidence base.

Creating an inclusive, evidence-based guideline is a vital first step, but guidelines can only be translated into practice if they are accepted and adopted by clinicians. As explored in the Background, there are various reasons why clinical guidelines, even those of high quality and validity, are not followed in practice. These include guidelines specific factors (e.g. credibility of the authors, the evidence based strategy, transparency and guideline complexity), Contextual factors (e.g. organisational characteristics, social and clinical norms and habits), Implementation factors (e.g. communication strategies, the use of incentives), and 'doctor related factor'. Doctors may not follow guidelines because they are unfamiliar with them, they disagree with the context, because they feel the guidelines are unrealistic or unachievable in their clinical context, or that the guideline is too rigid to allow for flexibility. Consequently, the revision or development of a new paediatric DS health surveillance guideline should aim to address these potential pitfalls. Much of this could be addressed by actively engaging with clinicians who are involved in the health surveillance of children with DS, at each stage of guidelines development, as well as providing a mechanism for 'user feedback' and regular guideline review.

The aims of this thesis incorporated a number of the priorities of patients and parents/carers that I had identified in the literature, and in my professional experience. In particular, I explored the themes of quality and consistency of routine health surveillance and clinician awareness of the existing guidelines, I expanded the knowledge base which is available to clinicians caring for individuals with DS (including the prevalence of DS associated morbidities and cancers across the life-course) and I identified gaps in the literature, which together with PPI collaboration, have the potential to guide future research priorities.

Overall, the findings presented in this thesis are a significant contribution to describing the current state of the health and care of children with DS in the UK, while also adding valuable novel data to the evidence base. I believe the findings provide important ground work to guide future research funding and resource allocation, and ultimately to improve the health and care of children with Down Syndrome.

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This study is based in part on data from the Clinical Practice Research Datalink obtained under licence from the UK Medicines and Healthcare products Regulatory Agency. The data is provided by patients and collected by the NHS as part of their care and support. The interpretation and conclusions contained in this study are those of the author/s alone. This study is also utilizes ONS data, provided by the ONS and HES data. Again, the interpretation and conclusions contained in this study are those of the author/s alone.

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APPENDIX

Appendix 1: An example clinic proforma, including the protocol for routine health surveillance, used for the review of children with DS in the community paediatric setting.

This proforma was developed by myself for use in the Community Paediatric department in North Middlesex University Hospital NHS Trust, January 2017.

Clinic date: ___/___/___ Age of patient:

Attended with:

Doctor seen by:

Other professionals present:

Current problems (in order of importance):

Other professionals involved (including site):

Current parental concerns / current & recent health:

SYSTEMATIC REVIEW:

Bladder and Bowel:

Constipated: Yes □ No □

Symptoms of coeliac disease: Yes □ No □

Feeding / diet:

Dental:

Last dental check:

Sleeping:

Snoring: present □ absent □

Sleep apnoea: present □ absent □

Vision:

Last vision check:

Hearing:

Last hearing check:

Other:

Medications (including dose and frequency):

Allergies:

IMMUNISATIONS:

Annual Influenza vaccine (from 6 months)*: Patient □ Household members □

RSV prophylaxis*: Indicated □ Given □

2 months DTaP/IPV/Hib, PCV, Men B, Rotavirus

3 months DTaP/IPV/Hib, Men C, Rotavirus

4 months DTaP/IPV/Hib, PCV, Men B

1 year Hib/MenC booster, PCV booster, Men B booster, MMR

2 – 6years years* Single dose pneumococcal

polysaccharide vaccine (PPV 23) (Pneumovax II)

3 years DTaP/IPV, MMR

Girls 12-13 years HPV (2 doses 6 months apart)

14 years Td/IPV, MenACWY

Schedule as per Spring 2016

*In addition to 'normal' schedule.

SOCIAL / FAMILY HISTORY:

(If previous genogram – note changes to family structure only)

Housing issues:

Current Benefits (DLA etc.):

Current Support services / voluntary sector input:

PHYSICAL EXAMINATION:

(Plot biometry data on Down's syndrome specific charts)

Height = (centile)

Weight = (centile)

OFC = (centile)

BMI = (centile)

BP = SaO2 =

General comments:

Cardiovascular:

Respiratory:

Abdominal:

Neurology:

ENT:

Eyes (Cataracts, Strabismus, Nystagmus, Visual behaviour):

Developmental observations:

Recommended minimum surveillance by age:

BIRTH • Karyotype

- ECHO <6 weeks
- FBC & film
- TFTs
- Vision (cataract)
- Universal hearing
- Guthrie

6 MONTHS • Formal audiology assessment by 12months □

- Ensure health surveillance at birth (see above) is complete □

1 YEAR • FBC, ferritin, TSH, T4, TPO antibodies, coeliac screen □

- Immunoglobulins, functional antibodies, Prevenar antibodies, lymphocyte subsets (immunology 1m after 12m immunisations) □
- Ophthalmology assessment by 18 months □
- Annual dental review □

2 YEARS • FBC, ferritin □

- Local Educational Authority notification □
- Annual hearing check □

- Advise need for single dose of Pneumovax II between 2-5years □
- Annual dental review □

3 YEARS
- FBC, ferritin, TSH, T4, TPO □
- Annual hearing check □
- Annual vision check □
- Annual dental review □
- Advise need for single dose of pneumovax II between 2-5years (if not had) □

4 YEARS
- FBC, ferritin □
- Ophthalmology assessment □
- Annual dental review □
- Annual hearing check □
- Advise need for single dose of pneumovax II between 2-5years (if not had) □

5 YEARS
- FBC, ferritin, TSH, T4, TPO □
- Annual hearing check □
- Annual vision check □
- Annual dental review □

6-14 YEARS
- Annual FBC, TFTs, TPO antibodies □
- 2 yearly hearing test □
- 2 yearly vision check □
- 2 yearly dental check □
- Annual dental review □

≥15 YEARS
- Annual FBC, U&E, LFTs, TFTs, glucose, HbA1c, Ca2+, vit D +/- AED levels □
- 2 yearly hearing test □
- 2 yearly vision check □
- Annual dental review □

Adulthood Single ECHO □

Additional plan:

Appendix 2: UK guidelines for the routine health surveillance of children with DS.

DOWN SYNDROME MEDICAL INTEREST GROUP (DSMIG)[392]

Cardiac disease

CARDIAC DISEASE: CONGENITAL AND ACQUIRED (Revised 2007)

(One of a set of guidelines drawn up by the Down's Syndrome Medical Interest Group)

1. Between 40 and 60% of babies with Down's syndrome have congenital heart defects. Of these 30 - 40% are complete atrioventricular septal defects (AVSD)1.2.3.. Most AVSD can be successfully treated if the diagnosis is made early and the baby referred for full corrective surgery before irreversible pulmonary vascular disease (PVD) is established 4.5.6.7.8. Other lesions can usually be approached with less surgical urgency.

2. There must be a high level of clinical suspicion of congenital heart disease (CHD) for all newborns with the syndrome. Despite overall awareness of the risk of serious CHD in children with Down's syndrome some with important and sometimes severe CHD continue to present too late for the best chance of an optimum cardiac outcome (personal communications. Archer, Dennis, Tulloh)

3. Irreversible PVD is more likely to develop quickly in children with Down's syndrome and AVSD

7.8.9.. Ideally surgery is desirable by 6 months 5.8 and there is some evidence that surgery before 4 months may achieve best possible outcome6.

4. I suggest that the surveillance goal should be to establish by age 6 weeks at the latest whether or not there is a significant cardiac problem. This is because from a practical point of view this should be achievable over a wide range of clinical settings in the UK and Republic of Ireland and it is sufficiently early to ensure that by the time surgery can take place very few babies will already have irreversible PVD. I suggest also that for babies potentially at high risk for PVD it is prudent to attempt to achieve this by age 2 weeks (see 5.1)

5. Diagnostic methods

Clinical examination alone is insufficient to detect cardiac disease in the newborn period. Even the most serious abnormalities can be missed 10. It is very unlikely however that a serious abnormality (AVSD or other major shunt lesion) requiring early intervention will be missed if the following course of action is taken.1.3.11.12.

5.1 Babies diagnosed with Down's syndrome in the early neonatal period

Shortly after diagnosis a careful clinical examination and ECG should be carried out. On the basis of this the degree of urgency for echocardiogram and expert cardiological assessment can be established as follows12:

• Those with abnormal clinical signs or ECG abnormality (in particular a superior QRS axis 13) are potentially at high risk for PVD and it is desirable that they are referred and seen within 2 weeks of birth for expert clinical assessment and echocardiogram by someone with appropriate paediatric cardiological training.

• Those with no abnormal clinical signs or ECG abnormality on initial examination may

nevertheless have cardiac disease 3.12.13. These babies should all be referred and seen within 6 weeks of birth by someone with appropriate paediatric cardiological training for further clinical assessment and echocardiogram

5.2 Babies diagnosed later in the neonatal period

These should have immediate ECG and clinical examination and accelerated referral to someone with appropriate paediatric cardiological training with the aim, wherever possible, of achieving the 6 week deadline given above.

5.3 Babies with a prenatal diagnosis of Down's syndrome

In the absence of evidence about the sensitivity of fetal echocardiography I suggest that those who had a fetal echocardiogram should still follow the above neonatal pathway.

5.4 Older children who have never had an echocardiogram should be dealt with as follows:

• Those with no symptoms or clinical signs and normal ECG should be referred routinely for further clinical assessment by someone with appropriate paediatric cardiological training

• Those who are symptomatic and/or have abnormal clinical signs or ECG should be referred urgently.

6. People with heart lesions are at increased risk of infective endocarditis. They and their parents

and carers should be given verbal and written advice about endocarditis prevention. Red cards from the British Heart Foundation14 are useful, and local paediatric cardiac centres will havetheir own preferred literature.

7. It must always be remembered that those with Down's syndrome and a normal heart at birth can, like other children, develop pulmonary vascular disease and right heart failure secondary to airway/respiratory problems 15.

8. It must be noted that occasionally, even in expert hands, echocardiography, particularly in the first few days after birth, may fail to diagnose AVSD and other major shunt lesions. Hence there should be a low threshold for repeating this investigation if symptoms or signs of cardiac disease are detected at any age even in the presence of 'normal' early echocardiogram. (Personal communications. Archer, Dennis, Ward)

9. From late adolescence onwards there is evidence of an increased incidence of asymptomatic mitral valve prolapse (MVP) with no clinical signs and of aortic regurgitation (AR)16.17.18.19. There is however insufficient evidence of benefit to make detailed recommendations about cardiac surveillance in adult life. MVP and AR are usually considered benign conditions but there may be implications for infective endocarditis prevention, particularly because of the high incidence of periodontal disease among this population20. Hence careful cardiac assessment may be indicated before some dental procedures 16.

There will be some whose MVP progresses to regurgitation (MVR). In order to identify these I recommend that auscultation of the heart should be included as part of routine medical monitoring on discharge from paediatric care and throughout adult life 21.Those with MVR should be monitored for signs of atrial fibrillation and/or left ventricular failure17.22. For some of these restriction of competitive sporting activities may be advised.22.23

10. Even if the above guidelines are effectively used there will still for some time to come be individuals for whom the difficult issues raised by the availability of heart lung transplant will

need to be considered. 24.
(References available at source).

Thyroid disease

THYROID DISORDER

(One of a set of guidelines drawn up by the Down's Syndrome Medical Interest Group)

1. At all ages thyroid disorder (usually hypothyroidism) occurs more frequently in people with Down's syndrome than in the general population [1.2.3.4.5]. Around 10% of the school age population have uncompensated hypothyroidism. The prevalence increases with age [6]. If undiagnosed, thyroid disorder constitutes a significant cause of preventable secondary handicap. Diagnosis on clinical grounds is unreliable [7.8]. Biochemical screening is essential. As in the general population those with significant abnormalities of any TFT should either be treated (if there is uncompensated hypothyroidism) or kept under close clinical and biochemical surveillance.
2. All babies in the U.K. have a neonatal screen for hypothyroidism [9]. For children with Down's syndrome each district should have a policy of screening after this, starting in infancy and continuing throughout life.
3. Biochemical testing, including estimation of T4, TSH, and thyroid antibodies should be carried out at least once every two years from age 1 and throughout life. [6.11].
4. Fingerprick dried blood spot TSH measurement (Guthrie) is being investigated. Preliminary evaluation suggests that this may prove an effective screening procedure [10]. If available, and if replacing venous testing (see 3 above) this should be carried out at least annually.
5. Transient changes may occur.[11.12]. Mildly raised TSH (not greater than 10mu/l) or the presence of antibodies with normal T4 and no clinical evidence of hypothyroidism does not usually warrant treatment [13.14]. It does however indicate increased likelihood of developing uncompensated hypothyroidism. Such people should therefore be tested more frequently than those with normal test results. A specialist opinion may be required.
6. Clinicians should always bear in mind the prevalence of thyroid disorder in people with Down's syndrome and have a low threshold for testing thyroid function if there is any clinical suspicion at times between biochemical testing.
7. As in the general population key clinical pointers are lethargy and/or changes in affect, cognition, growth, or weight.
8. Consideration of hypothyroidism is mandatory in the differential diagnosis of depression and dementia [15.16] .
9. The possibility of hyperthyroidism should also be born in mind [5.17].
(References available at source).

Hearing

HEARING IMPAIRMENT

(One of a set of guidelines drawn up by the Down's Syndrome Medical Interest Group.

Approved by BACDA and BAAP. Sept 2000. Reviewed and revised by BACDA 2004)

1. Well over 50% of people with Down's syndrome have significant hearing impairment which may be mild, moderate, severe or profound. Sensorineural and/or conductive loss may be present at any age. 3.4.5.7.17. Hearing impairment can be successfully managed in this population. If undetected it is likely to be a significant cause of preventable secondary handicap 3.10.12.13.21. Lifelong audiological surveillance is essential for all. The main cause of conductive loss is persistent otitis media with effusion (OME, glue ear). The natural history of OME and response to intervention differ from that in the general population hence local surveillance and management protocols need to be set up specific to people with Down's syndrome.3.5.9.19

2. People with Down's syndrome of all ages should have rapid access to specialist audiology services 3.

3. Because of an increased incidence of congenital sensorineural loss newborns should be included in targeted newborn hearing screening programmes wherever universal newborn hearing screening is not yet in place.1.14. This does not preclude the need for ongoing surveillance 8.

4. Guidance for parents of children with Down's syndrome should include discussion about hearing problems and their management, supported by good quality written information.15

5. All babies, regardless of any previous hearing screening results, should have a full audiological assessment between age 6 and 10 months. This should include measurement of auditory thresholds, impedance testing and otoscopy 18. To ensure inclusion of the child with Down's syndrome participation in existing child health hearing surveillance programmes should be encouraged.

6. Therefore by 10 months it should have been established whether or not a child has any degree of permanent hearing loss with or without OME. A clear management plan must have been agreed with the parents and intervention instigated where necessary.

7. In the second year (usually around 18 months) all children – whatever their previoushearing status - should have further audiological review carried out in a manner appropriate for a child with learning disability. This should include assessment of auditory thresholds, impedance testing and otoscopy. This should be repeated at least yearly until age 5 and thereafter 2 yearly for life. More frequent testing will be necessary if problems exist.

8. Transition of care from paediatric to adult services should involve direct transfer of care to a named person.

9. At all ages people with Down's syndrome have narrow ear canals which predispose to accumulation of wax4. This may affect impedance testing and hearing.

10. Most people with Down's syndrome are able to respond to standard tests – eg distraction; speech discrimination; pure tone audiometry (play or standard); and visual reinforcement audiometry – as long as these are carried out by testers with expertise in working with people with learning disability. Threshold measurement tests appropriate to developmental age must be used 6.20.

11. Because of increased incidence of sensorineural as well as conductive loss the frequency range tested should include 8000Hz whenever feasible as this may be an early warning of impending sensorineural deafness 11.22.
12. Diagnostic Auditory Brain Stem (ABR) responses in people with Down's syndrome must be interpreted with caution 7.22
13. As in the general population all those who are hearing impaired should have access to specialist hearing support services (Speech and Language Therapy; Teachers of the deaf; hearing Therapists etc)
14. At all ages particular attention should be paid to the treatment of suppurative nasal and ear conditions 3.16.
15. In adults with the syndrome hearing assessment is essential in the differential diagnosis of depression and dementia 7.
(References available at source).

Ophthalmic problems

OPHTHALMIC PROBLEMS (Revised 2012)

One of a set of guidelines drawn up by the Down Syndrome Medical Interest Group (DSMIG(UK))

1.There is a high prevalence of ocular disorder among people with Down syndrome. Refractive errors and/or squint may be present from an early age and persist into childhood (1,2,3). The majority of children with Down syndrome have reduced accommodation at near (2,4,5). Compared to the general population there is a tenfold increase in congenital cataract (6) and infantile glaucoma may also occur (7). Nystagmus is present in at least 10% (8) . Cataracts and keratoconus may develop in teenage years or later and studies suggest that these are approximately 4 times more common than in the adult general population (9). If untreated most of these disorders are a significant cause of preventable secondary handicap at all ages. Therefore there should be extra vigilance at all ages.
2. As with all children newborns with Down syndrome should be examined for congenital cataract and other eye anomalies by a trained person and this should be repeated at 6 weeks (10)
3. Visual behaviour must be monitored by the child's paediatrician particularly before the first formal ophthalmologic review. Those who start to squint or show other abnormalities of gaze, visual behaviour or attention should be referred for ophthalmological review.*
4. Between 18 months and 2 years all children with Down syndrome should have formal ocular/visual assessment by an orthoptist and ophthalmologist/optometrist in accordance with local arrangements. This should include orthoptic assessment, refraction, and fundus examination. At least one third will have ocular/visual defects by this age (1,11,12). Those with deviation from normal should be kept under appropriate specialist review. Refractive errors, most commonly hypermetropia, which often reduce spontaneously in other children, are likely to persist beyond infancy (3, 13). Correction for hypermetropia may be helpful at a younger

age than that for typically developing children especially since the majority will have defective accommodation (2, 4, 5).
5. Those with no abnormality at first review should nevertheless have further full ocular/visual assessment including refraction around age 4 years (14, 10). At this age at least 50% are likely to have refractive errors (1).
6. After age 4, due to the increased prevalence of disorders, eye checks should be at least 2 yearly throughout life by professionals with appropriate skills and expertise in managing this client group (14, 15). These may be optometrists (hospital or high-street based) or ophthalmologists. If hypermetropia is not present at age 4 it is not likely to occur later on, but myopia may develop at any age (3, 13).
7. Children and adults with Down syndrome should be expected to respond to standard vision testing procedures at appropriate developmental age but a distraction free environment and extra time may be necessary to optimise performance. Distance and near functioning vision should be checked at every review whenever developmentally possible and a prescription for near correction or bifocals considered at all ages * (13, 16, 17). Detail vision is likely to remain poorer than expected throughout life even when appropriate spectacles are worn(18,19)
8. Many High Street opticians/optometrists give an excellent service particularly for older children, but younger children and those who are difficult to examine in this setting should be seen in a specialist clinic.
9. Blepharitis has been reported to occur in up to 30% of children with Down syndrome (8,20) and can be managed in the usual way (21). Nasolacrimal duct obstruction also occurs commonly (20, 22) and may need specialist referral. *
10. In view of the high prevalence of ocular disorders (see item 1) and the communication difficulties encountered in this client group any child or adult with pain, and/or changing vision, and/or red eye should be referred in the normal way.
(References available at source).

Growth

GROWTH (Revised 2012)

One of a set of guidelines drawn up by the Down Syndrome Medical Interest Group (DSMIG UK)

Short stature is a recognised characteristic of most people with Down syndrome1.2. Average height at most ages is around the 2nd centile for the general population. Some children however also have additional medical conditions which may further jeopardize growth. These include congenital heart disease 3.4; sleep related upper airway obstruction 5; coeliac disease 6.7; nutritional inadequacy due to feeding problems 8; and thyroid hormone deficiency 9.10 which all occur more frequently among those with the syndrome. Regular surveillance of growth, general health, nutritional and thyroid status should aid in early identification of pathological causes of poor growth.

UK/Republic of Ireland growth charts for healthy children with Down syndrome from birth to 18 years are available and have been revised in 2011. 11.12. These reference values are

essential for assessing linear growth. However as many older children and adults with the syndrome are overweight 13.14 the reference values for weight should not be used as a standard that children should aim to achieve. Body Mass Index BMI information is included on the charts particularly to aid the assessment of those who may be overweight.

Recommendations:

1. I suggest that it is good practice to record and chart height and weight frequently in the first two years using the 2011 revised Down syndrome specific charts 11. Thereafter measurements should be made at least annually throughout childhood and at regular intervals in adult life. Regular measurements of this sort are likely to be sensitive early indicators of the many medical problems that are over represented in this population.
2. As in all children growth spurts and plateaux occur but among those with Down syndrome these tend to be more prolonged. They are not reflected in the smoothed curves of a reference chart.
3. As with all children head circumference should be measured at birth and 6 weeks and charted on the Down syndrome charts. Subsequent measurements can be made as clinically indicated.
4. Preterm babies

There are no published birth weight charts for preterm babies with Down syndrome who are born before 37 completed weeks. However as these weights differ little from the general population15 the neonatal and infant close monitoring (NICAM) chart may be used to give guidance until term16. Thereafter the Down syndrome charts should be used and measurements plotted using gestationally corrected age for at least a year.

5.Newborns and young babies

For babies with Down syndrome early weight loss may be more than 10% and it often takes longer than 2 weeks to regain birthweight17. By 4 weeks, if there is no serious medical problem, most will be on a centile close to their birth centile. Early weight loss greater than 10% which is not quickly recovered or undue delay in regaining birthweight (>4 weeks) indicates a need for careful clinical evaluation for feeding difficulties or major underlying pathology. Breast feeding should be encouraged and supported.

6.Underweight

Children below the 2nd centile for weight need evaluation. Some will be perfectly healthy. However some with heart problems, other additional medical needs, and feeding difficulties are also likely to be on lower centiles. If they grow roughly parallel to their centile this is reassuring, but if they fall away from the lowest centiles they should be assessed by a paediatrician and may need specialist feeding advice and possibly extra supplementary feeding.

7.

Overweight

There is a high prevalence of overweight and obesity among people with Down syndrome13.14. As with the general population weight is influenced by environmental14.18 as well as biological factors 19.

Appropriate anticipatory guidance regarding diet and physical activity should be given for all those with the syndrome.

The Down syndrome specific charts clearly reflect the tendency to overweight among the UK study sample particularly in later childhood and adult life 11.12. Hence the reference data should not be used as a standard that children should aim to achieve. Children over age 2 can be charted on the BMI conversion chart (see growth charts) particularly if there are concerns about overweight or if their weight lies above the 75th centile. Those with a BMI above the overweight or very overweight thresholds should be encouraged to lose weight and offered specialist referral for guidance if appropriate.
Thyroid function should always be checked in those with accelerated weight gain.
8.Puberty
The Down syndrome specific chart suggests an absence of pubertal growth spurt. However these children do have an adolescent growth spurt. It is usually less vigorous than in the general population and may occur at an earlier age. Final height is achieved earlier than in the general population20.21. If early onset of puberty occurs it may have a limiting effect on final height.
9. Growth hormone
The use of growth hormone in Down syndrome is still being evaluated. There is no evidence that it should be prescribed except in the unusual situation of concurrent primary growth hormone deficiency .22.23.24
10. The influence of parental height on target height appears to be variable 25.
(References available at source).

DEPARTMENT OF HEALTH AND SOCIAL CARE (DHSC)[393]
Adapted by the Royal College of General Practitioners, Syndrome Specific Medical health check guide – Down's Syndrome
Introduction
Down's syndrome results from increased genetic material on all or part of chromosome 21, usually as a consequence of Trisomy 21, and is characterized by intellectual disability and often comorbidities involving multiple organ systems.
The survival of people with Down's syndrome has improved dramatically in the past few decades, largely as a result of improved surgical repair of congenital heart defects. The median age at death is now the mid-50s, compared with less than 10 years of age in the 1970s. Respiratory infection and dementia are now leading causes of death in adults with Down's syndrome.
People with Down's syndrome generally do well with consistent schedules and can blossom in a setting of predictable routine. This also includes dietary habits and physical activity that prevent obesity.
History
As with all people with LD focus on an assessment of:
• eyesight and hearing
• feeding, bowel and bladder function
• behavioural problems and decline in skills.

The differential diagnosis for a decline in skills includes: depression, changes to routines, life events, hypothyroidism, sleep apnoea, hearing loss, vision loss, dementia, seizure disorder, developmental regression.
Important causes of unexplained weight loss include: coeliac disease and gastroesophageal reflux or dyspepsia, and swallowing problems.
Well over 50% of people with Down's syndrome have significant hearing impairment, which can range from mild to profound. Sensorineural and/ or conductive loss may be present at any age. If undetected it is likely to be a significant cause of preventable secondary handicap. The main cause of conductive loss is persistent Otitis media with effusion (glue ear).

About two thirds have problems affecting their eyesight, such as refractive errors, cataract, glaucoma and keratoconus.
Obesity is widespread in people with Down's syndrome (89-95%), likely due to lower activity levels and a lower metabolic rate, making exercise and energy restriction critical in maintaining a healthy weight.
One third, if not the majority of those with Down's syndrome, have obstructive sleep apnoea (OSA), which may due a small jaw and upper airways combined with macroglossia, as well as blocked nose and most of all obesity. OSA can occur at any age and cause daytime sleepiness, behavioural change, loss of skills and other symptoms suggestive of depression or dementia. Complete an Epworth sleepiness score and refer for sleep studies. Weight loss if obese as well as CPAP mask overnight can dramatically improve the symptoms of OSA and the wellbeing of patients.
Pneumonia, aspiration pneumonia and flu are a common causes for admission and the second most common cause of death of people with Down's syndrome. All adults with Down's syndrome are eligible for Influenza and Pneumococcal immunisation.
Swallowing difficulties (dysphagia) can present with coughing, gagging, sighing, burping, or throat clearing during mealtimes, and cause choking with aspiration. Evaluation consists of a modified barium swallow study in conjunction with a SALT assessment.
Gastro-oesophageal reflux is also common in people with Down's syndrome. Like dysphagia, it can present with weight loss, vomiting, decline in skills or behavioural changes.
Mental health problems affect 25-30%, mostly depression, anxiety, obsessivecompulsive tendencies, and behavioural issues. Depression is common in older adults, often triggered by bereavement or changes in their living situation. Discriminating depression from dementia can be difficult but is important, since the former as amenable to medical therapy. Symptoms more suggestive of depression include withdrawal and decreased appetite and speech. Autism is ten times more common than in the general population; it can be very difficult to treat, often requiring specialist input.
People with Down's syndrome have an increased risk of Alzheimer's dementia, with an earlier onset than in the general population. The prevalence is 10-22% in their 40s; 20-25% in their 50s; and 40-77% in those over 60 years, contributing to one third of deaths.

Although donepizil and memantine are increasingly used, there is currently no good evidence demonstrating their effectiveness in this population. They appear to be beneficial for some patients, however, hypotension, bradycardia or ataxia may require their discontinuation in some.
Women with Down's syndrome have an earlier menopause around 44 years on average.

Down's syndrome is an independent risk factor for osteoporosis, further increased by early menopause, anti-epileptic medication and other risk factors. There is a high risk of fractures in the over 50s.
Hypothyroidism affects 15-37%, increasing with age. Hyperthyroidism is also more common than in the general population.
Diabetes: Increased prevalence of Type 1 diabetes and Type 2 Diabetes associated with obesity. The onset of type 2 diabetes is often at a younger age than the general population and can present with subtle symptoms.
Skin conditions: Dry skin and eczema are particularly common and are managed in the usual way.
Cervical spine: Atlanto-axial instability has mostly been described in children. In adults, degenerative changes and cervical spondylosis are more common, with a prevalence of 35-70%. Routine cervical spine X-ray is not recommended, but I need to be alert to signs of spinal stenosis with cord compression and assess these promptly.
Congenital heart disease is common and usually treated surgically in early childhood. In adults, consider the possibility of acquired valve disease, specifically mitral valve prolapse (in 45%, often with mitral regurgitation) and aortic regurgitation. It may be asymptomatic and a murmur may not always be audible. The incidence of coronary artery disease in adults with Down's syndrome is decreased compared with the general population.
With the exception of childhood leukaemia, the incidence of cancer - whether hematologic or solid tumours - is also decreased in all age groups with Down's syndrome. Full blood counts frequently show leukopenia, macrocytosis and mild polycythemia, which do not appear to be of clinical relevance, but B12-deficiency and hypothyroidism should be excluded and the rare possibility of adult leukaemia be borne in mind.
Examination
1. Sensory
 Full assessment by optician/optometrist at least every 2 years.
 If examination is difficult, refer to specialist optician or ophthalmologist for assessment.
 Otoscopy annually - gentle examination as short auditory canals
 Auditory assessment every 2 years has been recommended (including auditory thresholds, impedance testing).
2. Dental

 Dental Review at least annually, as periodontal disease is common.
 Look for signs of oesophageal reflux.
 Ask about swallowing problems and aspiration.

3. Respiratory

 Examine nose for blockage, the oral cavity, and lungs for lower airway disease
 Ask about daytime sleepiness and sleep apnoea. Consider Epworth sleepiness score and sleep studies.

4. Cardiovascular

 Auscultation of the heart annually.
 A single Echocardiogram should be performed in adult life.
 Echocardiogram for new murmurs and signs of cardiac failure.
 Adults with a pre-existing structural abnormality should be informed of applicable prophylactic antibiotic protocols.

5. Gastrointestinal

 Ask for signs and symptoms of Coeliac Disease annually
 Coeliac antibody test in those with suspicious symptoms or signs: disordered bowel function with loose stools or new onset constipation, abdominal distension, general unhappiness and misery, arthritis, rash suggesting dermatitis herpetiformis.
 Coeliac antibody test in those with existing thyroid disease, diabetes or anaemia.

6. Endochrine

 Thyroid function blood tests (TFTs) including thyroid antibodies every 1 or 2 years.
 Check TFTs if weight gain or loss, generally unwell, possible diagnosis of depression or dementia.
 Consider HgbA1c annually (diabetes defined as greater than 48 mmol/mol) and finger prick blood glucose.
 Ask women over 40 about hot flushes and menopausal symptoms.
 Osteoporosis screening should start begin in their 40s.
 Screen early especially in the presence of risk factors, such as poor mobility or non-weight bearing status, anti-psychotic or anti-epileptic medication, poor nutritional status, or early menopause.

7. Mental Health

 From the age of 40, ask about symptoms of dementia, which include: loss of skills and independence, no longer remembering or managing routines, need for prompting, appearing confused, change in behaviour, also urinary and/or faecal incontinence, ataxia, seizures, impaired mobility.
 Ask family members and/or carers about these symptoms.
 When considering a dementia assessment and diagnosis, consider deafness, hypothyroidism, sleep apnoea and depression.

8. Orthopaedic

 Ask about signs of spinal stenosis associated with atlanto-axial instability, which

may be acute or chronic, such as: hyperreflexia, ataxia, clonus, unsteadiness, deterioration in bladder or bowel control, or quadriparesis, and consider urgent neurosurgical assessment if present.

Resources

Managing the care of adults with Down's syndrome, Clinical Review, BMJ 2014: http://www.bmj.com/content/349/bmj.g5596

Down's Syndrome Association: https://www.downs-syndrome.org.uk/forprofessionals/health-medical/annual-health-check-information-for-gps/

ROYAL COLLEGE OF PAEDIATRICS AND CHILD HEALTH (RCPCH)[387]

Appendix 1 of the RCPCH paediatric service specification, service for children and young people with Down Syndrome[387].

Service standards for specific medical problems associated with Down syndrome (DS), from diagnosis to transition:

	First year of life	Early years / pre-school	School Age
Thyroid	All children with DS must undergo the routine newborn blood spot screening test to exclude congenital hypothyroidism.	Thyroid function must be reviewed either: • Annually, on the basis of annual thyroid stimulating hormone blood spot test; or • Biennial serum thyroid function and antibody tests	
Vision	All children with DS must undergo an examination for red reflex to exclude congenital cataract, as part of the routine newborn examination.	By 2 years of age, children with DS must undergo a formal eye and vision test, including squint assessment. All children must also undergo a detailed visual assessment before school age (4 years), to include squint assessment, refraction and acuity.	School aged children with DS must undergo a detailed ophthalmological/optometric assessment a minimum of once every two years.
Hearing	All children with DS must undergo the routine newborn hearing screening test to exclude hearing impairment. Before the child's first birthday, children with DS must undergo a formal audiological review, including hearing assessment & impedance check.	Between one and four years of age, children with DS will undergo an annual audiological review, including hearing assessment & impedance check.	School age children with DS will undergo an audiological review, including hearing assessment & impedance check, a minimum of once every two years.

Breathing	Children with DS must be assessed for symptoms of sleep-related breathing disorder annually until commencing school, with further assessment (including overnight pulse oximetry) arranged where clinically indicated.		School-age children with DS who develop symptoms of sleep-related breathing disorders must be investigated (including overnight pulse oximetry) and managed promptly, including referral to ENT if appropriate.
Heart	By 6 weeks' of age, all children with DS must have a formal cardiological assessment (including echocardiography) to exclude congenital heart disease.	Children with DS must be reviewed annually for signs and symptoms of acquired valvular heart disease, with further assessment (including echocardiography and specialist cardiology referral arranged where clinically indicated.)	
Growth	Children with DS will undergo monitoring of height and weight (plotted on a UK DS-specific growth chart) on an annual basis.		
Haematology	All children with DS will have a blood film assessment in the neonatal period to exclude related blood disorders.		
Gastrointestinal	Assessment (and investigation as required) of common gastrointestinal problems, such as constipation, feeding difficulties and coeliac disease, must take place during each regular medical review.		
Spinal	Assessment (and investigation as required) of developing disorders of the cervical spine must take place during each regular medical review.		

Appendix 3: Mapping exercise, search terms

Pubmed

Search ((((((((((Adolescent[MeSH]OR baby OR babys OR baby's OR babies or babies' OR Child[MeSH]OR Infant[MeSH] OR juvenile OR juveniles OR juvenile's OR juveniles' OR juvenileadolescent OR juvenileonset OR neonate OR neonates OR neonate's OR neonates' OR neonatology OR neonatologist OR neonatologists OR neonatologist's OR neonatologists' OR neonatal OR neonatally OR newborn OR newborns OR newborn's OR newborns' OR new-born OR new-borns OR newborn's OR new-borns' OR Pediatrics[MeSH]OR preterm* or prematur* OR puber* OR pubescen* OR Schools[mesh]OR teen OR youth* OR young*)))) AND (("down syndrome"[Title/Abstract] OR "downs syndrome"[Title/Abstract] OR "down's syndrome"[Title/Abstract] OR "trisomy 21"[Title/Abstract] OR "Syndrome, Down"[Title/Abstract] OR "Syndrome, Down's"[Title/Abstract] OR "mongolism"[Title/Abstract] OR "mongoloid"[Title/Abstract] OR "langdon down disease"[Title/Abstract] OR "langdon down syndrome"[Title/Abstract] OR "trisomy G"[Title/Abstract])))) NOT ((Amniocentesis[Title/Abstract] OR "Antenatal diagnosis"[Title/Abstract] OR "Antenatal diagnostic"[Title/Abstract] OR "Antenatal screening"[Title/Abstract] OR "Antenatal test"[Title/Abstract] OR "Antenatal testing"[Title/Abstract] OR "Cell free fetal"[Title/Abstract] OR "Cell free foetal"[Title/Abstract] OR "Cell-free DNA"[Title/Abstract] OR "Cell-Free Fetal DNA"[Title/Abstract] OR "Cell-Free Foetal DNA"[Title/Abstract] OR "cff DNA"[Title/Abstract] OR "Chronic villous sampling"[Title/Abstract] OR "Fetal cell free"[Title/Abstract] OR "Foetal cell free "[Title/Abstract] OR "Fetal cell-free"[Title/Abstract] OR "Foetal cell-free"[Title/Abstract] OR "Fetal DNA"[Title/Abstract] OR "Foetal DNA"[Title/Abstract] OR "Invasive prenatal"[Title/Abstract] OR "Maternal Plasma"[Title/Abstract] OR "Maternal serum screening"[Title/Abstract] OR "NIPT"[Title/Abstract] OR "Non-invasive prenatal"[Title/Abstract] OR "Noninvasive prenatal"[Title/Abstract] OR "Prenatal diagnosis"[Title/Abstract] OR "Prenatal diagnostic"[Title/Abstract] OR "Prenatal screen"[Title/Abstract] OR "Prenatal screening"[Title/Abstract] OR "Prenatal test"[Title/Abstract] OR "Prenatal testing"[Title/Abstract] OR "Trimester screening"[Title/Abstract] OR "Trisomy screening"[Title/Abstract])))) NOT ((animals [mh] NOT humans [mh]))) NOT ((Mice[Title/Abstract] OR mouse[Title/Abstract]))) AND ("2000/01/01"[PDat] : "2016/12/31"[PDat])) Filters: Publication date from 2000/01/01 to 2016/12/31

Embase

Exp Down's syndrome (Down's syndrome OR idiocy, monogolian, OR langdon down disease OR langdon down syndrome OR Mongolian idiocy OR mongolism OR mongoloid idiocy OR mongolidism OR translocation 12 21 22 OR trisomy 21 syndrome) limit to Human and child<unspecificed age>

CINAHL Plus

Down syndrome (abs)

Limiters - Date of Publication: 20000101-20161231; Human; Age Related: All Child: 0-18 years; Age Groups: Infant, Newborn: birth-1 month, All Infant, All Child

Search modes - Boolean/Phrase

Appendix 4: Terms associated with exclusion

Search term	Number excluded (n=)
Fetal/foetal/fetus	88
Prenatal	35
Adult	147
Trimester	35
Non-DS	3
Alzeihmers / dementia	31
Femur	0
Mosaic	37
USS	53
Gestation	16
Pregnancy	24
Maternal risk	19
Dementia	33
Maternal serum	32
Abortion	8
Termination	7
Rett	14
Williams syndrome	7
Placenta	9
Maternal	85
Meiotic	7
Disjunction	13
Fragile x	8
Diagnosis	18
Embryo	3
Amniotic	11
Preimplantation	5
Translocation	27
Stillborn	3
Nasal	16
Nuchal	44
Invasive / cell-free	6
Prenatal	101
Antenatal	25
Mother	9

Appendix 5: Phenotyping code lists

MEDICAL CODE LISTS, READ CODES

ADHD

metadata	category	readcode	readterm	medcode
Name: ADHD_cprd	3	1P00.00	Hyperactive behaviour	10918
Version: 1	3	6A61.00	Attention deficit hyperactivity disorder annual review	101067
Source: CPRD	3	9Ol8.00	ADHD monitoring invitation first letter	99831
Author: C McKenna	3	9Ol9.00	ADHD monitoring invitation second letter	106362
Date: 19th October 2018	3	9OlA.00	ADHD monitoring invitation third letter	103937
Categories:	3	E2E..00	Childhood hyperkinetic syndrome	3775
1 = H/O	3	E2E..11	Overactive child syndrome	9972
2= Probable	3	E2E0.00	Child attention deficit disorder	5565
3 = Definite	3	E2E0000	Attention deficit without hyperactivity	34199
	3	E2E0100	Attention deficit with hyperactivity	9715
	3	E2E0z00	Child attention deficit disorder NOS	20467
	3	E2E1.00	Hyperkinesis with developmental delay	58069
	3	E2E2.00	Hyperkinetic conduct disorder	45263
	3	E2Ey.00	Other hyperkinetic manifestation	25469
	3	E2Ez.00	Hyperkinetic syndrome NOS	41769
	3	Eu84400	[X]Overactive disorder assoc mental retard/stereotype movts	52602
	3	Eu90.00	[X]Hyperkinetic disorders	1458
	3	Eu90000	[X]Disturbance of activity and attention	6512
	3	Eu90011	[X]Attention deficit hyperactivity disorder	6519
	3	Eu90100	[X]Hyperkinetic conduct disorder	33505
	3	Eu90111	[X]Hyperkinetic disorder associated with conduct disorder	45799
	3	Eu90200	[X]Deficits in attention motor control and perception	55322
	3	Eu90y00	[X]Other hyperkinetic disorders	6510
	3	Eu90z00	[X]Hyperkinetic disorder unspecified	50015
	3	Eu90z11	[X]Hyperkinetic reaction of childhood or adolescence NOS	97421
	3	Eu90z12	[X]Hyperkinetic syndrome NOS	96770
	3	Eu9y700	[X]Attention deficit disorder	26285
	3	Ry13.00	[D]Overactivity	24546
	3	ZS9..00	Disorders of attention and motor control	37994
	3	ZS91.00	Attention deficit disorder	28543
	3	ZS91.11	ADD - Attention deficit disorder	24808
	3	ZS91.12	[X]Attention deficit disorder	24753
	3	ZS93.00	Deficits in attention motor control and perception	39920
	3	ZS93.11	DAMP - Deficits in attention motor control and perception	35161

Anxiety/Depression

metadata	category	readcode	readterm	medcode
Name: AnxietyDepression_cprd	1	1466.00	H/O: anxiety state	3407
Version: 1	3	2257.00	O/E - depressed	1908
Source: CPRD	3	6659000	Antidepressant drug treatment started	102632
Author: C McKenna	3	13Y3.00	Manic-depression association member	56260
Date: 19th October 2018	3	1B17.00	Depressed	1996
Categories:	3	1B17.11	C/O - feeling depressed	4824
1 = H/O	3	1B1U.00	Symptoms of depression	9796
2= Probable	3	1B1U.11	Depressive symptoms	10438
3 = Definite	3	1B1V.00	C/O - panic attack	11890
	3	1Bb1.00	Fear of getting cancer	18967
	3	1BT..00	Depressed mood	10015
	3	1JJ..00	Suspected depression	100977
	3	225J.00	O/E - panic attack	19000
	3	285..00	NEUROTIC CONDITION, INSIGHT PRESENT	15811
	3	286..00	POOR INSIGHT INTO NEUROTIC CONDITION	5274
	3	388b.00	Depression anxiety stress scales anxiety score	19163
	3	388Z.00	Depression anxiety stress scales depression score	9970
	3	62T1.00	Puerperal depression	2923
	3	8BK0.00	Depression management programme	44848
	3	8CAa.00	Patient given advice about management of depression	30483
	3	8G94.00	Anxiety management training	9125
	3	8HHp.00	Referral for guided self-help for anxiety	28925
	3	8HHq.00	Referral for guided self-help for depression	32841
	3	9H90.00	Depression annual review	12399
	3	9H91.00	Depression medication review	12122
	3	9H92.00	Depression interim review	30405
	3	9HA0.00	On depression register	42931
	3	9k40.00	Depression - enhanced service completed	65435
	3	9Ov..00	Depression monitoring administration	51258
	3	9Ov0.00	Depression monitoring first letter	71009
	3	9Ov1.00	Depression monitoring second letter	72966
	3	9Ov2.00	Depression monitoring third letter	91105
	3	9Ov3.00	Depression monitoring verbal invite	88644

3	9Ov4.00	Depression monitoring telephone invite	85852
3	E001300	Presenile dementia with depression	27677
3	E002.00	Senile dementia with depressive or paranoid features	44674
3	E002100	Senile dementia with depression	21887
3	E002z00	Senile dementia with depressive or paranoid features NOS	41089
3	E004300	Arteriosclerotic dementia with depression	43292
3	E11..00	Affective psychoses	14656
3	E11..12	Depressive psychoses	2560
3	E112.00	Single major depressive episode	10610
3	E112.11	Agitated depression	5879
3	E112.12	Endogenous depression first episode	6546
3	E112.13	Endogenous depression first episode	6950
3	E112.14	Endogenous depression	595
3	E112000	Single major depressive episode, unspecified	34390
3	E112100	Single major depressive episode, mild	16506
3	E112200	Single major depressive episode, moderate	15155
3	E112300	Single major depressive episode, severe, without psychosis	15219
3	E112400	Single major depressive episode, severe, with psychosis	32159
3	E112500	Single major depressive episode, partial or unspec remission	43324
3	E112600	Single major depressive episode, in full remission	57409
3	E112z00	Single major depressive episode NOS	7011
3	E113.00	Recurrent major depressive episode	15099
3	E113.11	Endogenous depression - recurrent	6932
3	E113000	Recurrent major depressive episodes, unspecified	35671
3	E113100	Recurrent major depressive episodes, mild	29342
3	E113200	Recurrent major depressive episodes, moderate	14709
3	E113300	Recurrent major depressive episodes, severe, no psychosis	25697
3	E113400	Recurrent major depressive episodes, severe, with psychosis	24171
3	E113500	Recurrent major depressive episodes,partial/unspec remission	56273
1	E113600	Recurrent major depressive episodes, in full remission	55384
3	E113700	Recurrent depression	6482
3	E113z00	Recurrent major depressive episode NOS	25563
3	E114.00	Bipolar affective disorder, currently manic	3702
3	E114200	Bipolar affective disorder, currently manic, moderate	46434
3	E114300	Bipolar affect disord, currently manic, severe, no psychosis	16347

3	E114400	Bipolar affect disord, currently manic,severe with psychosis	55829
3	E114z00	Bipolar affective disorder, currently manic, NOS	57605
3	E115.00	Bipolar affective disorder, currently depressed	4677
3	E115.11	Manic-depressive - now depressed	12831
3	E115000	Bipolar affective disorder, currently depressed, unspecified	15923
3	E115100	Bipolar affective disorder, currently depressed, mild	35734
3	E115200	Bipolar affective disorder, currently depressed, moderate	27890
3	E115300	Bipolar affect disord, now depressed, severe, no psychosis	35607
3	E115400	Bipolar affect disord, now depressed, severe with psychosis	63701
1	E115600	Bipolar affective disorder, now depressed, in full remission	57465
3	E115z00	Bipolar affective disorder, currently depressed, NOS	37296
3	E116.00	Mixed bipolar affective disorder	31316
3	E116000	Mixed bipolar affective disorder, unspecified	31535
3	E116100	Mixed bipolar affective disorder, mild	24689
3	E116200	Mixed bipolar affective disorder, moderate	63150
3	E116300	Mixed bipolar affective disorder, severe, without psychosis	63284
3	E116400	Mixed bipolar affective disorder, severe, with psychosis	54195
3	E116z00	Mixed bipolar affective disorder, NOS	63583
3	E117.00	Unspecified bipolar affective disorder	14784
3	E117100	Unspecified bipolar affective disorder, mild	63698
3	E117200	Unspecified bipolar affective disorder, moderate	68647
3	E117400	Unspecified bipolar affective disorder,severe with psychosis	68326
3	E117z00	Unspecified bipolar affective disorder, NOS	27986
3	E118.00	Seasonal affective disorder	10825
3	E11y.00	Other and unspecified manic-depressive psychoses	60178
3	E11y000	Unspecified manic-depressive psychoses	11596
3	E11y200	Atypical depressive disorder	27491
3	E11yz00	Other and unspecified manic-depressive psychoses NOS	33426
3	E11z.00	Other and unspecified affective psychoses	41992
3	E11z000	Unspecified affective psychoses NOS	54607
3	E11z200	Masked depression	9183
3	E11zz00	Other affective psychosis NOS	33425
3	E130.00	Reactive depressive psychosis	8478
3	E130.11	Psychotic reactive depression	17770
3	E135.00	Agitated depression	1055

3	E200.00	Anxiety states	636
3	E200000	Anxiety state unspecified	6939
3	E200100	Panic disorder	4069
3	E200111	Panic attack	462
3	E200200	Generalised anxiety disorder	4659
3	E200300	Anxiety with depression	655
3	E200400	Chronic anxiety	1758
3	E200500	Recurrent anxiety	4634
3	E200z00	Anxiety state NOS	4534
3	E202.12	Phobic anxiety	9944
3	E202100	Agoraphobia with panic attacks	3076
3	E202B00	Cancer phobia	1510
3	E204.00	Neurotic depression reactive type	1131
3	E204.11	Postnatal depression	2639
3	E211.00	Affective personality disorder	14979
3	E211000	Unspecified affective personality disorder	16178
3	E211200	Depressive personality disorder	10455
3	E211300	Cyclothymic personality disorder	12707
3	E211z00	Affective personality disorder NOS	51497
3	E262000	CARDIAC NEUROSIS	15292
3	E280.00	Acute panic state due to acute stress reaction	11940
3	E290.00	Brief depressive reaction	1533
3	E290z00	Brief depressive reaction NOS	36246
3	E291.00	Prolonged depressive reaction	16632
3	E292000	Separation anxiety disorder	6221
3	E2B..00	Depressive disorder NEC	324
3	E2B0.00	Postviral depression	2972
3	E2B1.00	Chronic depression	4323
3	E2D0.00	Disturbance of anxiety and fearfulness childhood/adolescent	31522
3	E2D0000	Childhood and adolescent overanxiousness disturbance	35619
3	E2D0100	CHILDHOOD AND ADOLESCENT FEARFULNESS DISTURBANCE	56026
3	E2D0z00	Disturbance anxiety and fearfulness childhood/adolescent NOS	35594
3	Eu05300	[X]Organic mood [affective] disorders	24000
3	Eu05400	[X]Organic anxiety disorder	20773

3	Eu2040	[X]Post-schizophrenic depression	20785
3	Eu2510	[X]Schizoaffective disorder, depressive type	11055
3	Eu2511	[X]Schizoaffective psychosis, depressive type	35274
3	Eu2511	[X]Schizophreniform psychosis, depressive type	41022
3	Eu3..00	[X]Mood - affective disorders	5726
3	Eu31.00	[X]Bipolar affective disorder	6874
3	Eu31.11	[X]Manic-depressive illness	1531
3	Eu31.12	[X]Manic-depressive psychosis	6710
3	Eu31.13	[X]Manic-depressive reaction	66153
3	Eu3100	[X]Bipolar affective disorder, current episode hypomanic	16808
3	Eu3130	[X]Bipolar affect disorder cur epi mild or moderate depressn	16562
3	Eu3140	[X]Bipol aff disord, curr epis sev depress, no psychot symp	23713
3	Eu3150	[X]Bipolar affect dis cur epi severe depres with psyc symp	4732
3	Eu3160	[X]Bipolar affective disorder, current episode mixed	44693
3	Eu31z0	[X]Bipolar affective disorder, unspecified	33751
3	Eu32.00	[X]Depressive episode	4639
3	Eu32.11	[X]Single episode of depressive reaction	9055
3	Eu32.12	[X]Single episode of psychogenic depression	18510
3	Eu32.13	[X]Single episode of reactive depression	7604
3	Eu3200	[X]Mild depressive episode	11717
3	Eu3210	[X]Moderate depressive episode	9211
3	Eu3220	[X]Severe depressive episode without psychotic symptoms	9667
3	Eu3221	[X]Single episode agitated depressn w'out psychotic symptoms	41989
3	Eu3221	[X]Single episode major depression w'out psychotic symptoms	22806
3	Eu3221	[X]Single episode vital depression w'out psychotic symptoms	59386
3	Eu3230	[X]Severe depressive episode with psychotic symptoms	12099
3	Eu3231	[X]Single episode of major depression and psychotic symptoms	24117
3	Eu3231	[X]Single episode of psychogenic depressive psychosis	52678
3	Eu3231	[X]Single episode of psychotic depression	24112
3	Eu3231	[X]Single episode of reactive depressive psychosis	28863
3	Eu3240	[X]Mild depression	10667
3	Eu3250	[X]Major depression, mild	98346
3	Eu3260	[X]Major depression, moderately severe	98252
3	Eu3270	[X]Major depression, severe without psychotic symptoms	98414

3	Eu3280 0	[X]Major depression, severe with psychotic symptoms	98417
3	Eu32y0 0	[X]Other depressive episodes	6854
3	Eu32y1 1	[X]Atypical depression	10720
3	Eu32y1 2	[X]Single episode of masked depression NOS	56609
3	Eu32z0 0	[X]Depressive episode, unspecified	2970
3	Eu32z1 1	[X]Depression NOS	543
3	Eu32z1 2	[X]Depressive disorder NOS	3291
3	Eu32z1 3	[X]Prolonged single episode of reactive depression	28248
3	Eu32z1 4	[X] Reactive depression NOS	5987
3	Eu33.00	[X]Recurrent depressive disorder	3292
3	Eu33.11	[X]Recurrent episodes of depressive reaction	8851
3	Eu33.12	[X]Recurrent episodes of psychogenic depression	19696
3	Eu33.13	[X]Recurrent episodes of reactive depression	8902
3	Eu33.14	[X]Seasonal depressive disorder	28756
3	Eu33.15	[X]SAD - Seasonal affective disorder	8826
3	Eu3300 0	[X]Recurrent depressive disorder, current episode mild	29784
3	Eu3310 0	[X]Recurrent depressive disorder, current episode moderate	29520
3	Eu3320 0	[X]Recurr depress disorder cur epi severe without psyc sympt	33469
3	Eu3321 1	[X]Endogenous depression without psychotic symptoms	11329
3	Eu3321 2	[X]Major depression, recurrent without psychotic symptoms	11252
3	Eu3321 3	[X]Manic-depress psychosis,depressd,no psychotic symptoms	29451
3	Eu3321 4	[X]Vital depression, recurrent without psychotic symptoms	73991
3	Eu3330 0	[X]Recurrent depress disorder cur epi severe with psyc symp	47009
3	Eu3331 1	[X]Endogenous depression with psychotic symptoms	23731
3	Eu3331 2	[X]Manic-depress psychosis,depressed type+psychotic symptoms	28677
3	Eu3331 3	[X]Recurr severe episodes/major depression+psychotic symptom	32941
3	Eu3331 4	[X]Recurr severe episodes/psychogenic depressive psychosis	31757
3	Eu3331 5	[X]Recurrent severe episodes of psychotic depression	16861
3	Eu3331 6	[X]Recurrent severe episodes/reactive depressive psychosis	37764
3	Eu3340 0	[X]Recurrent depressive disorder, currently in remission	22116
3	Eu33y0 0	[X]Other recurrent depressive disorders	47731
3	Eu33z0 0	[X]Recurrent depressive disorder, unspecified	44300
3	Eu33z1 1	[X]Monopolar depression NOS	36616
3	Eu34.00	[X]Persistent mood affective disorders	42857

3	Eu3400	[X]Cyclothymia	21540
3	Eu3401	[X]Affective personality disorder	26839
3	Eu3401	[X]Cycloid personality	54848
3	Eu3401	[X]Cyclothymic personality	23854
3	Eu3410	[X]Dysthymia	7953
3	Eu3411	[X]Depressive neurosis	8584
3	Eu3411	[X]Depressive personality disorder	10290
3	Eu3411	[X]Neurotic depression	7737
3	Eu3411	[X]Persistant anxiety depression	15220
3	Eu34y0	[X]Other persistent mood affective disorders	50243
3	Eu34z0	[X]Persistent mood affective disorder, unspecified	39767
3	Eu3y.00	[X]Other mood affective disorders	28008
3	Eu3y00	[X]Other single mood affective disorders	50998
3	Eu3y01	[X]Mixed affective episode	30688
3	Eu3y10	[X]Other recurrent mood affective disorders	29921
3	Eu3y11	[X]Recurrent brief depressive episodes	19054
3	Eu3yy0	[X]Other specified mood affective disorders	29579
3	Eu3z.00	[X]Unspecified mood affective disorder	37090
3	Eu3z.11	[X]Affective psychosis NOS	31633
3	Eu4..00	[X]NEUROTIC, STRESS - RELATED AND SOMOFORM DISORDERS	23808
3	Eu40.00	[X]Phobic anxiety disorders	9386
3	Eu40y0	[X]Other phobic anxiety disorders	27685
3	Eu40z0	[X]Phobic anxiety disorder, unspecified	34064
3	Eu41.00	[X]Other anxiety disorders	5385
3	Eu4100	[X]Panic disorder [episodic paroxysmal anxiety]	8205
3	Eu4101	[X]Panic attack	6408
3	Eu4101	[X]Panic state	4081
3	Eu4110	[X]Generalized anxiety disorder	10344
3	Eu4111	[X]Anxiety neurosis	962
3	Eu4111	[X]Anxiety reaction	35825
3	Eu4111	[X]Anxiety state	50191
3	Eu4120	[X]Mixed anxiety and depressive disorder	11913
3	Eu4121	[X]Mild anxiety depression	7749

3	Eu41300	[X]Other mixed anxiety disorders	44321
3	Eu41y00	[X]Other specified anxiety disorders	24066
3	Eu41y11	[X]Anxiety hysteria	28167
3	Eu41z00	[X]Anxiety disorder, unspecified	23838
3	Eu41z11	[X]Anxiety NOS	25638
3	Eu45311	[X]CARDIAC NEUROSIS	44269
3	Eu45313	[X]GASTRIC NEUROSIS	63259
3	Eu46z00	[X]Neurotic disorder, unspecified	49628
3	Eu51511	[X]Dream anxiety disorder	17687
3	Eu53011	[X]Postnatal depression NOS	13307
3	Eu53012	[X]Postpartum depression NOS	4979
3	Eu930000	[X]Separation anxiety disorder of childhood	18032
3	Eu931000	[X]Phobic anxiety disorder of childhood	24351
3	Eu932000	[X]Social anxiety disorder of childhood	29907
3	Eu93y12	[X]Childhood overanxious disorder	61430
3	R007z13	[D]Postoperative depression	29527
3	Z4I7.00	Acknowledging anxiety	22159
3	Z4I7100	Recognising anxiety	62935
3	Z4I7200	Alleviating anxiety	28381
3	Z4I7211	Reducing anxiety	26295
3	Z4L1.00	Anxiety counselling	7999
3	ZR3U.00	Clinical anxiety scale	52243
1	ZV11100	[V]Personal history of affective disorder	15117
1	ZV11112	[V]Personal history of manic-depressive psychosis	22080

Arthritis (combined)

metadata	category	readcode	readterm	medcode
Name: ArthritisComb_cprd	1	1443.00	H/O: gout	3759
Version: 1	3	2377.00	O/E - ankyl.spondyl.chest def.	37400
Source: CPRD	3	6691.00	Initial gout assessment	14996
Author: C McKenna	3	6692.00	Follow-up gout assessment	35660
Date: 19th October 2018	3	6693.00	Joints gout affected	29658
Categories:	3	6695.00	Date gout treatment started	34006
1 = H/O	3	6696.00	Date of last gout attack	68209

2= Probable	3	6697.00	Gout associated problems	58746
3 = Definite	3	6698.00	Gout drug side effects	52103
	3	6699.00	Gout treatment changed	34105
	1	14G..11	H/O: arthritis	1503
	1	14G1.00	H/O: rheumatoid arthritis	6639
	1	14G2.00	H/O: osteoarthritis	9760
	3	1JG..00	Suspected inflammatory arthritis	94334
	3	2G26.00	O/E - hands - Heberden's nodes	17282
	3	2G27.00	O/E-hands-rheumatoid spindling	33264
	3	388p.00	BASDAI - Bath ankylosing spondylitis disease activity index	93639
	3	38DZ.00	Disease activity score in rheumatoid arthritis	100187
	3	38DZ000	Disease activity score 28 joint in rheumatoid arthritis	103829
	3	43b9.00	Rheumatoid arthritis particle agglutination test	14303
	3	43c6.00	Rheumatoid arthritis screening test	43544
	3	669..00	Gout monitoring	16475
	3	669A.00	Date gout treatment stopped	43646
	3	669Z.00	Gout monitoring NOS	52117
	3	66H..11	Arthritis monitoring	8111
	3	66H..13	Rheumatoid arthrit. monitoring	17412
	3	66HB000	Rheumatoid arthritis annual review	105507
	3	68F..00	Arthritis screen	16289
	3	68F1.00	Rheumatoid arthritis screen	16480
	3	68FZ.00	Arthritis screen NOS	65858
	3	7L0H100	Correction of pseudarthrosis of tibia	42604
	3	7L0H112	McFarland bone graft pseudoarthrosis of tibia	66803
	3	7P20300	Delivery of rehabilitation for rheumatoid arthritis	102088
	3	7P20400	Delivery of rehabilitation for osteoarthritis	100072
	3	9hQ0.00	Excepted fr osteoarthritis quality indicators: pt unsuitable	104033
	3	9hR..00	Exception reporting: rheumatoid arthritis quality indicators	106093
	3	9hR0.00	Except rheumatoid arthritis quality indicator: pt unsuitable	106118
	3	9hR1.00	Except rheumatoid arthritis qual indicator: informed dissent	106092
	3	9mM..00	Rheumatoid arthritis monitoring invitation	107340
	3	9mM0.00	Rheumatoid arthritis monitoring invitation first letter	107435
	3	9mM1.00	Rheumatoid arthritis monitoring invitation second letter	107575
	3	9mM2.00	Rheumatoid arthritis monitoring invitation third letter	107676
	3	9mM3.00	Rheumatoid arthritis monitoring verbal invitation	107606
	3	9mM4.00	Rheumatoid arthritis monitoring telephone invitation	107797
	3	AD55.00	Sarcoid arthropathy	40613
	3	C108H00	Insulin dependent diabetes mellitus with arthropathy	65616
	3	C108H11	Type I diabetes mellitus with arthropathy	62352

3	C108J00	Insulin dependent diab mell with neuropathic arthropathy	39809
3	C108J11	Type I diabetes mellitus with neuropathic arthropathy	60208
3	C108J12	Type 1 diabetes mellitus with neuropathic arthropathy	18230
3	C109G00	Non-insulin dependent diabetes mellitus with arthropathy	24693
3	C109G11	Type II diabetes mellitus with arthropathy	18143
3	C109G12	Type 2 diabetes mellitus with arthropathy	49869
3	C109H00	Non-insulin dependent d m with neuropathic arthropathy	40962
3	C109H11	Type II diabetes mellitus with neuropathic arthropathy	47816
3	C109H12	Type 2 diabetes mellitus with neuropathic arthropathy	66965
3	C10EH00	Type 1 diabetes mellitus with arthropathy	18642
3	C10EJ00	Type 1 diabetes mellitus with neuropathic arthropathy	54008
3	C10FG00	Type 2 diabetes mellitus with arthropathy	59253
3	C10FG11	Type II diabetes mellitus with arthropathy	103902
3	C10FH00	Type 2 diabetes mellitus with neuropathic arthropathy	35385
3	C10FH11	Type II diabetes mellitus with neuropathic arthropathy	109197
3	C32y200	Lipoid dermatoarthritis	67948
3	C34..00	Gout	709
3	C340.00	Gouty arthropathy	10080
3	C341.00	Gouty nephropathy	52969
3	C341z00	Gouty nephropathy NOS	61145
3	C342.00	Idiopathic gout	11462
3	C344.00	Drug-induced gout	44566
3	C345.00	Gout due to impairment of renal function	21687
3	C34y.00	Other specified gouty manifestation	28999
3	C34y000	Gouty tophi of ear	36481
3	C34y100	Gouty tophi of heart	93689
3	C34y200	Gouty tophi of other sites	4440
3	C34y300	Gouty iritis	50067
3	C34y400	Gouty neuritis	59344
3	C34y500	Gouty tophi of hand	9874
3	C34yz00	Other specified gouty manifestation NOS	27521
3	C34z.00	Gout NOS	24153
3	C370400	Arthropathy in cystic fibrosis	100610
3	F163200	Myelopathy due to spondylosis	8920
3	F337200	Nerve root and plexus compressions in spondylosis	23699
3	F371200	Polyneuropathy in rheumatoid arthritis	62401
3	F396400	Myopathy due to rheumatoid arthritis	31209
3	G557300	Gouty tophi of heart	57334
3	G5y8.00	Rheumatoid myocarditis	49787
3	G5yA.00	Rheumatoid carditis	43816

3	H570.00	Rheumatoid lung	9954
3	M160.00	Psoriatic arthropathy	476
3	M160.11	Psoriatic arthritis	96880
3	M160100	Distal interphalangeal psoriatic arthropathy	32149
3	M160200	Arthritis mutilans	21503
3	M160z00	Psoriatic arthropathy NOS	12500
3	N005.00	Adult Still's Disease	23834
3	N012.00	Arthropathy in Behcet's syndrome	68729
3	N012000	Arthropathy in Behcet's syndrome of unspecified site	71206
3	N012011	Behcet's syndrome arthropathy	58818
3	N012700	Arthropathy in Behcet's syndrome of the ankle and foot	100365
3	N012x00	Arthropathy in Behcet's syndrome of multiple sites	62867
3	N014000	Arthropathy with other bacterial disease, of unspec site	73424
3	N014700	Arthropathy with other bacterial disease, of ankle and foot	70792
3	N014800	Arthropathy in Whipple's disease	57894
3	N014y00	Arthropathy with other bacterial disease, of other spec site	100325
3	N015.00	Arthropathy associated with other viral diseases	16276
3	N015000	Arthropathy with other viral disease, of unspecified site	69369
3	N015300	Arthropathy with other viral disease, of forearm	68929
3	N015400	Arthropathy with other viral disease, of hand	67071
3	N015500	Arthropathy with other viral disease, of pelvic region/thigh	62816
3	N015600	Arthropathy with other viral disease, of lower leg	66344
3	N015700	Arthropathy with other viral disease, of ankle and foot	68251
3	N015x00	Arthropathy with other viral disease, of multiple sites	51643
3	N015z00	Arthropathy associated with other viral disease NOS	36054
3	N016.00	Arthropathy associated with mycoses	67631
3	N016300	Arthropathy associated with mycoses, of the forearm	53426
3	N016400	Arthropathy associated with mycoses, of the hand	94388
3	N016700	Arthropathy associated with mycoses, of the ankle and foot	50086
3	N016z00	Arthropathy associated with mycoses NOS	73621
3	N017100	Helminthiasis with arthropathy of the shoulder region	69822
3	N01w.00	Reactive arthropathy, unspecified	3936
3	N01w000	Reactive arthropathy of shoulder	53334
3	N01w100	Reactive arthropathy of sternoclavicular joint	99398
3	N01w300	Reactive arthropathy of elbow	61906
3	N01w500	Reactive arthropathy of wrist	58590
3	N01w600	Reactive arthropathy of MCP joint	68933
3	N01w700	Reactive arthropathy of PIP joint of finger	101937
3	N01w800	Reactive arthropathy of DIP joint of finger	103172
3	N01w900	Reactive arthropathy of hip	33790

3	N01wA00	Reactive arthropathy of sacro-iliac joint	94911
3	N01wB00	Reactive arthropathy of knee	53339
3	N01wD00	Reactive arthropathy of ankle	50465
3	N01wH00	Reactive arthropathy of 1st MTP joint	103289
3	N01wJ00	Reactive arthropathy of lesser MTP joint	107875
3	N01wK00	Reactive arthropathy of IP joint of toe	62937
3	N02..12	Crystal arthritis	29807
3	N023.00	Gouty arthritis	2857
3	N023100	Gouty arthritis of the shoulder region	72471
3	N023200	Gouty arthritis of the upper arm	97539
3	N023300	Gouty arthritis of the forearm	45465
3	N023400	Gouty arthritis of the hand	52101
3	N023600	Gouty arthritis of the lower leg	49775
3	N023700	Gouty arthritis of the ankle and foot	35664
3	N023800	Gouty arthritis of toe	93677
3	N023x00	Gouty arthritis of multiple sites	58064
3	N023y00	Gouty arthritis of other specified site	60541
3	N023z00	Gouty arthritis NOS	12594
3	N02yz00	Other crystal arthropathy NOS	95161
3	N02z.00	Crystal arthropathy NOS	56016
3	N02z000	Crystal arthropathy NOS, site unspecified	97557
3	N02z100	Crystal arthropathy NOS, of the shoulder region	103340
3	N02z300	Crystal arthropathy NOS, of the forearm	64930
3	N02z400	Crystal arthropathy NOS, of the hand	69244
3	N02z600	Crystal arthropathy NOS, of the lower leg	65661
3	N02z700	Crystal arthropathy NOS, of the ankle and foot	93356
3	N02z800	Crystal arthropathy NOS, of shoulder	103837
3	N02zA00	Crystal arthropathy NOS, of acromioclavicular joint	96398
3	N02zD00	Crystal arthropathy NOS, of wrist	44750
3	N02zE00	Crystal arthropathy NOS, of MCP joint	102054
3	N02zF00	Crystal arthropathy NOS, of PIP joint of finger	94440
3	N02zJ00	Crystal arthropathy NOS, of sacro-iliac joint	104366
3	N02zK00	Crystal arthropathy NOS, of knee	54225
3	N02zL00	Crystal arthropathy NOS, of tibio-fibular joint	66168
3	N02zM00	Crystal arthropathy NOS, of ankle	106813
3	N02zR00	Crystal arthropathy NOS, of 1st MTP joint	99423
3	N02zT00	Crystal arthropathy NOS, of IP joint of toe	99724
3	N02zx00	Crystal arthropathy NOS, of multiple sites	100839
3	N02zz00	Crystal arthropathy NOS	42089
3	N03..00	Arthropathy associated with disorders EC	44639

3	N030.00	Arthropathy associated with endocrine and metabolic disorder	62290
3	N030000	Diabetic cheiroarthropathy	18142
3	N030100	Diabetic Charcot arthropathy	27891
3	N030200	Arthropathy in amyloidosis	94141
3	N031000	Arthropathy in ulcerative colitis	17641
3	N031100	Arthropathy in Crohn's disease	20480
3	N031200	Arthropathy in Whipple's disease	42865
3	N031300	Arthropathy following intestinal bypass	63159
3	N032.00	Arthropathy associated with haematological disorders	95441
3	N032000	Arthropathy due to haemophilia	35315
3	N033.00	Arthropathy associated with dermatological disorders	44621
3	N034.00	Arthropathy associated with respiratory disorders	41765
3	N035.00	Neuropathic arthropathy	49575
3	N035.11	Charcot's arthropathy	8710
3	N035.12	Neuropathic arthritis	36643
3	N036.00	Arthropathy due to hypersensitivity reaction	56188
3	N03x.00	Other general diseases with associated arthropathy	101820
3	N03x000	Arthritis associated with other disease, shoulder	99997
3	N03x100	Arthritis associated with other disease, sternoclavic joint	94590
3	N03x200	Arthritis associated with other disease, acromioclavic joint	92962
3	N03x400	Arthritis associated with other disease, dist rad-uln joint	73413
3	N03x500	Arthritis associated with other disease, wrist	73928
3	N03x600	Arthritis associated with other disease, MCP joint	57901
3	N03x700	Arthritis associated with other disease, PIP joint of finger	73716
3	N03x800	Arthritis associated with other disease, DIP joint of finger	73774
3	N03x900	Arthritis associated with other disease, hip	73637
3	N03xA00	Arthritis associated with other disease, sacro-iliac joint	100356
3	N03xB00	Arthritis associated with other disease, knee	62037
3	N03xD00	Arthritis associated with other disease, ankle	96187
3	N03xE00	Arthritis associated with other disease, subtalar joint	96400
3	N03xF00	Arthritis associated with other disease, talonavicular joint	73751
3	N03xG00	Arthritis associated with other disease, other tarsal joint	99026
3	N03xH00	Arthritis associated with other disease, 1st MTP joint	72011
3	N03xK00	Arthritis associated with other disease, IP joint of toe	105650
3	N03y.00	Arthropathy associated with other conditions EC	45462
3	N03z.00	Arthropathy associated with disorders EC NOS	50006
3	N04..00	Rheumatoid arthritis and other inflammatory polyarthropathy	27603
3	N04..11	Inflammatory polyarthropathy	20615
3	N040.00	Rheumatoid arthritis	844
3	N040000	Rheumatoid arthritis of cervical spine	44743
3	N040100	Other rheumatoid arthritis of spine	44203

3	N040200	Rheumatoid arthritis of shoulder	21358
3	N040300	Rheumatoid arthritis of sternoclavicular joint	107963
3	N040400	Rheumatoid arthritis of acromioclavicular joint	100914
3	N040500	Rheumatoid arthritis of elbow	59738
3	N040600	Rheumatoid arthritis of distal radio-ulnar joint	63365
3	N040700	Rheumatoid arthritis of wrist	48832
3	N040800	Rheumatoid arthritis of MCP joint	42299
3	N040900	Rheumatoid arthritis of PIP joint of finger	41941
3	N040A00	Rheumatoid arthritis of DIP joint of finger	63198
3	N040B00	Rheumatoid arthritis of hip	49067
3	N040C00	Rheumatoid arthritis of sacro-iliac joint	100776
3	N040D00	Rheumatoid arthritis of knee	50863
3	N040E00	Rheumatoid arthritis of tibio-fibular joint	107791
3	N040F00	Rheumatoid arthritis of ankle	51239
3	N040G00	Rheumatoid arthritis of subtalar joint	73619
3	N040H00	Rheumatoid arthritis of talonavicular joint	70658
3	N040J00	Rheumatoid arthritis of other tarsal joint	71784
3	N040K00	Rheumatoid arthritis of 1st MTP joint	51238
3	N040L00	Rheumatoid arthritis of lesser MTP joint	99414
3	N040M00	Rheumatoid arthritis of IP joint of toe	107112
3	N040N00	Rheumatoid vasculitis	30548
3	N040P00	Seronegative rheumatoid arthritis	6916
3	N040Q00	Rheumatoid bursitis	18155
3	N040R00	Rheumatoid nodule	53621
3	N040S00	Rheumatoid arthritis - multiple joint	31054
3	N040T00	Flare of rheumatoid arthritis	8350
3	N041.00	Felty's syndrome	23552
3	N042.00	Other rheumatoid arthropathy + visceral/systemic involvement	49227
3	N042100	Rheumatoid lung disease	46436
3	N042200	Rheumatoid nodule	5723
3	N042z00	Rheumatoid arthropathy + visceral/systemic involvement NOS	37431
3	N043.00	Juvenile rheumatoid arthritis - Still's disease	4186
3	N043000	Juvenile rheumatoid arthropathy unspecified	50644
3	N043100	Acute polyarticular juvenile rheumatoid arthritis	47831
3	N043200	Pauciarticular juvenile rheumatoid arthritis	21533
3	N043300	Monarticular juvenile rheumatoid arthritis	36276
3	N043z00	Juvenile rheumatoid arthritis NOS	27557
3	N044.00	Chronic post-rheumatic arthropathy	3944
3	N045.00	Other juvenile arthritis	7196

3	N045000	Juvenile ankylosing spondylitis	42405
3	N045100	Juvenile seronegative polyarthritis	31181
3	N045200	Juvenile arthritis in psoriasis	28456
3	N045300	Juvenile arthritis in Crohn's disease	12575
3	N045400	Juvenile arthritis in ulcerative colitis	71083
3	N045500	Juvenile rheumatoid arthritis	31360
3	N045600	Pauciarticular onset juvenile chronic arthritis	46622
3	N047.00	Seropositive errosive rheumatoid arthritis	9707
3	N04X.00	"Seropositive rheumatoid arthritis, unspecified"	12019
3	N04y.00	Other specified inflammatory polyarthropathy	36597
3	N04y000	Rheumatoid lung	31724
3	N04y011	Caplan's syndrome	56838
3	N04y012	Fibrosing alveolitis associated with rheumatoid arthritis	28853
3	N04y100	Sero negative arthritis	4578
3	N04y111	Sero negative polyarthritis	10919
3	N04y200	Adult-onset Still's disease	32001
3	N04yz00	Other specified inflammatory polyarthropathy NOS	23833
3	N04z.00	Inflammatory polyarthropathy NOS	24747
3	N05..00	Osteoarthritis and allied disorders	3057
3	N05..11	Osteoarthritis	396
3	N050.00	Generalised osteoarthritis - OA	4353
3	N050000	Generalised osteoarthritis of unspecified site	38631
3	N050100	Generalised osteoarthritis of the hand	36327
3	N050111	Heberdens' nodes	4015
3	N050112	Bouchards' nodes	35919
3	N050200	Generalised osteoarthritis of multiple sites	23676
3	N050300	Bouchard's nodes with arthropathy	38018
3	N050400	Primary generalized osteoarthrosis	23646
3	N050500	Secondary multiple arthrosis	11256
3	N050600	Erosive osteoarthrosis	38019
3	N050700	Heberden's nodes with arthropathy	24432
3	N050z00	Generalised osteoarthritis NOS	34867
3	N051.00	Localised, primary osteoarthritis	32839
3	N051000	Localised, primary osteoarthritis of unspecified site	54224
3	N051100	Localised, primary osteoarthritis of the shoulder region	24022
3	N051200	Localised, primary osteoarthritis of the upper arm	24217
3	N051300	Localised, primary osteoarthritis of the forearm	34806
3	N051400	Localised, primary osteoarthritis of the hand	21350
3	N051500	Localised, primary osteoarthritis of the pelvic region/thigh	15839
3	N051600	Localised, primary osteoarthritis of the lower leg	21159
3	N051700	Localised, primary osteoarthritis of the ankle and foot	25793
3	N051800	Localised, primary osteoarthritis of other specified site	20472
3	N051900	Primary coxarthrosis, bilateral	24287
3	N051A00	Coxarthrosis resulting from dysplasia, bilateral	25812

3	N051B00	Primary gonarthrosis, bilateral	24146
3	N051C00	Primary arthrosis of first carpometacarpal joints, bilateral	36182
3	N051D00	Localised, primary osteoarthritis of the wrist	24958
3	N051E00	Localised, primary osteoarthritis of toe	28908
3	N051F00	Localised, primary osteoarthritis of elbow	18602
3	N051G00	Osteoarthritis of spinal facet joint	106678
3	N051z00	Localised, primary osteoarthritis NOS	20660
3	N052.00	Localised, secondary osteoarthritis	42045
3	N052000	Localised, secondary osteoarthritis of unspecified site	68712
3	N052100	Localised, secondary osteoarthritis of the shoulder region	33574
3	N052200	Localised, secondary osteoarthritis of the upper arm	41088
3	N052300	Localised, secondary osteoarthritis of the forearm	45815
3	N052400	Localised, secondary osteoarthritis of the hand	23638
3	N052500	Localised, secondary osteoarthritis of pelvic region/thigh	44041
3	N052600	Localised, secondary osteoarthritis of the lower leg	33479
3	N052700	Localised, secondary osteoarthritis of the ankle and foot	34035
3	N052800	Localised, secondary osteoarthritis of other specified site	32891
3	N052900	Post-traumatic coxarthrosis, bilateral	64503
3	N052A00	Post-traumatic gonarthrosis, bilateral	24392
3	N052B00	Post-traumatic arthrosis of first carpometacarpal jt bilat	60183
3	N052C00	Post-traumatic gonarthrosis, unilateral	50470
3	N052z00	Localised, secondary osteoarthritis NOS	57912
3	N053.00	Localised osteoarthritis, unspecified	34122
3	N053000	Localised osteoarthritis, unspecified, of unspecified site	49545
3	N053100	Localised osteoarthritis, unspecified, of shoulder region	15441
3	N053200	Localised osteoarthritis, unspecified, of the upper arm	59637
3	N053300	Localised osteoarthritis, unspecified, of the forearm	60537
3	N053400	Localised osteoarthritis, unspecified, of the hand	16242
3	N053500	Localised osteoarthritis, unspecified, pelvic region/thigh	20626
3	N053512	Hip osteoarthitis NOS	1104
3	N053600	Localised osteoarthritis, unspecified, of the lower leg	34804
3	N053611	Patellofemoral osteoarthritis	1296
3	N053700	Localised osteoarthritis, unspecified, of the ankle and foot	4461
3	N053800	Localised osteoarthritis, unspecified, of other spec site	18112
3	N053900	Arthrosis of first carpometacarpal joint, unspecified	21177
3	N053z00	Localised osteoarthritis, unspecified, NOS	31200
3	N054.00	Oligoarticular osteoarthritis, unspecified	21528
3	N054000	Oligoarticular osteoarthritis, unspec, of unspecified sites	48214
3	N054100	Oligoarticular osteoarthritis, unspecified, of shoulder	52095
3	N054200	Oligoarticular osteoarthritis, unspecified, of upper arm	97073
3	N054400	Oligoarticular osteoarthritis, unspecified, of hand	59616

3	N054500	Oligoarticular osteoarthritis, unspecified, of pelvis/thigh	68648
3	N054600	Oligoarticular osteoarthritis, unspecified, of lower leg	41090
3	N054700	Oligoarticular osteoarthritis, unspecified, of ankle/foot	72109
3	N054800	Oligoarticular osteoarthritis, unspecified, other spec sites	41985
3	N054900	Oligoarticular osteoarthritis, unspecified, multiple sites	57267
3	N054z00	Osteoarthritis of more than one site, unspecified, NOS	53858
3	N05z.00	Osteoarthritis NOS	5776
3	N05z.11	Joint degeneration	1509
3	N05z000	Osteoarthritis NOS, of unspecified site	35527
3	N05z100	Osteoarthritis NOS, of shoulder region	3147
3	N05z200	Osteoarthritis NOS, of the upper arm	50848
3	N05z211	Elbow osteoarthritis NOS	639
3	N05z300	Osteoarthritis NOS, of the forearm	24152
3	N05z311	Wrist osteoarthritis NOS	15206
3	N05z400	Osteoarthritis NOS, of the hand	658
3	N05z411	Finger osteoarthritis NOS	4490
3	N05z412	Thumb osteoarthritis NOS	1959
3	N05z500	Osteoarthritis NOS, pelvic region/thigh	4967
3	N05z511	Hip osteoarthritis NOS	2209
3	N05z600	Osteoarthritis NOS, of the lower leg	15144
3	N05z611	Knee osteoarthritis NOS	665
3	N05z700	Osteoarthritis NOS, of ankle and foot	15447
3	N05z711	Ankle osteoarthritis NOS	52897
3	N05z712	Foot osteoarthritis NOS	1312
3	N05z713	Toe osteoarthritis NOS	4878
3	N05z800	Osteoarthritis NOS, other specified site	15052
3	N05z900	Osteoarthritis NOS, of shoulder	5802
3	N05zA00	Osteoarthritis NOS, of sternoclavicular joint	3814
3	N05zB00	Osteoarthritis NOS, of acromioclavicular joint	2229
3	N05zC00	Osteoarthritis NOS, of elbow	19713
3	N05zD00	Osteoarthritis NOS, of distal radio-ulnar joint	65748
3	N05zE00	Osteoarthritis NOS, of wrist	9649
3	N05zF00	Osteoarthritis NOS, of MCP joint	7866
3	N05zG00	Osteoarthritis NOS, of PIP joint of finger	11032
3	N05zH00	Osteoarthritis NOS, of DIP joint of finger	9681
3	N05zJ00	Osteoarthritis NOS, of hip	6812
3	N05zK00	Osteoarthritis NOS, of sacro-iliac joint	34023
3	N05zL00	Osteoarthritis NOS, of knee	2487
3	N05zM00	Osteoarthritis NOS, of tibio-fibular joint	70425
3	N05zN00	Osteoarthritis NOS, of ankle	8202
3	N05zP00	Osteoarthritis NOS, of subtalar joint	40972

3	N05zQ00	Osteoarthritis NOS, of talonavicular joint	55388
3	N05zR00	Osteoarthritis NOS, of other tarsal joint	54350
3	N05zS00	Osteoarthritis NOS, of 1st MTP joint	6887
3	N05zT00	Osteoarthritis NOS, of lesser MTP joint	9010
3	N05zU00	Osteoarthritis NOS, of IP joint of toe	27834
3	N05zz00	Osteoarthritis NOS	27972
3	N060.11	Endemic polyarthritis	96456
3	N061.00	Traumatic arthropathy	15174
3	N061000	Traumatic arthropathy of unspecified site	23879
3	N061100	Traumatic arthropathy of the shoulder region	33463
3	N061200	Traumatic arthropathy of the upper arm	72766
3	N061300	Traumatic arthropathy of the forearm	70832
3	N061400	Traumatic arthropathy of the hand	67649
3	N061500	Traumatic arthropathy of the pelvic region and thigh	100720
3	N061600	Traumatic arthropathy of the lower leg	23818
3	N061700	Traumatic arthropathy of the ankle and foot	56341
3	N061800	Traumatic arthropathy of other specified site	72984
3	N061900	Traumatic arthropathy of multiple sites	98846
3	N061A00	Traumatic arthropathy of shoulder	60069
3	N061B00	Traumatic arthropathy of sternoclavicular joint	72799
3	N061C00	Traumatic arthropathy of acromioclavicular joint	72800
3	N061D00	Traumatic arthropathy-elbow	73127
3	N061F00	Traumatic arthropathy-wrist	62433
3	N061G00	Traumatic arthropathy of MCP joint	73081
3	N061H00	Traumatic arthropathy of PIP joint of finger	102716
3	N061K00	Traumatic arthropathy-hip	55762
3	N061L00	Traumatic arthropathy of sacro-iliac joint	73082
3	N061M00	Traumatic arthropathy-knee	59093
3	N061P00	Traumatic arthropathy-ankle	70130
3	N061Q00	Traumatic arthropathy of subtalar joint	95481
3	N061R00	Traumatic arthropathy of talonavicular joint	99531
3	N061S00	Traumatic arthropathy of other tarsal joint	109305
3	N061T00	Traumatic arthropathy of 1st MTP joint	67828
3	N061z00	Traumatic arthropathy NOS	65750
3	N062100	Allergic arthritis of the shoulder region	56249
3	N062300	Allergic arthritis of the forearm	96404
3	N062600	Allergic arthritis of the lower leg	73778
3	N062800	Allergic arthritis of other specified site	73749
3	N062900	Allergic arthritis of multiple sites	72240
3	N062z00	Allergic arthritis NOS	29465

3	N063.00	Climacteric arthritis	12410
3	N063.11	Menopausal arthritis	17051
3	N063000	Climacteric arthritis of unspecified site	55834
3	N063200	Climacteric arthritis of the upper arm	100054
3	N063400	Climacteric arthritis of the hand	69882
3	N063700	Climacteric arthritis of the ankle and foot	71838
3	N063800	Climacteric arthritis of other specified site	65722
3	N063900	Climacteric arthritis of multiple sites	70797
3	N063z00	Climacteric arthritis NOS	72249
3	N064.00	Transient arthropathy	10942
3	N064000	Transient arthropathy of unspecified site	70482
3	N064100	Transient arthropathy of the shoulder region	72626
3	N064200	Transient arthropathy of the upper arm	72223
3	N064400	Transient arthropathy of the hand	24602
3	N064500	Transient arthropathy of the pelvic region and thigh	69883
3	N064600	Transient arthropathy of the lower leg	52980
3	N064700	Transient arthropathy of the ankle and foot	57222
3	N064900	Transient arthropathy of multiple sites	62981
3	N064A00	Transient arthropathy of shoulder	61887
3	N064C00	Transient arthropathy of acromioclavicular joint	99513
3	N064D00	Transient arthropathy-elbow	104816
3	N064F00	Transient arthropathy-wrist	52906
3	N064G00	Transient arthropathy of MCP joint	99718
3	N064K00	Transient arthropathy-hip	44575
3	N064L00	Transient arthropathy of sacro-iliac joint	94284
3	N064M00	Transient arthropathy-knee	52979
3	N064T00	Transient arthropathy of 1st MTP joint	46031
3	N064z00	Transient arthropathy NOS	23648
3	N065.00	Unspecified polyarthropathy or polyarthritis	25020
3	N065.11	Polyarthropathy NEC	7454
3	N065000	Unspecified polyarthropathy of unspecified site	56322
3	N065100	Unspecified polyarthropathy of the shoulder region	62077
3	N065200	Unspecified polyarthropathy of the upper arm	57733
3	N065300	Unspecified polyarthropathy of the forearm	21309
3	N065400	Unspecified polyarthropathy of the hand	29655
3	N065500	Unspecified polyarthropathy of the pelvic region and thigh	100370
3	N065600	Unspecified polyarthropathy of the lower leg	63747
3	N065700	Unspecified polyarthropathy of the ankle and foot	62474
3	N065800	Unspecified polyarthropathy of other specified site	53871
3	N065900	Unspecified polyarthropathy of multiple sites	35629
3	N065A00	Generalised arthritis	17230

3	N065z00	Unspecified polyarthropathy or polyarthritis NOS	35936
3	N065z11	Polyarthritis	1670
3	N066.00	Unspecified monoarthritis	3853
3	N066000	Unspecified monoarthritis of unspecified site	63635
3	N066100	Unspecified monoarthritis of the shoulder region	15390
3	N066200	Unspecified monoarthritis of the upper arm	23812
3	N066300	Unspecified monoarthritis of the forearm	43652
3	N066400	Unspecified monoarthritis of the hand	29480
3	N066500	Unspecified monoarthritis of the pelvic region and thigh	64223
3	N066600	Unspecified monoarthritis of the lower leg	29949
3	N066700	Unspecified monoarthritis of the ankle and foot	29647
3	N066800	Unspecified monoarthritis of other specified site	40301
3	N066z00	Unspecified monoarthritis NOS	29443
3	N067.00	Ochronotic arthropathy	66305
3	N068.00	Haemophilic arthropathy	44535
3	N069.00	Arthropathy in neoplastic disease	103858
3	N06y.00	Other specified arthropathy	33500
3	N06y000	Other specified arthropathy of unspecified site	42887
3	N06y100	Other specified arthropathy of the shoulder region	28612
3	N06y200	Other specified arthropathy of the upper arm	106913
3	N06y300	Other specified arthropathy of the forearm	56306
3	N06y400	Other specified arthropathy of the hand	42408
3	N06y500	Other specified arthropathy of the pelvic region and thigh	44509
3	N06y600	Other specified arthropathy of the lower leg	70372
3	N06y700	Other specified arthropathy of the ankle and foot	65004
3	N06y800	Other specified arthropathy of other specified site	40314
3	N06y900	Other specified arthropathy of multiple sites	66723
3	N06yz00	Other specified arthropathy NOS	63820
3	N06z.00	Arthropathy NOS	2183
3	N06z.11	Arthritis	587
3	N06z000	Arthropathy NOS, of unspecified site	53314
3	N06z100	Arthropathy NOS, of the shoulder region	33674
3	N06z111	Shoulder arthritis NOS	8990
3	N06z200	Arthropathy NOS, of the upper arm	43308
3	N06z211	Elbow arthritis NOS	16591
3	N06z300	Arthropathy NOS, of the forearm	29425
3	N06z311	Wrist arthritis NOS	2474
3	N06z400	Arthropathy NOS, of the hand	23384
3	N06z411	Hand arthritis NOS	8969
3	N06z500	Arthropathy NOS, of the pelvic region and thigh	14733
3	N06z511	Hip arthritis NOS	7334
3	N06z600	Arthropathy NOS, of the lower leg	24909
3	N06z611	Knee arthritis NOS	2852
3	N06z700	Arthropathy NOS, of the ankle and foot	26382

3	N06z711	Ankle arthritis NOS	11257
3	N06z712	Foot arthritis NOS	3543
3	N06z800	Arthropathy NOS, of other specified site	11742
3	N06z900	Arthropathy NOS, of multiple sites	23934
3	N06zA00	Acute arthritis	11269
3	N06zB00	Chronic arthritis	4652
3	N06zz00	Arthropathy NOS	25736
3	N090.11	Hydrarthrosis	35025
3	N090W00	Intermittent hydrarthrosis	60170
3	N091.00	Haemarthrosis	2120
3	N091000	Haemarthrosis of unspecified site	55063
3	N091100	Haemarthrosis of the shoulder region	65637
3	N091200	Haemarthrosis of the upper arm	73019
3	N091211	Elbow haemarthrosis	52140
3	N091300	Haemarthrosis of the forearm	44579
3	N091400	Haemarthrosis of the hand	41519
3	N091500	Haemarthrosis of the pelvic region and thigh	72202
3	N091511	Hip haemarthrosis	96830
3	N091600	Haemarthrosis of the lower leg	45685
3	N091611	Haemarthrosis of the knee	60791
3	N091700	Haemarthrosis of the ankle and foot	41649
3	N091711	Haemarthrosis of the ankle	97913
3	N091800	Haemarthrosis of other specified site	72200
3	N091900	Haemarthrosis of multiple joints	56767
3	N091A00	Haemarthrosis of shoulder	54228
3	N091D00	Haemarthrosis of elbow	44583
3	N091F00	Haemarthrosis of wrist	49323
3	N091H00	Haemarthrosis of PIP joint of finger	89918
3	N091K00	Haemarthrosis of hip	44607
3	N091M00	Haemarthrosis of knee	27871
3	N091N00	Haemarthrosis of tibio-fibular joint	71979
3	N091P00	Haemarthrosis of ankle	49321
3	N091Q00	Haemarthrosis of subtalar joint	95034
3	N091S00	Haemarthrosis of other tarsal joint	95010
3	N091V00	Haemarthrosis of IP joint of toe	41964
3	N091z00	Haemarthrosis NOS	61175
3	N093.12	Intermittent hydrarthrosis	49790
3	N100.00	Ankylosing spondylitis	2184
3	N100.11	Marie - Strumpell spondylitis	40946
3	N11..00	Spondylosis and allied disorders	2001

3	N11..11	Arthritis of spine	2294
3	N11..12	Osteoarthritis of spine	7429
3	N110.00	Cervical spondylosis without myelopathy	2881
3	N110.11	Cervical spondylosis	771
3	N110.12	Osteoarthritis cervical spine	17092
3	N110000	Single-level cervical spondylosis without myelopathy	38501
3	N110100	Two-level cervical spondylosis without myelopathy	51531
3	N110200	Multiple-level cervical spondylosis without myelopathy	15744
3	N111.00	Cervical spondylosis with myelopathy	8208
3	N111000	Single-level cervical spondylosis with myelopathy	27583
3	N111100	Two-level cervical spondylosis with myelopathy	63192
3	N111200	Multiple-level cervical spondylosis with myelopathy	58865
3	N112.00	Thoracic spondylosis without myelopathy	18217
3	N112.11	Thoracic spondylosis	5183
3	N112000	Single-level thoracic spondylosis without myelopathy	69912
3	N112100	Two-level thoracic spondylosis without myelopathy	62914
3	N112200	Multiple-level thoracic spondylosis without myelopathy	50448
3	N112300	Dorsal spondylosis without myelopathy	18205
3	N113.00	Thoracic spondylosis with myelopathy	55628
3	N113000	Single-level thoracic spondylosis with myelopathy	64854
3	N113200	Multiple-level thoracic spondylosis with myelopathy	96103
3	N114.00	Lumbosacral spondylosis without myelopathy	15015
3	N114.11	Degeneration of lumbar spine	1565
3	N114.12	Lumbar spondylosis	1100
3	N114000	Single-level lumbosacral spondylosis without myelopathy	20791
3	N114100	Two-level lumbosacral spondylosis without myelopathy	52991
3	N114200	Multiple-level lumbosacral spondylosis without myelopathy	37097
3	N115.00	Lumbosacral spondylosis with myelopathy	11688
3	N115000	Single-level lumbosacral spondylosis with myelopathy	41516
3	N115100	Two-level lumbosacral spondylosis with myelopathy	45730
3	N115200	Multiple-level lumbosacral spondylosis with myelopathy	63578
3	N117.00	Ankylosing vertebral hyperostosis	18579
3	N119.00	Cervical spondylosis with radiculopathy	10121
3	N119000	Single-level cervical spondylosis with radiculopathy	55810
3	N119100	Two-level cervical spondylosis with radiculopathy	51318
3	N119200	Multiple-level cervical spondylosis with radiculopathy	56212
3	N11A.00	Cervical spondylosis with vascular compression	35851
3	N11B.00	Thoracic spondylosis with radiculopathy	19386
3	N11B000	Single-level thoracic spondylosis with radiculopathy	54852
3	N11B200	Multiple-level thoracic spondylosis with radiculopathy	93977
3	N11C.00	Lumbosacral spondylosis with radiculopathy	9834
3	N11C000	Single-level lumbosacral spondylosis with radiculopathy	54843

3	N11C100	Two-level lumbosacral spondylosis with radiculopathy	65641
3	N11C200	Multiple-level lumbosacral spondylosis with radiculopathy	48810
3	N11D.00	Osteoarthritis of spine	18826
3	N11D000	Osteoarthritis of cervical spine	41378
3	N11D100	Osteoarthritis of thoracic spine	47024
3	N11D200	Osteoarthritis of lumbar spine	22452
3	N11D300	Osteoarthritis of spine NOS	53184
3	N11E.00	Cervical spondylosis	96948
3	N11z.00	Spondylosis NOS	3447
3	N11z.11	Osteoarthritis spine	829
3	N11z000	Spondylosis without myelopathy, NOS	56594
3	N11z100	Spondylosis with myelopathy, NOS	35838
3	N11zz00	Spondylosis NOS	17766
3	N212000	Periarthritis of shoulder	10555
3	N214200	Periarthritis of wrist	16583
3	N21z100	Periarthritis NOS	14900
3	N312.00	Hypertrophic pulmonary osteoarthropathy	6332
3	N338100	Pseudoarthrosis - fracture nonunion	12879
3	N33zC00	Pseudarthrosis after fusion or arthrodesis	42098
3	Nyu0100	[X]Arthritis+polyarthritis due/other specfd bacterial agents	96160
3	Nyu0500	[X]Reactive arthropathy in other diseases CE	73921
3	Nyu1000	[X]Rheumatoid arthritis+involvement/other organs or systems	106440
3	Nyu1100	[X]Other seropositive rheumatoid arthritis	93715
3	Nyu1200	[X]Other specified rheumatoid arthritis	70221
3	Nyu1500	[X]Other juvenile arthritis	94854
3	Nyu1700	[X]Other secondary gout	94539
3	Nyu1B00	[X]Other specified arthritis	69960
3	Nyu1G00	[X]Seropositive rheumatoid arthritis, unspecified	56202
3	Nyu2.00	[X]Arthrosis	18795
3	Nyu2000	[X]Other polyarthrosis	53741
3	Nyu2100	[X]Other primary coxarthrosis	10854
3	Nyu2400	[X]Other secondary coxarthrosis, bilateral	73948
3	Nyu2500	[X]Other primary gonarthrosis	43474
3	Nyu2511	[X] Unilateral primary gonarthrosis	24079
3	Nyu2700	[X]Other secondary gonarthrosis, bilateral	73952
3	Nyu2800	[X]Other secondary gonarthrosis	73930
3	Nyu2811	[X] Unilateral secondary gonarthrosis	24145
3	Nyu2D00	[X]Other specified arthrosis	51360
3	Nyu2E11	[X] Unilateral secondary coxarthrosis	24326
3	Nyu2F00	[X]Post-traumatic arthrosis of other joints	67336

3		Nyu6300	[X]Other spondylosis with radiculopathy	71477
3		Nyu6400	[X]Other spondylosis	55238
3		NyuC700	[X]Other hypertrophic osteoarthropathy	105535
3		PF6y600	Congenital pseudarthrosis of tibia	48469
3		ZR1U.00	Arthritis impact measurement scale	50535
3		ZR1U.11	AIMS - Arthritis impact measurement scale	100719
3		ZR1U200	Arthritis impact measurement scale II	67350
1		ZV13400	[V]Personal history of arthritis	10327
2		ZV7y100	[V]Screening for rheumatoid arthritis	6766

Atlantoaxial instability

metadata	category	readcode	readterm	medcode
Name: AtlantoaxialInstab_cprd	3	Nyu5700	[X]Other recurrent atlantoaxial subluxation	94363
Version: 1	3	N1y0.00	Recurrent atlantoaxial subluxation with myelopathy	8667
Source: CPRD	3	N14890	Cervical spine instability	31344
Author: C McKenna	3	N14880	Atlanto-axial instability	18171
Date: 19th October 2018	3	N14870	Atlanto-occipital instability	12669
Categories:	3	S570200	Atlanto-axial joint sprain	67908
1 = H/O	3	S498200	Closed subluxation atlanto-axial joint	31587
2= Probable	3	7J22700	Posterior fusion atlantoaxial joint us transarticular screw	99490
3 = Definite	3	7J22012	Gallie fusion of atlantoaxial joint	68082
	3	S499200	Open subluxation atlanto-axial joint	46597
	3	S490200	Closed dislocation atlanto-axial joint	47830
	3	7N94000	[SO]Atlanto-occipital joint	33893

Autism

metadata	category	readcode	readterm	medcode
Name: autism_cprd	3	E140.12	Autism	1276
Version: 1	3	Eu84500	[X]Asperger's syndrome	2950
Source: CPRD	3	Eu84000	[X]Childhood autism	3637
Author: C McKenna	3	E140.13	Childhood autism	7302
Date: 19th October 2018	3	Eu84011	[X]Autistic disorder	9982
Categories:	3	E140.00	Infantile autism	22098
1 = H/O	3	Eu84100	[X]Atypical autism	24044
2= Probable	3	1J9..00	Suspected autism	26343
3 = Definite	3	Eu84112	[X]Mental retardation with autistic features	34174
	3	E140z00	Infantile autism NOS	36662
	3	ZT4f400	Does not respond to communication by others	37888
	3	ZT4f200	Unable to responds to communication by others	40012

	3	Eu84z11	[X]Autistic spectrum disorder	42941
	3	E140.11	Kanner's syndrome	43444
	3	Eu84012	[X]Infantile autism	50337
	3	Eu84511	[X]Autistic psychopathy	51375
	3	ZT4f500	Difficulty responding to communication by others	52207
	3	E140000	Active infantile autism	63251
	3	E140100	Residual infantile autism	69016
	3	Eu84z00	[X]Pervasive developmental disorder, unspecified	44327
	3	Eu84.00	[X]Pervasive developmental disorders	7226
	3	Eu84y00	[X]Other pervasive developmental disorders	47948

Cataract

metadata	category	readcode	readterm	medcode
Name: cataract_cprd	1	1483.00	H/O: cataract	5518
Version: 1	3	7263.12	Extracapsular extraction of cataract	6330
Source: CPRD	3	7264.11	Intracapsular extraction of cataract	4260
Author: C McKenna	3	7266.11	Other extraction of cataract	5361
Date: 19th October 2018	3	7263011	Needling of lens for cataract	23883
Categories:	3	7266100	Discission of cataract	38641
1 = H/O	3	7267600	Cataract extraction and insertion of intraocular lens	103508
2= Probable	1	14N9.00	H/O: R cataract extraction	28513
3 = Definite	1	14NA.00	H/O: L cataract extraction	28515
	1	14NC.00	H/O: Bilateral cataract extraction	11970
	3	22E5.00	O/E - cataract present	1622
	3	2BT..00	Cataract observation	64196
	3	2BT0.00	O/E - Right cataract present	6547
	3	2BT1.00	O/E - Left cataract present	9931
	3	2BT2.00	O/E - Right cataract absent	21108
	3	8H5H.00	Referral for cataract extraction	11767
	3	8HTV.00	Referral to cataract clinic	11941
	3	8LC0.00	Cataract operation planned	94348
	3	C108F00	Insulin dependent diabetes mellitus with diabetic cataract	44260
	3	C108F11	Type I diabetes mellitus with diabetic cataract	17545
	3	C109E00	Non-insulin depend diabetes mellitus with diabetic cataract	69278
	3	C109E11	Type II diabetes mellitus with diabetic cataract	48192
	3	C109E12	Type 2 diabetes mellitus with diabetic cataract	44779
	3	C10EF00	Type 1 diabetes mellitus with diabetic cataract	49554
	3	C10EF12	Insulin dependent diabetes mellitus with diabetic cataract	100770
	3	C10FE00	Type 2 diabetes mellitus with diabetic cataract	44982
	3	C10FE11	Type II diabetes mellitus with diabetic cataract	93727
	3	F46..00	Cataract	296
	3	F460.00	Infantile, juvenile and presenile cataracts	41668

3	F460000	Unspecified infantile cataract	44794
3	F460100	Unspecified juvenile cataract	63491
3	F460200	Unspecified presenile cataract	57805
3	F460300	Anterior subcapsular polar cataract	59125
3	F460400	Posterior subcapsular polar cataract	4242
3	F460500	Cortical cataract	7257
3	F460600	Lamellar zonular cataract	45190
3	F460700	Nuclear cataract	7793
3	F460x00	Combined nonsenile cataract	94474
3	F460y00	Other nonsenile cataract	70403
3	F460z00	Nonsenile cataract NOS	58078
3	F461.00	Senile cataract	10010
3	F461000	Unspecified senile cataract	47566
3	F461200	Coronary cataract	50932
3	F461300	Punctate cataract	26097
3	F461400	Incipient cataract NOS	48148
3	F461500	Immature cataract NOS	23631
3	F461600	Anterior subcapsular polar senile cataract	92358
3	F461700	Posterior subcapsular polar senile cataract	5325
3	F461800	Cortical senile cataract	22022
3	F461900	Nuclear senile cataract	6876
3	F461A00	Total, mature senile cataract	33793
3	F461B00	Hypermature cataract	51162
3	F461B11	Morgagni cataract	63640
3	F461x00	Combined senile cataract	70257
3	F461y00	Other senile cataract	49085
3	F461z00	Senile cataract NOS	29770
2	F462.00	Traumatic cataract	3897
2	F462000	Unspecified traumatic cataract	62605
3	F462200	Total traumatic cataract	73419
3	F462z00	Traumatic cataract NOS	50638
3	F463.00	Cataract secondary to ocular disease	48228
3	F463000	Unspecified cataracta complicata	62188
3	F463200	Cataract in eye inflammatory disorder	54130
3	F463300	Cataract with neovascularization	61325
3	F463400	Cataract in degenerative disorder	19371
3	F463z00	Cataract secondary to ocular disorder NOS	46169
3	F464.00	Cataract due to other disorder	71291
3	F464000	Diabetic cataract	10659
3	F464100	Tetanic cataract	45952
3	F464200	Myotonic cataract	60883
3	F464300	Cataract associated with other syndromes	58625
3	F464400	Drug induced cataract	58120
3	F464600	Radiation induced cataract	66093

3	F464z00	Cataract due to other disorder NOS	94430
3	F465.00	After cataract	33482
3	F465000	Unspecified secondary cataract	24467
3	F465200	Other after cataract with vision normal	89585
3	F465300	After-cataract with vision obscured	26850
3	F465z00	After cataract NOS	44487
3	F466.00	Bilateral cataracts	703
3	F46y.00	Other cataract	4358
3	F46yz00	Other cataract NOS	15589
3	F46z.00	Cataract NOS	6317
3	F46z000	Immature cortical cataract	44294
3	F4B4B00	Keratopathy following cataract surgery	104553
3	F4B4C00	Bullous aphakic keratopathy following cataract surgery	105971
3	F4K2D00	Vitreous syndrome following cataract surgery	42452
3	FyuE000	[X]Other senile cataract	101939
3	FyuE100	[X]Other specified cataract	70201
3	FyuE400	[X]Cataract in other diseases classified elsewhere	49297
3	P33..00	Congenital cataract and lens anomalies	4148
3	P330.00	Congenital cataract, unspecified	299
3	P331.00	Capsular and subcapsular cataract	59914
3	P331000	Capsular cataract	18089
3	P331100	Subcapsular cataract	11255
3	P331z00	Capsular or subcapsular cataract NOS	88738
3	P332.00	Cortical and zonular cataract	96385
3	P332000	Cortical cataract - congenital	60425
3	P332100	Zonular cataract	63429
3	P332z00	Cortical or zonular cataract NOS	98962
3	P333.00	Nuclear cataract - congenital	63212
3	P334000	Total congenital cataract	39081
3	P334z00	Total or subtotal congenital cataract NOS	71623
3	P33y.00	Other specified congenital cataract or lens anomaly	70700
3	P33y000	Blue dot cataract	27898
3	P33y100	Congenital membranous cataract	99424
3	P33yz00	Other congenital cataract or lens anomaly NOS	90279
3	P33z.00	Congenital cataract or lens anomaly NOS	45926
3	ZV45611	[V]State following cataract extraction	4459
3	ZV7A200	[V]Screening for cataract	17983

Chronic kidney disease

metadata Name:	category	readcode	readterm	medcode
chronicKidneyDisease_cprd	1	14D1.00	H/O: nephritis	8828
Version: 1	1	14V2.00	H/O: renal dialysis	20196

Source: CPRD	1	14V2.11	H/O: kidney dialysis	44422
Author: C McKenna	3	1Z1..00	Chronic renal impairment	12720
Date: 19th October 2018	3	1Z10.00	Chronic kidney disease stage 1	29013
Categories:	3	1Z11.00	Chronic kidney disease stage 2	12586
1 = H/O	3	1Z12.00	Chronic kidney disease stage 3	12566
2= Probable	3	1Z13.00	Chronic kidney disease stage 4	12479
3 = Definite	3	1Z14.00	Chronic kidney disease stage 5	12585
	3	1Z15.00	Chronic kidney disease stage 3A	94965
	3	1Z16.00	Chronic kidney disease stage 3B	95179
	3	1Z17.00	Chronic kidney disease stage 1 with proteinuria	94789
	3	1Z17.11	CKD stage 1 with proteinuria	97980
	3	1Z18.00	Chronic kidney disease stage 1 without proteinuria	95572
	3	1Z19.00	Chronic kidney disease stage 2 with proteinuria	95146
	3	1Z19.11	CKD stage 2 with proteinuria	97979
	3	1Z1A.00	Chronic kidney disease stage 2 without proteinuria	95121
	3	1Z1A.11	CKD stage 2 without proteinuria	97978
	3	1Z1B.00	Chronic kidney disease stage 3 with proteinuria	94793
	3	1Z1B.11	CKD stage 3 with proteinuria	95145
	3	1Z1C.00	Chronic kidney disease stage 3 without proteinuria	95123
	3	1Z1C.11	CKD stage 3 without proteinuria	95188
	3	1Z1D.00	Chronic kidney disease stage 3A with proteinuria	95408
	3	1Z1D.11	CKD stage 3A with proteinuria	95571
	3	1Z1E.00	Chronic kidney disease stage 3A without proteinuria	95175
	3	1Z1E.11	CKD stage 3A without proteinuria	95176
	3	1Z1F.00	Chronic kidney disease stage 3B with proteinuria	95178
	3	1Z1F.11	CKD stage 3B with proteinuria	95180
	3	1Z1G.00	Chronic kidney disease stage 3B without proteinuria	95177
	3	1Z1G.11	CKD stage 3B without proteinuria	100633
	3	1Z1H.00	Chronic kidney disease stage 4 with proteinuria	95122
	3	1Z1J.00	Chronic kidney disease stage 4 without proteinuria	95406
	3	1Z1J.11	CKD stage 4 without proteinuria	97587
	3	1Z1K.00	Chronic kidney disease stage 5 with proteinuria	95508
	3	1Z1L.00	Chronic kidney disease stage 5 without proteinuria	95405
	3	1Z1L.11	CKD stage 5 without proteinuria	97683
	3	4N2..00	Dialysis fluid glucose level	86419
	3	7A60600	Creation of graft fistula for dialysis	60302
	3	7A61900	Ligation of arteriovenous dialysis fistula	96347
	3	7B00.00	Transplantation of kidney	2997
	3	7B00000	Autotransplant of kidney	55151
	3	7B00100	Transplantation of kidney from live donor	11745

3	7B00111	Allotransplantation of kidney from live donor	66705
3	7B00200	Transplantation of kidney from cadaver	24361
3	7B00211	Allotransplantation of kidney from cadaver	98364
3	7B00300	Allotransplantation of kidney from cadaver, heart-beating	89924
3	7B00y00	Other specified transplantation of kidney	70874
3	7B00z00	Transplantation of kidney NOS	5504
3	7B01.00	Total nephrectomy	867
3	7B01.11	Total excision of kidney	7568
3	7B01000	Radical nephrectomy	6136
3	7B01011	Nephrectomy and excision of perirenal tissue	68574
3	7B01100	Nephroureterectomy-unspecified	1600
3	7B01200	Bilateral nephrectomy	51039
3	7B01300	Heminephrectomy for horseshoe kidney	34834
3	7B01311	Excision of half of horseshoe kidney	60919
3	7B01400	Simple nephrectomy - other	29120
3	7B01500	Transplant nephrectomy	48121
3	7B01511	Excision of rejected transplanted kidney	72004
3	7B01600	Simple nephrectomy -live donor	37007
3	7B01700	Nephroureterectomy with open lower ureterectomy	35225
3	7B01800	Nephroureterectomy with pluck lower ureterectomy	49535
3	7B01y00	Other specified total nephrectomy	56892
3	7B01z00	Total nephrectomy NOS	34366
3	7B06300	Exploration of renal transplant	26862
3	7L1A.11	Dialysis for renal failure	11773
3	7L1A000	Renal dialysis	20073
3	7L1A100	Peritoneal dialysis	2994
3	7L1A200	Haemodialysis NEC	2996
3	7L1A400	Automated peritoneal dialysis	88597
3	7L1A500	Continuous ambulatory peritoneal dialysis	30756
3	7L1A600	Peritoneal dialysis NEC	64828
3	7L1B.11	Placement ambulatory dialysis apparatus - compens renal fail	36442
3	7L1B000	Insertion of ambulatory peritoneal dialysis catheter	8037

3	7L1B100	Removal of ambulatory peritoneal dialysis catheter	23773
3	7L1C000	Insertion of temporary peritoneal dialysis catheter	30709
3	8L50.00	Renal transplant planned	17253
3	A786.00	Haemorrhagic nephrosonephritis	67197
3	A844100	Plasmodium malariae malaria with nephropathy	49046
3	C104.00	Diabetes mellitus with renal manifestation	16502
3	C104.11	Diabetic nephropathy	2475
3	C104000	Diabetes mellitus, juvenile type, with renal manifestation	93922
3	C104100	Diabetes mellitus, adult onset, with renal manifestation	35105
3	C104y00	Other specified diabetes mellitus with renal complications	13279
3	C104z00	Diabetes mellitis with nephropathy NOS	35107
3	C108000	Insulin-dependent diabetes mellitus with renal complications	46963
3	C108011	Type I diabetes mellitus with renal complications	61344
3	C108012	Type 1 diabetes mellitus with renal complications	21983
3	C108D00	Insulin dependent diabetes mellitus with nephropathy	57621
3	C108D11	Type I diabetes mellitus with nephropathy	66872
3	C109000	Non-insulin-dependent diabetes mellitus with renal comps	52303
3	C109011	Type II diabetes mellitus with renal complications	50225
3	C109012	Type 2 diabetes mellitus with renal complications	18209
3	C109C00	Non-insulin dependent diabetes mellitus with nephropathy	59365
3	C109C11	Type II diabetes mellitus with nephropathy	64571
3	C109C12	Type 2 diabetes mellitus with nephropathy	24836
3	C10E000	Type 1 diabetes mellitus with renal complications	47582
3	C10ED00	Type 1 diabetes mellitus with nephropathy	10418
3	C10EK00	Type 1 diabetes mellitus with persistent proteinuria	30323
3	C10EL00	Type 1 diabetes mellitus with persistent microalbuminuria	30294
3	C10F000	Type 2 diabetes mellitus with renal complications	18777
3	C10F011	Type II diabetes mellitus with renal complications	57278
3	C10FC00	Type 2 diabetes mellitus with nephropathy	12640
3	C10FL00	Type 2 diabetes mellitus with persistent proteinuria	26054
3	C10FL11	Type II diabetes mellitus with persistent proteinuria	60796
3	C10FM00	Type 2 diabetes mellitus with persistent microalbuminuria	18390
3	C10FM11	Type II diabetes mellitus with persistent microalbuminuria	85991

3	D310100	Henoch-Schonlein nephritis	22897
3	K0...00	Nephritis, nephrosis and nephrotic syndrome	2773
3	K00..00	Acute glomerulonephritis	2088
3	K00..11	Acute nephritis	5417
3	K000.00	Acute proliferative glomerulonephritis	29384
3	K001.00	Acute nephritis with lesions of necrotising glomerulitis	67460
3	K00y.00	Other acute glomerulonephritis	63599
3	K00y000	Acute glomerulonephritis in diseases EC	20027
3	K00y100	Acute exudative nephritis	94261
3	K00y200	Acute focal nephritis	48261
3	K00y300	Acute diffuse nephritis	55100
3	K00yz00	Other acute glomerulonephritis NOS	47838
3	K00z.00	Acute glomerulonephritis NOS	20129
3	K01..00	Nephrotic syndrome	2999
3	K010.00	Nephrotic syndrome with proliferative glomerulonephritis	9840
3	K011.00	Nephrotic syndrome with membranous glomerulonephritis	1803
3	K012.00	Nephrotic syndrome+membranoproliferative glomerulonephritis	99644
3	K013.00	Nephrotic syndrome with minimal change glomerulonephritis	29634
3	K013.11	Lipoid nephrosis	40349
3	K013.12	Steroid sensitive nephrotic syndrome	57926
3	K014.00	Nephrotic syndrome, minor glomerular abnormality	23913
3	K015.00	Nephrotic syndrome, focal and segmental glomerular lesions	22852
3	K016.00	Nephrotic syndrome, diffuse membranous glomerulonephritis	19316
3	K017.00	Nephrotic syn difus mesangial prolifertiv glomerulonephritis	21947
3	K018.00	Nephrotic syn,difus endocapilary proliftv glomerulonephritis	50472
3	K019.00	Nephrotic syn,diffuse mesangiocapillary glomerulonephritis	21989
3	K01A.00	Nephrotic syndrome, dense deposit disease	56987
3	K01B.00	Nephrotic syndrome, diffuse crescentic glomerulonephritis	17365
3	K01w.00	Congenital nephrotic syndrome	63786
3	K01w000	Finnish nephrosis syndrome	72303
3	K01x000	Nephrotic syndrome in amyloidosis	47922
3	K01x100	Nephrotic syndrome in diabetes mellitus	2471
3	K01x111	Kimmelstiel - Wilson disease	45499
3	K01x200	Nephrotic syndrome in malaria	99201
3	K01x300	Nephrotic syndrome in polyarteritis nodosa	58750

3	K01x400	Nephrotic syndrome in systemic lupus erythematosus	47672
3	K01x411	Lupus nephritis	22205
3	K01y.00	Nephrotic syndrome with other pathological kidney lesions	94373
3	K01z.00	Nephrotic syndrome NOS	27427
3	K02..00	Chronic glomerulonephritis	7804
3	K02..11	Nephritis - chronic	10647
3	K02..12	Nephropathy - chronic	11875
3	K020.00	Chronic proliferative glomerulonephritis	34998
3	K021.00	Chronic membranous glomerulonephritis	10809
3	K022.00	Chronic membranoproliferative glomerulonephritis	61494
3	K023.00	Chronic rapidly progressive glomerulonephritis	65064
3	K02y.00	Other chronic glomerulonephritis	60960
3	K02y000	Chronic glomerulonephritis + diseases EC	97758
3	K02y200	Chronic focal glomerulonephritis	4669
3	K02y300	Chronic diffuse glomerulonephritis	65400
3	K02yz00	Other chronic glomerulonephritis NOS	63615
3	K02z.00	Chronic glomerulonephritis NOS	15097
3	K03..00	Nephritis and nephropathy unspecified	33580
3	K03..11	Nephritis and nephropathy unspecified	4850
3	K03..12	Nephropathy, unspecified	11873
3	K030.00	Proliferative nephritis unspecified	16008
3	K031.00	Membranous nephritis unspecified	5291
3	K032.00	Membranoproliferative nephritis unspecified	12465
3	K032000	Focal membranoproliferative glomerulonephritis	67995
3	K032300	Anaphylactoid glomerulonephritis	62868
3	K032400	Familial glomerulonephritis in Alport's syndrome	24384
3	K032500	Other familial glomerulonephritis	57072
3	K032600	Berger's IgA or IgG nephropathy	21423
3	K032y00	Nephritis unsp+OS membranoprolif glomerulonephritis lesion	67193
3	K032y11	Hypocomplementaemic persistent glomerulonephritis NEC	50305
3	K032y13	Mesangioproliferative glomerulonephritis NEC	36342
3	K032y14	Mesangiocapillary glomerulonephritis NEC	41881
3	K032y15	Mixed membranous and proliferative glomerulonephritis NEC	97388
3	K032z00	Nephritis unsp+membranoprolif glomerulonephritis lesion NOS	94350
3	K033.00	Rapidly progressive nephritis unspecified	58164
3	K03T.00	Tubulo-interstit nephritis, not specif as acute or chron	23990
3	K03U.00	Unspecif nephr synd, diff concentric glomerulonephritis	36125

3	K03V.00	Unspecified nephritic syndrome, dense deposit disease	60128
3	K03W.00	Unsp nephrit synd, diff endocap prolif glomerulonephritis	62520
3	K03X.00	Unsp nephrit synd, diff mesang prolif glomerulonephritis	30301
3	K03y.00	Other nephritis and nephrosis unspecified	35065
3	K03y000	Other nephritis and nephrosis in diseases EC	27335
3	K03y200	Other interstitial nephritis	34669
3	K03yz00	Other nephritis and nephrosis NOS	44055
3	K03z.00	Unspecified glomerulonephritis NOS	5182
3	K05..00	Chronic renal failure	512
3	K05..11	Chronic uraemia	10081
3	K05..12	End stage renal failure	53852
3	K050.00	End stage renal failure	6712
3	K072.00	Glomerulosclerosis	7190
3	K08y500	Acute interstitial nephritis	9379
3	K0A..00	Glomerular disease	8668
3	K0A0.00	Acute nephritic syndrome	31581
3	K0A0100	Acute nephritic syndrome, focal+segmental glomerular lesions	66136
3	K0A0200	Acute nephritic syn, diffuse membranous glomerulonephritis	66503
3	K0A0300	Acut neph syn, diffuse mesangial prolifrative glomnephritis	55389
3	K0A0500	Acute neph syn, diffuse mesangiocapillary glomerulonephritis	54312
3	K0A0700	Acute nephrotic syndrm diffuse crescentic glomerulonephritis	61814
3	K0A1.00	Rapidly progressive nephritic syndrome	71174
3	K0A1100	Rapid progres nephritic syn focal+segmental glomerulr lesion	97734
3	K0A1200	Rapid progres neph syn diffuse membranous glomerulonephritis	41285
3	K0A1300	Rpd prog neph syn df mesangial prolifratv glomerulonephritis	58060
3	K0A1600	Rapid progressive nephritic syndrome, dense deposit disease	50200
3	K0A1700	Rapid progres nephritic syn df crescentic glomerulonephritis	62320
3	K0A2000	Recurrent+persistnt haematuria minor glomerular abnormality	95546
3	K0A2100	Recur+persist haematuria, focal+segmental glomerular lesions	68364
3	K0A2200	Recur+persist haematuria difus membranous glomerulonephritis	61317
3	K0A2300	Recur+persist haemuria df mesangial prolif glomerulnephritis	49642
3	K0A2500	Recur+persist hmuria df mesangiocapilary glomerulonephritis	60484
3	K0A2700	Recur+persist haematuria difus crescentic glomerulonephritis	60856
3	K0A2800	IgA nephropathy	85659

3	K0A3.00	Chronic nephritic syndrome	21297
3	K0A3000	Chronic nephritic syndrome, minor glomerular abnormality	66505
3	K0A3100	Chronic nephritic syndrm focal+segmental glomerular lesions	40413
3	K0A3200	Chron nephritic syndrom difuse membranous glomerulonephritis	57168
3	K0A3300	Chron neph syn difus mesangial prolifrtiv glomerulonephritis	56893
3	K0A3500	Chronic neph syn difus mesangiocapillary glomerulonephritis	73026
3	K0A3600	Chronic nephritic syndrome, dense deposit disease	60198
3	K0A3700	Chronic nephritic syn diffuse crescentic glomerulonephritis	60857
3	K0A5000	Hereditary nephropathy NEC, minor glomerular abnormality	51113
3	K0A5100	Hereditary nephropathy NEC,focal+segmnt glomerular lesion	41239
3	K0A5200	Hereditry nephropathy NEC,difus membran glomerulnephritis	44270
3	K0A5600	Hereditary nephropathy, NEC, dense deposit disease	91738
3	K0D..00	End-stage renal disease	8330
3	K0y..00	Other specified nephritis, nephrosis or nephrotic syndrome	49150
3	K0z..00	Nephritis, nephrosis and nephrotic syndrome NOS	15780
3	K190X00	Persistent proteinuria, unspecified	16465
3	Kyu0900	[X]Unsp nephrit synd, diff mesang prolif glomerulonephritis	71709
3	Kyu5G00	[X]Persistent proteinuria, unspecified	64030
3	SP01500	Mechanical complication of dialysis catheter	48639
3	SP05613	[X] Peritoneal dialysis associated peritonitis	46438
3	SP07G00	Stenosis of arteriovenous dialysis fistula	59315
3	TA02000	Accid cut,puncture,perf,h'ge - kidney dialysis	96184
3	TA22000	Failure of sterile precautions during kidney dialysis	69266
3	TB00100	Kidney transplant with complication, without blame	54990
3	TB00111	Renal transplant with complication, without blame	18774
3	TB11.00	Kidney dialysis with complication, without blame	28158
3	TB11.11	Renal dialysis with complication, without blame	66714
3	Z1A2.00	Haemodialysis training	74905
3	Z919.00	Care of haemodialysis equipment	60446
3	Z919100	Priming haemodialysis lines	72336
3	Z919300	Reversing haemodialysis lines	60498
3	Z91A.00	Peritoneal dialysis bag procedure	63502
3	ZV42000	[V]Kidney transplanted	5911

3	ZV45100	[V]Renal dialysis status	22252
3	ZV56.00	[V]Aftercare involving intermittent dialysis	60743
3	ZV56011	[V]Aftercare involving renal dialysis NOS	46145
3	ZV56100	[V]Preparatory care for dialysis	52088
3	ZV56y00	[V]Other specified aftercare involving intermittent dialysis	63488
3	ZV56y11	[V]Aftercare involving peritoneal dialysis	45160
3	ZV56z00	[V]Unspecified aftercare involving intermittent dialysis	63038
3	ZVu3G00	[X]Other dialysis	69760

Coeliac disease

metadata	category	readcode	readterm	medcode
Name: coeliac_cprd	3	J690.00	Coeliac disease	1515
Version: 1	3	J690.13	Gluten enteropathy	3509
Source: CPRD	3	8B55.00	Gluten-free diet	5662
Author: C McKenna	3	13B2.00	Gluten free diet	5664
Date: 19th October 2018	3	J690.18	Gluten intolerance	12217
Categories:	3	8CA4200	Pt advised re gluten free diet	18729
1 = H/O	3	J690z00	Coeliac disease NOS	44310
2= Probable	3	ZC2C200	Dietary advice for coeliac disease	45925
3 = Definite	3	J690000	Congenital coeliac disease	62397
	3	J690100	Acquired coeliac disease	63195
	2	J695.00	Non-coeliac gluten sensitivity	97008
	2	J695.11	Non-coeliac gluten intolerance	97144
	3	68W4.00	Coeliac disease autoantibody profile positive	98297
	3	6648.00	Coeliac disease monitoring	102315
	3	6648000	Coeliac disease annual review	102617
	3	8IAp.00	Coeliac disease annual review declined	103379
	3	9mB..00	Coeliac disease monitoring invitation	106282
	3	9mB1.00	Coeliac disease monitoring invitation first letter	106326
	3	13YB.00	Coeliac UK member	107845

Congenital cardiac disease

metadata	category	readcode	readterm	medcode
Name: CongenCardiac_cprd	3	7902.00	Correction of tetralogy of Fallot	5477
Version: 1	3	7902.11	Repair of tetralogy of Fallot	12844
Source: CPRD	3	7903.00	Atrial inversion ops for transposition of great vessels	6945
Author: C McKenna	3	7903.12	Senning correction for transposition of great vessels	37987
Date: 19th October 2018	3	7903.13	Atrial inversion operations for transposition of great art	89968
Categories:	3	7904.00	Other correction of transposition of great vessels	28355

1 = H/O	3	7905.00	Correction of total anomalous pulmonary venous connection	28943
2= Probable	3	7906.00	Closure of defect of atrioventricular septum	32163
3 = Definite	3	7906.11	Repair of defect of the atrioventricular septum	73476
	3	7907.00	Closure of defect of interatrial septum	34902
	3	7908.00	Closure of defect of interventricular septum	36575
	3	7909.00	Closure of defect of unspecified septum of heart	30340
	3	2126800	Ostium secundum atrial septal defect resolved	104307
	3	7902000	Correct Fallot tetralogy- valved right ventr outflow conduit	16538
	3	7902100	Correct Fallot tetralogy- right ventric outflow conduit NEC	73029
	3	7902200	Correct Fallot tetralogy- right ventricular outflow patch	99198
	3	7902300	Revision of correction of tetralogy of Fallot	70857
	3	7902400	Repair of tetralogy of Fallot using transannular patch	88842
	3	7902500	Repair of tetralogy of Fallot with absent pulmonary valve	88479
	3	7902600	Repair Fallot-type pulmonary atresia aortopulmonary collater	93719
	3	7906400	Primary closure of defect of atrioventricular septum NEC	48331
	3	7906500	Revision of closure of defect of atrioventricular septum	39885
	3	7908100	Close defect interventricular septum using pericardial patch	50626
	3	7908500	Closure of multiple interventricular septal defects	94023
	3	7908511	Repair of multiple interventricular septal defects	98273
	3	7908600	Closure interventricular septal defect us intraop trans pros	65234
	3	7908611	Repair interventricular septal defect us intraop trans pros	92020
	3	7910213	Carpentier prosthetic replacement of mitral valve	49592
	1	14AV.00	History of ventricular septal defect	99786
	1	14H1.00	H/O: cardiac anomaly	18820
	3	24M..00	Spontaneous closure of ventricular septal defect	104345
	3	66g..00	Congenital heart condition monitoring	72576
	3	790..00	Heart wall, septum and chamber operations	39810
	3	7902y00	Other specified correction of tetralogy of Fallot	65401
	3	7902z00	Correction of tetralogy of Fallot NOS	19956
	3	7902z11	Repair of tetralogy of Fallot NOS	108402
	3	7903y00	Atrial inversion op for transposition of great vessels OS	69200
	3	7903z00	Atrial inversion op for transposition of great vessels NOS	58886
	3	7904y00	Other correction of transposition of great vessels OS	64470
	3	7904z00	Other correction of transposition of great vessels NOS	38411
	3	7905y00	Correction of total anomalous pulmonary venous connection OS	105154
	3	7905z00	Correction total anomalous pulmonary venous connection NOS	73820
	3	7906y00	Other specified closure of defect of atrioventricular septum	57270
	3	7906z00	Closure of defect of atrioventricular septum NOS	38436

3	7907z00	Closure of defect of interatrial septum NOS	16191
3	790F100	Correction of partial anomalous pulmonary venous drainage	44117
3	790F200	Repair of cor triatriatum	99829
3	790G100	Repair of atrium NEC	73602
3	790J.00	Other repair of transposition of great arteries	90605
3	790Jz00	Other repair of transposition of great arteries NOS	108021
3	790K.00	Repair of double outlet ventricle	89231
3	790K100	Repair of Fallot-type double outlet right ventricle	107122
3	790K200	Repair of double outlet right ventricle	98443
3	790M400	Biventricular repair of hypoplastic left heart syndrome	96637
3	791A200	Repair of subaortic stenosis	20940
3	791A300	Repair of supraaortic stenosis	62293
3	7A00000	Correction of persistent truncus arteriosus	56081
3	7A01.00	Open correction of patent ductus arteriosus	21090
3	7A01.11	Open correction of patent ductus arteriosus (PDA)	7342
3	7A01000	Division of patent ductus arteriosus	50019
3	7A01100	Ligation of patent ductus arteriosus	9573
3	7A01200	Closure of patent ductus arteriosus NEC	36668
3	7A01300	Revision of correction of patent ductus arteriosus	63163
3	7A01y00	Other specified open correction of patent ductus arteriosus	106081
3	7A01z00	Open correction of patent ductus arteriosus NOS	2728
3	7A02000	Percut transluminal prosth occlusion patent ductus arterios	12889
3	7A02011	Percut translum prosth occlus patent ductus arteriosus (PDA)	19188
3	7A18111	Hamilton repair coarctation of aorta using subclavian flap	92330
3	7A18600	Repair of interrupted aortic arch	67046
3	9NiY.00	Did not attend congenital heart disease clinic	104046
3	9RD0.00	Transfer of care from paediatric congenital heart service	63297
3	G130.00	Mitral and aortic stenosis	8274
3	G361.00	Atrial septal defect/curr comp folow acut myocardal infarct	23708
3	G362.00	Ventric septal defect/curr comp fol acut myocardal infarctn	37657
3	G541100	Aortic stenosis, non-rheumatic	999
3	G541300	Aortic stenosis alone, cause unspecified	2343
3	G541500	Aortic stenosis	9591
3	G543z00	Pulmonary valve disorders NOS	19957
3	G551.00	Hypertrophic obstructive cardiomyopathy	8010
3	G554011	Congestive obstructive cardiomyopathy	68766
3	G554400	Primary dilated cardiomyopathy	7535
3	G558200	Dystrophic cardiomyopathy	64837
3	G5y9.00	Cardiac septal defect, acquired	29180
3	Gyu1000	[X]Other mitral valve diseases	53756
3	L185.11	Congenital heart disease in pregnancy	61935

3	P5...00	Bulbus cordis and cardiac septal closure anomalies	31518
3	P5...11	Cardiac septal defects	21943
3	P5...12	Congenital heart disease, septal and bulbar anomalies	23754
3	P5...13	Heart septal defects	18785
3	P5…13	Heart septal defects	18785
3	P50..00	Common aorto-pulmonary trunk	4964
3	P50..11	Aortic septal defect	37405
3	P50..12	Common truncus	98893
3	P500.00	Absent septum between aorta and pulmonary artery	72604
3	P500.11	Persistent truncus arteriosus	61914
3	P500.12	Truncus arteriosus	45187
3	P501.00	Aortic septal defect	45505
3	P501.11	Aortopulmonary window	51418
3	P501.12	Aorticopulmonary septal defect	65330
3	P502.00	Persistent truncus arteriosus	66245
3	P502.11	Truncus arteriosus	41371
3	P50z.00	Common aorto-pulmonary trunk NOS	94344
3	P51..00	Transposition of great vessels	2816
3	P510.00	Total great vessel transposition	69858
3	P511.00	Double outlet right ventricle	1778
3	P511100	Dextratransposition of aorta	23988
3	P511200	Incomplete great vessel transposition	102980
3	P511300	Taussig-Bing syndrome	40025
3	P511z00	Double outlet right ventricle NOS	65318
3	P512.00	Corrected great vessel transposition	63390
3	P51y.00	Other specified transposition of great vessels	62169
3	P51y.11	Transposition of aorta	61100
3	P51z.00	Great vessel transposition NOS	73539
3	P51z.11	Transposition of arterial trunk NEC	100622
3	P52..00	Tetralogy of Fallot	4864
3	P520.00	Tetralogy of Fallot, unspecified	38967
3	P520.11	Ventricular septal defect in Fallot's tetralogy	23692
3	P520.12	Dextraposition of aorta in Fallot's tetralogy	71252
3	P521.00	Pentalogy of Fallot	51649
3	P52z.00	Tetralogy of Fallot NOS	63046
3	P53..00	Common ventricle	19969
3	P54..00	Ventricular septal defect	246
3	P540.00	Ventricular septal defect, unspecified	42132
3	P541.00	Interventricular septal defect	56575
3	P542.00	Left ventricle to right atrial communication	67657
3	P543.00	Eisenmenger's complex	9011
3	P544.00	Gerbode's defect	51897
3	P545.00	Roger's disease	20153
3	P54y.00	Other specified ventricular septal defect	54772

3	P54z.00	Ventricular septal defect NOS	34067
3	P55..00	Ostium secundum atrial septal defect	7474
3	P550.00	Atrial septal defect NOS	3255
3	P550.11	Auricular septal defect NOS	40673
3	P550.12	Interatrial septal defect NEC	28174
3	P550.13	Interauricular septal defect	72577
3	P551.00	Patent foramen ovale	3625
3	P552.00	Persistent ostium secundum	37816
3	P553.00	Lutembacher's syndrome	59144
3	P55y.00	Other specified ostium secundum atrial septal defect	53088
3	P55y.11	Other specified atrial septal defect	18395
3	P55z.00	Ostium secundum atrial septal defect NOS	54243
3	P56..00	Endocardial cushion defects	63340
3	P561.00	Ostium primum defect	51053
3	P561.11	Persistent ostium primum	93161
3	P56y.00	Other specified endocardial cushion defects	101393
3	P56z.00	Endocardial cushion defects NOS	49702
3	P56z000	Common atrium	55535
3	P56z011	Cor triloculare biventriculare	61715
3	P56z100	Common atrioventricular canal	43049
3	P56z200	Common atrioventricular-type ventricular septal defect	44896
3	P56zz00	Endocardial cushion defects NOS	73816
3	P58..00	Double outlet left ventricle	46117
3	P59..00	Isomerism of atrial appendages	9361
3	P5X..00	Congenital malforms of cardiac chambers+connections unsp	48205
3	P5y..00	Other heart bulb and septal closure defect	66401
3	P5z..00	Heart bulb or septal closure defects NOS	54196
3	P6...00	Other congenital heart anomalies	5621
3	P60..00	Pulmonary valve anomalies	39992
3	P600.00	Pulmonary valve anomaly, unspecified	69940
3	P601.00	Congenital atresia of the pulmonary valve	3862
3	P601000	Hypoplasia of pulmonary valve	54488
3	P601z00	Congenital atresia of pulmonary valve NOS	93561
3	P602.00	Congenital pulmonary stenosis	22778
3	P602100	Congenital fusion of pulmonary valve segment	45452
3	P602z00	Congenital pulmonary stenosis NOS	33919
3	P603.00	Right hypoplastic heart syndrome	21851
3	P603.11	Pseudotruncus arteriosus	68982
3	P60z.00	Other pulmonary valve anomalies	44478
3	P60z000	Congenital insufficiency of the pulmonary valve	107150
3	P60z100	Fallot's trilogy	52607
3	P60zz00	Other pulmonary valve anomaly NOS	70880
3	P61..00	Congenital tricuspid atresia and stenosis	12752

3	P610.00	Congenital tricuspid atresia	21272
3	P611.00	Congenital tricuspid stenosis	69169
3	P61z.00	Congenital tricuspid atresia or stenosis NOS	100065
3	P62..00	Ebstein's anomaly	23709
3	P63..00	Congenital aortic valve stenosis	6886
3	P64..00	Congenital aortic valve insufficiency	8636
3	P640.00	Congenital aortic valve insufficiency, unspecified	58734
3	P641.00	Bicuspid aortic valve	3300
3	P64z.00	Congenital aortic valve insufficiency NOS	6843
3	P65..00	Congenital mitral stenosis	57091
3	P65..11	Duroziez's disease	68888
3	P650.00	Congenital mitral stenosis, unspecified	90551
3	P651.00	Fused commissure of the mitral valve	73592
3	P652.00	Parachute deformity of the mitral valve	63069
3	P65z.00	Congenital mitral stenosis NOS	100291
3	P66..00	Congenital mitral insufficiency	61651
3	P67..00	Hypoplastic left heart syndrome	20772
3	P68..00	Congenital heart disease	89256
3	P6W..00	Congenital malformation of aortic and mitral valves unsp	46825
3	P6X..00	Congenital malformation of tricuspid valve, unspecified	50529
3	P6y..00	Other specified heart anomalies	24789
3	P6y0.00	Subaortic stenosis	16539
3	P6y1.00	Cor triatriatum	34668
3	P6y2.00	Pulmonary infundibular stenosis	9401
3	P6y3.00	Obstructive heart anomaly NEC	99128
3	P6y3000	Uhl's disease	32748
3	P6y3z00	Obstructive heart anomaly NEC NOS	97818
3	P6y4.00	Coronary artery anomaly	25481
3	P6y4000	Congenital absence of coronary artery	71956
3	P6y4100	Single coronary artery	62163
3	P6y4400	Anomalous coronary artery communication	31373
3	P6y4411	Congenital coronary arterio-venous fistula	28705
3	P6y4500	Congenital coronary aneurysm	49901
3	P6y4z00	Coronary artery anomaly NOS	53546
3	P6y5.00	Congenital heart block	24533
3	P6y5000	Congenital heart block, unspecified	68097
3	P6y5100	Congenital complete atrio-ventricular heart block	52310
3	P6y5200	Congenital incomplete atrio-ventricular heart block	102167
3	P6y5z00	Congenital heart block NOS	70992
3	P6y6.00	Heart and cardiac apex malposition	71678
3	P6y6.11	Ectopic heart	20466
3	P6y6000	Dextrocardia	3774
3	P6y6100	Levocardia	72259

3	P6y6111	Laevocardia	69556
3	P6y6200	Mesocardia	72405
3	P6y6300	Ectopia cordis	50284
3	P6y6z00	Heart or cardiac apex malposition NOS	92426
3	P6y7.00	Myocardial bridge of coronary artery	52615
3	P6yy.00	Other specified heart anomalies	24854
3	P6yy.11	Hypoplastic aortic orifice or valve	44767
3	P6yy.12	Hypoplasia of heart NOS	9232
3	P6yy000	Atresia of cardiac vein	93089
3	P6yy100	Hypoplasia of cardiac vein	68063
3	P6yy200	Congenital cardiomegaly	34007
3	P6yy300	Congenital left ventricular diverticulum	49133
3	P6yy400	Congenital pericardial defect	50362
3	P6yy411	Congenital absence of pericardium	101896
3	P6yy500	Congenital anomaly of myocardium	68894
3	P6yy700	Atresia of heart valve NEC	37451
3	P6yy900	Congenital epicardial cyst	23752
3	P6yyA00	Hemicardia	95785
3	P6yyC00	Fusion of mitral valve cusps	98317
3	P6yyz00	Other specified heart anomalies NOS	24714
3	P6z..00	Congenital heart anomaly NOS	247
3	P6z..11	Chiari's malformation	8279
3	P6z0.00	Unspecified anomaly of heart valve	26626
3	P6z1100	Anomalous ventricular bands	64778
3	P6z2.00	Acyanotic congenital heart disease NOS	38968
3	P6z3.00	Cyanotic congenital heart disease NOS	3863
3	P6z3.11	Blue baby	7262
3	P6zz.00	Congenital heart anomaly NOS	11982
3	P70..00	Patent ductus arteriosus	2727
3	P71..00	Coarctation of aorta	3301
3	P710.00	Hypoplasia of aortic arch, unspecified	57932
3	P711.00	Preductal coarctation of aorta	72295
3	P711.13	Preductal aortic stenosis	106756
3	P712.00	Postductal coarctation of aorta	70853
3	P712.12	Postductal interruption of aorta	64953
3	P712.13	Postductal aortic stenosis	49279
3	P713.00	Interruption of aortic arch	37323
3	P713.11	Stenosis of aortic arch	16731
3	P71z.00	Coarctation of aorta NOS	59907
3	P721.00	Aortic arch anomalies	30725
3	P721000	Anomalous origin of the aortic arch	67286
3	P721200	Double aortic arch	46530
3	P721600	Vascular ring, aorta	90486
3	P721z00	Aortic arch anomalies NOS	34176

3	P722400	Supra-valvular aortic stenosis	53964
3	P73..00	Pulmonary artery anomalies	11127
3	P732.00	Pulmonary artery atresia	31112
3	P733.00	Coarctation of the pulmonary artery	18982
3	P734.00	Hypoplasia of the pulmonary artery	54487
3	P735.00	Stenosis of pulmonary artery	2670
3	P738.00	Atresia of pulmonary artery with septal defect	32508
3	P741.00	Total anomalous pulmonary venous return	51941
3	P741z00	Total anomalous pulmonary venous return NOS	68784
3	P742.00	Partial anomalous pulmonary venous return	46176
3	P74z600	Scimitar syndrome	36606
3	P74z700	Transposition of pulmonary veins	71874
3	P7W..00	Congenital malformation of circulatory system, unspecif	29738
3	P7X..00	Congenital malformation of great arteries, unspecified	45910
3	PK3..00	Situs inversus	20062
3	PK33.00	Complete situs inversus with dextrocardia	36416
3	Pyu2100	[X]Other congenital malformations of cardiac septa	101322
3	Pyu2200	[X]Other congenital malformations of pulmonary valve	109008
3	Pyu2700	[X]Other congenital malformations of pulmonary artery	107639
3	Pyu2G00	[X]Congenital malformation of tricuspid valve, unspecified	107496
3	Pyu2H00	[X]Congenital malformation of aortic and mitral valves unsp	107710
3	Pyu2K00	[X]Congenital malformation of circulatory system, unspecif	108747
3	Q48y100	Congenital cardiac failure	20822

Congenital gastrointestinal disease

metadata	category	readcode	readterm	medcode
Name: CongenGastro_cprd	3	7606200	Correction of congenital atresia of oesophagus	43818
Version: 1	3	7733300	Reanastomosis rectum-anal canal correct cong rectal atresia	33725
Source: CPRD	3	761B100	Repair of congenital atresia of pylorus	39917
Author: C McKenna	3	7726y11	Duhamel Hirschsprung abdoperin	21059
Date: 19th October 2018	3	7726y12	Soave endorectal pull through op for Hirschsprung's disease	68527
Categories:	3	7726y13	Swenson Hirschsprung proctect	48226
1 = H/O	3	J103.00	Oesophageal stricture and stenosis	16713
2= Probable	3	J103z00	Oesophageal stricture and stenosis NOS	41141
3 = Definite	3	J50z200	Stenosis of intestine NOS	35852
	3	J527.00	Megacolon excluding Hirschsprung's disease	35863
	3	J572000	Stenosis of rectum	5334
	3	J572111	Anal stenosis	4856
	3	J572z00	Stenosis of rectum and anus NOS	53581

3	PA3..00	Oesophageal atresia, stenosis and fistula	37408
3	PA30.00	Atresia of oesophagus	4122
3	PA31.11	Congenital oesophageal stenosis	49707
3	PA37.00	Atresia of oesophagus with tracheo-oesophageal fistula	33655
3	PA3y.00	Other specified oesophageal atresia, stenosis or fistula	29767
3	PA3z.00	Oesophageal atresia, stenosis or fistula NOS	5801
3	PA5..00	Congenital hypertrophic pyloric stenosis	2469
3	PA50.00	Congenital pyloric hypertrophy	63866
3	PA52.00	Congenital pyloric stenosis	3263
3	PA52.11	Congenital pyloric stricture	69528
3	PA5y.00	Other specified congenital pyloric obstruction	22586
3	PA5z.00	Congenital pyloric obstruction NOS	60432
3	PB1..00	Small intestine atresia and stenosis	60083
3	PB10.00	Atresia of small intestine	33584
3	PB1000	Atresia of small intestine, unspecified	40252
3	PB1010	Atresia of duodenum	19039
3	PB1030	Atresia of jejunum	52687
3	PB10z0	Small intestine atresia NOS	70579
3	PB12.00	Congenital obstruction of small intestine	66309
3	PB13.00	Congenital stenosis of small intestine	59399
3	PB1310	Congenital stenosis of jejunum	67021
3	PB1320	Congenital stenosis of ileum	69712
3	PB13z0	Congenital stenosis of small intestine NOS	99366
3	PB13z1	Congenital stricture of small intestine	47939
3	PB1z.00	Small intestine atresia or stenosis NOS	25042
3	PB2..00	Atresia and stenosis of large intestine/rectum/anal canal	51672
3	PB2..11	Atresia large intestine	27598
3	PB2..12	Stenosis large intestine	50109
3	PB21.00	Atresia of large intestine	31468
3	PB2110	Atresia of colon	23593
3	PB2120	Atresia of rectum	46123
3	PB2150	Atresia of rectum with fistula	71153
3	PB22.00	Congenital obstruction of large intestine	65762
3	PB2411	Congenital stenosis of anus without mention of fistula	49089
3	PB2501	Congenital stenosis of rectum with fistula	88890
3	PB2511	Congenital stenosis of rectum without mention of fistula	101122
3	PB2z.00	Atresia and stenosis of large intestine/rectum/anus NOS	35968
3	PB3..00	Hirschsprung's disease and allied congenital conditions	56630
3	PB3..11	Aganglionosis	94813

3	PB30.00	Hirschsprung's disease	8546
3	PB3000	Long segment Hirschsprung's disease	63395
3	PB3010	Short segment Hirschsprung's disease	70868
3	PB30z00	Hirschsprung's disease NOS	70582
3	PB33.00	Total intestinal aganglionosis	52258
3	PB33.11	Aganglionic macrocolon	65511
3	PB33.12	Congenital aganglionic megacolon	53517
3	PB3z.00	Hirschsprung's disease and allied congenital conditions NOS	59085

Dementia

metadata	category	readcode	readterm	medcode
Name: Dementia_cprd	3	1B1A.12	Memory loss symptom	5777
Version: 1	3	1B1A.13	Memory disturbance	2908
Source: CPRD	3	1B1A100	Short-term memory loss	103453
Author: C McKenna	3	1JA2.00	Suspected dementia	104155
Date: 19th October 2018	1	6AB..00	Dementia annual review	12710
Categories:	3	8BPa.00	Antipsychotic drug therapy for dementia	109047
1 = H/O	3	8Hla.00	Referral to dementia care advisor	103445
2= Probable	3	8T05.00	Referral to dementia service	106627
3 = Definite	3	9Ou..00	Dementia monitoring administration	85853
	3	9Ou1.00	Dementia monitoring first	49674
	3	9Ou2.00	Dementia monitoring second letter	83576
	3	9Ou3.00	Dementia monitoring third letter	89036
	3	9Ou4.00	Dementia monitoring verbal invite	89037
	3	9Ou5.00	Dementia monitoring telephone invite	65235
	3	E00..11	Senile dementia	1916
	3	E00..12	Senile/presenile dementia	1350
	3	E000.00	Uncomplicated senile dementia	7323
	3	E001.00	Presenile dementia	15165
	3	E001000	Uncomplicated presenile dementia	42602
	3	E001100	Presenile dementia with delirium	49513
	3	E001200	Presenile dementia with paranoia	30032
	3	E001300	Presenile dementia with depression	27677
	3	E001z00	Presenile dementia NOS	38438
	3	E002.00	Senile dementia with depressive or paranoid features	44674
	3	E002000	Senile dementia with paranoia	18386
	3	E002100	Senile dementia with depression	21887
	3	E002z00	Senile dementia with depressive or paranoid features NOS	41089

3	E003.00	Senile dementia with delirium	37015
3	E004.00	Arteriosclerotic dementia	19477
3	E004.11	Multi infarct dementia	8634
3	E004000	Uncomplicated arteriosclerotic dementia	43089
3	E004100	Arteriosclerotic dementia with delirium	56912
3	E004200	Arteriosclerotic dementia with paranoia	55467
3	E004300	Arteriosclerotic dementia with depression	43292
3	E004z00	Arteriosclerotic dementia NOS	42279
3	E041.00	Dementia in conditions EC	25386
3	E2A0.00	Frontal lobe syndrome	31453
3	Eu00.00	[X]Dementia in Alzheimer's disease	7664
3	Eu00000	[X]Dementia in Alzheimer's disease with early onset	49263
3	Eu00011	[X]Presenile dementia,Alzheimer's type	25704
3	Eu00012	[X]Primary degen dementia, Alzheimer's type, presenile onset	60059
3	Eu00013	[X]Alzheimer's disease type 2	61528
3	Eu00100	[X]Dementia in Alzheimer's disease with late onset	38678
3	Eu00111	[X]Alzheimer's disease type 1	46762
3	Eu00112	[X]Senile dementia,Alzheimer's type	11379
3	Eu00113	[X]Primary degen dementia of Alzheimer's type, senile onset	43346
3	Eu00200	[X]Dementia in Alzheimer's dis, atypical or mixed type	30706
3	Eu00z00	[X]Dementia in Alzheimer's disease, unspecified	29386
3	Eu00z11	[X]Alzheimer's dementia unspec	8195
3	Eu01.00	[X]Vascular dementia	6578
3	Eu01.11	[X]Arteriosclerotic dementia	9565
3	Eu01000	[X]Vascular dementia of acute onset	46488
3	Eu01100	[X]Multi-infarct dementia	11175
3	Eu01111	[X]Predominantly cortical dementia	55838
3	Eu01200	[X]Subcortical vascular dementia	8934
3	Eu01300	[X]Mixed cortical and subcortical vascular dementia	31016
3	Eu01y00	[X]Other vascular dementia	55313
3	Eu01z00	[X]Vascular dementia, unspecified	19393
3	Eu02.00	[X]Dementia in other diseases classified elsewhere	12621
3	Eu02000	[X]Dementia in Pick's disease	28402
3	Eu02200	[X]Dementia in Huntington's disease	37014
3	Eu02300	[X]Dementia in Parkinson's disease	9509
3	Eu02500	[X]Lewy body dementia	26270
3	Eu02y00	[X]Dementia in other specified diseases classif elsewhere	64267
3	Eu02z00	[X] Unspecified dementia	4693
3	Eu02z11	[X] Presenile dementia NOS	48501
3	Eu02z13	[X] Primary degenerative dementia NOS	34944
3	Eu02z14	[X] Senile dementia NOS	4357
3	Eu02z16	[X] Senile dementia, depressed or paranoid type	27759

3	Eu04100	[X]Delirium superimposed on dementia	53446
3	F11..00	Other cerebral degenerations	31892
3	F110.00	Alzheimer's disease	1917
3	F110000	Alzheimer's disease with early onset	16797
3	F110100	Alzheimer's disease with late onset	32057
3	F111.00	Pick's disease	11136
3	F116.00	Lewy body disease	7572
3	F118.00	Frontotemporal degeneration	104534
3	F11z.00	Cerebral degeneration NOS	5651
3	F21y200	Binswanger's disease	5095
3	Fyu3000	[X]Other Alzheimer's disease	59122
3	ZS7C500	Language disorder of dementia	55222

Diabetes mellitus (combined)

metadata	category	readcode	readterm	medcode
Name: DMcombined_cprd	1	1434.00	H/O: diabetes mellitus	6813
Version: 1	3	3881.00	Education score - diabetes	12703
Source: CPRD	3	3882.00	Diabetes well being questionnaire	34528
Author: C McKenna	3	6761.00	Diabetic pre-pregnancy counselling	49884
Date: 19th October 2018	3	7276.00	Pan retinal photocoagulation for diabetes	11599
Categories:	3	9360.00	Patient held diabetic record issued	52237
1 = H/O	1	2126300	Diabetes resolved	28622
2= Probable	3	13AB.00	Diabetic lipid lowering diet	21689
3 = Definite	3	13AC.00	Diabetic weight reducing diet	13078
	3	13B1.00	Diabetic diet	13074
	3	13Y1.00	Diabetic association member	46533
	1	14F4.00	H/O: Admission in last year for diabetes foot problem	7045
	1	14P3.00	H/O: insulin therapy	17236
	3	212H.00	Diabetes resolved	18766
	3	2BBF.00	Retinal abnormality - diabetes related	22967
	3	2BBk.00	O/E - right eye stable treated prolif diabetic retinopathy	47328
	3	2BBL.00	O/E - diabetic maculopathy present both eyes	9835
	3	2BBM.00	O/E - diabetic maculopathy absent both eyes	47144
	3	2BBo.00	O/E - sight threatening diabetic retinopathy	52630
	3	2BBP.00	O/E - right eye background diabetic retinopathy	11433
	3	2BBQ.00	O/E - left eye background diabetic retinopathy	11129
	3	2BBR.00	O/E - right eye preproliferative diabetic retinopathy	13099
	3	2BBS.00	O/E - left eye preproliferative diabetic retinopathy	13103
	3	2BBT.00	O/E - right eye proliferative diabetic retinopathy	13097
	3	2BBV.00	O/E - left eye proliferative diabetic retinopathy	13101
	3	2BBW.00	O/E - right eye diabetic maculopathy	13102

3	2BBX.00	O/E - left eye diabetic maculopathy	13108
3	2G51000	Foot abnormality - diabetes related	27921
3	2G5A.00	O/E - Right diabetic foot at risk	17095
3	2G5B.00	O/E - Left diabetic foot at risk	26664
3	2G5C.00	Foot abnormality - diabetes related	18056
3	2G5E.00	O/E - Right diabetic foot at low risk	26666
3	2G5F.00	O/E - Right diabetic foot at moderate risk	31157
3	2G5G.00	O/E - Right diabetic foot at high risk	31171
3	2G5H.00	O/E - Right diabetic foot - ulcerated	35316
3	2G5I.00	O/E - Left diabetic foot at low risk	26667
3	2G5J.00	O/E - Left diabetic foot at moderate risk	31156
3	2G5K.00	O/E - Left diabetic foot at high risk	31172
3	2G5L.00	O/E - Left diabetic foot - ulcerated	35116
3	2G5V.00	O/E - right chronic diabetic foot ulcer	62384
3	2G5W.00	O/E - left chronic diabetic foot ulcer	49640
3	66A..00	Diabetic monitoring	3550
3	66A1.00	Initial diabetic assessment	13070
3	66A2.00	Follow-up diabetic assessment	608
3	66A3.00	Diabetic on diet only	7563
3	66A4.00	Diabetic on oral treatment	1684
3	66A5.00	Diabetic on insulin	8842
3	66A8.00	Has seen dietician - diabetes	13069
3	66A9.00	Understands diet - diabetes	38078
3	66Aa.00	Diabetic diet - poor compliance	25636
3	66AA.11	Injection sites - diabetic	20696
3	66Ab.00	Diabetic foot examination	22823
3	66Ac.00	Diabetic peripheral neuropathy screening	10977
3	66AD.00	Fundoscopy - diabetic check	13196
3	66Af.00	Patient diabetes education review	32619
3	66AG.00	Diabetic drug side effects	53238
3	66AH.00	Diabetic treatment changed	16490
3	66AI.00	Diabetic - good control	13071
3	66AJ.00	Diabetic - poor control	2378
3	66AJ.11	Unstable diabetes	9013
3	66AJ100	Brittle diabetes	2478
3	66AJz00	Diabetic - poor control NOS	22023
3	66Ak.00	Diabetic monitoring - lower risk albumin excretion	66475
3	66Al.00	Diabetic monitoring - higher risk albumin excretion	61470
3	66AM.00	Diabetic - follow-up default	17886
3	66An.00	Diabetes type 1 review	85660
3	66Ao.00	Diabetes type 2 review	83532
3	66AP.00	Diabetes: practice programme	12506
3	66AQ.00	Diabetes: shared care programme	12675
3	66AR.00	Diabetes management plan given	8836

3	66AS.00	Diabetic annual review	6125
3	66AT.00	Annual diabetic blood test	18167
3	66AU.00	Diabetes care by hospital only	12307
3	66AV.00	Diabetic on insulin and oral treatment	28769
3	66AW.00	Diabetic foot risk assessment	50175
3	66AX.00	Diabetes: shared care in pregnancy - diabetol and obstet	46577
3	66AY.00	Diabetic diet - good compliance	26604
3	66AZ.00	Diabetic monitoring NOS	13067
3	679L.00	Health education - diabetes	13057
3	679R.00	Patient offered diabetes structured education programme	12682
3	68A7.00	Diabetic retinopathy screening	18311
3	68A9.00	Diabetic retinopathy screening offered	19739
3	68AB.00	Diabetic digital retinopathy screening offered	61021
3	7L10000	Continuous subcutaneous infusion of insulin	36798
3	7L19800	Subcutaneous injection of insulin	17817
3	889A.00	Diab mellit insulin-glucose infus acute myocardial infarct	61670
3	8A12.00	Diabetic crisis monitoring	47341
3	8A13.00	Diabetic stabilisation	24363
3	8A17.00	Self monitoring of blood glucose	17478
3	8A18.00	Self monitoring of urine glucose	17846
3	8A19.00	Self monitoring of blood and urine glucose	42217
3	8A1A.00	Self monitoring urine ketones	55140
3	8B3l.00	Diabetes medication review	11471
3	8BL2.00	Patient on maximal tolerated therapy for diabetes	12213
3	8CA4100	Pt advised re diabetic diet	8414
3	8CAQ.00	Advice about blood glucose control	12483
3	8CP2.00	Transition of diabetes care options discussed	28856
3	8CR2.00	Diabetes clinical management plan	63412
3	8CS0.00	Diabetes care plan agreed	47032
3	8H2J.00	Admit diabetic emergency	7059
3	8H3O.00	Non-urgent diabetic admission	35321
3	8H7r.00	Refer to diabetic foot screener	11677
3	8HBG.00	Diabetic retinopathy 12 month review	11018
3	8HBH.00	Diabetic retinopathy 6 month review	18662
3	8Hg4.00	Discharged from care of diabetes specialist nurse	47058
3	8HHy.00	Referral to diabetic register	57723
3	8Hj0.00	Referral to diabetes structured education programme	47011
3	8Hj3.00	Referral to DAFNE diabetes structured education programme	93704
3	8Hj4.00	Referral to DESMOND diabetes structured education programme	93657
3	8Hj5.00	Referral to XPERT diabetes structured education programme	93870
3	8Hl1.00	Referral for diabetic retinopathy screening	64142
3	8HLE.00	Diabetology D.V. done	47370
3	8HTe.00	Referral to diabetes preconception counselling clinic	50937

3	8HTk.00	Referral to diabetic eye clinic	19381
3	8I3k.00	Insulin therapy declined	58159
3	8I3W.00	Diabetic foot examination declined	18824
3	8I3X.00	Diabetic retinopathy screening refused	12262
3	8I57.00	Patient held diabetic record declined	58639
3	8I6F.00	Diabetic retinopathy screening not indicated	18747
3	8I6G.00	Diabetic foot examination not indicated	12247
3	8I81.00	Did not complete diabetes structured education programme	95094
3	8I82.00	Did not complete DAFNE diabetes structured education program	97809
3	8I83.00	Did not complete DESMOND diabetes structured educat program	95093
3	8I84.00	Did not complete XPERT diabetes structured education program	94956
3	93C4.00	Patient consent given for addition to diabetic register	57389
3	9h4..00	Exception reporting: diabetes quality indicators	28574
3	9h41.00	Excepted from diabetes qual indicators: Patient unsuitable	11041
3	9h42.00	Excepted from diabetes quality indicators: Informed dissent	11348
3	9N0m.00	Seen in diabetic nurse consultant clinic	38103
3	9N0n.00	Seen in community diabetes specialist clinic	32739
3	9N0o.00	Seen in community diabetic specialist nurse clinic	38129
3	9N1i.00	Seen in diabetic foot clinic	10824
3	9N1o.00	Seen in multidisciplinary diabetic clinic	95813
3	9N1Q.00	Seen in diabetic clinic	2379
3	9N1v.00	Seen in diabetic eye clinic	9974
3	9N2d.00	Seen by diabetologist	46521
3	9N2i.00	Seen by diabetic liaison nurse	12507
3	9N4I.00	DNA - Did not attend diabetic clinic	9145
3	9N4p.00	Did not attend diabetic retinopathy clinic	30648
3	9NiA.00	Did not attend diabetes structured education programme	95553
3	9NiD.00	Did not attend DESMOND diabetes structured education program	95159
3	9NiE.00	Did not attend XPERT diabetes structured education programme	94955
3	9Nl4.00	Seen by general practitioner special interest in diabetes	97281
3	9NM0.00	Attending diabetes clinic	6430
3	9NN8.00	Under care of diabetologist	54601
3	9NN9.00	Under care of diabetes specialist nurse	11930
3	9NND.00	Under care of diabetic foot screener	11094
3	9OL..00	Diabetes monitoring admin.	9897
3	9OL1.00	Attends diabetes monitoring	13197
3	9OL2.00	Refuses diabetes monitoring	26603
3	9OL3.00	Diabetes monitoring default	22130
3	9OL4.00	Diabetes monitoring 1st letter	13194
3	9OL5.00	Diabetes monitoring 2nd letter	13195
3	9OL6.00	Diabetes monitoring 3rd letter	12030

3	9OL7.00	Diabetes monitor.verbal invite	31240
3	9OL8.00	Diabetes monitor.phone invite	31141
3	9OL9.00	Diabetes monitoring deleted	54846
3	9OLA.00	Diabetes monitor. check done	13192
3	9OLA.11	Diabetes monitored	20900
3	9OLB.00	Attended diabetes structured education programme	26605
3	9OLD.00	Diabetic patient unsuitable for digital retinal photography	35383
3	9OLF.00	Diabetes structured education programme completed	94186
3	9OLG.00	Attended XPERT diabetes structured education programme	94011
3	9OLH.00	Attended DAFNE diabetes structured education programme	93390
3	9OLJ.00	DAFNE diabetes structured education programme completed	93491
3	9OLK.00	DESMOND diabetes structured education programme completed	93529
3	9OLL.00	XPERT diabetes structured education programme completed	93631
3	9OLM.00	Diabetes structured education programme declined	93854
3	9OLZ.00	Diabetes monitoring admin.NOS	31241
3	C10..00	Diabetes mellitus	711
3	C100.00	Diabetes mellitus with no mention of complication	38986
3	C100000	Diabetes mellitus, juvenile type, no mention of complication	24490
3	C100011	Insulin dependent diabetes mellitus	1038
3	C100100	Diabetes mellitus, adult onset, no mention of complication	14803
3	C100111	Maturity onset diabetes	14889
3	C100112	Non-insulin dependent diabetes mellitus	506
3	C100z00	Diabetes mellitus NOS with no mention of complication	50972
3	C101.00	Diabetes mellitus with ketoacidosis	1682
3	C101000	Diabetes mellitus, juvenile type, with ketoacidosis	53200
3	C101100	Diabetes mellitus, adult onset, with ketoacidosis	54856
3	C101y00	Other specified diabetes mellitus with ketoacidosis	38617
3	C101z00	Diabetes mellitus NOS with ketoacidosis	42505
3	C102.00	Diabetes mellitus with hyperosmolar coma	21482
3	C102000	Diabetes mellitus, juvenile type, with hyperosmolar coma	40023
3	C102100	Diabetes mellitus, adult onset, with hyperosmolar coma	43139
3	C102z00	Diabetes mellitus NOS with hyperosmolar coma	72345
3	C103.00	Diabetes mellitus with ketoacidotic coma	15690
3	C103000	Diabetes mellitus, juvenile type, with ketoacidotic coma	42567
3	C103100	Diabetes mellitus, adult onset, with ketoacidotic coma	68843
3	C103y00	Other specified diabetes mellitus with coma	59288
3	C103z00	Diabetes mellitus NOS with ketoacidotic coma	65062
3	C104.00	Diabetes mellitus with renal manifestation	16502
3	C104.11	Diabetic nephropathy	2475
3	C104000	Diabetes mellitus, juvenile type, with renal manifestation	93922
3	C104100	Diabetes mellitus, adult onset, with renal manifestation	35105

3	C104y00	Other specified diabetes mellitus with renal complications	13279
3	C104z00	Diabetes mellitus with nephropathy NOS	35107
3	C105.00	Diabetes mellitus with ophthalmic manifestation	33254
3	C105000	Diabetes mellitus, juvenile type, + ophthalmic manifestation	69748
3	C105100	Diabetes mellitus, adult onset, + ophthalmic manifestation	41389
3	C105y00	Other specified diabetes mellitus with ophthalmic complicatn	47377
3	C105z00	Diabetes mellitus NOS with ophthalmic manifestation	34283
3	C106.00	Diabetes mellitus with neurological manifestation	16230
3	C106.11	Diabetic amyotrophy	59903
3	C106.12	Diabetes mellitus with neuropathy	7795
3	C106.13	Diabetes mellitus with polyneuropathy	16491
3	C106000	Diabetes mellitus, juvenile, + neurological manifestation	67853
3	C106100	Diabetes mellitus, adult onset, + neurological manifestation	39317
3	C106y00	Other specified diabetes mellitus with neurological comps	61523
3	C106z00	Diabetes mellitus NOS with neurological manifestation	22573
3	C107.00	Diabetes mellitus with peripheral circulatory disorder	35399
3	C107.11	Diabetes mellitus with gangrene	32403
3	C107.12	Diabetes with gangrene	32556
3	C107000	Diabetes mellitus, juvenile +peripheral circulatory disorder	70448
3	C107100	Diabetes mellitus, adult, + peripheral circulatory disorder	63357
3	C107200	Diabetes mellitus, adult with gangrene	33807
3	C107300	IDDM with peripheral circulatory disorder	69124
3	C107400	NIDDM with peripheral circulatory disorder	56803
3	C107z00	Diabetes mellitus NOS with peripheral circulatory disorder	65025
3	C108.00	Insulin dependent diabetes mellitus	1647
3	C108.11	IDDM-Insulin dependent diabetes mellitus	18505
3	C108.12	Type 1 diabetes mellitus	17858
3	C108.13	Type I diabetes mellitus	24423
3	C108000	Insulin-dependent diabetes mellitus with renal complications	46963
3	C108011	Type I diabetes mellitus with renal complications	61344
3	C108012	Type 1 diabetes mellitus with renal complications	21983
3	C108100	Insulin-dependent diabetes mellitus with ophthalmic comps	49276
3	C108200	Insulin-dependent diabetes mellitus with neurological comps	52283
3	C108211	Type I diabetes mellitus with neurological complications	49146
3	C108212	Type 1 diabetes mellitus with neurological complications	61829
3	C108300	Insulin dependent diabetes mellitus with multiple complicatn	52104
3	C108400	Unstable insulin dependent diabetes mellitus	26855
3	C108411	Unstable type I diabetes mellitus	60107
3	C108412	Unstable type 1 diabetes mellitus	97474
3	C108500	Insulin dependent diabetes mellitus with ulcer	44443
3	C108511	Type I diabetes mellitus with ulcer	51957

3	C108512	Type 1 diabetes mellitus with ulcer	68390
3	C108600	Insulin dependent diabetes mellitus with gangrene	60499
3	C108700	Insulin dependent diabetes mellitus with retinopathy	6509
3	C108711	Type I diabetes mellitus with retinopathy	38161
3	C108712	Type 1 diabetes mellitus with retinopathy	41049
3	C108800	Insulin dependent diabetes mellitus - poor control	6791
3	C108811	Type I diabetes mellitus - poor control	46850
3	C108812	Type 1 diabetes mellitus - poor control	45914
3	C108900	Insulin dependent diabetes maturity onset	31310
3	C108911	Type I diabetes mellitus maturity onset	63017
3	C108912	Type 1 diabetes mellitus maturity onset	97446
3	C108A00	Insulin-dependent diabetes without complication	56448
3	C108A11	Type I diabetes mellitus without complication	95992
3	C108B00	Insulin dependent diabetes mellitus with mononeuropathy	24694
3	C108B11	Type I diabetes mellitus with mononeuropathy	99231
3	C108C00	Insulin dependent diabetes mellitus with polyneuropathy	41716
3	C108D00	Insulin dependent diabetes mellitus with nephropathy	57621
3	C108D11	Type I diabetes mellitus with nephropathy	66872
3	C108E00	Insulin dependent diabetes mellitus with hypoglycaemic coma	44440
3	C108E11	Type I diabetes mellitus with hypoglycaemic coma	42729
3	C108E12	Type 1 diabetes mellitus with hypoglycaemic coma	70766
3	C108F00	Insulin dependent diabetes mellitus with diabetic cataract	44260
3	C108F11	Type I diabetes mellitus with diabetic cataract	17545
3	C108G00	Insulin dependent diab mell with peripheral angiopathy	64446
3	C108H00	Insulin dependent diabetes mellitus with arthropathy	65616
3	C108H11	Type I diabetes mellitus with arthropathy	62352
3	C108J00	Insulin dependent diab mell with neuropathic arthropathy	39809
3	C108J11	Type I diabetes mellitus with neuropathic arthropathy	60208
3	C108J12	Type 1 diabetes mellitus with neuropathic arthropathy	18230
3	C108y00	Other specified diabetes mellitus with multiple comps	46290
3	C108z00	Unspecified diabetes mellitus with multiple complications	64449
3	C109.00	Non-insulin dependent diabetes mellitus	4513
3	C109.11	NIDDM - Non-insulin dependent diabetes mellitus	5884
3	C109.12	Type 2 diabetes mellitus	17859
3	C109.13	Type II diabetes mellitus	18219
3	C109000	Non-insulin-dependent diabetes mellitus with renal comps	52303
3	C109011	Type II diabetes mellitus with renal complications	50225
3	C109012	Type 2 diabetes mellitus with renal complications	18209
3	C109100	Non-insulin-dependent diabetes mellitus with ophthalm comps	50429
3	C109111	Type II diabetes mellitus with ophthalmic complications	59725
3	C109112	Type 2 diabetes mellitus with ophthalmic complications	70316
3	C109200	Non-insulin-dependent diabetes mellitus with neuro comps	55842
3	C109211	Type II diabetes mellitus with neurological complications	67905

3	C109212	Type 2 diabetes mellitus with neurological complications	45919
3	C109300	Non-insulin-dependent diabetes mellitus with multiple comps	62146
3	C109400	Non-insulin dependent diabetes mellitus with ulcer	34912
3	C109411	Type II diabetes mellitus with ulcer	55075
3	C109412	Type 2 diabetes mellitus with ulcer	65704
3	C109500	Non-insulin dependent diabetes mellitus with gangrene	40401
3	C109511	Type II diabetes mellitus with gangrene	62107
3	C109512	Type 2 diabetes mellitus with gangrene	46150
3	C109600	Non-insulin-dependent diabetes mellitus with retinopathy	17262
3	C109611	Type II diabetes mellitus with retinopathy	58604
3	C109612	Type 2 diabetes mellitus with retinopathy	42762
3	C109700	Non-insulin dependent diabetes mellitus - poor control	8403
3	C109711	Type II diabetes mellitus - poor control	24458
3	C109712	Type 2 diabetes mellitus - poor control	45913
3	C109800	Reaven's syndrome	39406
3	C109900	Non-insulin-dependent diabetes mellitus without complication	29979
3	C109A00	Non-insulin dependent diabetes mellitus with mononeuropathy	72320
3	C109A11	Type II diabetes mellitus with mononeuropathy	50813
3	C109B00	Non-insulin dependent diabetes mellitus with polyneuropathy	45467
3	C109B11	Type II diabetes mellitus with polyneuropathy	47409
3	C109C00	Non-insulin dependent diabetes mellitus with nephropathy	59365
3	C109C11	Type II diabetes mellitus with nephropathy	64571
3	C109C12	Type 2 diabetes mellitus with nephropathy	24836
3	C109D00	Non-insulin dependent diabetes mellitus with hypoglyca coma	43785
3	C109D11	Type II diabetes mellitus with hypoglycaemic coma	56268
3	C109D12	Type 2 diabetes mellitus with hypoglycaemic coma	61071
3	C109E00	Non-insulin depend diabetes mellitus with diabetic cataract	69278
3	C109E11	Type II diabetes mellitus with diabetic cataract	48192
3	C109E12	Type 2 diabetes mellitus with diabetic cataract	44779
3	C109F00	Non-insulin-dependent d m with peripheral angiopath	54212
3	C109F11	Type II diabetes mellitus with peripheral angiopathy	54899
3	C109F12	Type 2 diabetes mellitus with peripheral angiopathy	60699
3	C109G00	Non-insulin dependent diabetes mellitus with arthropathy	24693
3	C109G11	Type II diabetes mellitus with arthropathy	18143
3	C109G12	Type 2 diabetes mellitus with arthropathy	49869
3	C109H00	Non-insulin dependent d m with neuropathic arthropathy	40962
3	C109H11	Type II diabetes mellitus with neuropathic arthropathy	47816
3	C109H12	Type 2 diabetes mellitus with neuropathic arthropathy	66965
3	C109J00	Insulin treated Type 2 diabetes mellitus	18278
3	C109J11	Insulin treated non-insulin dependent diabetes mellitus	37648
3	C109J12	Insulin treated Type II diabetes mellitus	18264
3	C109K00	Hyperosmolar non-ketotic state in type 2 diabetes mellitus	36633

3	C10A.00	Malnutrition-related diabetes mellitus	52236
3	C10A000	Malnutrition-related diabetes mellitus with coma	66675
3	C10A100	Malnutrition-related diabetes mellitus with ketoacidosis	33969
3	C10A500	Malnutritn-relat diabetes melitus wth periph circul complctn	100347
3	C10B.00	Diabetes mellitus induced by steroids	11551
3	C10B000	Steroid induced diabetes mellitus without complication	26108
3	C10C.00	Diabetes mellitus autosomal dominant	43453
3	C10C.11	Maturity onset diabetes in youth	46624
3	C10C.12	Maturity onset diabetes in youth type 1	98392
3	C10D.00	Diabetes mellitus autosomal dominant type 2	36695
3	C10D.11	Maturity onset diabetes in youth type 2	59991
3	C10E.00	Type 1 diabetes mellitus	1549
3	C10E.11	Type I diabetes mellitus	12455
3	C10E.12	Insulin dependent diabetes mellitus	51261
3	C10E000	Type 1 diabetes mellitus with renal complications	47582
3	C10E100	Type 1 diabetes mellitus with ophthalmic complications	47649
3	C10E112	Insulin-dependent diabetes mellitus with ophthalmic comps	98071
3	C10E200	Type 1 diabetes mellitus with neurological complications	42831
3	C10E300	Type 1 diabetes mellitus with multiple complications	47650
3	C10E311	Type I diabetes mellitus with multiple complications	91942
3	C10E312	Insulin dependent diabetes mellitus with multiple complicat	45276
3	C10E400	Unstable type 1 diabetes mellitus	43921
3	C10E411	Unstable type I diabetes mellitus	49949
3	C10E412	Unstable insulin dependent diabetes mellitus	54600
3	C10E500	Type 1 diabetes mellitus with ulcer	18683
3	C10E511	Type I diabetes mellitus with ulcer	93878
3	C10E512	Insulin dependent diabetes mellitus with ulcer	98704
3	C10E600	Type 1 diabetes mellitus with gangrene	69993
3	C10E700	Type 1 diabetes mellitus with retinopathy	18387
3	C10E711	Type I diabetes mellitus with retinopathy	95343
3	C10E712	Insulin dependent diabetes mellitus with retinopathy	93875
3	C10E800	Type 1 diabetes mellitus - poor control	35288
3	C10E812	Insulin dependent diabetes mellitus - poor control	72702
3	C10E900	Type 1 diabetes mellitus maturity onset	40682
3	C10E911	Type I diabetes mellitus maturity onset	96235
3	C10E912	Insulin dependent diabetes maturity onset	97849
3	C10EA00	Type 1 diabetes mellitus without complication	69676
3	C10EA11	Type I diabetes mellitus without complication	62613
3	C10EB00	Type 1 diabetes mellitus with mononeuropathy	68105
3	C10EC00	Type 1 diabetes mellitus with polyneuropathy	46301
3	C10EC11	Type I diabetes mellitus with polyneuropathy	91943

3	C10ED00	Type 1 diabetes mellitus with nephropathy	10418
3	C10EE00	Type 1 diabetes mellitus with hypoglycaemic coma	39070
3	C10EF00	Type 1 diabetes mellitus with diabetic cataract	49554
3	C10EG00	Type 1 diabetes mellitus with peripheral angiopathy	93468
3	C10EH00	Type 1 diabetes mellitus with arthropathy	18642
3	C10EJ00	Type 1 diabetes mellitus with neuropathic arthropathy	54008
3	C10EK00	Type 1 diabetes mellitus with persistent proteinuria	30323
3	C10EL00	Type 1 diabetes mellitus with persistent microalbuminuria	30294
3	C10EM00	Type 1 diabetes mellitus with ketoacidosis	10692
3	C10EM11	Type I diabetes mellitus with ketoacidosis	62209
3	C10EN00	Type 1 diabetes mellitus with ketoacidotic coma	40837
3	C10EN11	Type I diabetes mellitus with ketoacidotic coma	66145
3	C10EP00	Type 1 diabetes mellitus with exudative maculopathy	22871
3	C10EP11	Type I diabetes mellitus with exudative maculopathy	97894
3	C10EQ00	Type 1 diabetes mellitus with gastroparesis	55239
3	C10ER00	Latent autoimmune diabetes mellitus in adult	95636
3	C10F.00	Type 2 diabetes mellitus	758
3	C10F.11	Type II diabetes mellitus	22884
3	C10F000	Type 2 diabetes mellitus with renal complications	18777
3	C10F011	Type II diabetes mellitus with renal complications	57278
3	C10F100	Type 2 diabetes mellitus with ophthalmic complications	47321
3	C10F200	Type 2 diabetes mellitus with neurological complications	34268
3	C10F211	Type II diabetes mellitus with neurological complications	98616
3	C10F300	Type 2 diabetes mellitus with multiple complications	65267
3	C10F311	Type II diabetes mellitus with multiple complications	43227
3	C10F400	Type 2 diabetes mellitus with ulcer	49074
3	C10F411	Type II diabetes mellitus with ulcer	91646
3	C10F500	Type 2 diabetes mellitus with gangrene	12736
3	C10F600	Type 2 diabetes mellitus with retinopathy	18496
3	C10F611	Type II diabetes mellitus with retinopathy	49655
3	C10F700	Type 2 diabetes mellitus - poor control	25627
3	C10F711	Type II diabetes mellitus - poor control	47315
3	C10F800	Reaven's syndrome	54773
3	C10F811	Metabolic syndrome X	39481
3	C10F900	Type 2 diabetes mellitus without complication	47954
3	C10F911	Type II diabetes mellitus without complication	53392
3	C10FA00	Type 2 diabetes mellitus with mononeuropathy	62674
3	C10FA11	Type II diabetes mellitus with mononeuropathy	95351
3	C10FB00	Type 2 diabetes mellitus with polyneuropathy	18425
3	C10FB11	Type II diabetes mellitus with polyneuropathy	50527

3	C10FC00	Type 2 diabetes mellitus with nephropathy	12640
3	C10FC11	Type II diabetes mellitus with nephropathy	102201
3	C10FD00	Type 2 diabetes mellitus with hypoglycaemic coma	46917
3	C10FD11	Type II diabetes mellitus with hypoglycaemic coma	98723
3	C10FE00	Type 2 diabetes mellitus with diabetic cataract	44982
3	C10FE11	Type II diabetes mellitus with diabetic cataract	93727
3	C10FF00	Type 2 diabetes mellitus with peripheral angiopathy	37806
3	C10FG00	Type 2 diabetes mellitus with arthropathy	59253
3	C10FH00	Type 2 diabetes mellitus with neuropathic arthropathy	35385
3	C10FJ00	Insulin treated Type 2 diabetes mellitus	1407
3	C10FJ11	Insulin treated Type II diabetes mellitus	64668
3	C10FK00	Hyperosmolar non-ketotic state in type 2 diabetes mellitus	34450
3	C10FL00	Type 2 diabetes mellitus with persistent proteinuria	26054
3	C10FL11	Type II diabetes mellitus with persistent proteinuria	60796
3	C10FM00	Type 2 diabetes mellitus with persistent microalbuminuria	18390
3	C10FM11	Type II diabetes mellitus with persistent microalbuminuria	85991
3	C10FN00	Type 2 diabetes mellitus with ketoacidosis	32627
3	C10FP00	Type 2 diabetes mellitus with ketoacidotic coma	51756
3	C10FQ00	Type 2 diabetes mellitus with exudative maculopathy	25591
3	C10FR00	Type 2 diabetes mellitus with gastroparesis	63690
3	C10FS00	Maternally inherited diabetes mellitus	95539
3	C10G.00	Secondary pancreatic diabetes mellitus	51697
3	C10G000	Secondary pancreatic diabetes mellitus without complication	96506
3	C10H.00	Diabetes mellitus induced by non-steroid drugs	61122
3	C10H000	DM induced by non-steroid drugs without complication	67212
3	C10J.00	Insulin autoimmune syndrome	68517
3	C10K.00	Type A insulin resistance	37957
3	C10K000	Type A insulin resistance without complication	56885
3	C10M.00	Lipoatrophic diabetes mellitus	43857
3	C10N.00	Secondary diabetes mellitus	22487
3	C10N000	Secondary diabetes mellitus without complication	94383
3	C10N100	Cystic fibrosis related diabetes mellitus	93380
3	C10y.00	Diabetes mellitus with other specified manifestation	33343
3	C10y100	Diabetes mellitus, adult, + other specified manifestation	63371
3	C10yy00	Other specified diabetes mellitus with other spec comps	10098
3	C10yz00	Diabetes mellitus NOS with other specified manifestation	70821
3	C10z.00	Diabetes mellitus with unspecified complication	45491
3	C10z000	Diabetes mellitus, juvenile type, + unspecified complication	68792
3	C10z100	Diabetes mellitus, adult onset, + unspecified complication	63762
3	C10zy00	Other specified diabetes mellitus with unspecified comps	64283

3	C10zz00	Diabetes mellitus NOS with unspecified complication	64357
3	C11y000	Steroid induced diabetes	32193
3	C314.11	Renal diabetes	11848
3	C350011	Bronzed diabetes	23479
3	Cyu2.00	[X]Diabetes mellitus	52212
3	Cyu2000	[X]Other specified diabetes mellitus	41686
3	F171100	Autonomic neuropathy due to diabetes	17067
3	F345000	Diabetic mononeuritis multiplex	44033
3	F35z000	Diabetic mononeuritis NOS	17247
3	F372.00	Polyneuropathy in diabetes	31790
3	F372.11	Diabetic polyneuropathy	5002
3	F372.12	Diabetic neuropathy	2342
3	F372000	Acute painful diabetic neuropathy	48078
3	F372100	Chronic painful diabetic neuropathy	35785
3	F372200	Asymptomatic diabetic neuropathy	24571
3	F381300	Myasthenic syndrome due to diabetic amyotrophy	39420
3	F381311	Diabetic amyotrophy	2340
3	F3y0.00	Diabetic mononeuropathy	37315
3	F420.00	Diabetic retinopathy	1323
3	F420000	Background diabetic retinopathy	7069
3	F420100	Proliferative diabetic retinopathy	3286
3	F420200	Preproliferative diabetic retinopathy	2986
3	F420300	Advanced diabetic maculopathy	10099
3	F420400	Diabetic maculopathy	3837
3	F420500	Advanced diabetic retinal disease	47584
3	F420600	Non proliferative diabetic retinopathy	10755
3	F420700	High risk proliferative diabetic retinopathy	30477
3	F420800	High risk non proliferative diabetic retinopathy	65463
3	F420z00	Diabetic retinopathy NOS	11626
3	F440700	Diabetic iritis	17313
3	F464000	Diabetic cataract	10659
3	G73y000	Diabetic peripheral angiopathy	34152
3	K01x100	Nephrotic syndrome in diabetes mellitus	2471
3	K01x111	Kimmelstiel - Wilson disease	45499
3	L180500	Pre-existing diabetes mellitus, insulin-dependent	50960
3	L180600	Pre-existing diabetes mellitus, non-insulin-dependent	50609
3	L180X00	Pre-existing diabetes mellitus, unspecified	55431
3	M037200	Cellulitis in diabetic foot	7328
3	M21yC00	Insulin lipohypertrophy	38076
3	M21yC11	Insulin site lipohypertrophy	43493
3	M271000	Ischaemic ulcer diabetic foot	24327
3	M271100	Neuropathic diabetic ulcer - foot	11663
3	M271200	Mixed diabetic ulcer - foot	9881

3	N030000	Diabetic cheiroarthropathy	18142
3	N030011	Diabetic cheiropathy	57333
3	N030100	Diabetic Charcot arthropathy	27891
3	Q441.00	Neonatal diabetes mellitus	21472
3	R054200	[D]Gangrene of toe in diabetic	53634
3	R054300	[D]Widespread diabetic foot gangrene	31053
3	TJ23.00	Adverse reaction to insulins and antidiabetic agents	68928
3	TJ23z00	Adverse reaction to insulins and antidiabetic agents NOS	61210
3	U602311	[X] Adverse reaction to insulins and antidiabetic agents	65684
3	ZC2C800	Dietary advice for diabetes mellitus	10642
3	ZC2C900	Dietary advice for type I diabetes	69043
3	ZC2CA00	Dietary advice for type II diabetes	25041
3	ZL22500	Under care of diabetic liaison nurse	45250
3	ZLA2500	Seen by diabetic liaison nurse	8618
3	ZLD7500	Discharge by diabetic liaison nurse	58133
3	ZRB4.00	Diabetes clinic satisfaction questionnaire	68546
3	ZRB4.11	CSQ - Diabetes clinic satisfaction questionnaire	91164
3	ZRB5.00	Diabetes treatment satisfaction questionnaire	94699
3	ZRB5.11	DTSQ - Diabetes treatment satisfaction questionnaire	68818
3	ZRB6.00	Diabetes wellbeing questionnaire	38130
3	ZRB6.11	DWBQ - Diabetes wellbeing questionnaire	97824
3	ZRBa.00	Education score - diabetes	67664
3	ZRbH.00	Perceived control of insulin-dependent diabetes	32359
3	ZV65312	[V]Dietary counselling in diabetes mellitus	16881

Type 1 diabetes mellitus

metadata	category	readcode	readterm	medcode
Name: DMT1_cprd	3	66An.00	Diabetes type 1 review	85660
Version: 1	3	C100000	Diabetes mellitus, juvenile type, no mention of complication	24490
Source: CPRD	3	C101000	Diabetes mellitus, juvenile type, with ketoacidosis	53200
Author: C McKenna	3	C102000	Diabetes mellitus, juvenile type, with hyperosmolar coma	40023
Date: 19th October 2018	3	C103000	Diabetes mellitus, juvenile type, with ketoacidotic coma	42567
Categories:	3	C104000	Diabetes mellitus, juvenile type, with renal manifestation	93922
1 = H/O	3	C105000	Diabetes mellitus, juvenile type, + ophthalmic manifestation	69748
2= Probable	3	C106000	Diabetes mellitus, juvenile, + neurological manifestation	67853
3 = Definite	3	C107000	Diabetes mellitus, juvenile +peripheral circulatory disorder	70448
	3	C108.12	Type 1 diabetes mellitus	17858
	3	C108.13	Type I diabetes mellitus	24423
	3	C108011	Type I diabetes mellitus with renal complications	61344
	3	C108012	Type 1 diabetes mellitus with renal complications	21983

3	C108211	Type I diabetes mellitus with neurological complications	49146
3	C108212	Type 1 diabetes mellitus with neurological complications	61829
3	C108411	Unstable type I diabetes mellitus	60107
3	C108412	Unstable type 1 diabetes mellitus	97474
3	C108511	Type I diabetes mellitus with ulcer	51957
3	C108512	Type 1 diabetes mellitus with ulcer	68390
3	C108711	Type I diabetes mellitus with retinopathy	38161
3	C108712	Type 1 diabetes mellitus with retinopathy	41049
3	C108811	Type I diabetes mellitus - poor control	46850
3	C108812	Type 1 diabetes mellitus - poor control	45914
3	C108911	Type I diabetes mellitus maturity onset	63017
3	C108912	Type 1 diabetes mellitus maturity onset	97446
3	C108A11	Type I diabetes mellitus without complication	95992
3	C108B11	Type I diabetes mellitus with mononeuropathy	99231
3	C108D11	Type I diabetes mellitus with nephropathy	66872
3	C108E11	Type I diabetes mellitus with hypoglycaemic coma	42729
3	C108E12	Type 1 diabetes mellitus with hypoglycaemic coma	70766
3	C108F11	Type I diabetes mellitus with diabetic cataract	17545
3	C108H11	Type I diabetes mellitus with arthropathy	62352
3	C108J11	Type I diabetes mellitus with neuropathic arthropathy	60208
3	C108J12	Type 1 diabetes mellitus with neuropathic arthropathy	18230
3	C109J12	Insulin treated Type II diabetes mellitus	18264
3	C10C.12	Maturity onset diabetes in youth type 1	98392
3	C10E.00	Type 1 diabetes mellitus	1549
3	C10E.11	Type I diabetes mellitus	12455
3	C10E000	Type 1 diabetes mellitus with renal complications	47582
3	C10E100	Type 1 diabetes mellitus with ophthalmic complications	47649
3	C10E200	Type 1 diabetes mellitus with neurological complications	42831
3	C10E300	Type 1 diabetes mellitus with multiple complications	47650
3	C10E311	Type I diabetes mellitus with multiple complications	91942
3	C10E400	Unstable type 1 diabetes mellitus	43921
3	C10E411	Unstable type I diabetes mellitus	49949
3	C10E500	Type 1 diabetes mellitus with ulcer	18683
3	C10E511	Type I diabetes mellitus with ulcer	93878
3	C10E600	Type 1 diabetes mellitus with gangrene	69993
3	C10E700	Type 1 diabetes mellitus with retinopathy	18387
3	C10E711	Type I diabetes mellitus with retinopathy	95343
3	C10E800	Type 1 diabetes mellitus - poor control	35288
3	C10E900	Type 1 diabetes mellitus maturity onset	40682
3	C10E911	Type I diabetes mellitus maturity onset	96235
3	C10EA00	Type 1 diabetes mellitus without complication	69676
3	C10EA11	Type I diabetes mellitus without complication	62613
3	C10EB00	Type 1 diabetes mellitus with mononeuropathy	68105
3	C10EC00	Type 1 diabetes mellitus with polyneuropathy	46301

	3	C10EC11	Type I diabetes mellitus with polyneuropathy	91943
	3	C10ED00	Type 1 diabetes mellitus with nephropathy	10418
	3	C10EE00	Type 1 diabetes mellitus with hypoglycaemic coma	39070
	3	C10EF00	Type 1 diabetes mellitus with diabetic cataract	49554
	3	C10EG00	Type 1 diabetes mellitus with peripheral angiopathy	93468
	3	C10EH00	Type 1 diabetes mellitus with arthropathy	18642
	3	C10EJ00	Type 1 diabetes mellitus with neuropathic arthropathy	54008
	3	C10EK00	Type 1 diabetes mellitus with persistent proteinuria	30323
	3	C10EL00	Type 1 diabetes mellitus with persistent microalbuminuria	30294
	3	C10EM00	Type 1 diabetes mellitus with ketoacidosis	10692
	3	C10EM11	Type I diabetes mellitus with ketoacidosis	62209
	3	C10EN00	Type 1 diabetes mellitus with ketoacidotic coma	40837
	3	C10EN11	Type I diabetes mellitus with ketoacidotic coma	66145
	3	C10EP00	Type 1 diabetes mellitus with exudative maculopathy	22871
	3	C10EP11	Type I diabetes mellitus with exudative maculopathy	97894
	3	C10EQ00	Type 1 diabetes mellitus with gastroparesis	55239
	3	C10z000	Diabetes mellitus, juvenile type, + unspecified complication	68792
	3	ZC2C900	Dietary advice for type I diabetes	69043

Type 2 diabetes mellitus

metadata	category	readcode	readterm	medcode
Name: DMT2_cprd	3	66Ao.00	Diabetes type 2 review	83532
Version: 1	3	C100100	Diabetes mellitus, adult onset, no mention of complication	14803
Source: CPRD	3	C100111	Maturity onset diabetes	14889
Author: C McKenna	3	C100112	Non-insulin dependent diabetes mellitus	506
Date: 19th October 2018	3	C101100	Diabetes mellitus, adult onset, with ketoacidosis	54856
Categories:	3	C102100	Diabetes mellitus, adult onset, with hyperosmolar coma	43139
1 = H/O	3	C103100	Diabetes mellitus, adult onset, with ketoacidotic coma	68843
2= Probable	3	C104100	Diabetes mellitus, adult onset, with renal manifestation	35105
3 = Definite	3	C105100	Diabetes mellitus, adult onset, + ophthalmic manifestation	41389
	3	C106100	Diabetes mellitus, adult onset, + neurological manifestation	39317
	3	C107100	Diabetes mellitus, adult, + peripheral circulatory disorder	63357
	3	C107200	Diabetes mellitus, adult with gangrene	33807
	3	C107400	NIDDM with peripheral circulatory disorder	56803
	3	C109.00	Non-insulin dependent diabetes mellitus	4513
	3	C109.11	NIDDM - Non-insulin dependent diabetes mellitus	5884
	3	C109.12	Type 2 diabetes mellitus	17859
	3	C109.13	Type II diabetes mellitus	18219
	3	C109000	Non-insulin-dependent diabetes mellitus with renal comps	52303
	3	C109011	Type II diabetes mellitus with renal complications	50225
	3	C109012	Type 2 diabetes mellitus with renal complications	18209

3	C109100	Non-insulin-dependent diabetes mellitus with ophthalm comps	50429
3	C109111	Type II diabetes mellitus with ophthalmic complications	59725
3	C109112	Type 2 diabetes mellitus with ophthalmic complications	70316
3	C109200	Non-insulin-dependent diabetes mellitus with neuro comps	55842
3	C109211	Type II diabetes mellitus with neurological complications	67905
3	C109212	Type 2 diabetes mellitus with neurological complications	45919
3	C109300	Non-insulin-dependent diabetes mellitus with multiple comps	62146
3	C109400	Non-insulin dependent diabetes mellitus with ulcer	34912
3	C109411	Type II diabetes mellitus with ulcer	55075
3	C109412	Type 2 diabetes mellitus with ulcer	65704
3	C109500	Non-insulin dependent diabetes mellitus with gangrene	40401
3	C109511	Type II diabetes mellitus with gangrene	62107
3	C109512	Type 2 diabetes mellitus with gangrene	46150
3	C109600	Non-insulin-dependent diabetes mellitus with retinopathy	17262
3	C109611	Type II diabetes mellitus with retinopathy	58604
3	C109612	Type 2 diabetes mellitus with retinopathy	42762
3	C109700	Non-insulin dependent diabetes mellitus - poor control	8403
3	C109711	Type II diabetes mellitus - poor control	24458
3	C109712	Type 2 diabetes mellitus - poor control	45913
3	C109900	Non-insulin-dependent diabetes mellitus without complication	29979
3	C109A00	Non-insulin dependent diabetes mellitus with mononeuropathy	72320
3	C109A11	Type II diabetes mellitus with mononeuropathy	50813
3	C109B00	Non-insulin dependent diabetes mellitus with polyneuropathy	45467
3	C109B11	Type II diabetes mellitus with polyneuropathy	47409
3	C109C00	Non-insulin dependent diabetes mellitus with nephropathy	59365
3	C109C11	Type II diabetes mellitus with nephropathy	64571
3	C109C12	Type 2 diabetes mellitus with nephropathy	24836
3	C109D00	Non-insulin dependent diabetes mellitus with hypoglyca coma	43785
3	C109D11	Type II diabetes mellitus with hypoglycaemic coma	56268
3	C109D12	Type 2 diabetes mellitus with hypoglycaemic coma	61071
3	C109E00	Non-insulin depend diabetes mellitus with diabetic cataract	69278
3	C109E11	Type II diabetes mellitus with diabetic cataract	48192
3	C109E12	Type 2 diabetes mellitus with diabetic cataract	44779
3	C109F00	Non-insulin-dependent d m with peripheral angiopath	54212
3	C109F11	Type II diabetes mellitus with peripheral angiopathy	54899
3	C109F12	Type 2 diabetes mellitus with peripheral angiopathy	60699
3	C109G00	Non-insulin dependent diabetes mellitus with arthropathy	24693
3	C109G11	Type II diabetes mellitus with arthropathy	18143
3	C109G12	Type 2 diabetes mellitus with arthropathy	49869
3	C109H00	Non-insulin dependent d m with neuropathic arthropathy	40962
3	C109H11	Type II diabetes mellitus with neuropathic arthropathy	47816
3	C109H12	Type 2 diabetes mellitus with neuropathic arthropathy	66965

3	C109J00	Insulin treated Type 2 diabetes mellitus	18278
3	C109J11	Insulin treated non-insulin dependent diabetes mellitus	37648
3	C109K00	Hyperosmolar non-ketotic state in type 2 diabetes mellitus	36633
3	C10C.11	Maturity onset diabetes in youth	46624
3	C10D.00	Diabetes mellitus autosomal dominant type 2	36695
3	C10D.11	Maturity onset diabetes in youth type 2	59991
3	C10ER00	Latent autoimmune diabetes mellitus in adult	95636
3	C10F.00	Type 2 diabetes mellitus	758
3	C10F.11	Type II diabetes mellitus	22884
3	C10F000	Type 2 diabetes mellitus with renal complications	18777
3	C10F011	Type II diabetes mellitus with renal complications	57278
3	C10F100	Type 2 diabetes mellitus with ophthalmic complications	47321
3	C10F200	Type 2 diabetes mellitus with neurological complications	34268
3	C10F211	Type II diabetes mellitus with neurological complications	98616
3	C10F300	Type 2 diabetes mellitus with multiple complications	65267
3	C10F311	Type II diabetes mellitus with multiple complications	43227
3	C10F400	Type 2 diabetes mellitus with ulcer	49074
3	C10F411	Type II diabetes mellitus with ulcer	91646
3	C10F500	Type 2 diabetes mellitus with gangrene	12736
3	C10F600	Type 2 diabetes mellitus with retinopathy	18496
3	C10F611	Type II diabetes mellitus with retinopathy	49655
3	C10F700	Type 2 diabetes mellitus - poor control	25627
3	C10F711	Type II diabetes mellitus - poor control	47315
3	C10F900	Type 2 diabetes mellitus without complication	47954
3	C10F911	Type II diabetes mellitus without complication	53392
3	C10FA00	Type 2 diabetes mellitus with mononeuropathy	62674
3	C10FA11	Type II diabetes mellitus with mononeuropathy	95351
3	C10FB00	Type 2 diabetes mellitus with polyneuropathy	18425
3	C10FB11	Type II diabetes mellitus with polyneuropathy	50527
3	C10FC00	Type 2 diabetes mellitus with nephropathy	12640
3	C10FC11	Type II diabetes mellitus with nephropathy	102201
3	C10FD00	Type 2 diabetes mellitus with hypoglycaemic coma	46917
3	C10FD11	Type II diabetes mellitus with hypoglycaemic coma	98723
3	C10FE00	Type 2 diabetes mellitus with diabetic cataract	44982
3	C10FE11	Type II diabetes mellitus with diabetic cataract	93727
3	C10FF00	Type 2 diabetes mellitus with peripheral angiopathy	37806
3	C10FG00	Type 2 diabetes mellitus with arthropathy	59253
3	C10FH00	Type 2 diabetes mellitus with neuropathic arthropathy	35385
3	C10FJ00	Insulin treated Type 2 diabetes mellitus	1407
3	C10FJ11	Insulin treated Type II diabetes mellitus	64668
3	C10FK00	Hyperosmolar non-ketotic state in type 2 diabetes mellitus	34450
3	C10FL00	Type 2 diabetes mellitus with persistent proteinuria	26054
3	C10FL11	Type II diabetes mellitus with persistent proteinuria	60796
3	C10FM00	Type 2 diabetes mellitus with persistent microalbuminuria	18390

3	C10FM11	Type II diabetes mellitus with persistent microalbuminuria	85991
3	C10FN00	Type 2 diabetes mellitus with ketoacidosis	32627
3	C10FP00	Type 2 diabetes mellitus with ketoacidotic coma	51756
3	C10FQ00	Type 2 diabetes mellitus with exudative maculopathy	25591
3	C10FR00	Type 2 diabetes mellitus with gastroparesis	63690
3	C10y100	Diabetes mellitus, adult, + other specified manifestation	63371
3	C10z100	Diabetes mellitus, adult onset, + unspecified complication	63762
3	L180600	Pre-existing diabetes mellitus, non-insulin-dependent	50609
3	ZC2CA00	Dietary advice for type II diabetes	25041

Duchenne/ muscular dystrophy/ myopathy

metadata	category	readcode	readterm	medcode
Name: DuchenneMyop_cprd	3	F152111	Duchenne Aran muscular atrophy	7470
Version: 1	3	F390.00	Congenital hereditary muscular dystrophy	64690
Source: CPRD	3	F390300	Myotubular myopathy	25429
Author: C McKenna	3	F390500	Congenital myopathy	103722
Date: 19th October 2018	3	F390z00	Congenital hereditary muscular dystrophy NOS	22174
Categories:	3	F391.00	Hereditary progressive muscular dystrophy	68118
1 = H/O	3	F391000	Duchenne muscular dystrophy	5393
2= Probable	3	F391200	Pelvic muscular dystrophy	91544
3 = Definite	3	F391300	Other limb-girdle muscular dystrophy	28210
	3	F391400	Facioscapulohumeral muscular dystrophy	36671
	3	F391500	Distal (Gower's) muscular dystrophy	66726
	3	F391800	Becker muscular dystrophy	32749
	3	F391A00	Emery-Dreifuss muscular dystrophy	34985
	3	F391B00	Cardiomyopathy in Duchenne muscular dystrophy	44272
	3	F391y00	Other specified hereditary progressive muscular dystrophy	71128
	3	F391z00	Hereditary progressive muscular dystrophy NOS	21425
	3	F397.00	Proximal myopathy	17392
	3	F39B.00	Muscular dystrophy	5964
	3	F39z.00	Myopathy or muscular dystrophy NOS	1632
	3	G558100	Cardiomyopathy in myotonic dystrophy	27683

Eczema

metadata	category	readcode	readterm	medcode
Name: Eczema_cprd	1	14F1.00	H/O: eczema	2859
Version: 1	3	M12..12	Contact eczema	5391
Source: CPRD	3	M12z300	Hand eczema	3699
Author: C McKenna	3	M102.00	Infectious eczematoid dermatitis	6728
Date: 19th October 2018	3	G831.00	Varicose veins of the leg with eczema	5983

Categories:	3	M114.00	Allergic (intrinsic) eczema	5869
1 = H/O	3	C391211	Thrombocytopenic eczema with immunodeficiency	42439
2= Probable	3	M119.00	Discoid eczema	4684
3 = Definite	3	M11A.00	Asteatotic eczema	102327
	3	F4D3112	Contact eczema - eyelids	15879
	3	M12z100	Eczema NOS	230
	3	8HTu.00	Referral to eczema clinic	100100
	3	G832.00	Varicose veins of the leg with ulcer and eczema	16079
	3	A540.00	Eczema herpeticum - Kaposi's varicelliform eruption	5395
	3	M1y2.00	Gravitational eczema	102515
	3	Myu2.00	[X]Dermatitis and eczema	39721
	3	M112.00	Infantile eczema	610
	3	M113.00	Flexural eczema	1240
	3	M12z111	Discoid eczema	1095
	3	26C4.00	Nipple eczema	10920
	3	G831.11	Varicose eczema	1217
	3	M12z400	Erythrodermic eczema	8994
	3	F4D3000	Eczematous eyelid dermatitis	29779
	3	M111.00	Atopic dermatitis/eczema	1741
	3	F502400	Acute eczematoid otitis extern	10254
	3	M07y.11	Pustular eczema	15372
	2	M101.12	Seborrhoeic eczema	653
	3	Myu2200	[X]Exacerbation of eczema	22764
	3	M12..00	Contact dermatitis and other eczemas	6399
	3	M12z200	Infected eczema	1424
	3	F502411	Eczema of external ear	6218
	3	M102.11	Pustular eczema	5000
	3	M11..00	Atopic dermatitis and related conditions	13223
	3	M11z.00	Atopic dermatitis NOS	6180

Skin, other

metadata	category	readcode	readterm	medcode
Name: SkinOther_cprd	3	M161B00	Psoriasis plantaris	2945
Version: 1	3	M161500	Psoriasis geographica	21633
Source: CPRD	3	M166.00	Palmoplantar pustular psoriasis	105229
Author: C McKenna	3	M161A00	Psoriasis palmaris	8014
Date: 19th October 2018	3	M161J00	Flexural psoriasis	107494
Categories:	3	M16..00	Psoriasis and similar disorders	3733
1 = H/O	3	M161400	Psoriasis discoidea	18755
2= Probable	3	M161600	Guttate psoriasis	3193

3 = Definite	3	M16y000	Scalp psoriasis	11761
	3	M161700	Psoriasis gyrata	65839
	3	M161C00	Psoriasis punctata	24136
	3	M161300	Psoriasis diffusa	42008
	3	M161F00	Psoriasis vulgaris	30210
	3	M160000	Psoriasis spondylitica	26368
	3	Myu3000	[X]Other psoriasis	66711
	3	M161H00	Erythrodermic psoriasis	17094
	3	M161z00	Psoriasis NOS	172
	3	M161200	Psoriasis circinata	30272
	3	M16y.00	Other psoriasis and similar disorders	41149
	1	14F2.00	H/O: psoriasis	3437
	3	M16z.00	Psoriasis and similar disorders NOS	30975
	3	M161E00	Psoriasis universalis	20222
	3	M161100	Psoriasis annularis	21104
	3	38Gg.00	Psoriasis area and severity index	106363
	3	N045200	Juvenile arthritis in psoriasis	28456
	3	M161D00	Pustular psoriasis	4231
	3	M161000	Psoriasis unspecified	162
	3	M161900	Psoriasis ostracea	60169
	3	M161F11	Chronic large plaque psoriasis	93511
	3	M161800	Psoriasis inveterata	48257
	3	M161.00	Other psoriasis	22501
	3	M170400	Lichen planus hypertrophicus	7983
	3	Myu3200	[X]Other lichen planus	53843
	3	M170700	Lichen planus obtusus	67900
	3	M170z00	Lichen planus NOS	38416
	3	M170900	Follicular lichen planus	43358
	3	M170100	Lichen planus annularis	38610
	3	M170800	Subacute active lichen planus	57469
	3	M170000	Lichen planus actinicus	43912
	3	M170.00	Lichen planus	1621
	3	M170300	Lichen planus bullosus	22154
	3	M170500	Lichen planus linearis	40455

3	M170200	Lichen planus atrophicus	18954
3	M144300	Foliaceous pemphigus	32219
3	M144000	Benign pemphigus	52474
3	M144800	Drug-induced pemphigus	106167
3	M144.00	Pemphigus	15415
3	M145100	Benign pemphigus NOS	17808
3	M144600	Pemphigus vulgaris	25738
3	M144700	Wildfire pemphigus	67527
3	Myu1000	[X]Other pemphigus	97478
3	43mb.00	Pemphigus antibody level	34602
3	68E0.00	Pemphigus/pemphigoid screening	85987
3	M144200	Erythematous pemphigus	49282
3	M144500	Pemphigus vegetans	57451
3	M144z00	Pemphigus NOS	53763
3	PH33111	Benign familial chronic pemphigus	49284
3	M146z00	Benign mucous membrane pemphigoid NOS	58079
3	M145.00	Pemphigoid	2646
3	M145z00	Pemphigoid NOS	58116
3	M142.11	Juvenile pemphigoid	17810
3	M146.00	Benign mucous membrane pemphigoid	37532
3	M146011	Cicatricial pemphigoid	40275
3	M146000	Benign mucous membrane pemphigoid with no eye involvement	71937
3	M145000	Bullous pemphigoid	9880
3	F4Cy100	Ocular pemphigoid	37617
3	43mc.00	Pemphigoid antibody level	34601
3	M146100	Ocular pemphigoid	45463
3	Myu1200	[X]Other pemphigoid	70199
3	M118.00	Infantile seborrhoeic dermatitis	3580
3	M101.11	Seborrhoeic dermatitis capitis	7425
3	Myu2000	[X]Other seborrhoeic dermatitis	48473
3	M101.00	Seborrhoeic dermatitis	359
3	M118z00	Infantile seborrhoeic dermatitis NOS	21266
3	M118000	Infantile seborrhoeic dermatitis capitis	45407
3	F4E5311	Vitiligo of eyelid	43328
3	M295100	Vitiligo	975
3	M223.00	Seborrhoeic keratosis	919

metadata	category	readcode	readterm	medcode
Name: Epilepsy_cprd	1	1473.00	H/O: epilepsy	3783
Version: 1	3	2822.00	O/E - grand mal fit	7811
Source: CPRD	3	2823.00	O/E - petit mal fit	7809
Author: C McKenna	3	2824.00	O/E - focal (Jacksonian) fit	57277
Date: 19th October 2018	3	2824.11	O/E - Jacksonian fit	39530
Categories:	3	2825.00	O/E - psychomotor fit	51517
1 = H/O	3	2826.00	O/E - salaam attack	31663
2= Probable	3	2828.00	Absence seizure	8097
3 = Definite	3	6671.00	Initial epilepsy assessment	45746
	3	6674.00	Epilepsy associated problems	50012
	3	6675.00	Fit frequency	8262
	3	6677.00	Epilepsy drug side effects	13073
	3	6679.00	Epilepsy treatment started	34473
	1	2126000	Epilepsy resolved	8385
	3	Eu80300	[X]Acquired aphasia with epilepsy [Landau - Kleffner]	43679
	3	F132100	Progressive myoclonic epilepsy	37644
	3	F250y00	Other specified generalised nonconvulsive epilepsy	59185
	3	F250z00	Generalised nonconvulsive epilepsy NOS	44252
	3	F251.00	Generalised convulsive epilepsy	26144
	3	F251011	Tonic-clonic epilepsy	22804
	3	F251100	Neonatal myoclonic epilepsy	37782
	3	F251y00	Other specified generalised convulsive epilepsy	45927
	3	F251z00	Generalised convulsive epilepsy NOS	40806
	3	F254.00	Partial epilepsy with impairment of consciousness	32288
	3	F254100	Psychomotor epilepsy	23634
	3	F254200	Psychosensory epilepsy	36203
	3	F254300	Limbic system epilepsy	55665
	3	F254z00	Partial epilepsy with impairment of consciousness NOS	31920
	3	F255.00	Partial epilepsy without impairment of consciousness	26015
	3	F255100	Sensory induced epilepsy	48134
	3	F255200	Somatosensory epilepsy	37592
	3	F255400	Visual reflex epilepsy	55739
	3	F255y00	Partial epilepsy without impairment of consciousness OS	26733
	3	F25A.00	Juvenile myoclonic epilepsy	19363
	2	F25B.00	Alcohol-induced epilepsy	30604
	2	F25C.00	Drug-induced epilepsy	30816
	3	F25D.00	Menstrual epilepsy	56359

3	F25E.00	Stress-induced epilepsy	65673
3	F25y.00	Other forms of epilepsy	38307
3	1B1W.00	Transient epileptic amnesia	38919
3	1B63.00	Had a fit	1902
3	1B63.11	Fit - had one, symptom	3652
3	1B64.00	Had a convulsion	9085
3	1B64.11	Convulsion - symptom	7808
3	1JA0.00	Suspected epilepsy	12811
3	1O30.00	Epilepsy confirmed	22341
1	212J.00	Epilepsy resolved	12848
3	282..00	O/E - fit/convulsion	32662
3	282..11	O/E - a convulsion	6072
3	282..13	O/E - a seizure	7275
3	282Z.00	O/E - fit/convulsion NOS	38457
3	667..00	Epilepsy monitoring	6983
3	667B.00	Nocturnal epilepsy	4602
3	667C.00	Epilepsy control good	19550
3	667E.00	Epilepsy care arrangement	19551
1	667F.00	Seizure free >12 months	11015
3	667G.00	Epilepsy restricts employment	26620
3	667H.00	Epilepsy prevents employment	50702
3	667J.00	Epilepsy impairs education	40863
3	667N.00	Epilepsy severity	22991
3	667P.00	No seizures on treatment	13219
3	667Q.00	1 to 12 seizures a year	26618
3	667R.00	2 to 4 seizures a month	13221
3	667S.00	1 to 7 seizures a week	19549
3	667T.00	Daily seizures	18899
3	667V.00	Many seizures a day	39160
3	667W.00	Emergency epilepsy treatment since last appointment	46603
3	667Z.00	Epilepsy monitoring NOS	36696
3	8BL3.00	Patient on maximal tolerated anticonvulsant therapy	11752
3	9N0r.00	Seen in epilepsy clinic	47117
3	9Of0.00	Epilepsy screen invite 1	34346
3	9Of1.00	Epilepsy screen invite 2	34362
3	9Of7.00	Epilepsy monitoring call third letter	98977
3	Eu05212	[X]Schizophrenia-like psychosis in epilepsy	31877
3	Eu05y11	[X]Epileptic psychosis NOS	6709
3	Eu06013	[X]Limbic epilepsy personality	48462
3	F132200	Myoclonic encephalopathy	45602
3	F25..00	Epilepsy	573
3	F25.z.11	Fit (in known epileptic) NOS	3607
3	F250.00	Generalised nonconvulsive epilepsy	11186
3	F250000	Petit mal (minor) epilepsy	2907

3	F250011	Epileptic absences	1715
3	F250100	pykno-epilepsy	99548
3	F250200	Epileptic seizures - atonic	24309
3	F250300	Epileptic seizures - akinetic	31830
3	F250400	Juvenile absence epilepsy	17399
3	F250500	Lennox-Gastaut syndrome	34792
3	F251000	Grand mal (major) epilepsy	988
3	F251111	Otohara syndrome	49340
3	F251200	Epileptic seizures - clonic	18471
3	F251300	Epileptic seizures - myoclonic	4801
3	F251400	Epileptic seizures - tonic	5152
3	F251500	Tonic-clonic epilepsy	8187
3	F251600	Grand mal seizure	5668
3	F252.00	Petit mal status	215809
3	F253.00	Grand mal status	5117
3	F253.11	Status epilepticus	4093
3	F254000	Temporal lobe epilepsy	3175
3	F254400	Epileptic automatism	34079
3	F254500	Complex partial epileptic seizure	11394
3	F255000	Jacksonian; focal or motor epilepsy	9569
3	F255011	Focal epilepsy	5525
3	F255012	Motor epilepsy	65699
3	F255300	Visceral reflex epilepsy	73542
3	F255311	Partial epilepsy with autonomic symptoms	98870
3	F255500	Unilateral epilepsy	68946
3	F255600	Simple partial epileptic seizure	40105
3	F255z00	Partial epilepsy without impairment of consciousness NOS	27526
3	F256.00	Infantile Spasms	4478
3	F256.11	Lightning spasms	224846
3	F256.12	West Syndrome	39023
3	F256000	Hypsarrhthymia	7945
3	F256100	Salaam attacks	23415
3	F256z00	Infantile Spasms NOS	49322
3	F257.00	Kojevnikov's epilepsy	71719
3	F259.00	Early infant epileptic encephalopathy with suppression bursts	37906
3	F259.11	Ohtahara syndrome	51998
3	F25F.00	Photosensitive epilepsy	30635
3	F25G.00	Severe myoclonic epilepsy in infancy	108409
3	F25H.00	Generalised seizure	106571
3	F25X.00	Status epilepticus; unspecified	6271
3	F25y000	Cursive (running) epilepsy	55260
3	F25y100	Gelastic epilepsy	53483
3	F25y200	Locl-rlt(foc)(part)idiop epilep&epilptic syn seiz locl onset	9887
3	F25y300	Complex partial status epilepticus	25330

3	F25y400	Benign Rolandic epilepsy	19170
3	F25y500	Panayiotopoulos syndrome	96641
3	F25yz00	Other forms of epilepsy NOS	9979
3	F25z.00	Epilepsy NOS	9747
3	Fyu5000	[X]Other generalized epilepsy and epileptic syndromes	99731
3	Fyu5100	[X]Other epilepsy	69831
3	Fyu5200	[X]Other status epilepticus	59120
3	Fyu5900	[X]Status epilepticus; unspecified	71801
3	Q480.00	Convulsions in newborn	20005
3	Q480.11	Fits in newborn	21839
3	Q480.12	Seizures in newborn	13304
3	R003.00	[D]Convulsions	1137
3	R003100	[D]Convulsions, infantile	27647
2	R003211	[D]Fit (in non epileptic) NOS	6721
3	R003400	[D]Nocturnal seizure	99834
3	R003y00	[D]Other specified convulsion	25865
3	R003z00	[D]Convulsion NOS	15077
3	R003z11	[D]Seizure NOS	1306
3	Ryu7100	[X]Other and unspecified convulsions	72608
3	SC20000	Traumatic epilepsy	4109
3	SL6..11	Anticonvulsant poisoning	62030
3	ZS82.00	Acquired epileptic aphasia	49889
3	ZS82.11	Landau-Kleffner syndrome	59806

Glaucoma

metadata	category	readcode	readterm	medcode
Name: Glaucoma_cprd	1	1482.00	H/O: glaucoma	8955
Version: 1	3	7259.00	Operations following glaucoma surgery	46069
Source: CPRD	3	7275.00	Pan retinal photocoagulation for glaucoma	11059
Author: C McKenna	3	7259000	Needling of bleb following glaucoma surgery	65079
Date: 19th October 2018	3	7259100	Injection of bleb following glaucoma surgery	89934
Categories:	3	7259200	Revision of bleb NEC following glaucoma surgery	88595
1 = H/O	3	7259300	Removal of releasable suture following glaucoma surgery	91442
2= Probable	3	7259400	Laser suture lysis following glaucoma surgery	93967
3 = Definite	3	66T1.00	Glaucoma monitoring	2399
	3	7259y00	Other specified operations following glaucoma surgery	88142
	3	7259z00	Operations following glaucoma surgery NOS	95852
	3	F442100	Glaucomatocyclitic crises	29764
	3	F45..00	Glaucoma	2074
	3	F450.00	Borderline glaucoma	8971
	3	F450000	Unspecified preglaucoma	24860
	3	F450100	Open angle glaucoma with borderline intraocular pressure	10070

3	F450200	Borderline glaucoma with anatomical narrow angle	35748
3	F450300	Borderline glaucoma steroid responder	36737
3	F450400	Ocular hypertension	1611
3	F450z00	Borderline glaucoma NOS	9260
3	F451.00	Open-angle glaucoma	1798
3	F451000	Unspecified open-angle glaucoma	42447
3	F451100	Primary open-angle glaucoma	4581
3	F451111	Simple chronic glaucoma	30649
3	F451200	Low tension glaucoma	9469
3	F451211	Normal pressure glaucoma	53879
3	F451300	Pigmentary glaucoma	12251
3	F451400	Glaucoma of childhood	58645
3	F451500	Open-angle glaucoma residual stage	72394
3	F451z00	Open-angle glaucoma NOS	28189
3	F452.00	Primary angle-closure glaucoma	2823
3	F452.11	Closed angle glaucoma	6315
3	F452000	Unspecified primary angle-closure glaucoma	20520
3	F452100	Intermittent primary angle-closure glaucoma	44817
3	F452200	Acute primary angle-closure glaucoma	28536
3	F452300	Chronic primary angle-closure glaucoma	35446
3	F452400	Primary angle-closure glaucoma residual stage	67413
3	F452z00	Primary angle-closure glaucoma NOS	39120
2	F453.00	Steroid-induced glaucoma	35528
2	F453100	Steroid-induced glaucoma residual stage	68094
2	F453z00	Steroid-induced glaucoma NOS	48132
3	F454.00	Glaucoma due to disease EC	41854
3	F454000	Glaucoma due to chamber angle anomaly	69195
3	F454100	Glaucoma due to iris anomaly	67341
3	F454200	Glaucoma due to other anterior segment anomaly	96707
3	F454300	Glaucoma due to systemic syndrome	64851
3	F454400	Glaucoma in endocrine, nutritional and metabolic diseases	68633
3	F454z00	Glaucoma due to disease NOS	41804
3	F455.00	Glaucoma associated with disorders of the lens	54262
3	F455000	Phacolytic glaucoma	44798
3	F455100	Pseudoexfoliation glaucoma	18743
3	F455z00	Glaucoma associated with disorders of the lens NOS	34354
3	F456.00	Glaucoma associated with other ocular disorders	53127
3	F456000	Glaucoma due to unspecified ocular disorder	22805
3	F456100	Glaucoma due to pupillary block	37876
3	F456200	Glaucoma due to ocular inflammation	26870
3	F456300	Glaucoma due to ocular vascular disorder	41794
3	F456400	Glaucoma due to ocular tumour or cyst	48479
3	F456500	Glaucoma due to ocular trauma	22528
3	F456600	Neovascular glaucoma	11058

3	F456611	Rubeotic glaucoma	9213
3	F456z00	Glaucoma associated with other ocular disorders NOS	53521
3	F45y.00	Other specified forms of glaucoma	28505
3	F45y000	Hypersecretion glaucoma	63660
3	F45y100	Glaucoma due to episode of increased venous pressure	65193
3	F45y200	Low tension glaucoma	8132
3	F45yz00	Other specified glaucoma NOS	44295
3	F45z.00	Glaucoma NOS	8001
3	F4H1400	Optic disc glaucomatous atrophy	20230
3	FyuG.00	[X]Glaucoma	52888
3	FyuG000	[X]Other glaucoma	70195
3	FyuG100	[X]Glaucoma in endocrine,nutritional+metabolic diseases CE	98647

Gastroesophageal reflux

metadata	category	readcode	readterm	medcode
Name: Reflux_cprd	3	J10y400	Oesopheal reflux without mention of oesophagitis	25610
Version: 1	3	760L000	Antireflux fundoplication using thoracic approach	14713
Source: CPRD	3	J101100	Reflux oesophagitis	2535
Author: C McKenna	3	760L300	Antireflux gastropexy	45360
Date: 19th October 2018	3	J101113	Oesophageal reflux with oesophagitis	16605
Categories:	3	J101112	Gastro-oesophageal reflux with oesophagitis	7104
1 = H/O	3	760Lz00	Antireflux operation NOS	28619
2= Probable	3	K100400	Nonobstructive reflux-associated chronic pyelonephritis	35360
3 = Definite	3	760L400	Antireflux procedure and gastroplasty HFQ	103564
	3	760L.00	Antireflux operations	18211
	3	171J.00	Reflux cough	19470
	3	760L111	Antireflux procedure using thoracic approach NEC	68276
	3	760L.11	Oesophageal reflux operations	17263
	3	J10y412	Gastro-oesophageal reflux	984
	3	J10y413	Acid reflux	2281
	3	J10y411	Oesophageal reflux	1327
	3	760Ly00	Other specified antireflux operation	34005
	3	J101111	Acid reflux	15054
	3	1957.00	Gastric reflux	7577
	3	760L311	Antireflux gastroplasty	48146
	3	J101z00	Oesophagitis NOS	14760
	3	J101.00	Oesophagitis	592
	3	J101600	Ulcerative oesophagitis	5283
	3	J101115	Regurgitant oesophagitis	16450
	3	J101114	Peptic oesophagitis	15579

Hearing impairment

metadata	category	readcode	readterm	medcode
Name: HearingImpairment_cprd	3	3134.00	Auditory/vestib. test abnormal	8441
Version: 1	3	313440	Hearing test bilateral abnormality	10509
Source: CPRD	3	313460	Hearing test right abnormality	17981
Author: C McKenna	3	731950	Fitting external hearing prosthesis bone anchored fixtures	101755
Date: 19th October 2018	3	1C16.00	Deteriorating hearing	17699
Categories:	3	1C17.00	Hearing aid problem	47475
1 = H/O	3	2BL5.0	O/E - completely deaf	26539
2= Probable	3	2BM3.0	O/E tune fork=perceptive deaf	30355
3 = Definite	3	8D2..11	Auditory aid provision	42584
	3	8D21.0	Provide head worn hearing aid	58602
	3	8D24.0	Replace hearing aid battery	52853
	3	9O6B.0	Child hearing screen failure referred to specialist	8247
	3	F58010	Presbyacusis	1752
	3	F58011	Senile presbyacusis	30208
	3	F59..00	Hearing loss	412
	3	F59020	Conductive hearing loss due to disorder of tympanic membrane	52758
	3	F59030	Conductive hearing loss due to disorder of middle ear	31748
	3	F590z0	Conductive hearing loss NOS	33583
	3	F591.14	Perceptive hearing loss	12829
	3	F59100	Unspecified perceptive hearing loss	2061
	3	F59120	Neural hearing loss	6846
	3	F59170	Sensorineurl hear loss,unilat unrestrict hear/contralat side	29191
	3	F591A0	Bilateral congenital sensorineural hearing loss	107323
	3	F591z0	Perceptive hearing loss NOS	16393
	3	F595.00	Low frequency deafness	44282
	3	F597.00	Mild acquired hearing loss	99753
	3	F598.00	Moderate acquired hearing loss	100127
	3	F5A..00	Hearing impairment	96245
	3	Fy1..00	Combined visual and hearing impairment	103907
	3	P40z.00	Other and unspecified ear anomaly with hearing impaired	27313
	3	SJ15.12	Deafness - traumatic - NOS	12339
	3	Z8B530	Does use hearing aid	19417
	3	Z91110	Fit hearing aid	7344
	3	Z91150	Checking hearing aid	30394

3	Z911B00	Attention to hearing aid	42879
3	Z911E00	Fit ear mould for existing hearing aid	58826
3	Z961.00	Provision of guide help for visual and hearing impairment	38717
3	ZE3..00	Distorted hearing	26058
3	ZE63.00	Hearing worse	11184
3	ZE8220	Hearing for conversational voice impaired	36807
3	ZE84.12	Hearing for speech	39997
3	ZE86.00	Difficulty hearing in noise	30334
3	ZE87.12	Difficulty hearing	19666
3	ZE87.13	Hard of hearing	22102
3	ZE87.16	HL - Hearing loss	12324
3	ZE87.17	HOH - Hard of hearing	7891
3	ZE87.18	Hearing impairment	18008
3	ZV53200	[V]Fitting or adjustment of hearing aid	2876

Hyperthyroidism

metadata	category	readcode	readterm	medcode
Name: Hyperthyroidism_cprd	1	1431.00	H/O: hyperthyroidism	6245
Version: 1	1	1431.11	H/O: thyrotoxicosis	8038
Source: CPRD	3	212P.00	Hyperthyroidism resolved	26362
Author: C McKenna	3	C02..00	Thyrotoxicosis	677
Date: 19th October 2018	3	C02..11	Hyperthyroidism	1472
Categories:	3	C02..12	Toxic goitre	10760
1 = H/O	3	C020.00	Toxic diffuse goitre	23315
2= Probable	3	C020.11	Basedow's disease	44405
3 = Definite	3	C020.12	Graves' disease	5257
	3	C020000	Toxic diffuse goitre with no crisis	26702
	3	C020100	Toxic diffuse goitre with crisis	57011
	3	C020z00	Toxic diffuse goitre NOS	49334
	3	C021.00	Toxic uninodular goitre	53280
	3	C021000	Toxic uninodular goitre with no crisis	26869
	3	C021z00	Toxic uninodular goitre NOS	61498
	3	C022.00	Toxic multinodular goitre	11426
	3	C022000	Toxic multinodular goitre with no crisis	46985
	3	C022z00	Toxic multinodular goitre NOS	53981
	3	C023.00	Toxic nodular goitre unspecified	15790
	3	C023000	Toxic nodular goitre unspecified with no crisis	68512
	3	C023z00	Toxic nodular goitre NOS	49361
	3	C024.00	Thyrotoxicosis from ectopic thyroid nodule	49508

3	C024000	Thyrotoxicosis from ectopic thyroid nodule with no crisis	64656
3	C024z00	Thyrotoxicosis from ectopic thyroid nodule NOS	56270
3	C02y.00	Thyrotoxicosis of other specified origin	43136
3	C02y000	Thyrotoxicosis of other specified origin with no crisis	51273
3	C02yz00	Thyrotoxicosis of other specified origin NOS	34220
3	C02z.00	Thyrotoxicosis without mention of goitre or other cause	15565
3	C02z000	Thyrotoxicosis without mention of goitre or cause no crisis	26701
3	C02z100	Thyrotoxicosis without mention of goitre, cause with crisis	3194
3	C02zz00	Thyrotoxicosis NOS	26699
3	Cyu1300	[X]Other thyrotoxicosis	72690
3	F381600	Myasthenic syndrome due to thyrotoxicosis	47695
3	F395400	Myopathy due to thyrotoxicosis	48167
3	F4G2000	Thyrotoxic exophthalmos	1567
3	G557500	Thyrotoxic heart disease	20035
3	Q443.00	Neonatal thyrotoxicosis	48010
3	C05..00	Thyroiditis	1346
3	C050.00	Acute thyroiditis	4898
3	C050000	Acute nonsuppurative thyroiditis	67972
3	C050100	Acute suppurative thyroiditis	70773
3	C050200	Abscess of thyroid	29296
3	C050z00	Acute thyroiditis NOS	42323
3	C051.00	Subacute thyroiditis	30799
3	C051.11	De Quervain's thyroiditis	21747
3	C052.00	Chronic lymphocytic thyroiditis	26833
3	C052.11	Autoimmune thyroiditis	3857
3	C053.00	Chronic fibrous thyroiditis	70244
3	C053.11	Riedel's thyroiditis	53667
3	C054.00	Iatrogenic thyroiditis	61026
3	C05y.00	Other and unspecified chronic thyroiditis	65444
3	C05y400	Chronic thyroiditis with transient thyrotoxicosis	65907
3	C05z.00	Thyroiditis NOS	20909
3	Cyu1400	[X]Other chronic thyroiditis	95335
3	L181500	Postpartum thyroiditis	11947
3	C02y.11	Factitia thyrotoxicosis	58138
3	C02y200	Thyrotoxicosis factitia	64856

Hypothyroidism

metadata	category	readcode	readterm	medcode
Name: Hypothyroidism_cprd	3	C04..13	Hypothyroidism	273
Version: 1	3	C0A5.00	Subclinical iodine-deficiency hypothyroidism	718

Source: CPRD	3	C04..11	Myxoedema	1619
Author: C McKenna	3	C04..00	Acquired hypothyroidism	3290
Date: 19th October 2018	3	C052.12	Hashimoto's disease	3436
Categories:	1	1432.00	H/O: hypothyroidism	3611
1 = H/O	3	C04z.00	Hypothyroidism NOS	3941
2= Probable	3	C03..00	Congenital hypothyroidism	10097
3 = Definite	3	C134300	TSH - thyroid-stimulating hormone deficiency	11146
	3	C041000	Irradiation hypothyroidism	11322
	3	C04..12	Thyroid deficiency	14704
	3	C043000	Hypothyroidism resulting from para-aminosalicylic acid	15743
	3	C04z.13	Hypothyroid goitre, acquired	18282
	3	9Oj3.00	Hypothyroidism monitoring verbal invite	19367
	3	C04z.11	Pretibial myxoedema - hypothyroid	20310
	3	C04z.12	Thyroid insufficiency	23014
	3	C04y.00	Other acquired hypothyroidism	24748
	3	C043.00	Other iatrogenic hypothyroidism	25913
	3	C03z.12	Cretinism	27533
	3	9Oj..00	Hypothyroidism monitoring administration	28735
	3	C040.00	Postsurgical hypothyroidism	28852
	3	C03y000	Congenital hypothyroidism with diffuse goitre	31612
	3	C046.00	Autoimmune myxoedema	31971
	3	C042.00	Iodine hypothyroidism	34221
	3	C043z00	Iatrogenic hypothyroidism NOS	38976
	3	C0A1.00	Congenital iodine-deficiency syndrome, myxoedematous type	39166
	3	44qV.00	Congenital hypothyroidism screening test	43861
	3	9Oj0.00	Hypothyroidism monitoring first letter	46057
	3	9Oj1.00	Hypothyroidism monitoring second letter	46630
	3	9Oj2.00	Hypothyroidism monitoring third letter	46640
	3	C031.00	Goitrous cretin	47449
	3	C040.11	Post ablative hypothyroidism	47521
	3	F11x500	Cerebral degeneration due to myxoedema	47658
	3	C041.00	Other postablative hypothyroidism	50275
	3	C044.00	Postinfectious hypothyroidism	50860
	3	F395300	Myopathy due to myxoedema	51416
	3	C03z.00	Congenital hypothyroidism NOS	51481
	3	C041z00	Postablative hypothyroidism NOS	51706
	3	C04z000	Premature puberty due to hypothyroidism	56722
	3	Q433700	Neonatal jaundice with congenital hypothyroidism	58833
	3	C04z100	Myxoedema coma	59702

3	F381400	Myasthenic syndrome due to hypothyroidism	61069
3	C03..11	Cretinism	67513
3	C03y.00	Other specified congenital hypothyroidism	69290
3	Cyu1100	[X]Other sp cified hypothyroidism	73107
3	9Oj4.00	Hypothyroidism monitoring telephone invitation	85661
3	8CR5.00	Hypothyroidism clinical management plan	85955
3	C03y100	Congenital hypothyroidism without goitre	93159
3	C03z.11	Congenital thyroid insufficiency	93323
3	C043200	Hypothyroidism resulting from resorcinol	94915
3	C047.00	Subclinical hypothyroidism	95830
3	66BB.00	Hypothyroidism annual review	95885
3	C043100	Hypothyroidism resulting from phenylbutazone	97090
3	1JM..00	Suspected hypothyroidism	102442
3	1IC..00	Congenital hypothyroidism not suspected	104582
3	8IEf.00	Congenital hypothyroidism screening declined	107806
3	1JM0.00	Suspected congenital hypothyroidism	108482

Inflammatory Bowel Disease

metadata	category	readcode	readterm	medcode
Name: IBD_cprd	1	14C4.11	H/O: ulcerative colitis	5749
Version: 1	3	J41..00	Idiopathic proctocolitis	5133
Source: CPRD	3	J41..12	Ulcerative colitis and/or proctitis	1784
Author: C McKenna	3	J410.00	Ulcerative proctocolitis	6650
Date: 19th October 2018	3	J410000	Ulcerative ileocolitis	48732
Categories:	3	J410100	Ulcerative colitis	704
1 = H/O	3	J410300	Ulcerative proctitis	8347
2= Probable	3	J410400	Exacerbation of ulcerative colitis	22516
3 = Definite	3	J410z00	Ulcerative proctocolitis NOS	33456
	3	J411.00	Ulcerative (chronic) enterocolitis	30433
	3	J412.00	Ulcerative (chronic) ileocolitis	42822
	3	J41y.00	Other idiopathic proctocolitis	24550
	3	J41yz00	Other idiopathic proctocolitis NOS	43090
	3	J41z.00	Idiopathic proctocolitis NOS	15207
	3	Jyu4100	[X]Other ulcerative colitis	53743
	3	N031000	Arthropathy in ulcerative colitis	17641
	3	N045400	Juvenile arthritis in ulcerative colitis	71083
	3	J08z900	Orofacial Crohn's disease	29616
	3	J40..00	Regional enteritis - Crohn's disease	11286
	3	J40..11	Crohn's disease	593

3	J400200	Crohn's disease of the terminal ileum	28476
3	J400300	Crohn's disease of the ileum unspecified	66238
3	J400400	Crohn's disease of the ileum NOS	39278
3	J400500	Exacerbation of Crohn's disease of small intestine	36913
3	J400z00	Crohn's disease of the small bowel NOS	9359
3	J401200	Exacerbation of Crohn's disease of large intestine	39037
3	J401z00	Crohn's disease of the large bowel NOS	20688
3	J401z11	Crohn's colitis	6538
3	J40z.11	Crohn's disease NOS	59994
3	Jyu4000	[X]Other Crohn's disease	69959
3	N031100	Arthropathy in Crohn's disease	20480
3	N045300	Juvenile arthritis in Crohn's disease	12575
3	ZR3S.00	Crohn's disease activity index	11337
3	ZR3S.11	CDAI - Crohn's disease activity index	11119
3	J4...12	Inflammatory bowel disease	1796
3	J400.00	Regional enteritis of the small bowel	51576
3	J402.00	Regional ileocolitis	15773
3	J410200	Ulcerative rectosigmoiditis	24858
3	J4...11	Colitis - noninfective	1561
3	J41..11	Mucous colitis and/or proctitis	23950
3	J413.00	Ulcerative pancolitis	104259
3	J43..00	Other non-infective inflammatory gastroenteritis and colitis	42531
3	J431200	Toxic enterocolitis	68825
3	J431300	Toxic colitis	29435
3	J435.00	Pouchitis	11775
3	J437.00	Colitis	96919
3	J438.00	Left sided colitis	104556
3	J4z2.00	Non-infective ileitis NOS	9788
3	J4z3.00	Non-infective colitis NOS	8301
3	J4z5.00	Exacerbation of non-infective colitis	30662
3	J4z6.00	Indeterminate colitis	96976

Iron deficiency

metadata	category	readcode	readterm	medcode
Name: IronDefic_cprd	3	42R2.00	Serum iron low	15535
Version: 1	1	1451.00	H/O: anaemia - iron deficient	31214
Source: CPRD	3	L182500	Iron deficiency anaemia of pregnancy	1668
Author: C McKenna	3	D00..00	Iron deficiency anaemias	795
Date: 19th October 2018	3	D000.00	Iron deficiency anaemia due to chronic blood loss	27726
Categories:	3	D000.12	Iron deficiency anaemia due to blood loss	48338
1 = H/O	3	D001.00	Iron deficiency anaemia due to dietary causes	21127
2= Probable	3	D00y.00	Other specified iron deficiency anaemia	33420

3 = Definite	3	D00yz00	Other specified iron deficiency anaemia NOS	9537
	3	D00z.00	Unspecified iron deficiency anaemia	18137
	3	D00zz00	Iron deficiency anaemia NOS	15439
	3	Dyu0000	[X]Other iron deficiency anaemias	4858
	3	D00..11	Hypochromic - microcytic anaemia	882
	3	D00..12	Microcytic - hypochromic anaemia	539
	3	D00y100	Microcytic hypochromic anaemia	4839
	3	D00zz00	Iron deficiency anaemia NOS	15439
	3	D00y.00	Other specified iron deficiency anaemia	33420
	3	C294300	Iron deficiency	5619
	3	D00..00	Iron deficiency anaemias	795
	3	D00z.00	Unspecified iron deficiency anaemia	18137
	3	D00yz00	Other specified iron deficiency anaemia NOS	9537
	3	D001.00	Iron deficiency anaemia due to dietary causes	21127
	3	42R2.00	Serum iron low	15535

Ischaemic Heart Disease

metadata	category	readcode	readterm	medcode
Name: IchaemiaHeartDisease_cprd	1	14A5.00	H/O: angina pectoris	6336
Version: 1	1	14A6.00	H/O: heart failure	15058
Source: CPRD	1	14AJ.00	H/O: Angina in last year	57062
Author: C McKenna	1	14AM.00	H/O: Heart failure in last year	46912
Date: 19th October 2018	3	173..13	Shortness of breath symptom	5349
Categories:	3	1J60.00	Suspected heart failure	21235
1 = H/O	3	1O1..00	Heart failure confirmed	9913
2= Probable	3	23E1.00	O/E - pulmonary oedema	5155
3 = Definite	3	323..00	ECG: myocardial infarction	7783
	3	388D.00	New York Heart Assoc classification heart failure symptoms	46672
	3	662f.00	New York Heart Association classification - class I	18853
	3	662g.00	New York Heart Association classification - class II	13189
	3	662h.00	New York Heart Association classification - class III	19066
	3	662i.00	New York Heart Association classification - class IV	51214
	3	662K.00	Angina control	13185
	3	662K000	Angina control - good	19542
	3	662K100	Angina control - poor	15373
	3	662K200	Angina control - improving	14782
	3	662K300	Angina control - worsening	29300
	3	662Kz00	Angina control NOS	15349
	3	662p.00	Heart failure 6 month review	83502
	3	662T.00	Congestive heart failure monitoring	12366

3	662W.00	Heart failure annual review	30779
3	679X.00	Heart failure education	95835
3	792..11	Coronary artery bypass graft operations	737
3	7920y00	Saphenous vein graft replacement of coronary artery OS	7137
3	7920z00	Saphenous vein graft replacement coronary artery NOS	51515
3	7928y00	Transluminal balloon angioplasty of coronary artery OS	41547
3	7928z00	Transluminal balloon angioplasty of coronary artery NOS	732
3	792B00	Endarterectomy of coronary artery NEC	22020
3	792D.00	Other bypass of coronary artery	34963
3	792Dy00	Other specified other bypass of coronary artery	3159
3	792Dz00	Other bypass of coronary artery NOS	33471
3	792y.00	Other specified operations on coronary artery	31571
3	793G.00	Perc translumin balloon angioplasty stenting coronary artery	43939
3	8B27.00	Antianginal therapy	45960
3	8B29.00	Cardiac failure therapy	24503
3	8CL3.00	Heart failure care plan discussed with patient	32945
3	8H2S.00	Admit heart failure emergency	32898
3	8HBE.00	Heart failure follow-up	17851
3	8Hg8.00	Discharge from practice nurse heart failure clinic	91288
3	8HHz.00	Referral to heart failure exercise programme	70619
3	8Hk0.00	Referred to heart failure education group	71235
3	8L40.00	Coronary artery bypass graft operation planned	101121
3	9h1..00	Exception reporting: LVD quality indicators	34213
3	9h11.00	Excepted from LVD quality indicators: Patient unsuitable	11613
3	9h12.00	Excepted from LVD quality indicators: Informed dissent	28649
3	9hH..00	Exception reporting: heart failure quality indicators	90935
3	9hH0.00	Excepted heart failure quality indicators: Patient unsuitabl	30749
3	9hH1.00	Excepted heart failure quality indicators: Informed dissent	64062
3	9N0k.00	Seen in heart failure clinic	12627
3	9N2p.00	Seen by community heart failure nurse	19002
3	9N4s.00	Did not attend practice nurse heart failure clinic	95021
3	9N4w.00	Did not attend heart failure clinic	83481
3	9N6T.00	Referred by heart failure nurse specialist	69062
3	9On..00	Left ventricular dysfunction monitoring administration	18793
3	9On0.00	Left ventricular dysfunction monitoring first letter	60710
3	9On1.00	Left ventricular dysfunction monitoring second letter	60721
3	9On2.00	Left ventricular dysfunction monitoring third letter	72341
3	9On3.00	Left ventricular dysfunction monitoring verbal invite	92305

3	9On4.00	Left ventricular dysfunction monitoring telephone invite	96484
3	9Or..00	Heart failure monitoring administration	32911
3	9Or0.00	Heart failure review completed	19380
3	9Or1.00	Heart failure monitoring telephone invite	90193
3	9Or2.00	Heart failure monitoring verbal invite	90192
3	9Or3.00	Heart failure monitoring first letter	72965
3	9Or4.00	Heart failure monitoring second letter	72386
3	9Or5.00	Heart failure monitoring third letter	89650
3	G1yz100	Rheumatic left ventricular failure	22262
3	G210.00	Malignant hypertensive heart disease	50157
3	G210000	Malignant hypertensive heart disease without CCF	95334
3	G210100	Malignant hypertensive heart disease with CCF	72668
3	G211100	Benign hypertensive heart disease with CCF	52127
3	G21z100	Hypertensive heart disease NOS with CCF	62718
3	G230.00	Malignant hypertensive heart and renal disease	67232
3	G232.00	Hypertensive heart&renal dis wth (congestive) heart failure	21837
3	G234.00	Hyperten heart&renal dis+both(congestv)heart and renal fail	57987
3	G3...00	Ischaemic heart disease	240
3	G3...11	Arteriosclerotic heart disease	24783
3	G3...12	Atherosclerotic heart disease	20416
3	G3...13	IHD - Ischaemic heart disease	1792
3	G30..00	Acute myocardial infarction	241
3	G30..11	Attack - heart	13566
3	G30..12	Coronary thrombosis	2491
3	G30..13	Cardiac rupture following myocardial infarction (MI)	30421
3	G30..14	Heart attack	1204
3	G30..15	MI - acute myocardial infarction	1677
3	G30..16	Thrombosis - coronary	13571
3	G30..17	Silent myocardial infarction	17689
3	G300.00	Acute anterolateral infarction	12139
3	G301.00	Other specified anterior myocardial infarction	5387
3	G301000	Acute anteroapical infarction	40429
3	G301100	Acute anteroseptal infarction	17872
3	G301z00	Anterior myocardial infarction NOS	14897
3	G302.00	Acute inferolateral infarction	8935
3	G303.00	Acute inferoposterior infarction	29643
3	G304.00	Posterior myocardial infarction NOS	23892
3	G305.00	Lateral myocardial infarction NOS	14898
3	G306.00	True posterior myocardial infarction	63467
3	G307.00	Acute subendocardial infarction	3704

3	G307000	Acute non-Q wave infarction	9507
3	G307100	Acute non-ST segment elevation myocardial infarction	10562
3	G308.00	Inferior myocardial infarction NOS	1678
3	G309.00	Acute Q-wave infarct	30330
3	G30A.00	Mural thrombosis	17133
3	G30B.00	Acute posterolateral myocardial infarction	32854
3	G30X.00	Acute transmural myocardial infarction of unspecif site	29758
3	G30X000	Acute ST segment elevation myocardial infarction	12229
3	G30y.00	Other acute myocardial infarction	34803
3	G30y000	Acute atrial infarction	28736
3	G30y100	Acute papillary muscle infarction	62626
3	G30y200	Acute septal infarction	41221
3	G30yz00	Other acute myocardial infarction NOS	46017
3	G30z.00	Acute myocardial infarction NOS	14658
3	G31..00	Other acute and subacute ischaemic heart disease	27951
3	G310.00	Postmyocardial infarction syndrome	23579
3	G310.11	Dressler's syndrome	15661
3	G311.00	Preinfarction syndrome	36523
3	G311.11	Crescendo angina	4656
3	G311.12	Impending infarction	39655
3	G311.13	Unstable angina	1431
3	G311.14	Angina at rest	19655
3	G311000	Myocardial infarction aborted	61072
3	G311011	MI - myocardial infarction aborted	55137
3	G311100	Unstable angina	7347
3	G311200	Angina at rest	17307
3	G311300	Refractory angina	34328
3	G311400	Worsening angina	18118
3	G311500	Acute coronary syndrome	11983
3	G311z00	Preinfarction syndrome NOS	54251
3	G312.00	Coronary thrombosis not resulting in myocardial infarction	39449
3	G31y.00	Other acute and subacute ischaemic heart disease	9413
3	G31y000	Acute coronary insufficiency	9276
3	G31y100	Microinfarction of heart	68357
3	G31y200	Subendocardial ischaemia	39693

3	G31y300	Transient myocardial ischaemia	21844
3	G31yz00	Other acute and subacute ischaemic heart disease NOS	27977
3	G32..00	Old myocardial infarction	4017
3	G32..11	Healed myocardial infarction	16408
1	G32..12	Personal history of myocardial infarction	17464
3	G33..00	Angina pectoris	1430
3	G330.00	Angina decubitus	20095
3	G330000	Nocturnal angina	18125
3	G330z00	Angina decubitus NOS	29902
3	G331.00	Prinzmetal's angina	12986
3	G331.11	Variant angina pectoris	11048
3	G332.00	Coronary artery spasm	36854
3	G33z.00	Angina pectoris NOS	25842
3	G33z000	Status anginosus	66388
3	G33z100	Stenocardia	54535
3	G33z200	Syncope anginosa	7696
3	G33z300	Angina on effort	1414
3	G33z400	Ischaemic chest pain	32450
3	G33z500	Post infarct angina	9555
3	G33z600	New onset angina	26863
3	G33z700	Stable angina	12804
3	G33zz00	Angina pectoris NOS	28554
3	G34..00	Other chronic ischaemic heart disease	28138
3	G340.00	Coronary atherosclerosis	5413
3	G340.11	Triple vessel disease of the heart	1655
3	G340.12	Coronary artery disease	1344
3	G340000	Single coronary vessel disease	3999
3	G340100	Double coronary vessel disease	5254
3	G342.00	Atherosclerotic cardiovascular disease	36609
3	G343.00	Ischaemic cardiomyopathy	7320
3	G344.00	Silent myocardial ischaemia	29421
3	G34y.00	Other specified chronic ischaemic heart disease	34633
3	G34y000	Chronic coronary insufficiency	24540
3	G34y100	Chronic myocardial ischaemia	23078
3	G34yz00	Other specified chronic ischaemic heart disease NOS	35713
3	G34z.00	Other chronic ischaemic heart disease NOS	15754
3	G34z000	Asymptomatic coronary heart disease	18889

3	G35..00	Subsequent myocardial infarction	18842
3	G350.00	Subsequent myocardial infarction of anterior wall	45809
3	G351.00	Subsequent myocardial infarction of inferior wall	38609
3	G353.00	Subsequent myocardial infarction of other sites	72562
3	G35X.00	Subsequent myocardial infarction of unspecified site	46166
3	G36..00	Certain current complication follow acute myocardial infarct	36423
3	G360.00	Haemopericardium/current comp folow acut myocard infarct	24126
3	G361.00	Atrial septal defect/curr comp folow acut myocardal infarct	23708
3	G362.00	Ventric septal defect/curr comp fol acut myocardal infarctn	37657
3	G363.00	Ruptur cardiac wall w'out haemopericard/cur comp fol ac MI	59189
3	G364.00	Ruptur chordae tendinae/curr comp fol acute myocard infarct	59940
3	G365.00	Rupture papillary muscle/curr comp fol acute myocard infarct	69474
3	G366.00	Thrombosis atrium,auric append&vent/curr comp foll acute MI	29553
3	G37..00	Cardiac syndrome X	8568
3	G38..00	Postoperative myocardial infarction	32272
3	G380.00	Postoperative transmural myocardial infarction anterior wall	46112
3	G381.00	Postoperative transmural myocardial infarction inferior wall	46276
3	G384.00	Postoperative subendocardial myocardial infarction	41835
3	G38z.00	Postoperative myocardial infarction, unspecified	68748
3	G3y..00	Other specified ischaemic heart disease	22383
3	G3z..00	Ischaemic heart disease NOS	1676
3	G400.00	Acute cor pulmonale	8464
3	G41z.11	Chronic cor pulmonale	5695
3	G554000	Congestive cardiomyopathy	5141
3	G554011	Congestive obstructive cardiomyopathy	68766
3	G58..00	Heart failure	2062
3	G58..11	Cardiac failure	1223
3	G580.00	Congestive heart failure	398
3	G580.11	Congestive cardiac failure	2906
3	G580.12	Right heart failure	10079
3	G580.13	Right ventricular failure	10154
3	G580.14	Biventricular failure	9524
3	G580000	Acute congestive heart failure	23707
3	G580100	Chronic congestive heart failure	32671
3	G580200	Decompensated cardiac failure	27884
3	G580300	Compensated cardiac failure	11424
3	G580400	Congestive heart failure due to valvular disease	94870

3	G581.00	Left ventricular failure	884
3	G581.11	Asthma - cardiac	23481
3	G581.12	Pulmonary oedema - acute	43618
3	G581.13	Impaired left ventricular function	5942
3	G581000	Acute left ventricular failure	5255
3	G582.00	Acute heart failure	27964
3	G58z.00	Heart failure NOS	4024
3	G58z.11	Weak heart	12590
3	G58z.12	Cardiac failure NOS	17278
3	G5yy600	Atrial thrombosis	30454
3	G5yy700	Left ventricular thrombosis	21854
3	G5yy900	Left ventricular systolic dysfunction	8966
3	G5yyA00	Left ventricular diastolic dysfunction	12550
3	G70..00	Atherosclerosis	5640
3	G70..11	Arteriosclerosis	996
3	G700.00	Aortic atherosclerosis	1318
3	G70z.00	Arteriosclerotic vascular disease NOS	3995
3	G74..11	Arterial embolus and thrombosis	8998
3	G74..12	Thrombosis - arterial	9364
3	G74..13	Arterial embolic and thrombotic occlusion	28004
3	Gyu3.00	[X]Ischaemic heart diseases	52517
3	Gyu3000	[X]Other forms of angina pectoris	39546
3	H54..00	Pulmonary congestion and hypostasis	30214
3	H541.00	Pulmonary congestion	1585
3	H541000	Chronic pulmonary oedema	26082
3	H541z00	Pulmonary oedema NOS	7321
3	H54z.00	Pulmonary congestion and hypostasis NOS	61229
3	H584.00	Acute pulmonary oedema unspecified	558
3	H584z00	Acute pulmonary oedema NOS	5293
3	P6y4.00	Coronary artery anomaly	25481
3	R2y1000	[D]Cardiorespiratory failure	20324
3	SP07600	Coronary artery bypass graft occlusion	12734
3	ZRad.00	New York Heart Assoc classification heart failure symptoms	26242
3	ZV45K00	[V]Presence of coronary artery bypass graft	5030
3	ZV45K11	[V]Presence of coronary artery bypass graft - CABG	5674

Non-accidental injury/ child abuse

metadata	category	readcode	readterm	medcode

Name: NAIchildAbuse_cprd	2	63CB.00	Risk of non-accidental injury	16226
Version: 1	3	SN55200	Non-accidental injury to child	2886
Source: CPRD	3	1J31.00	Suspected non-accidental injury to child	107432
Author: C McKenna	3	SN55211	NAI - non-accidental injury to child	9655
Date: 19th October 2018	1	6254.00	A/N care: H/O child abuse	33009
Categories:	3	1J30.00	Suspected sexual abuse of child	107403
1 = H/O	3	SN55z11	Child abuse NEC	23777
2= Probable	3	14XG.00	Victim of domestic abuse	107316
3 = Definite	3	SN57100	Sexual abuse	3879
	2	13ZW.00	At risk of sexual abuse	35408
	3	E250300	Nondependent alcohol abuse in remission	31569
	2	13ZR.00	At risk of emotional/psychological abuse	52024
	3	Z41..00	Abuse counselling	36393
	3	13W3.00	Child abuse in family	40032
	3	ZV4G500	[V]Problems related to alleged physical abuse of child	22625
	1	14X1.00	History of sexual abuse	7387
	2	13ZT.00	At risk of physical abuse	26008
	3	14X5.00	Victim of physical abuse	12537
	3	14X7.00	Victim of emotional abuse	48546
	3	SN55012	Emotional abuse of child	40785
	3	ZV4G400	[V]Problem relatd/alleg sex abuse cld by person prim sup grp	24008
	3	SN55500	Physical abuse of child	30588
	1	14X..00	History of abuse	8170
	3	Z412.00	Physical abuse counselling	35230
	3	ZV4F900	[V]Probs rel alleg sex abuse child by pers out prim sup grp	24072
	3	Z352.11	Child abuse investigation	67173
	3	ZV61200	[V]Child abuse	9602
	3	Z411.00	Sexual abuse counselling	28782
	3	1J3..00	Suspected child abuse	4060
	1	14X0.00	History of physical abuse	8605
	1	14X2.00	History of emotional abuse	10074
	3	14X6.00	Victim of sexual abuse	22840
	3	1J32.00	Suspected victim of child neglect	107302
	3	SN55z13	Neglect affecting child NEC	8031
	3	Z787700	Neglect of physical illness	60238
	3	ZV61212	[V]Child neglect	9749
	3	TE40.12	Accident due to neglect of helpless person	63765
	3	U3M..00	[X]Neglect and abandonment	31434
	3	Z787400	Neglect of personal hygiene	32226
	3	Z787800	Neglect of common dangers	100585
	3	13ZV.00	At risk of neglect by others	32757

3	U3My.00	[X]Neglect and abandonment, by other specified persons	60597
3	222R.00	Neglected appearance	103925
3	U3Mz.00	[X]Neglect and abandonment, by unspecified person	108983
3	Z787200	Neglect of clothes	61590
3	Z787500	Neglect of physical health	35270
3	ZVu4B00	[X]Other problems related to neglect in upbringing	101308
1	ZV1B400	[V]Personal history of neglect	99709
3	U3M1.00	[X]Neglect and abandonment, by parent	32228
3	ZV4H400	[V]Other problems related to neglect in upbringing	44086
3	ZV4H300	[V]Emotional neglect of child	28520
3	U3M2.00	[X]Neglect and abandonment, by acquaintance or friend	29968
3	13WT400	Child protection category neglect	104377
3	Z787600	Neglect of dental care	43823
3	SN57000	Neglect or abandonment	25192
3	13WT100	Child protection category emotional	104786
3	8CM6.00	Child protection plan	94516
3	13WT000	Child protection category	104904
3	9H3..00	Court of protection cert	2682
3	13Id.00	On child protection register	84157
3	13Iv.00	Subject to child protection plan	95907
3	13IM.00	Child on protection register	7215
3	13IO.00	Child removed from protection register	7325
3	Z351.00	Immediate protection of child	62870
3	13Iv000	Unborn child subject to child protection plan	104301
1	13Iw.00	No longer subject to child protection plan	96043
3	ZH11900	Surveillance for child protection	42936
3	13WT300	Child protection category sexual	105070
3	Z35..00	Child protection procedure	9529
3	13WT400	Child protection category neglect	104377
3	13WT.00	Child protection observation	104272
3	Z331.00	Child protection plan	64183
3	Z331100	Intra-agency protection plan	100176
3	13WT200	Child protection category physical	105005
3	64c..00	Child protection procedure	9530
2	Z352.00	Child protection investigation	24892

Obesity

metadata	category	readcode	readterm	medcode
Name: Obesity_cprd	3	C380.00	Obesity	430
Version: 1	3	22A4.11	O/E - overweight	2839
Source: CPRD	3	66C4.00	Has seen dietician - obesity	3176
Author: C McKenna	3	22A5.11	O/E - obese	7984
Date: 19th October 2018	3	C380300	Morbid obesity	8854
Categories:	3	22K4.00	Body mass index index 25-29 - overweight	9015
1 = H/O	3	ZC2CM00	Dietary advice for obesity	10728
2= Probable	3	C38z000	Simple obesity NOS	11401
3 = Definite	3	66C..00	Obesity monitoring	11461
	3	22K5.00	Body mass index 30+ - obesity	13278
	1	1444.00	H/O: obesity	16196
	3	66CE.00	Reason for obesity therapy - occupational	17444
	3	ZV65319	[V]Dietary counselling in obesity	17477
	3	9OK..11	Obesity clinic administration	21744
	3	22K7.00	Body mass index 40+ - severely obese	22556
	3	C380400	Central obesity	22695
	3	C380500	Generalised obesity	25968
	1	66C7.00	Treatment of obesity stopped	27570
	3	66C2.00	Follow-up obesity assessment	29538
	3	9OK..00	Obesity monitoring admin.	32843
	3	C380200	Extreme obesity with alveolar hypoventilation	38059
	3	66C6.00	Treatment of obesity started	38632
	3	66C1.00	Initial obesity assessment	38658
	3	C380000	Obesity due to excess calories	38799
	3	66CZ.00	Obesity monitoring NOS	40153
	3	9OKA.00	Obesity monitoring check done	47439
	3	L161.12	Maternal obesity syndrome	48330
	3	C380100	Drug-induced obesity	49250
	3	9OK4.00	Obesity monitoring 1st letter	49409
	3	9OK1.00	Attends obesity monitoring	52034
	3	9OK3.00	Obesity monitoring default	52036
	1	212Q.00	Obesity resolved	52703
	3	9OKZ.00	Obesity monitoring admin.NOS	52735
	3	Cyu7.00	[X]Obesity and other hyperalimentation	52782
	3	9OK6.00	Obesity monitoring 3rd letter	55585
	3	9OK5.00	Obesity monitoring 2nd letter	55586
	3	222A.00	O/E - obese	59780
	3	66C5.00	Treatment of obesity changed	64712
	3	C38..00	Obesity and other hyperalimentation	66406
	2	9OK2.00	Refuses obesity monitoring	67516
	3	9OK8.00	Obesity monitor phone invite	67517
	3	Cyu7000	[X]Other obesity	69757

	3	C38z.00	Obesity and other hyperalimentation NOS	70898
	2	9OK7.00	Obesity monitoring verbal inv.	70950
	2	9OK9.00	Obesity monitoring deleted	73304
	3	66CM.00	Risk health associ overweight and obesity, at increased risk	102150
	3	66CN.00	Risk health associated overweight and obesity, at high risk	102514
	3	22AA.00	Overweight	103499
	3	C38y011	Obesity hypoventilation syndrome	103574
	3	C380600	Adult-onset obesity	104129
	3	C380700	Lifelong obesity	104421
	3	66CL.00	Risk health associa overweight obesity, at no increased risk	104724
	3	66CS.00	Inter risk hlth overwght obesity adv diet phys act cons drug	104887
	3	66CP.00	Risk health associ overweight and obesity, at very high risk	106010
	3	C380800	Childhood obesity	106771

Schizophrenia

metadata	category	readcode	readterm	medcode
Name: Schizophrenia_cprd	1	1464.00	H/O: schizophrenia	6325
Version: 1	3	212T.00	Psychosis, schizophrenia + bipolar affective disord resolved	19345
Source: CPRD	3	212W.00	Schizophrenia resolved	88275
Author: C McKenna	1	ZV11000	[V]Personal history of schizophrenia	22104
Date: 19th October 2018	3	13Y2.00	Schizophrenia association member	67943
Categories:	3	E103.00	Paranoid schizophrenia	1494
1 = H/O	3	E103000	Unspecified paranoid schizophrenia	33383
2= Probable	3	E103200	Chronic paranoid schizophrenia	31362
3 = Definite	3	E103300	Acute exacerbation of subchronic paranoid schizophrenia	51322
	3	E103400	Acute exacerbation of chronic paranoid schizophrenia	53032
	3	E103500	Paranoid schizophrenia in remission	36172
	3	E103z00	Paranoid schizophrenia NOS	9281
	3	Eu20000	[X]Paranoid schizophrenia	16764
	3	Eu20011	[X]Paraphrenic schizophrenia	50060
	3	E101.00	Hebephrenic schizophrenia	30619
	3	E101000	Unspecified hebephrenic schizophrenia	66506
	3	E101400	Acute exacerbation of chronic hebephrenic schizophrenia	97919
	3	E101500	Hebephrenic schizophrenia in remission	67768
	3	E101z00	Hebephrenic schizophrenia NOS	48054
	3	Eu20100	[X]Hebephrenic schizophrenia	43405
	3	Eu20111	[X]Disorganised schizophrenia	53985
	3	E102.00	Catatonic schizophrenia	25546
	3	E102000	Unspecified catatonic schizophrenia	58716
	3	E102z00	Catatonic schizophrenia NOS	63867

3	Eu20200	[X]Catatonic schizophrenia	61501
3	Eu20211	[X]Catatonic stupor	20572
3	Eu20212	[X]Schizophrenic catalepsy	64533
3	Eu20213	[X]Schizophrenic catatonia	35877
3	Eu20214	[X]Schizophrenic flexibilatis cerea	31493
3	E10..00	Schizophrenic disorders	854
3	E100.00	Simple schizophrenia	32222
3	E100.11	Schizophrenia simplex	73295
3	E100000	Unspecified schizophrenia	15733
3	E100100	Subchronic schizophrenia	23616
3	E100200	Chronic schizophrenic	3984
3	E100300	Acute exacerbation of subchronic schizophrenia	57666
3	E100400	Acute exacerbation of chronic schizophrenia	44498
3	E100500	Schizophrenia in remission	58687
3	E100z00	Simple schizophrenia NOS	53625
3	E104.00	Acute schizophrenic episode	576
3	E106.00	Residual schizophrenia	38063
3	E10y.00	Other schizophrenia	39062
3	E10y.11	Cenesthopathic schizophrenia	92994
3	E10y000	Atypical schizophrenia	33338
3	E10yz00	Other schizophrenia NOS	49761
3	E10z.00	Schizophrenia NOS	8407
3	Eu20.00	[X]Schizophrenia	34236
3	Eu20300	[X]Undifferentiated schizophrenia	60013
3	Eu20311	[X]Atypical schizophrenia	91547
3	Eu20500	[X]Residual schizophrenia	64264
3	Eu20511	[X]Chronic undifferentiated schizophrenia	24107
3	Eu20600	[X]Simple schizophrenia	35848
3	Eu20y00	[X]Other schizophrenia	49420
3	Eu20y12	[X]Schizophreniform disord NOS	94001
3	Eu20y13	[X]Schizophrenifrm psychos NOS	18053
3	Eu20z00	[X]Schizophrenia, unspecified	34966
3	E105.00	Latent schizophrenia	66410
3	E105200	Chronic latent schizophrenia	94299
3	E105500	Latent schizophrenia in remission	96883
3	E212200	Schizotypal personality	61969
3	Eu2..00	[X]Schizophrenia, schizotypal and delusional disorders	17281
3	Eu21.00	[X]Schizotypal disorder	39316
3	Eu21.11	[X]Latent schizophrenic reaction	91511
3	Eu21.12	[X]Borderline schizophrenia	54387
3	Eu21.13	[X]Latent schizophrenia	64993
3	Eu21.14	[X]Prepsychotic schizophrenia	62449
3	Eu21.15	[X]Prodromal schizophrenia	40386
3	Eu21.16	[X]Pseudoneurotic schizophrenia	49852

3	Eu21.17	[X]Pseudopsychopathic schizophrenia	71250
3	Eu21.18	[X]Schizotypal personality disorder	26859
3	E107.00	Schizo-affective schizophrenia	2117
3	E107000	Unspecified schizo-affective schizophrenia	58862
3	E107100	Subchronic schizo-affective schizophrenia	61098
3	E107200	Chronic schizo-affective schizophrenia	43800
3	E107300	Acute exacerbation subchronic schizo-affective schizophrenia	58866
3	E107400	Acute exacerbation of chronic schizo-affective schizophrenia	63478
3	E107500	Schizo-affective schizophrenia in remission	56438
3	E107z00	Schizo-affective schizophrenia NOS	10575
3	Eu25.00	[X]Schizoaffective disorders	9422
3	Eu25000	[X]Schizoaffective disorder, manic type	33847
3	Eu25011	[X]Schizoaffective psychosis, manic type	16905
3	Eu25012	[X]Schizophreniform psychosis, manic type	51903
3	Eu25100	[X]Schizoaffective disorder, depressive type	11055
3	Eu25111	[X]Schizoaffective psychosis, depressive type	35274
3	Eu25112	[X]Schizophreniform psychosis, depressive type	41022
3	Eu25200	[X]Schizoaffective disorder, mixed type	33693
3	Eu25212	[X]Mixed schizophrenic and affective psychosis	37580
3	Eu25y00	[X]Other schizoaffective disorders	58532
3	Eu25z00	[X]Schizoaffective disorder, unspecified	37681
3	Eu25z11	[X]Schizoaffective psychosis NOS	33410

Sleep Disordered Breathing

metadata	category	readcode	readterm	medcode
Name: SDB_cprd	3	R005311	[D]Sleep apnoea syndrome	2506
Version: 1	3	R060B00	[D]Snoring	2578
Source: CPRD	3	1C7..00	Snoring symptoms	5636
Author: C McKenna	3	Fy03.00	Sleep apnoea	7603
Date: 19th October 2018	3	Fy03.11	Obstructive sleep apnoea	8148
Categories:	3	R005312	[D]Syndrome sleep apnoea	20438
1 = H/O	3	H5B0.00	Obstructive sleep apnoea	20748
2= Probable	3	H5B..00	Sleep apnoea	23779
3 = Definite	3	C38y.11	Pickwickian syndrome	24755
	3	Q318.00	Primary sleep apnoea of newborn	26871
	3	1C72.00	Snores	29370
	3	1C7Z.00	Snoring symptom NOS	29641
	3	R005300	[D]Hypersomnia with sleep apnoea	36301
	3	8A43.00	Apnoea alarm monitoring	37667
	3	C380200	Extreme obesity with alveolar hypoventilation	38059
	3	C38y000	Pickwickian syndrome	38294
	3	Fy04.00	Sleep-related respiratory failure	38686
	3	R005100	[D]Insomnia with sleep apnoea	48539

3	7527800	Injection snoreplasty	56712
3	7P1B000	Polysomnography	83545
2	8HTn.00	Referral to sleep clinic	95887
3	C38y011	Obesity hypoventilation syndrome	103574

Stroke

metadata	category	readcode	readterm	medcode
Name: SDB_cprd	2	1JA1.00	Suspected cerebrovascular disease	40098
Version: 1	2	1JA1011	Suspected stroke	102554
Source: CPRD	3	1M4..00	Central post-stroke pain	100639
Author: C McKenna	3	38G3.00	Hyperten, abnorm renal/liver funct, stroke, BLED score	103690
Date: 19th October 2018	3	661M700	Stroke self-management plan agreed	107195
Categories:	1	662e.00	Stroke/CVA annual review	18686
1 = H/O	1	662e.11	Stroke annual review	107886
2= Probable	3	662M.00	Stroke monitoring	10792
3 = Definite	1	662M100	Stroke 6 month review	105100
	3	662M200	Stroke initial post discharge review	104505
	1	662o.00	Haemorrhagic stroke monitoring	28914
	3	7P24200	Delivery of rehabilitation for stroke	55351
	3	8HBJ.00	Stroke / transient ischaemic attack referral	13707
	3	8Hd6.00	Admission to stroke unit	105520
	3	8HHM.00	Ref to multidisciplinary stroke function improvement service	56458
	3	8HTQ.00	Referral to stroke clinic	18804
	3	9N0p.00	Seen in stroke clinic	32959
	1	9N4X.00	DNA - Did not attend stroke clinic	18687
	1	9Om..00	Stroke/transient ischaemic attack monitoring administration	31218
	1	9Om0.00	Stroke/transient ischaemic attack monitoring first letter	28753
	1	9Om1.00	Stroke/transient ischaemic attack monitoring second letter	34245
	1	9Om2.00	Stroke/transient ischaemic attack monitoring third letter	34375
	1	9Om4.00	Stroke/transient ischaemic attack monitoring telephone invte	89913
	3	Fyu5500	[X]Other transnt cerebral ischaemic attacks+related syndroms	63746
	3	G6...00	Cerebrovascular disease	2418
	3	G61..00	Intracerebral haemorrhage	5051
	3	G61..11	CVA - cerebrovascular accid due to intracerebral haemorrhage	6960
	3	G61..12	Stroke due to intracerebral haemorrhage	18604
	3	G610.00	Cortical haemorrhage	31595
	3	G611.00	Internal capsule haemorrhage	40338
	3	G612.00	Basal nucleus haemorrhage	46316
	3	G613.00	Cerebellar haemorrhage	13564
	3	G614.00	Pontine haemorrhage	7912
	3	G615.00	Bulbar haemorrhage	62342

3	G616.00	External capsule haemorrhage	30045
3	G617.00	Intracerebral haemorrhage, intraventricular	30202
3	G618.00	Intracerebral haemorrhage, multiple localized	57315
3	G61X.00	Intracerebral haemorrhage in hemisphere, unspecified	31060
3	G61X000	Left sided intracerebral haemorrhage, unspecified	28314
3	G61X100	Right sided intracerebral haemorrhage, unspecified	19201
3	G61z.00	Intracerebral haemorrhage NOS	3535
3	G630.00	Basilar artery occlusion	32447
3	G632.00	Vertebral artery occlusion	40847
3	G63y000	Cerebral infarct due to thrombosis of precerebral arteries	23671
3	G63y100	Cerebral infarction due to embolism of precerebral arteries	24446
3	G64..00	Cerebral arterial occlusion	8837
3	G64..11	CVA - cerebral artery occlusion	5363
3	G64..12	Infarction - cerebral	569
3	G64..13	Stroke due to cerebral arterial occlusion	6155
3	G640.00	Cerebral thrombosis	16517
3	G640000	Cerebral infarction due to thrombosis of cerebral arteries	36717
3	G641.00	Cerebral embolism	15019
3	G641.11	Cerebral embolus	34758
3	G641000	Cerebral infarction due to embolism of cerebral arteries	27975
3	G64z.00	Cerebral infarction NOS	3149
3	G64z.11	Brainstem infarction NOS	15252
3	G64z.12	Cerebellar infarction	5602
3	G64z000	Brainstem infarction	25615
3	G64z100	Wallenberg syndrome	47642
3	G64z111	Lateral medullary syndrome	5185
3	G64z200	Left sided cerebral infarction	9985
3	G64z300	Right sided cerebral infarction	10504
3	G64z400	Infarction of basal ganglia	26424
3	G65..00	Transient cerebral ischaemia	504
3	G65..11	Drop attack	3132
3	G65..12	Transient ischaemic attack	1433
3	G65..13	Vertebro-basilar insufficiency	2417
3	G650.00	Basilar artery syndrome	23942
3	G650.11	Insufficiency - basilar artery	5268
3	G651.00	Vertebral artery syndrome	33377
3	G651000	Vertebro-basilar artery syndrome	21118
3	G652.00	Subclavian steal syndrome	23465
3	G653.00	Carotid artery syndrome hemispheric	44765
3	G654.00	Multiple and bilateral precerebral artery syndromes	50594
3	G655.00	Transient global amnesia	6489
3	G656.00	Vertebrobasilar insufficiency	10794
3	G65y.00	Other transient cerebral ischaemia	19354

3	G65z.00	Transient cerebral ischaemia NOS	1895
3	G65z000	Impending cerebral ischaemia	55247
3	G65z100	Intermittent cerebral ischaemia	16507
3	G65zz00	Transient cerebral ischaemia NOS	15788
3	G66..00	Stroke and cerebrovascular accident unspecified	1469
3	G66..11	CVA unspecified	1298
3	G66..12	Stroke unspecified	6253
3	G66..13	CVA - Cerebrovascular accident unspecified	6116
3	G660.00	Middle cerebral artery syndrome	18689
3	G661.00	Anterior cerebral artery syndrome	19280
3	G662.00	Posterior cerebral artery syndrome	19260
3	G663.00	Brain stem stroke syndrome	8443
3	G664.00	Cerebellar stroke syndrome	17322
3	G665.00	Pure motor lacunar syndrome	33499
3	G666.00	Pure sensory lacunar syndrome	51767
3	G667.00	Left sided CVA	7780
3	G668.00	Right sided CVA	12833
3	G669.00	Cerebral palsy, not congenital or infantile, acute	16956
3	G671.00	Generalised ischaemic cerebrovascular disease NOS	40053
3	G671100	Chronic cerebral ischaemia	24385
3	G671z00	Generalised ischaemic cerebrovascular disease NOS	12555
3	G673200	Carotid artery dissection	12634
3	G676000	Cereb infarct due cerebral venous thrombosis, nonpyogenic	39344
3	G677000	Occlusion and stenosis of middle cerebral artery	51759
3	G677100	Occlusion and stenosis of anterior cerebral artery	57527
3	G677200	Occlusion and stenosis of posterior cerebral artery	65770
3	G677300	Occlusion and stenosis of cerebellar arteries	55602
3	G677400	Occlusion+stenosis of multiple and bilat cerebral arteries	71274
3	G679.00	Small vessel cerebrovascular disease	98188
3	G67y.00	Other cerebrovascular disease OS	34117
3	G67z.00	Other cerebrovascular disease NOS	37493
3	G68..00	Late effects of cerebrovascular disease	23361
1	G683.00	Sequelae of cerebral infarction	39403
3	G68W.00	Sequelae/other + unspecified cerebrovascular diseases	51138
3	G68X.00	Sequelae of stroke,not specfd as h'morrhage or infarction	6228
3	G6W..00	Cereb infarct due unsp occlus/stenos precerebr arteries	40758
3	G6X..00	Cerebrl infarctn due/unspcf occlusn or sten/cerebrl artrs	33543
3	G6y..00	Other specified cerebrovascular disease	51311
3	G6z..00	Cerebrovascular disease NOS	10062
3	Gyu6.00	[X]Cerebrovascular diseases	73901
3	Gyu6100	[X]Other subarachnoid haemorrhage	65745
3	Gyu6200	[X]Other intracerebral haemorrhage	53810
3	Gyu6300	[X]Cerebrl infarctn due/unspcf occlusn or sten/cerebrl artrs	91627
3	Gyu6400	[X]Other cerebral infarction	53745

3	Gyu6500	[X]Occlusion and stenosis of other precerebral arteries	90572
3	Gyu6600	[X]Occlusion and stenosis of other cerebral arteries	92036
3	Gyu6A00	[X]Other cerebrovascular disorders in diseases CE	99367
3	Gyu6F00	[X]Intracerebral haemorrhage in hemisphere, unspecified	96630
3	Gyu6G00	[X]Cereb infarct due unsp occlus/stenos precerebr arteries	94482
3	L440.12	Stroke in the puerperium	56279
1	ZLEP.00	Discharge from stroke serv	42248

Undescended testis

metadata	category	readcode	readterm	medcode
Name: undescendedTestis_cprd	3	PC5..00	Undescended testicle	634
Version: 1	3	B470.00	Malignant neoplasm of undescended testis	64602
Source: CPRD	3	B470200	Seminoma of undescended testis	7740
Author: C McKenna	3	PC5z.00	Undescended testicle NOS	28215
Date: 19th October 2018	3	B470300	Teratoma of undescended testis	36325
Categories:	3	PC5z000	Undescended testis, unilateral	6794
1 = H/O	3	PC5z100	Undescended testis, bilateral	6451
2= Probable	3	B470z00	Malignant neoplasm of undescended testis NOS	96429
3 = Definite	3	PC50.00	Cryptorchidism	10965
	3	PC50000	Cryptorchidism, unilateral	44918
	3	PC50z00	Cryptorchidism NOS	33424
	3	PC50100	Cryptorchidism, bilateral	47565

Vitamin D deficiency

metadata	category	readcode	readterm	medcode
Name: vitDdefic_cprd	3	66p..00	Vitamin D deficiency monitoring	107250
Version: 1	3	8I7F.00	Combined calcium and vitamin D3 preparation not tolerated	56468
Source: CPRD	3	C28A.00	Vitamin D-dependent rickets	105896
Author: C McKenna	3	9mP0000	Vitamin D deficiency monitoring first letter	108831
Date: 19th October 2018	3	8B73.00	Vitamin D supplements	53111
Categories:	3	85D0.00	Injection of vitamin D	102445
1 = H/O	3	9mP..00	Vitamin D deficiency monitoring administration	107324
2= Probable	3	C2B..00	Vitamin D insufficiency	106409
3 = Definite	3	66p0.00	Vitamin D deficiency annual review	107460
	3	C28..00	Vitamin D deficiency	11974

MEDICAL CODE LISTS, ICD-10 CODES

ADHD

metadata	icd_term	icd_code	Category
Name: ADHD_HES	Hyperkinetic disorders	F90	3
Version: 1	Disturbance of activity and attention	F90.0	3
Source: HES	Hyperkinetic conduct disorder	F90.1	3
Author: C McKenna	Other hyperkinetic disorders	F90.8	3
Date: 19th October 2018	Hyperkinetic disorder, unspecified	F90.9	3
Categories:			
1 = H/O			
2= Probable			
3 = Definite			

Anxiety/Depression

metadata	icd_term	icd_code	Category
Name: AnxietyDepression_HES	Phobic anxiety disorders	F40	3
Version: 1	Other anxiety disorders	F41	3
Source: HES	Organic anxiety disorder	F06.4	3
Author: C McKenna	Separation anxiety disorder of childhood	F93.0	3
Date: 19th October 2018	Social anxiety disorder of childhood	F93.2	3
Categories:	Phobic anxiety disorder of childhood	F93.1	3
1 = H/O	Manic episode	F30	3
2= Probable	Bipolar affective disorder	F31	3
3 = Definite	Depressive episode	F32	3
	Recurrent depressive disorder	F33	3
	Persistent mood [affective] disorders	F34	3
	Other mood [affective] disorders	F38	3
	Unspecified mood [affective] disorder	F39	3

Arthritis (combined)

metadata	icd_term	icd_code	Category
Name: ArthritisComb_HES	Reactive arthropathies	M02	3
Version: 1	Seropositive rheumatoid arthritis	M05	3
Source: HES	Other rheumatoid arthritis	M06	3
Author: C McKenna	Psoriatic and enteropathic arthropathies	M07	3
Date: 19th October 2018	Juvenile arthritis	M08	3
Categories:	Juvenile arthritis in diseases classified elsewhere	M09	3
1 = H/O	Gout	M10	3
2= Probable	Other crystal arthropathies	M11	3
3 = Definite	Other arthritis	M13	3
	Arthropathies in other diseases classified elsewhere	M14	3
	Polyarthrosis	M15	3
	Coxarthrosis [arthrosis of hip]	M16	3
	Gonarthrosis [arthrosis of knee]	M17	3
	Arthrosis of first carpometacarpal joint	M18	3

Other arthrosis	M19	3
Other spondylosis with myelopathy	M471	3
Other spondylosis with radiculopathy	M472	3
Other spondylosis	M478	3
Spondylosis, unspecified	M479	3
Gouty arthropathy due to enzyme defects and other inherited disorders	M140	3
Rheumatoid carditis	I528	3
Rheumatoid lung disease	J990	3
Felty's syndrome	M050	3
Rheumatoid lung disease	M051	3
Rheumatoid vasculitis	M052	3
Rheumatoid arthritis with involvement of oth organs and sys	M053	3
Other seropositive rheumatoid arthritis	M058	3
Seropositive rheumatoid arthritis, unspecified	M059	3
Seronegative rheumatoid arthritis	M060	3
Adult-onset Still's disease	M061	3
Rheumatoid bursitis	M062	3
Rheumatoid nodule	M063	3
Other specified rheumatoid arthritis	M068	3
Rheumatoid arthritis, unspecified	M069	3
Juvenile rheumatoid arthritis	M080	3
Juvenile arthritis with systemic onset	M082	3
Juvenile polyarthritis (seronegative)	M083	3
Pauciarticular juvenile arthritis	M084	3
Ankylosing spondylitis (excludes juvenile ank spond)	M45X	3
Ankylosing spondylitis multiple sites in spine	M450	3
Ankylosing spondylitis occipito-atlanto-axial region	M451	3
Ankylosing spondylitis cervical region	M452	3
Ankylosing spondylitis cervicothoracic region	M453	3
Ankylosing spondylitis thoracic region	M454	3
Ankylosing spondylitis thoracolumbar region	M455	3
Ankylosing spondylitis lumbar region	M456	3
Ankylosing spondylitis lumbosacral region	M457	3
Ankylosing spondylitis sacral & sacrococcygeal region	M458	3
Ankylosing spondylitis site unspecified	M459	3

Atlantoaxial instability

metadata	icd_term	icd_code	Category
Name: AtlantoaxialInstab_HES	Spinal instabilities	M53.2	3
Version: 1	Other cervical disc displacement	M50.2	3
Source: HES	Cervical disc disorder with radiculopathy	M50.1	3
Author: C McKenna			

Date: 19th October 2018
Categories:
1 = H/O
2= Probable
3 = Definite

Autism

metadata	icd_term	icd_code	Category
Name: Autism_HES	Pervasive developmental disorders	F84	3
Version: 1			
Source: HES			
Author: C McKenna			
Date: 19th October 2018			
Categories:			
1 = H/O			
2= Probable			
3 = Definite			

Cataract

metadata	icd_term	icd_code	Category
Name: Cataract_HES	Senile cataract	H25	3
Version: 1	Other cataract	H26	3
Source: HES	Congenital cataract	Q12.0	3
Author: C McKenna			
Date: 19th October 2018			
Categories:			
1 = H/O			
2= Probable			
3 = Definite			

Chronic kidney disease

metadata	icd_term	icd_code	Category
Name: ChronicKidneyDisease_HES	Chronic kidney disease	N18	3
Version: 1	Unspecified kidney failure	N19	3
Source: HES	Chronic nephritic syndrome	N03	3
Author: C McKenna	Nephrotic syndrome	N04	3
Date: 19th October 2018	Unspecified nephritic syndrome	N05	3
Categories:	Chronic tubulo-interstitial nephritis	N11	3
1 = H/O	Unspecified contracted kidney	N26	3
2= Probable	Dependence on renal dialysis	Z99.2	3
3 = Definite	Renal tubulo-interstitial disorders in transplant rejection	N16.5	3

Kidney transplant failure and rejection	T86.1	3
Kidney transplant status	Z94.0	3
Kidney dialysis: abnormal reaction to	Y84.1	3

Coeliac disease

metadata	icd_term	icd_code	Category
Name: Coeliac_HES	Coeliac disease	K90.0	3
Version: 1			
Source: HES			
Author: C McKenna			
Date: 19th October 2018			
Categories:			
1 = H/O			
2= Probable			
3 = Definite			

Congenital cardiac disease

metadata	icd_term	icd_code	Category
Name: CongenCardiac_HES	Other congenital malformations of heart	Q24	3
Version: 1	Congenital malformations of great arteries	Q25	3
Source: HES	Congenital malformations of great veins	Q26	3
Author: C McKenna	Congenital malformations of cardiac septa	Q21	3
Date: 19th October 2018	Congenital malformations of pulmonary and tricuspid valves	Q22	3
Categories:	Congenital malformations of aortic and mitral valves	Q23	3
1 = H/O	Congenital malformations of cardiac chambers and connections	Q20	3
2= Probable			
3 = Definite			

Congenital gastrointestinal disease

metadata	icd_term	icd_code	Category
Name: CongenGastro_HES	Congenital hypertrophic pyloric stenosis	Q40.0	3
Version: 1	Congenital absence, atresia and stenosis of small intestine	Q41	3
Source: HES	Congenital absence, atresia and stenosis of large intestine	Q42	3
Author: C McKenna	Hirschsprung disease	Q43.1	3
Date: 19th October 2018	Atresia of oesophagus without fistula	Q39.0	3
Categories:	Atresia of oesophagus with tracheo-oesophageal fistula	Q39.1	3

1 = H/O	Congenital tracheo-oesophageal fistula without atresia	Q39.2	3
2= Probable	Congenital stenosis and stricture of oesophagus	Q39.3	3
3 = Definite			

Dementia

metadata	icd_term	icd_code	Category
Name: Dementia_HES	Dementia in Alzheimer disease	F00	3
Version: 1	Vascular dementia	F01	3
Source: HES	Dementia in other diseases classified elsewhere	F02	3
Author: C McKenna	Unspecified dementia	F03	3
Date: 19th October 2018	Organic amnesic syndrome, not induced by alcohol and other psychoactive substances	F04	3
Categories:	Delirium superimposed on dementia	F05.1	3
1 = H/O	Alzheimer disease	G30	3
2= Probable			
3 = Definite			

Diabetes mellitus (combined)

metadata	icd_term	icd_code	Category
Name: DMcombined_HES	Insulin-dependent diabetes mellitus	E10	3
Version: 1	Non-insulin-dependent diabetes mellitus	E11	3
Source: HES	Other specified diabetes mellitus	E13	3
Author: C McKenna	Unspecified diabetes mellitus	E14	3
Date: 19th October 2018	Special screening examination for those with diabetes mellitus	Z13.1	3
Categories:	Abnormal glucose tolerance test	R73.0	3
1 = H/O	Diabetic polyneuropathy	G63.2	3
2= Probable	Diabetic cataract	H28.0	3
3 = Definite	Diabetic retinopathy	H36.0	3

Duchene/ muscular dystrophy/ myopathy

metadata	icd_term	icd_code	Category
Name: DuchenneMyop_HES	Muscular dystrophy	G71.0	3
Version: 1	Congenital myopathies	G71.2	3
Source: HES	Myotonic disorders	G71.1	3
Author: C McKenna			
Date: 19th October 2018			
Categories:			

1 = H/O
2= Probable
3 = Definite

Eczema

metadata	icd_term	icd_code	Category
Name: Eczema_HES	Atopic dermatitis	L20	3
Version: 1			
Source: HES			
Author: C McKenna			
Date: 19th October 2018			
Categories:			
1 = H/O			
2= Probable			
3 = Definite			

Skin, other

metadata	icd_term	icd_code	Category
Name: SkinOther_HES	Psoriasis	L40	3
Version: 1	Juvenile arthritis in psoriasis	M09.0	3
Source: HES	Other psoriatic arthropathies	M07.3	3
Author: C McKenna	Lichen planus	L43	3
Date: 19th October 2018	Pemphigus	L10	3
Categories:	Pemphigoid	L12	3
1 = H/O	Seborrhoeic dermatitis	L21	3
2= Probable	Vitiligo	L80	3
3 = Definite	Seborrhoeic keratosis	L82	3

Epilepsy

metadata	icd_term	icd_code	Category
Name: Epilepsy_HES	Epilepsy	G40	3
Version: 1	Acquired aphasia with epilepsy [Landau-Kleffner]	F80.3	3
Source: HES	Status epilepticus	G41	3
Author: C McKenna			
Date: 19th October 2018			
Categories:			
1 = H/O			
2= Probable			
3 = Definite			

Glaucoma

metadata	icd_term	icd_code	Category

metadata	icd_term	icd_code	Category
Name: Glaucoma_HES	Glaucoma	H40	3
Version: 1	Congenital glaucoma	Q15.0	3
Source: HES	Glaucoma in diseases classified elsewhere	H42	3
Author: C McKenna			
Date: 19th October 2018			
Categories:			
1 = H/O			
2= Probable			
3 = Definite			

Gastroesophageal reflux

metadata	icd_term	icd_code	Category
Name: GORD_HES	Gastro-oesophageal reflux disease	K21	3
Version: 1	Oesophagitis	K20	3
Source: HES			
Author: C McKenna			
Date: 19th October 2018			
Categories:			
1 = H/O			
2= Probable			
3 = Definite			

Hearing impairment

metadata	icd_term	icd_code	Category
Name: HearingImpairment_HES	Conductive and sensorineural hearing loss	H90	3
Version: 1	Other hearing loss	H91	3
Source: HES			
Author: C McKenna			
Date: 19th October 2018			
Categories:			
1 = H/O			
2= Probable			
3 = Definite			

Hyperthyroidism

metadata	icd_term	icd_code	Category
Name: Hyperthyroidism_HES	Thyrotoxicosis [hyperthyroidism]	E05	3
Version: 1			
Source: HES			
Author: C McKenna			
Date: 19th October 2018			
Categories:			

1 = H/O

2= Probable

3 = Definite

Hypothyroidism

metadata	icd_term	icd_code	Category
Name: Hypothyroidism_HES	Subclinical iodine-deficiency hypothyroidism	E02	3
Version: 1	Other hypothyroidism	E03	3
Source: HES	Systemic atrophy primarily affecting central nervous system in myxoedema	G132	3
Author: C McKenna			
Date: 19th October 2018			
Categories:			
1 = H/O			
2= Probable			
3 = Definite			

Inflammatory Bowel Disease

metadata	icd_term	icd_code	Category
Name: IBD_HES	Crohn disease [regional enteritis]	K50	3
Version: 1	Ulcerative colitis	K51	3
Source: HES	Other noninfective gastroenteritis and colitis	K52	3
Author: C McKenna			
Date: 19th October 2018			
Categories:			
1 = H/O			
2= Probable			
3 = Definite			

Iron deficiency

metadata	icd_term	icd_code	Category
Name: IronDefic_HES	Iron deficiency	E61.1	3
Version: 1	Iron deficiency anaemia	D50	3
Source: HES			
Author: C McKenna			
Date: 19th October 2018			
Categories:			
1 = H/O			
2= Probable			
3 = Definite			

Ischaemic Heart Disease

metadata	icd_term	icd_code	Category
Name: IschaemiaHeartDisease_HES	Angina pectoris	I20	3
Version: 1	Acute myocardial infarction	I21	3
Source: HES	Subsequent myocardial infarction	I22	3
Author: C McKenna	Certain current complications following acute myocardial infarction	I23	3
Date: 19th October 2018	Other acute ischaemic heart diseases	I24	3
Categories:	Chronic ischaemic heart disease	I25	3
1 = H/O			
2= Probable			
3 = Definite			

Non-accidental injury/ child abuse

metadata	icd_term	icd_code	Category
Name: NAIchildAbuse_HES	Effects of other deprivation	T73	3
Version: 1	Maltreatment syndromes	T74	3
Source: HES	Problems related to negative life events in childhood	Z61	3
Author: C McKenna	Reactive attachment disorder of childhood	F94.1	2
Date: 19th October 2018			
Categories:			
1 = H/O			
2= Probable			
3 = Definite			

Obesity

metadata	icd_term	icd_code	Category
Name: Obesity_HES	Obesity	E66	3
Version: 1			
Source: HES			
Author: C McKenna			
Date: 19th October 2018			
Categories:			
1 = H/O			
2= Probable			
3 = Definite			

Schizophrenia

metadata	icd_term	icd_code	Category
Name: Schizophrenia_HES	Schizophrenia	F20	3
Version: 1	Schizotypal disorder	F21	3
Source: HES	Persistent delusional disorders	F22	3
Author: C McKenna	Schizoaffective disorders	F25	3

Date: 19th October 2018

Categories:

1 = H/O

2= Probable

3 = Definite

Sleep Disordered Breathing

metadata	icd_term	icd_code	Category
Name: SDB_HES	Extreme obesity with alveolar hypoventilation	E66.2	3
Version: 1	Sleep apnoea	G47.3	3
Source: HES	Unspecified Sleep Apnea	G47.30	3
Author: C McKenna	Obstructive Sleep Apnea	G47.33	3
Date: 19th October 2018	Sleep Related Nonobstructive Alveolar Hypoventilatio	G47.34	3
Categories:	Sleep Related Hypoventilation/Hypoxemia	G47.36	3
1 = H/O	Other Sleep Apnea	G47.39	3
2= Probable	Primary sleep apnoea of newborn	P28.3	3
3 = Definite			

Stroke

metadata	icd_term	icd_code	Category
Name: Stroke_HES	Subarachnoid haemorrhage	I60	3
Version: 1	Intracerebral haemorrhage	I61	3
Source: HES	Other nontraumatic intracranial haemorrhage	I62	3
Author: C McKenna	Cerebral infarction	I63	3
Date: 19th October 2018	Stroke, not specified as haemorrhage or infarction	I64	3
Categories:	Occlusion and stenosis of precerebral arteries, not resulting in cerebral infarction	I65	2
1 = H/O	Occlusion and stenosis of cerebral arteries, not resulting in cerebral infarction	I66	2
2= Probable	Dissection of cerebral arteries, nonruptured	I67.0	2
3 = Definite	Sequelae of cerebrovascular disease	I69	1

Undescended testis

metadata	icd_term	icd_code	Category
Name: UndescendedTestis_HES	Undescended testicle	Q53	3
Version: 1			
Source: HES			
Author: C McKenna			
Date: 19th October 2018			
Categories:			
1 = H/O			
2= Probable			

3 = Definite

Vitamin D deficiency

metadata	icd_term	icd_code	Category
Name: VitDdefic_HES	Vitamin D deficiency	E55	3
Version: 1			
Source: HES			
Author: C McKenna			
Date: 19th October 2018			
Categories:			
1 = H/O			
2= Probable			
3 = Definite			

DEVELOPMENT OF MEDICAL CODE LISTS, READ CODES

ADHD

ADHD READ FINAL	34
Code browser	40
Peer reviewed publications	13
Caliber portal	0
Duplicates	13
Inappropriate	6
Search terms	ADHD, hyperactive, hyperkinetic, overactive, attention deficit

Alexander, Myriam, et al. "Morbidity and medication in a large population of individuals with Down syndrome compared to the general population." Developmental Medicine & Child Neurology 58.3 (2016): 246-254.

Anxiety/Depression

ANX DEP FINAL	262
Code browser	202
Peer reviewed publications	224
Caliber portal	190
Duplicates	293
Inappropriate	40
Search terms	Depression, Depressive, Anxiety, Anxious, Neurotic, Personality, Affective

Alexander, Myriam, et al. "Morbidity and medication in a large population of individuals with Down syndrome compared to the general population." Developmental Medicine & Child Neurology 58.3 (2016): 246-254.

Arthritis (combined)

ARTH FINAL	629
Code browser	630
Peer reviewed publications	0
Caliber portal	276
Duplicates	78
Inappropriate	199
Search terms	Arthritis, arthropath, rheumatoid, gout, arthrosis, spondylosis, spondylitis

Atlantoaxial instability

ATLANTO FINAL	12
Code browser	12
Peer reviewed publications	0
Caliber portal	0
Duplicates	0
Inappropriate	0
Search terms	atlantoaxial, atlanto-occipital, cervical spine instability

Autism

AUSTISM FINAL	22
Code browser	22
Peer reviewed publications	24
Caliber portal	0
Duplicates	15
Inappropriate	9
Search terms	Autism, Asperger, pervasive, autistic

Cataract

FINAL	110
Code browser	109
Peer reviewed publications	35
Caliber portal	0
Duplicates	33
Inappropriate	1
Search terms	cataract, lens

Chronic kidney disease

FINAL	254
Code browser	242
Peer reviewed publications	0
Caliber portal	254
Duplicates	242
Inappropriate	0
Search terms	renal failure, kidney failure, chronic kidney, dialysis, proteinurina, nephrotic, nephritis

Coeliac disease

FINAL	19
Code browser	17
Peer reviewed publications	9
Caliber portal	0
Duplicates	7
Inappropriate	0
Search terms	coeliac, gluten

Alexander, Myriam, et al. "Morbidity and medication in a large population of individuals with Down syndrome compared to the general population." Developmental Medicine & Child Neurology 58.3 (2016): 246-254.

Congenital cardiac disease

FINAL	282
Code browser	709
Peer reviewed publications	200
Caliber portal	232
Duplicates	464
Inappropriate	395
Search terms	cyanotic, congenital heart, fallot, atrial septal defects, ventricular septal defect, dextrocardia, aortic stenosis, atrioventricular septal defect, biscuspid aortic value, congenital cardiomyopathy, congenital heart block, double ouytlet right ventricle, spetal defects, coarctation of aortic arch, interupted aortic arch, patent ductus arteriosis, scimitar, pulmonary venous, pentalogy

Alexander, Myriam, et al. "Morbidity and medication in a large population of individuals with Down syndrome compared to the general population." Developmental Medicine & Child Neurology 58.3 (2016): 246-254.

Kuyateh, Fatmatta, et al. "validation of Congenital Cardiac Malformations in the General Practice Research Database: 723." Pharmacoepidemiology and Drug Safety 21 (2012): 336-337.

Congenital gastrointestinal disease

FINAL	60
Code browser	342
Peer reviewed publications	41
Caliber portal	0
Duplicates	41
Inappropriate	282
Search terms	Congenital atresia, congenital stenosis, congenital obstruction, hirschprung, Aganglion, pyloric stenosis, pyloric hypertrophy

Alexander, Myriam, et al. "Morbidity and medication in a large population of individuals with Down syndrome compared to the general population." Developmental Medicine & Child Neurology 58.3 (2016): 246-254.

Dementia

FINAL	81
Code browser	112
Peer reviewed publications	76
Caliber portal	77
Duplicates	153
Inappropriate	31
Search terms	Dementia, Alzheimer, memory loss, senile, pick's, lewy body, frontotemporal degeneration

Alexander, Myriam, et al. "Morbidity and medication in a large population of individuals with Down syndrome compared to the general population." Developmental Medicine & Child Neurology 58.3 (2016): 246-254.

Diabetes mellitus (combined)

FINAL	509
Code browser	600
Peer reviewed publications	283
Caliber portal	793
Duplicates	883
Inappropriate	284
Search terms	Diabetes, diabetic, mellitus, metabolic syndrome, insulin

Alexander, Myriam, et al. "Morbidity and medication in a large population of individuals with Down syndrome compared to the general population." Developmental Medicine & Child Neurology 58.3 (2016): 246-254.

Type 1 diabetes mellitus

FINAL	75
Code browser	600
Peer reviewed publications	0
Caliber portal	793
Duplicates	600
Inappropriate	718
Search terms	Diabetes, diabetic, mellitus, metabolic syndrome, insulin

Type 2 diabetes mellitus

FINAL	115
Code browser	600
Peer reviewed publications	0
Caliber portal	793
Duplicates	600
Inappropriate	678
Search terms	Diabetes, diabetic, mellitus, metabolic syndrome, insulin

Duchene/ muscular dystrophy/ myopathy

FINAL	20
Code browser	24
Peer reviewed publications	0
Caliber portal	0
Duplicates	0
Inappropriate	4
Search terms	duchenne, becker, myotonic, myopathy, muscular dystrophy

Eczema

FINAL	34
Code browser	35
Peer reviewed publications	0
Caliber portal	0
Duplicates	0
Inappropriate	1
Search terms	eczema, atopic dermatitis

Skin, other

FINAL	78
Code browser	78
Peer reviewed publications	0
Caliber portal	84
Duplicates	78
Inappropriate	6
Search terms	Psoriasis, psoriatic, lichen plaus, pemphigus, pemphigoid, seborrhoeic dermatitis, vitiligo, seborrhoeic keratosis

Epilepsy

FINAL	148
Code browser	0
Peer reviewed publications	167
Caliber portal	0
Duplicates	0
Inappropriate	19
Search terms	Epilepsy, epileptic, status epilepticus, fit, seizure, tonic clonic, grand mal, petit mal, convulsion, infantile spasm, rolandic, salaam, anticonvulsant

Glaucoma

FINAL	72
Code browser	80
Peer reviewed publications	2
Caliber portal	72
Duplicates	74
Inappropriate	8
Search terms	Glaucoma, ocular hypertension

Alexander, Myriam, et al. "Morbidity and medication in a large population of individuals with Down syndrome compared to the general population." Developmental Medicine & Child Neurology 58.3 (2016): 246-254.

Gastroesophageal reflux

FINAL	25
Code browser	40
Peer reviewed publications	6
Caliber portal	0
Duplicates	6
Inappropriate	15
Search terms	Oesopheal reflux, antireflux, acid reflux, gastric reflux, oesophagitis

Hearing impairment

FINAL	48
Code browser	194
Peer reviewed publications	296
Caliber portal	0
Duplicates	194
Inappropriate	248
Search terms	Hearing, presbyacusis

Alexander, Myriam, et al. "Morbidity and medication in a large population of individuals with Down syndrome compared to the general population." Developmental Medicine & Child Neurology 58.3 (2016): 246-254.

Hyperthyroidism

FINAL	57
Code browser	72
Peer reviewed publications	
Caliber portal	57
Duplicates	57
Inappropriate	15
Search terms	Hyperthyroid, thryrotoxicosis, goitre, thyroiditis

Hypothyroidism

FINAL	57
Code browser	54
Peer reviewed publications	45
Caliber portal	49
Duplicates	94
Inappropriate	3
Search terms	Hypothyroid, thryoid deficien, thyroid insuffic, cretinism, myxoedema, hashimoto

Alexander, Myriam, et al. "Morbidity and medication in a large population of individuals with Down syndrome compared to the general population." Developmental Medicine & Child Neurology 58.3 (2016): 246-254.

Inflammatory Bowel Disease

FINAL	51
Code browser	16
Peer reviewed publications	0
Caliber portal	35
Duplicates	0

Inappropriate	0
Search terms	Colitis, crohn, enteritis, ileitis

Iron deficiency

FINAL	23
Code browser	115
Peer reviewed publications	0
Caliber portal	9
Duplicates	9
Inappropriate	92
Search terms	Iron deficency,anaemia, serum iron

Ischaemic Heart Disease

FINAL	244
Code browser	250
Peer reviewed publications	101
Caliber portal	131
Duplicates	232
Inappropriate	6
Search terms	angina, heart failure, cardiac failure, myocardial infarction, heart attack, ventricular dysfunction, ischaemic heart disease, coronary, atherosclero

Alexander, Myriam, et al. "Morbidity and medication in a large population of individuals with Down syndrome compared to the general population." Developmental Medicine & Child Neurology 58.3 (2016): 246-254.

Non-accidental injury/ child abuse

FINAL	76
Code browser	170
Peer reviewed publications	0
Caliber portal	0
Duplicates	0
Inappropriate	94
Search terms	non-accidental, abuse, neglect, child protection

Obesity

FINAL	55
Code browser	50
Peer reviewed publications	45
Caliber portal	78

Duplicates	23
Inappropriate	95
Search terms	Obesity, obese, overweight

Alexander, Myriam, et al. "Morbidity and medication in a large population of individuals with Down syndrome compared to the general population." Developmental Medicine & Child Neurology 58.3 (2016): 246-254.

Schizophrenia

FINAL	90
Code browser	110
Peer reviewed publications	99
Caliber portal	90
Duplicates	189
Inappropriate	20
Search terms	Schizophreni, schizo,

Alexander, Myriam, et al. "Morbidity and medication in a large population of individuals with Down syndrome compared to the general population." Developmental Medicine & Child Neurology 58.3 (2016): 246-254.

Sleep Disordered Breathing

FINAL	22
Code browser	28
Peer reviewed publications	9
Caliber portal	11
Duplicates	22
Inappropriate	4
Search terms	sleep apnoea, apnoea, hypoventilation, pickwickan, snor, polysom, sleep, insom, respiratory failure

Alexander, Myriam, et al. "Morbidity and medication in a large population of individuals with Down syndrome compared to the general population." Developmental Medicine & Child Neurology 58.3 (2016): 246-254.

Stroke

FINAL	128
Code browser	305
Peer reviewed publications	0
Caliber portal	156
Duplicates	156
Inappropriate	177
Search terms	Stroke, transient ischaemic attack, cerebrovascular, intracerebral haemorrhage, cerebral infarct, cerebral ischaemia, cerebral embolism, cerebral haem,

Undescended testis

FINAL	12
Code browser	12
Peer reviewed publications	0
Caliber portal	0
Duplicates	0
Inappropriate	0
Search terms	Undescended testi, cryptorchidism

Vitamin D deficiency

FINAL	10
Code browser	42
Peer reviewed publications	0
Caliber portal	0
Duplicates	0
Inappropriate	32
Search terms	Vitamin D

DEVELOPMENT OF MEDICAL CODE LISTS, ICD-10

ADHD

FINAL	5
Code browser	5
Peer reviewed publications	0
Caliber portal	0
Duplicates	0
Inappropriate	0
Search terms	ADHD, hyerkinetic

Anxiety/Depression

FINAL	14
Code browser	14
Peer reviewed publications	0
Caliber portal	15
Duplicates	14
Inappropriate	1

Search terms	Depression, Anxiety

Arthritis (combined)

FINAL	49
Code browser	49
Peer reviewed publications	0
Caliber portal	42
Duplicates	42
Inappropriate	0
Search terms	Arthritis, arthropath, rheumatoid, gout, arthrosis, spondylosis, spondylitis

Atlantoaxial instability

FINAL	3
Code browser	3
Peer reviewed publications	0
Caliber portal	0
Duplicates	0
Inappropriate	0
Search terms	atlantoaxial, atlanto-occipital, cervical disc, cervical spine

Autism

FINAL	1
Code browser	1
Peer reviewed publications	0
Caliber portal	0
Duplicates	0
Inappropriate	0
Search terms	Autism, asperger, pervasive, autistic

Cataract

FINAL	3
Code browser	3
Peer reviewed publications	0
Caliber portal	0
Duplicates	0
Inappropriate	0
Search terms	cataract, lens

Chronic kidney disease

FINAL	12
Code browser	12
Peer reviewed publications	0
Caliber portal	26
Duplicates	12
Inappropriate	14
Search terms	renal failure, kidney failure, chronic kidney, dialysis, proteinurina, nephrotic, nephritis

Coeliac disease

FINAL	1
Code browser	1
Peer reviewed publications	0
Caliber portal	0
Duplicates	0
Inappropriate	0
Search terms	coeliac, gluten

Congenital cardiac disease

FINAL	7
Code browser	7
Peer reviewed publications	0
Caliber portal	0
Duplicates	0
Inappropriate	0
Search terms	congenital heart, congenital cardiac

Congenital gastrointestinal disease

FINAL	8
Code browser	8
Peer reviewed publications	0
Caliber portal	0
Duplicates	0
Inappropriate	0
Search terms	Congenital atresia, congenital stenosis, congenital obstruction, hirschprung, Aganglion, pyloric stenosis, pyloric hypertrophy

Dementia

FINAL	7
Code browser	7
Peer reviewed publications	0
Caliber portal	5
Duplicates	5
Inappropriate	0
Search terms	Dementia, Alzheimer

Diabetes mellitus (combined)

FINAL	9
Code browser	9
Peer reviewed publications	0
Caliber portal	34
Duplicates	9
Inappropriate	25
Search terms	Diabetes, diabetic, insulin

Duchene/ muscular dystrophy/ myopathy

FINAL	3
Code browser	3
Peer reviewed publications	0
Caliber portal	0
Duplicates	0
Inappropriate	0
Search terms	duchenne, becker, myotonic, myopathy, dystrophy

Eczema

FINAL	1
Code browser	1
Peer reviewed publications	0
Caliber portal	0
Duplicates	0
Inappropriate	0
Search terms	eczema, atopic dermatitis

Skin, other

FINAL	9

Code browser	0
Peer reviewed publications	0
Caliber portal	28
Duplicates	0
Inappropriate	19
Search terms	Psoriasis, psoriatic, lichen plaus, pemphigus, pemphigoid, seborrhoeic dermatitis, vitiligo, seborrhoeic keratosis

Epilepsy

FINAL	3

Code browser	3
Peer reviewed publications	0
Caliber portal	0
Duplicates	0
Inappropriate	0
Search terms	Epilepsy, epileptic, status epilepticus, seizure, convulsion

Glaucoma

FINAL	3

Code browser	3
Peer reviewed publications	0
Caliber portal	10
Duplicates	3
Inappropriate	7
Search terms	Glaucoma, ocular hypertension

Gastroesophageal reflux

FINAL	2

Code browser	2
Peer reviewed publications	0
Caliber portal	0
Duplicates	0
Inappropriate	0
Search terms	GORD, gastro-oessophageal reflux, oesophagitis

Hearing impairment

FINAL	2

Code browser	2

Peer reviewed publications	0
Caliber portal	0
Duplicates	0
Inappropriate	0
Search terms	Hearing, presbyacusis

Hyperthyroidism

FINAL	1
Code browser	1
Peer reviewed publications	0
Caliber portal	11
Duplicates	1
Inappropriate	10
Search terms	Hyperthyroid, thryrotoxicosis, goitre, thyroiditis

Hypothyroidism

FINAL	3
Code browser	3
Peer reviewed publications	0
Caliber portal	3
Duplicates	0
Inappropriate	0
Search terms	Hypothyroid, myxoedema

Inflammatory Bowel Disease

FINAL	3
Code browser	3
Peer reviewed publications	0
Caliber portal	9
Duplicates	3
Inappropriate	6
Search terms	Crohn, ulcerative colitis, inflammatory bowel disease

Iron deficiency

FINAL	2
Code browser	2
Peer reviewed publications	0
Caliber portal	9

Duplicates	2
Inappropriate	7
Search terms	Iron deficiency, anaemia

Ischaemic Heart Disease

FINAL	6
Code browser	6
Peer reviewed publications	0
Caliber portal	6
Duplicates	6
Inappropriate	0
Search terms	angina, myocardial, heart disease, ischaemic

Non-accidental injury/ child abuse

FINAL	4
Code browser	4
Peer reviewed publications	0
Caliber portal	0
Duplicates	0
Inappropriate	0
Search terms	non-accidental, abuse, neglect, child protection,

Obesity

FINAL	1
Code browser	1
Peer reviewed publications	0
Caliber portal	1
Duplicates	1
Inappropriate	0
Search terms	Obesity, obese, overweight

Schizophrenia

FINAL	4
Code browser	4
Peer reviewed publications	0
Caliber portal	3
Duplicates	3
Inappropriate	0

Search terms	Schizophrenia, schizophrenic, schizoaffective

Sleep Disordered Breathing

FINAL	8
Code browser	49
Peer reviewed publications	0
Caliber portal	2
Duplicates	2
Inappropriate	41
Search terms	sleep disordered breathing, sleep, apnoea, hypoventilation, obesity, somnia

Stroke

FINAL	9
Code browser	9
Peer reviewed publications	0
Caliber portal	22
Duplicates	9
Inappropriate	13
Search terms	Stroke, cerebral infarction, cerebrovascular, transient ischaemic attack

Undescended testis

FINAL	1
Code browser	1
Peer reviewed publications	0
Caliber portal	0
Duplicates	0
Inappropriate	0
Search terms	Undescended testicle, cryptorchidism

Vitamin D deficiency

FINAL	1
Code browser	1
Peer reviewed publications	0
Caliber portal	0
Duplicates	0
Inappropriate	0
Search terms	Vitamin D

CANCER CODE LISTS, READ CODES

Bladder

metadata	category	readcode	readterm	medcode
Name: bladder_cprd	1	ZV10511	[V]Personal history of malignant neoplasm of bladder	35816
Version: 1	2	1J09.00	Suspected bladder cancer	9303
Source: CPRD	3	B49..00	Malignant neoplasm of urinary bladder	779
Author: C McKenna	3	B490.00	Malignant neoplasm of trigone of urinary bladder	38862
Date: 19th October 2018	3	B491.00	Malignant neoplasm of dome of urinary bladder	44996
Categories:	3	B492.00	Malignant neoplasm of lateral wall of urinary bladder	35963
1 = H/O	3	B493.00	Malignant neoplasm of anterior wall of urinary bladder	19162
2= Probable	3	B494.00	Malignant neoplasm of posterior wall of urinary bladder	42012
3 = Definite	3	B495.00	Malignant neoplasm of bladder neck	41571
	3	B49y.00	Malignant neoplasm of other site of urinary bladder	36949
	3	B49y000	Malignant neoplasm, overlapping lesion of bladder	47801
	3	B49z.00	Malignant neoplasm of urinary bladder NOS	31102
	3	B581100	Secondary malignant neoplasm of bladder	22146
	3	ByuC500	[X]2ndry malignant neoplasm/bladder+oth+unsp urinary organs	97091
	3	B498.00	Local recurrence of malignant tumour of urinary bladder	105388
	3	BB41.11	[M]Urinary bladder papilloma	1904
	3	B496.00	Malignant neoplasm of ureteric orifice	28241
	3	B497.00	Malignant neoplasm of urachus	42023

Bone

metadata	category	readcode	readterm	medcode
Name: bone_cprd	3	BBV3.00	[M]Fibroblastic osteosarcoma	21447
Version: 1	3	BBV5.00	[M]Osteosarcoma in Paget's disease of bone	60631
Source: CPRD	3	BBVA.00	[M] Small cell osteosarcoma	29337
Author: C McKenna	3	BBV1.00	[M]Osteosarcoma NOS	8660
Date: 19th October 2018	3	BBV2.00	[M]Chondroblastic osteosarcoma	24539
Categories:	3	B30z000	Osteosarcoma	19437
1 = H/O	3	BBVz.00	[M]Osteoma or osteosarcoma NOS	48271
2= Probable	3	BBV..12	[M]Parosteal osteosarcoma	63571
3 = Definite	3	BBV..00	[M]Osteomas and osteosarcomas	39522
	3	BBV4.00	[M]Telangiectatic osteosarcoma	22561
	3	BBY0.00	[M]Ewing's sarcoma	4473
	3	BBV7.00	[M]Osteoid osteoma NOS	33993
	3	B73..12	Osteoma	4794
	3	BBV0.00	[M]Osteoma NOS	44556
	3	BBV8.11	[M]Giant osteoid osteoma	21224
	3	B30..12	Osteoma	29735
	3	BBW4.11	[M]Fibrochondrosarcoma	68220

	3	BBV1.12	[M]Osteochondrosarcoma	59310
	3	BBW9.00	[M]Mesenchymal chondrosarcoma	52684
	3	BBW6.00	[M]Juxtacortical chondrosarcoma	63659
	3	BBV9.00	[M]Myxoid chondrosarcoma	4118
	3	BBW4.00	[M]Chondrosarcoma NOS	7941
	3	BBa5.00	[M]Chordoma	21758
	3	BBF3.00	[M]Spindle cell sarcoma	31026

Brain/ CNS

metadata	category	readcode	readterm	medcode
Name: brainCNS_cprd	3	B51..00	Malignant neoplasm of brain	18617
Version: 1	3	B510.00	Malignant neoplasm cerebrum (excluding lobes and ventricles)	15711
Source: CPRD	3	B51000	Malignant neoplasm of basal ganglia	48073
Author: C McKenna	3	B51010	Malignant neoplasm of cerebral cortex	61399
Date: 19th October 2018	3	B51030	Malignant neoplasm of globus pallidus	99913
Categories:	3	B51040	Malignant neoplasm of hypothalamus	70942
1 = H/O	3	B51050	Malignant neoplasm of thalamus	62126
2= Probable	3	B510z0	Malignant neoplasm of cerebrum NOS	54133
3 = Definite	3	B511.00	Malignant neoplasm of frontal lobe	42426
	3	B51..11	Cerebral tumour - malignant	10851
	3	B512.00	Malignant neoplasm of temporal lobe	46792
	3	B51200	Malignant neoplasm of hippocampus	67236
	3	B512z0	Malignant neoplasm of temporal lobe NOS	47556
	3	B513.00	Malignant neoplasm of parietal lobe	19226
	3	B514.00	Malignant neoplasm of occipital lobe	39088
	3	B515.00	Malignant neoplasm of cerebral ventricles	52511
	3	B51500	Malignant neoplasm of choroid plexus	46789
	3	B516.00	Malignant neoplasm of cerebellum	45154
	3	B517.00	Malignant neoplasm of brain stem	44089
	3	B51700	Malignant neoplasm of cerebral peduncle	64557
	3	B51710	Malignant neoplasm of medulla oblongata	49132
	3	B51720	Malignant neoplasm of midbrain	93537
	3	B51730	Malignant neoplasm of pons	91240
	3	B517z0	Malignant neoplasm of brain stem NOS	68641
	3	B51y.00	Malignant neoplasm of other parts of brain	71139
	3	B51y00	Malignant neoplasm of corpus callosum	59170
	3	B51y20	Malignant neoplasm; overlapping lesion of brain	65241

3	B51yz00	Malignant neoplasm of other part of brain NOS	100733
3	B51z.00	Malignant neoplasm of brain NOS	41520

Breast

metadata	category	readcode	readterm	medcode
Name: breast_cprd	1	ZV10300	[V]Personal history of malignant neoplasm of breast	16639
Version: 2	3	B340000	Malignant neoplasm of nipple of female breast	23380
Source: CPRD	3	B340100	Malignant neoplasm of areola of female breast	64686
Author: C McKenna/C Parisinos/ V Kuan	3	B340.00	Malignant neoplasm of nipple and areola of female breast	26853
Date: 19th October 2018	3	B340z00	Malignant neoplasm of nipple or areola of female breast NOS	59831
Categories:	3	B341.00	Malignant neoplasm of central part of female breast	31546
1 = H/O	3	B342.00	Malignant neoplasm of upper-inner quadrant of female breast	29826
2= Probable	3	B343.00	Malignant neoplasm of lower-inner quadrant of female breast	45222
3 = Definite	3	B344.00	Malignant neoplasm of upper-outer quadrant of female breast	23399
	3	B345.00	Malignant neoplasm of lower-outer quadrant of female breast	42070
	3	B346.00	Malignant neoplasm of axillary tail of female breast	20685
	3	B347.00	Malignant neoplasm, overlapping lesion of breast	49148
	3	B34..00	Malignant neoplasm of female breast	3968
	3	B34..11	Ca female breast	348
	3	B34y000	Malignant neoplasm of ectopic site of female breast	95057
	3	B34y.00	Malignant neoplasm of other site of female breast	56715
	3	B34yz00	Malignant neoplasm of other site of female breast NOS	38475
	3	B34z.00	Malignant neoplasm of female breast NOS	9470
	3	B350000	Malignant neoplasm of nipple of male breast	68480
	3	B350100	Malignant neoplasm of areola of male breast	67884
	3	B350.00	Malignant neoplasm of nipple and areola of male breast	54494
	3	B35..00	Malignant neoplasm of male breast	19423
	3	B35z000	Malignant neoplasm of ectopic site of male breast	95323
	3	B35z.00	Malignant neoplasm of other site of male breast	54202
	3	B35zz00	Malignant neoplasm of male breast NOS	48809
	3	B36..00	Local recurrence of malignant tumour of breast	105488
	3	B830000	Lobular carcinoma in situ of breast	10387
	3	B830100	Intraductal carcinoma in situ of breast	18694
	3	B830.00	Carcinoma in situ of breast	7833

3	BB91.00	[M]Infiltrating duct carcinoma	8351
3	BB91.11	[M]Duct carcinoma NOS	21833
3	BB910000	[M]Intraductal papillary adenocarcinoma with invasion	30189
3	BB96.00	[M]Noninfiltrating intraductal papillary adenocarcinoma	102593
3	BB911000	[M]Infiltrating duct and lobular carcinoma	39760
3	BB92.00	[M]Comedocarcinoma, noninfiltrating	62871
3	BB93.00	[M]Comedocarcinoma NOS	58131
3	BB94.00	[M]Juvenile breast carcinoma	40359
3	BB94.11	[M]Secretory breast carcinoma	67701
3	BB9J.00	[M]Paget's disease, mammary	12300
3	BB9J.11	[M]Paget's disease, breast	60803
3	BB9K000	[M]Paget's disease and intraductal carcinoma of breast	12480
3	BB9K.00	[M]Paget's disease and infiltrating breast duct carcinoma	42542
3	BB9M.00	[M]Intracystic carcinoma NOS	3969
3	Byu6.00	[X]Malignant neoplasm of breast	12499
3	ByuFG00	[X]Other carcinoma in situ of breast	53803

Cervix

metadata	category	readcode	readterm	medcode
Name: cervix_cprd	3	685C.00	Ca cervix screen abnormal	448
Version: 1	3	B41..00	Malignant neoplasm of cervix uteri	2747
Source: CPRD	3	B41..11	Cervical carcinoma (uterus)	3230
Author: C McKenna	3	B831.00	Carcinoma in situ of cervix uteri	3279
Date: 19th October 2018	3	B831.11	CIN III - carcinoma in situ of cervix	4087
Categories:	3	K551z00	Dysplasia of cervix NOS	12913
1 = H/O	3	K551200	Squamous metaplasia of cervix	17548
2= Probable	1	ZV10411	[V]Personal history of malignant neoplasm of cervix uteri	23936
3 = Definite	3	B831000	Carcinoma in situ of endocervix	24228
	2	1J06.00	Suspected cervical cancer	26872
	3	B41z.00	Malignant neoplasm of cervix uteri NOS	28311
	3	B41y.00	Malignant neoplasm of other site of cervix	32955
	3	B41yz00	Malignant neoplasm of other site of cervix NOS	43435
	3	BB2N.00	[M]Intraepit neop,grade III,of cervix, vulva and vagina	44534
	3	B410.00	Malignant neoplasm of endocervix	48820
	3	B831100	Carcinoma in situ of exocervix	50126
	3	B410z00	Malignant neoplasm of endocervix NOS	50285
	3	B411.00	Malignant neoplasm of exocervix	50297

3	B410100	Malignant neoplasm of endocervical gland	53103
3	B410000	Malignant neoplasm of endocervical canal	57235
3	B41y100	Malignant neoplasm of squamocolumnar junction of cervix	57719
3	B412.00	Malignant neoplasm, overlapping lesion of cervix uteri	58094
3	ByuFA00	[X]Carcinoma in situ of other parts of cervix	72695
3	B58y200	Secondary malignant neoplasm of cervix uteri	73616
3	B41y000	Malignant neoplasm of cervical stump	95505
3	B58y211	Secondary cancer of the cervix	97832

Colorectal

metadata	category	readcode	readterm	medcode
Name: colorectal_cprd	1	ZV10011	[V]Personal history of malignant neoplasm of anus	68018
Version: 2	1	ZV10014	[V]Personal history of malignant neoplasm of large intestine	57727
Source: CPRD	1	ZV10017	[V]Personal history of malignant neoplasm of rectum	62785
Author: C McKenna/C Parisinos/ V Kuan	3	B130.00	Malignant neoplasm of hepatic flexure of colon	9088
Date: 19th October 2018	3	B131.00	Malignant neoplasm of transverse colon	6935
Categories:	3	B132.00	Malignant neoplasm of descending colon	10864
1 = H/O	3	B133.00	Malignant neoplasm of sigmoid colon	2815
2= Probable	3	B134.00	Malignant neoplasm of caecum	3811
3 = Definite	3	B134.11	Carcinoma of caecum	22163
	3	B135.00	Malignant neoplasm of appendix	18632
	3	B136.00	Malignant neoplasm of ascending colon	10946
	3	B137.00	Malignant neoplasm of splenic flexure of colon	18619
	3	B138.00	Malignant neoplasm, overlapping lesion of colon	93478
	3	B139.00	Hereditary nonpolyposis colon cancer	101700
	3	B13..00	Malignant neoplasm of colon	1220
	3	B13y.00	Malignant neoplasm of other specified sites of colon	48231
	3	B13z.00	Malignant neoplasm of colon NOS	28163
	3	B13z.11	Colonic cancer	9118
	3	B140.00	Malignant neoplasm of rectosigmoid junction	27855
	3	B141.00	Malignant neoplasm of rectum	1800
	3	B141.11	Carcinoma of rectum	7219
	3	B141.12	Rectal carcinoma	5901
	3	B142000	Malignant neoplasm of cloacogenic zone	46159

3	B142.00	Malignant neoplasm of anal canal	24370
3	B142.11	Anal carcinoma	9491
3	B143.00	Malignant neoplasm of anus unspecified	27897
3	B14..00	Malignant neoplasm of rectum, rectosigmoid junction and anus	35357
3	B14y.00	Malig neop other site rectum, rectosigmoid junction and anus	55659
3	B14z.00	Malignant neoplasm rectum,rectosigmoid junction and anus NOS	50974
3	B1z0.11	Cancer of bowel	11628
3	9Ow1.00	Bowel cancer detected by national screening programme	94000
3	68W2400	Bowel scope (flexible sigmoidoscopy) screen: cancer detected	10895

Hepatobiliary

metadata	category	readcode	readterm	medcode
Name: liverbiliary_cprd	1	ZV10015	[V]Personal history of malignant neoplasm of liver	58177
Version: 2	3	B150000	Primary carcinoma of liver	16126
Source: CPRD	3	B150100	Hepatoblastoma of liver	31210
Author: C McKenna/C Parisinos/ V Kuan	3	B150200	Primary angiosarcoma of liver	68410
Date: 19th October 2018	3	B150300	Hepatocellular carcinoma	22187
Categories:	3	B150.00	Primary malignant neoplasm of liver	25535
1 = H/O	3	B150z00	Primary malignant neoplasm of liver NOS	44399
2= Probable	3	BB5D500	[M]Hepatocellular carcinoma NOS	40240
3 = Definite	3	BB5D512	[M]Hepatoma, malignant	26814
	3	BB5D513	[M]Liver cell carcinoma	25641
	3	BB5D800	[M]Hepatocellular carcinoma, fibrolamellar	46771
	3	B151000	Malignant neoplasm of interlobular bile ducts	65124
	3	B151200	Malignant neoplasm of intrahepatic biliary passages	89593
	3	B151400	Malignant neoplasm of intrahepatic gall duct	58088
	3	B151.00	Malignant neoplasm of intrahepatic bile ducts	16915
	3	B151z00	Malignant neoplasm of intrahepatic bile ducts NOS	61643
	3	B161000	Malignant neoplasm of cystic duct	72445
	3	B161100	Malignant neoplasm of hepatic duct	52537
	3	B161200	Malignant neoplasm of common bile duct	7982
	3	B161211	Carcinoma common bile duct	36495

3	B161300	Malignant neoplasm of sphincter of Oddi	105613
3	B161.00	Malignant neoplasm of extrahepatic bile ducts	23433
3	B161z00	Malignant neoplasm of extrahepatic bile ducts NOS	74896
3	B162.00	Malignant neoplasm of ampulla of Vater	10949
3	B163.00	Malignant neoplasm, overlapping lesion of biliary tract	35039
3	BB5D100	[M]Cholangiocarcinoma	8711
3	BB5D111	[M]Bile duct carcinoma	40438
3	BB5D300	[M]Bile duct cystadenocarcinoma	41313
3	BB5D700	[M]Combined hepatocellular carcinoma and cholangiocarcinoma	107299
3	BB5D711	[M]Hepatocholangiocarcinoma	110147
3	B153.00	Secondary malignant neoplasm of liver	36147
3	B160.00	Malignant neoplasm of gallbladder	16105

Gastroesophageal

metadata	category	readcode	readterm	medcode
Name: liverbiliary_cprd	3	B10..00	Malignant neoplasm of oesophagus	1062
Version: 2	3	B10z.11	Oesophageal cancer	4865
Source: CPRD	3	B801.00	Carcinoma in situ of oesophagus	8244
Author: C McKenna/C Parisinos/ V Kuan	3	B11..00	Malignant neoplasm of stomach	8386
Date: 19th October 2018	3	B11z.00	Malignant neoplasm of stomach NOS	14800
Categories:	3	B112.00	Malignant neoplasm of pyloric antrum of stomach	19318
1 = H/O	3	B111.00	Malignant neoplasm of pylorus of stomach	21620
2= Probable	3	B110100	Malignant neoplasm of cardio-oesophageal junction of stomach	22894
3 = Definite	3	BB55.00	Linitis plastica	27440
	3	B10z.00	Malignant neoplasm of oesophagus NOS	30700
	3	B110.00	Malignant neoplasm of cardia of stomach	32022
	3	B113.00	Malignant neoplasm of fundus of stomach	32362
	3	B110z00	Malignant neoplasm of cardia of stomach NOS	37859
	3	B111100	Malignant neoplasm of pyloric canal of stomach	41215
	3	B101.00	Malignant neoplasm of thoracic oesophagus	41362
	3	B115.00	Malignant neoplasm of lesser curve of stomach unspecified	42193
	3	B105.00	Malignant neoplasm of lower third of oesophagus	42416

	3	B114.00	Malignant neoplasm of body of stomach	43572
	3	B801z00	Carcinoma in situ of oesophagus NOS	44228
	3	B111000	Malignant neoplasm of prepylorus of stomach	48237
	1	ZV10018	[V]Personal history of malignant neoplasm of stomach	49447
	3	B103.00	Malignant neoplasm of upper third of oesophagus	50789
	1	ZV10016	[V]Personal history of malignant neoplasm of oesophagus	51001
	3	B117.00	Malignant neoplasm, overlapping lesion of stomach	51690
	3	B10y.00	Malignant neoplasm of other specified part of oesophagus	53591
	3	B104.00	Malignant neoplasm of middle third of oesophagus	54171
	3	B11y.00	Malignant neoplasm of other specified site of stomach	55019
	3	B116.00	Malignant neoplasm of greater curve of stomach unspecified	55434
	3	B801200	Carcinoma in situ of lower 1/3 oesophagus	56077
	3	B111z00	Malignant neoplasm of pylorus of stomach NOS	59092
	3	B100.00	Malignant neoplasm of cervical oesophagus	61695
	3	B102.00	Malignant neoplasm of abdominal oesophagus	63470
	3	B801100	Carcinoma in situ of middle 1/3 oesophagus	64274
	3	B11y000	Malignant neoplasm of anterior wall of stomach NEC	65312
	3	B11yz00	Malignant neoplasm of other specified site of stomach NOS	65372
	3	B106.00	Malignant neoplasm, overlapping lesion of oesophagus	67497
	3	B110111	Malignant neoplasm of gastro-oesophageal junction	94278
	3	B119.00	Siewert type III adenocarcinoma	96094
	3	B11y100	Malignant neoplasm of posterior wall of stomach NEC	96802
	3	B118.00	Siewert type II adenocarcinoma	97499
	3	B107.00	Siewert type I adenocarcinoma	98142
	3	B801000	Carcinoma in situ of upper 1/3 oesophagus	99155
	3	B110000	Malignant neoplasm of cardiac orifice of stomach	100584
	3	B11..11	Gastric neoplasm	10368

Leukaemia

metadata	category	readcode	readterm	medcode
Name: leukaemia_cprd	1	1429.00	H/O: * leukaemia	17177
Version: 1	2	1J02.00	Suspected leukaemia	19692
Source: CPRD	3	B624.12	Hairy cell leukaemia	87335

Author: C McKenna
Date: 19th October 2018

Categories:

1 = H/O

2= Probable

3 = Definite

3	B631.00	Plasma cell leukaemia	39187
3	B64..00	Lymphoid leukaemia	19372
3	B64..11	Lymphatic leukaemia	4222
3	B640.00	Acute lymphoid leukaemia	4251
3	B640000	B-cell acute lymphoblastic leukaemia	104325
3	B641.00	Chronic lymphoid leukaemia	8625
3	B641.11	Chronic lymphatic leukaemia	27790
3	B641000	B-cell chronic lymphocytic leukaemia	104328
3	B641011	Chronic lymphocytic leukaemia of B-cell type	107017
3	B641100	Clinical stage A chronic lymphocytic leukaemia	107052
3	B641200	Clinical stage B chronic lymphocytic leukaemia	106924
3	B641300	Clinical stage C chronic lymphocytic leukaemia	107163
3	B642.00	Subacute lymphoid leukaemia	72774
3	B64y.00	Other lymphoid leukaemia	49725
3	B64y100	Prolymphocytic leukaemia	31586
3	B64y200	Adult T-cell leukaemia	37461
3	B64y300	B-cell prolymphocytic leukaemia	108656
3	B64y400	T-cell prolymphocytic leukaemia	107643
3	B64y500	Adult T-cell lymphoma/leukaemia (HTLV-1-associated)	104939
3	B64yz00	Other lymphoid leukaemia NOS	38331
3	B64z.00	Lymphoid leukaemia NOS	38914
3	B65..00	Myeloid leukaemia	7176
3	B650.00	Acute myeloid leukaemia	4413
3	B651.00	Chronic myeloid leukaemia	10726
3	B651.11	Chronic granulocytic leukaemia	31701
3	B651000	Chronic eosinophilic leukaemia	100786
3	B651100	Chronic myeloid leukaemia, BCR/ABL positive	105957
3	B651200	Chronic neutrophilic leukaemia	102783
3	B651300	Atypical chronic myeloid leukaemia, BCR/ABL negative	107236
3	B651z00	Chronic myeloid leukaemia NOS	27520
3	B652.00	Subacute myeloid leukaemia	63475
3	B654.00	Acute myeloblastic leukaemia	104788
3	B65y100	Acute promyelocytic leukaemia	27664
3	B65yz00	Other myeloid leukaemia NOS	66089
3	B65z.00	Myeloid leukaemia NOS	33344
3	B66..00	Monocytic leukaemia	35875
3	B66..11	Histiocytic leukaemia	108715
3	B66..12	Monoblastic leukaemia	67700
3	B660.00	Acute monocytic leukaemia	19974
3	B661.00	Chronic monocytic leukaemia	27458
3	B662.00	Subacute monocytic leukaemia	101606
3	B663.00	Acute monoblastic leukaemia	108424
3	B66y.00	Other monocytic leukaemia	99015
3	B66yz00	Other monocytic leukaemia NOS	103645

3	B66z.00	Monocytic leukaemia NOS	93342
3	B67..00	Other specified leukaemia	37272
3	B670.00	Acute erythraemia and erythroleukaemia	42539
3	B672.00	Megakaryocytic leukaemia	57671
3	B672.11	Thrombocytic leukaemia	65777
3	B673.00	Mast cell leukaemia	65721
3	B67y.00	Other and unspecified leukaemia	94174
3	B67y000	Lymphosarcoma cell leukaemia	72197
3	B67yz00	Other and unspecified leukaemia NOS	99413
3	B67z.00	Other specified leukaemia NOS	30632
3	B68..00	Leukaemia of unspecified cell type	25191
3	B680.00	Acute leukaemia NOS	4072
3	B681.00	Chronic leukaemia NOS	16416
3	B682.00	Subacute leukaemia NOS	54793
3	B68y.00	Other leukaemia of unspecified cell type	34692
3	B68z.00	Leukaemia NOS	4250
3	B69..00	Myelomonocytic leukaemia	20440
3	B690.00	Acute myelomonocytic leukaemia	61500
3	B691.00	Chronic myelomonocytic leukaemia	22050
3	B692.00	Subacute myelomonocytic leukaemia	104475
3	B693.00	Juvenile myelomonocytic leukaemia	105069
3	BBr..00	[M]Leukaemias	4637
3	BBr0.00	[M]Leukaemias unspecified	40420
3	BBr0000	[M]Leukaemia NOS	41734
3	BBr0100	[M]Acute leukaemia NOS	6316
3	BBr0111	[M]Blast cell leukaemia	22071
3	BBr0112	[M]Blastic leukaemia	64963
3	BBr0113	[M]Stem cell leukaemia	63570
3	BBr0200	[M]Subacute leukaemia NOS	72179
3	BBr0300	[M]Chronic leukaemia NOS	31750
3	BBr0400	[M]Aleukaemic leukaemia NOS	72310
3	BBr0z00	[M]Leukaemia unspecified, NOS	59929
3	BBr2.00	[M]Lymphoid leukaemias	48155
3	BBr2000	[M]Lymphoid leukaemia NOS	12146
3	BBr2011	[M]Lymphatic leukaemia	20635
3	BBr2100	[M]Acute lymphoid leukaemia	37410
3	BBr2300	[M]Chronic lymphoid leukaemia	41500
3	BBr2500	[M]Prolymphocytic leukaemia	46048
3	BBr2600	[M]Burkitt's cell leukaemia	50928
3	BBr2700	[M]Adult T-cell leukaemia/lymphoma	29335
3	BBr3.00	[M]Plasma cell leukaemias	64618
3	BBr4.00	[M]Erythroleukaemias	46444
3	BBr4000	[M]Erythroleukaemia	70935
3	BBr4z00	[M]Erythroleukaemia NOS	100927

	3	BBr6.00	[M]Myeloid leukaemias	35697
	3	BBr6000	[M]Myeloid leukaemia NOS	71850
	3	BBr6011	[M]Granulocytic leukaemia NOS	37723
	3	BBr6100	[M]Acute myeloid leukaemia	54585
	3	BBr6200	[M]Subacute myeloid leukaemia	106483
	3	BBr6300	[M]Chronic myeloid leukaemia	52942
	3	BBr6311	[M]Naegeli-type monocytic leukaemia	66694
	3	BBr6600	[M]Acute promyelocytic leukaemia	57316
	3	BBr6700	[M]Acute myelomonocytic leukaemia	46263
	3	BBr6800	[M]Chronic myelomonocytic leukaemia	48049
	3	BBr6900	[M]Juvenile myelomonocytic leukaemia	108964
	3	BBr6z00	[M]Other myeloid leukaemia NOS	62330
	3	BBr7000	[M]Basophilic leukaemia	106197
	3	BBr8.00	[M]Eosinophilic leukaemias	57713
	3	BBr8000	[M]Eosinophilic leukaemia	71377
	3	BBr8z00	[M]Eosinophilic leukaemia NOS	107773
	3	BBr9000	[M]Monocytic leukaemia NOS	73088
	3	BBrA.00	[M]Miscellaneous leukaemias	73066
	3	BBrA100	[M]Megakaryocytic leukaemia	72222
	3	BBrA111	[M]Thrombocytic leukaemia	69299
	3	BBrA400	[M]Hairy cell leukaemia	5915
	3	BBrA500	[M]Acute megakaryoblastic leukaemia	49327
	3	BBrAz00	[M]Miscellaneous leukaemia NOS	108316
	3	BBrz.00	[M]Leukaemia NOS	42297
	3	ByuD500	[X]Other lymphoid leukaemia	67029
	3	ByuD600	[X]Other myeloid leukaemia	61693
	3	ByuD700	[X]Other monocytic leukaemia	89762
	3	ByuD800	[X]Other specified leukaemias	89329
	3	ByuD900	[X]Other leukaemia of unspecified cell type	65165
	1	ZV10600	[V]Personal history of leukaemia	36693
	1	ZV10611	[V]Personal history of lymphoid leukaemia	94597
	3	ZV67811	[V]Follow-up examination after chemotherapy for leukaemia	53477

Lung

metadata	category	readcode	readterm	medcode
Name: lung_cprd	1	ZV10100	[V]Personal history of malig neop of trachea/bronchus/lung	49289
Version: 2	1	ZV10111	[V]Personal history of malignant neoplasm of bronchus	32246

Source: CPRD	1	ZV1011 2	[V]Personal history of malignant neoplasm of lung	29284
Author: C McKenna/C Parisinos/ V Kuan	3	B22010 0	Malignant neoplasm of mucosa of trachea	103946
Date: 19th October 2018	3	B220.0 0	Malignant neoplasm of trachea	15221
Categories:	3	B220z0 0	Malignant neoplasm of trachea NOS	37810
1 = H/O	3	B22100 0	Malignant neoplasm of carina of bronchus	17391
2= Probable	3	B22110 0	Malignant neoplasm of hilus of lung	33444
3 = Definite	3	B221.0 0	Malignant neoplasm of main bronchus	12870
	3	B221z0 0	Malignant neoplasm of main bronchus NOS	21698
	3	B22200 0	Malignant neoplasm of upper lobe bronchus	31700
	3	B22210 0	Malignant neoplasm of upper lobe of lung	25886
	3	B222.0 0	Malignant neoplasm of upper lobe, bronchus or lung	10358
	3	B222.1 1	Pancoast's syndrome	20170
	3	B222z0 0	Malignant neoplasm of upper lobe, bronchus or lung NOS	44169
	3	B22300 0	Malignant neoplasm of middle lobe bronchus	41523
	3	B22310 0	Malignant neoplasm of middle lobe of lung	39923
	3	B223.0 0	Malignant neoplasm of middle lobe, bronchus or lung	31268
	3	B223z0 0	Malignant neoplasm of middle lobe, bronchus or lung NOS	54134
	3	B22400 0	Malignant neoplasm of lower lobe bronchus	18678
	3	B22410 0	Malignant neoplasm of lower lobe of lung	12582
	3	B224.0 0	Malignant neoplasm of lower lobe, bronchus or lung	31188
	3	B224z0 0	Malignant neoplasm of lower lobe, bronchus or lung NOS	42566
	3	B225.0 0	Malignant neoplasm of overlapping lesion of bronchus & lung	36371
	3	B22..00	Malignant neoplasm of trachea, bronchus and lung	13243
	3	B22y.0 0	Malignant neoplasm of other sites of bronchus or lung	38961
	3	B22z.00	Malignant neoplasm of bronchus or lung NOS	3903
	3	B22z.11	Lung cancer	2587
	3	BB5S20 0	[M]Bronchiolo-alveolar adenocarcinoma	34015
	3	BB5S21 1	[M]Alveolar cell carcinoma	36530
	3	BB5S21 2	[M]Bronchiolar carcinoma	16723
	3	BB5S40 0	[M]Alveolar adenocarcinoma	57802
	3	Byu200 0	[X]Malignant neoplasm of bronchus or lung, unspecified	40595
	3	BBK37 00	[M]Alveolar rhabdomyosarcoma	42082
	3	BB5T1 00	[M]Papillary adenocarcinoma NOS	35348

3	BB5Tz00	[M]Papillary adenoma or adenocarcinoma NOS	96494
3	BB5T.00	[M]Papillary adenomas and adenocarcinomas	42273
3	BBLA.11	[M]Pneumoblastoma	61082
3	BBLM.00	[M]Pulmonary blastoma	48348
3	BB5Sz00	[M]Respiratory tract adenoma or adenocarcinoma NOS	36221
3	BB5S.00	[M]Respiratory tract adenomas and adenocarcinomas	26848
3	Byu2.00	[X]Malignant neoplasm of respiratory and intrathoracic orga	35325
3	B226.00	Mesothelioma	7484
3	Byu5011	Mesothelioma of the lung	21715

Lymphoma

metadata	category	readcode	readterm	medcode
Name: lymphoma_cprd	2	1J04.00	Suspected lymphoma	19083
Version: 1	3	4M2..00	Lymphoma staging system	40991
Source: CPRD	3	4M20.00	Lymphoma stage I	60918
Author: C McKenna	3	4M21.00	Lymphoma stage II	94935
Date: 19th October 2018	3	4M22.00	Lymphoma stage III	32240
Categories:	3	4M23.00	Lymphoma stage IV	71672
1 = H/O	3	A789600	HIV disease resulting in Burkitt's lymphoma	44617
2= Probable	3	A789700	HIV dis resulting oth types of non-Hodgkin's lymphoma	66367
3 = Definite	3	AyuC600	[X]HIV disease resulting in other non-Hodgkin's lymphoma	69767
	3	B602.00	Burkitt's lymphoma	21402
	3	B602100	Burkitt's lymphoma of lymph nodes of head, face and neck	59115
	3	B602200	Burkitt's lymphoma of intrathoracic lymph nodes	100006
	3	B602300	Burkitt's lymphoma of intra-abdominal lymph nodes	97577
	3	B602500	Burkitt's lymphoma of lymph nodes of inguinal region and leg	92380
	3	B602z00	Burkitt's lymphoma NOS	71304
	3	B61..11	Hodgkin lymphoma	104291
	3	B617.00	Nodular lymphocyte predominant Hodgkin lymphoma	104895
	3	B618.00	Nodular sclerosis classical Hodgkin lymphoma	105841
	3	B619.00	Mixed cellularity classical Hodgkin lymphoma	108775
	3	B61B.00	Lymphocyte-rich classical Hodgkin lymphoma	106597
	3	B61C.00	Other classical Hodgkin lymphoma	104484
	3	B61z.11	Hodgkin lymphoma NOS	106349
	3	B620.00	Nodular lymphoma (Brill - Symmers disease)	5179
	3	B620000	Nodular lymphoma of unspecified site	66327
	3	B620100	Nodular lymphoma of lymph nodes of head, face and neck	45264
	3	B620200	Nodular lymphoma of intrathoracic lymph nodes	105203

3	B620300	Nodular lymphoma of intra-abdominal lymph nodes	92068
3	B620500	Nodular lymphoma of lymph nodes of inguinal region and leg	94995
3	B620800	Nodular lymphoma of lymph nodes of multiple sites	58082
3	B620z00	Nodular lymphoma NOS	65701
3	B627.00	Non - Hodgkin's lymphoma	3604
3	B627.11	Non-Hodgkin lymphoma	104391
3	B627000	Follicular non-Hodgkin's small cleaved cell lymphoma	28639
3	B627100	Follicular non-Hodg mixed sml cleavd & lge cell lymphoma	70842
3	B627200	Follicular non-Hodgkin's large cell lymphoma	49262
3	B627300	Diffuse non-Hodgkin's small cell (diffuse) lymphoma	50668
3	B627400	Diffuse non-Hodgkin's small cleaved cell (diffuse) lymphoma	108182
3	B627500	Diffuse non-Hodgkin mixed sml & lge cell (diffuse) lymphoma	50695
3	B627600	Diffuse non-Hodgkin's immunoblastic (diffuse) lymphoma	53551
3	B627700	Diffuse non-Hodgkin's lymphoblastic (diffuse) lymphoma	17460
3	B627800	Diffuse non-Hodgkin's lymphoma undifferentiated (diffuse)	65180
3	B627900	Mucosa-associated lymphoma	95715
3	B627A00	Diffuse non-Hodgkin's large cell lymphoma	101114
3	B627B00	Other types of follicular non-Hodgkin's lymphoma	31576
3	B627C00	Follicular non-Hodgkin's lymphoma	21549
3	B627C11	Follicular lymphoma NOS	17182
3	B627D00	Diffuse non-Hodgkin's centroblastic lymphoma	70509
3	B627E00	Diffuse large B-cell lymphoma	102594
3	B627G00	Mediastinal (thymic) large B-cell lymphoma	105038
3	B627W00	Unspecified B-cell non-Hodgkin's lymphoma	31794
3	B627X00	Diffuse non-Hodgkin's lymphoma, unspecified	39798
3	B628.00	Follicular lymphoma	104152
3	B628000	Follicular lymphoma grade 1	105889
3	B628100	Follicular lymphoma grade 2	105095
3	B628200	Follicular lymphoma grade 3	107166
3	B628300	Follicular lymphoma grade 3a	105020
3	B628400	Follicular lymphoma grade 3b	107973
3	B628500	Diffuse follicle centre lymphoma	106969
3	B628600	Cutaneous follicle centre lymphoma	108719
3	B628700	Other types of follicular lymphoma	106063
3	B62E.00	T/NK-cell lymphoma	105085
3	B62E100	Anaplastic large cell lymphoma, ALK-positive	105559
3	B62E200	Anaplastic large cell lymphoma, ALK-negative	105955
3	B62E300	Cutaneous T-cell lymphoma	104862
3	B62E500	Hepatosplenic T-cell lymphoma	107949
3	B62E600	Enteropathy-associated T-cell lymphoma	105709

3	B62E700	Subcutaneous panniculitic T-cell lymphoma	105925
3	B62E800	Blastic NK-cell lymphoma	105375
3	B62E900	Angioimmunoblastic T-cell lymphoma	105636
3	B62Ew00	Other mature T/NK-cell lymphoma	104934
3	B62F.00	Nonfollicular lymphoma	106884
3	B62F.11	Non-follicular lymphoma	106867
3	B62F000	Small cell B-cell lymphoma	104386
3	B62F100	Mantle cell lymphoma	104620
3	B62F200	Lymphoblastic (diffuse) lymphoma	104412
3	B62x.00	Malignant lymphoma otherwise specified	17887
3	B62x000	T-zone lymphoma	90201
3	B62x100	Lymphoepithelioid lymphoma	57737
3	B62x200	Peripheral T-cell lymphoma	12464
3	B62x600	True histiocytic lymphoma	95630
3	B62xX00	Oth and unspecif peripheral & cutaneous T-cell lymphomas	44318
3	B62y.00	Malignant lymphoma NOS	12335
3	B62y000	Malignant lymphoma NOS of unspecified site	57427
3	B62y100	Malignant lymphoma NOS of lymph nodes of head, face and neck	50696
3	B62y200	Malignant lymphoma NOS of intrathoracic lymph nodes	72725
3	B62y300	Malignant lymphoma NOS of intra-abdominal lymph nodes	42579
3	B62y400	Malignant lymphoma NOS of lymph nodes of axilla and arm	34089
3	B62y500	Malignant lymphoma NOS of lymph node inguinal region and leg	63105
3	B62y600	Malignant lymphoma NOS of intrapelvic lymph nodes	71262
3	B62y700	Malignant lymphoma NOS of spleen	60092
3	B62y800	Malignant lymphoma NOS of lymph nodes of multiple sites	15504
3	B62yz00	Malignant lymphoma NOS	15027
3	B64y500	Adult T-cell lymphoma/leukaemia (HTLV-1-associated)	104939
3	BBB1.00	[M]Adenolymphoma	3710
3	BBg..00	[M]Lymphomas, NOS or diffuse	17178
2	BBg0.00	[M]Lymphomatous tumour, benign	49131
3	BBg1.00	[M]Malignant lymphoma NOS	36114
3	BBg1.11	[M]Lymphoma NOS	1483
3	BBg1000	[M]Malignant lymphoma, diffuse NOS	23711
3	BBg2.00	[M]Malignant lymphoma, non Hodgkin's type	16460
3	BBg2.11	[M]Non Hodgkins lymphoma	3371
3	BBg3.00	[M]Malignant lymphoma, undifferentiated cell type NOS	71117
3	BBg4.00	[M]Malignant lymphoma, stem cell type	46931
3	BBg5.00	[M]Malignant lymphoma, convoluted cell type NOS	69301
3	BBg7.00	[M]Malignant lymphoma, lymphoplasmacytoid type	41754
3	BBg8.00	[M]Malignant lymphoma, immunoblastic type	48253
3	BBgA.00	[M]Malignant lymphoma, centroblastic-centrocytic, diffuse	68964
3	BBgB.00	[M]Malignant lymphoma, follicular centre cell NOS	41841

3	BBgC.00	[M]Malignant lymphoma, lymphocytic, well differentiated NOS	69980
3	BBgC.11	[M]Lymphocytic lymphoma NOS	21463
3	BBgD.00	[M]Malig lymphoma, lymphocytic, intermediate different NOS	51852
3	BBgE.00	[M]Malignant lymphoma, centrocytic	39906
3	BBgG.00	[M]Malignant lymphoma, lymphocytic, poorly different NOS	72196
3	BBgG.12	[M]Lymphoblastic lymphoma NOS	34352
3	BBgJ.00	[M]Malignant lymphoma, centroblastic type NOS	60275
3	BBgK.00	[M]Malig lymphoma, follicular centre cell, non-cleaved NOS	66603
3	BBgL.00	[M]Malignant lymphoma, small lymphocytic NOS	46877
3	BBgM.00	[M]Malignant lymphoma, small cleaved cell, diffuse	31726
3	BBgN.00	[M]Malign lymphoma,lymphocytic,intermediate differn, diffuse	61251
3	BBgP.00	[M]Malignant lymphoma, mixed small and large cell, diffuse	71652
3	BBgQ.00	[M]Malignant lymphomatous polyposis	58015
3	BBgR.00	[M]Malignant lymphoma, large cell, diffuse NOS	33869
3	BBgS.00	[M]Malignant lymphoma, large cell, cleaved, diffuse	63994
3	BBgT.00	[M]Malignant lymphoma, large cell, noncleaved, diffuse	71619
3	BBgV.00	[M]Malignant lymphoma, small cell, noncleaved, diffuse	51680
3	BBgz.00	[M]Lymphoma, diffuse or NOS	51895
3	BBk..00	[M]Lymphomas, nodular or follicular	20437
3	BBk0.00	[M]Malignant lymphoma, nodular NOS	63699
3	BBk0.13	[M]Giant follicular lymphoma	49253
3	BBk2.00	[M]Malignant lymphoma, centroblastic-centrocytic, follicular	98961
3	BBk3.00	[M]Malig lymphoma, lymphocytic, well differentiated,nodular	106970
3	BBk7.00	[M]Malignant lymphoma, centroblastic type, follicular	97852
3	BBkz.00	[M]Lymphoma, nodular or follicular NOS	40513
3	BBm4.00	[M]True histiocytic lymphoma	57544
3	BBm5.00	[M] Peripheral T-cell lymphoma NOS	40766
3	BBm9.00	[M] Monocytoid B-cell lymphoma	31492
3	BBmD.00	[M] Cutaneous lymphoma	16774
3	BBmH.00	[M] Large cell lymphoma	18383
3	BBr2700	[M]Adult T-cell leukaemia/lymphoma	29335
3	BBv0.00	[M]Monocytoid B-cell lymphoma	31749
3	BBv2.00	[M]AngiocentricT-cell lymphoma	27965
3	ByuD100	[X]Other types of follicular non-Hodgkin's lymphoma	67518
3	ByuD200	[X]Other types of diffuse non-Hodgkin's lymphoma	98596
3	ByuD300	[X]Other specified types of non-Hodgkin's lymphoma	64336
3	ByuDC00	[X]Diffuse non-Hodgkin's lymphoma, unspecified	64515

3	ByuDE00	[X]Unspecified B-cell non-Hodgkin's lymphoma	63375
3	ByuDF00	[X]Non-Hodgkin's lymphoma, unspecified type	8649
3	ByuDF11	[X]Non-Hodgkin's lymphoma NOS	7940
3	M162800	Lymphomatoid papulosis	26111
3	B6...00	Malignant neoplasm of lymphatic and haemopoietic tissue	12323
3	B60..00	Lymphosarcoma and reticulosarcoma	41369
3	B601.00	Lymphosarcoma	27416
3	B61..00	Hodgkin's disease	2462
3	B610.00	Hodgkin's paragranuloma	65489
3	B611.00	Hodgkin's granuloma	44196
3	B612.00	Hodgkin's sarcoma	64036
3	B61z.00	Hodgkin's disease NOS	53397
3	B61z000	Hodgkin's disease NOS, unspecified site	61662
3	B61zz00	Hodgkin's disease NOS	42461
3	B62..00	Other malignant neoplasm of lymphoid and histiocytic tissue	33333
3	B62z.00	Malignant neoplasms of lymphoid and histiocytic tissue nos	65434
3	B62z000	Unspec malig neop lymphoid/histiocytic of unspecified site	108037
3	B62zz00	Lymphoid and histiocytic malignancy nos	95792
3	B6y..00	Malignant neoplasm lymphatic or haematopoietic tissue OS	30646
3	B6z..00	Malignant neoplasm lymphatic or haematopoietic tissue nos	49301
3	BBg6.00	[M]Lymphosarcoma nos	99655
3	BBgC.12	[M]Lymphocytic lymphosarcoma nos	60504
3	BBgG.11	[M]Lymphoblastic lymphosarcoma nos	67203
3	BBgG.13	[M]Lymphoblastoma nos	52591
3	BBgH.00	[M]Prolymphocytic lymphosarcoma	72241
3	BBk0.12	[M]Follicular lymphosarcoma nos	27562
3	BBs..00	[M]Misc myeloproliferative and lymphoproliferative disorders	30139
3	BBs5.00	[M]Chronic lymphoproliferative disease	9673
3	BBsz.00	[M]Misc myeloproliferative or lymphoproliferative dis nos	37692
3	ByuD.00	[X]Malignant neoplasms of lymphoid, haematopoietic and rela	40740
3	ByuD500	[X]Other lymphoid leukaemia	67029
3	ByuDA00	[X]Oth spcf mal neoplsm/lymphoid,haematopoietic+rltd tissue	105025
1	ZV10611	[V]Personal history of lymphoid leukaemia	94597

Melanoma

metadata	category	readcode	readterm	medcode
Name: melanoma_cprd	1	1425000	H/O Malignant melanoma	7761
Version: 2	3	4M3..00	Breslow depth staging for melanoma	57294

		4M70.00	Clark melanoma level 1	101198
Source: CPRD	3			
Author: C McKenna/C Parisinos/ V Kuan	3	4M71.00	Clark melanoma level 2	104609
		4M72.00	Clark melanoma level 3	96280
Date: 19th October 2018	3			
		4M73.00	Clark melanoma level 4	102116
Categories:	3			
		4M74.00	Clark melanoma level 5	108866
1 = H/O	3			
		7G03J00	Excision of melanoma	8640
2= Probable	3			
		B32..0	Malignant melanoma of skin	865
3 = Definite	3			
		B320.0	Malignant melanoma of lip	70637
	3	0		
		B321.0	Malignant melanoma of eyelid including canthus	54632
	3	0		
		B322.0	Malignant melanoma of ear and external auricular canal	57260
	3	0		
		B3220	Malignant melanoma of auricle (ear)	59061
	3	00		
		B3221	Malignant melanoma of external auditory meatus	102145
	3	00		
		B322z00	Malignant melanoma of ear and external auricular canal NOS	73744
	3			
		B323.0	Malignant melanoma of other and unspecified parts of face	47252
	3	0		
		B3230	Malignant melanoma of external surface of cheek	41278
	3	00		
		B3231	Malignant melanoma of chin	71136
	3	00		
		B3232	Malignant melanoma of eyebrow	47094
	3	00		
		B3233	Malignant melanoma of forehead	68133
	3	00		
		B3234	Malignant melanoma of external surface of nose	45139
	3	00		
		B3235	Malignant melanoma of temple	58958
	3	00		
		B323z00	Malignant melanoma of face NOS	67806
	3			
		B324.0	Malignant melanoma of scalp and neck	65625
	3	0		
		B3240	Malignant melanoma of scalp	55881
	3	00		
		B3241	Malignant melanoma of neck	45306
	3	00		
		B324z00	Malignant melanoma of scalp and neck NOS	99257
	3			
		B325.0	Malignant melanoma of trunk (excluding scrotum)	38689
	3	0		
		B3250	Malignant melanoma of axilla	49814
	3	00		
		B3251	Malignant melanoma of breast	32768
	3	00		
		B3252	Malignant melanoma of buttock	53629
	3	00		
		B3253	Malignant melanoma of groin	34259
	3	00		
		B3254	Malignant melanoma of perianal skin	109002
	3	00		
		B3255	Malignant melanoma of perineum	95629
	3	00		

3	B3256 00	Malignant melanoma of umbilicus	43715
3	B3257 00	Malignant melanoma of back	43463
3	B3258 00	Malignant melanoma of chest wall	51209
3	B325z 00	Malignant melanoma of trunk, excluding scrotum, NOS	45760
3	B326.0 0	Malignant melanoma of upper limb and shoulder	65164
3	B3260 00	Malignant melanoma of shoulder	50505
3	B3261 00	Malignant melanoma of upper arm	54685
3	B3262 00	Malignant melanoma of fore-arm	45755
3	B3263 00	Malignant melanoma of hand	62475
3	B3264 00	Malignant melanoma of finger	25602
3	B3265 00	Malignant melanoma of thumb	63997
3	B326z 00	Malignant melanoma of upper limb or shoulder NOS	55292
3	B327.0 0	Malignant melanoma of lower limb and hip	46255
3	B3270 00	Malignant melanoma of hip	73536
3	B3271 00	Malignant melanoma of thigh	51873
3	B3272 00	Malignant melanoma of knee	54305
3	B3273 00	Malignant melanoma of popliteal fossa area	39878
3	B3274 00	Malignant melanoma of lower leg	37872
3	B3275 00	Malignant melanoma of ankle	42714
3	B3276 00	Malignant melanoma of heel	61246
3	B3277 00	Malignant melanoma of foot	41490
3	B3278 00	Malignant melanoma of toe	36899
3	B3279 00	Malignant melanoma of great toe	53369
3	B327z 00	Malignant melanoma of lower limb or hip NOS	64327
3	B32y.0 0	Malignant melanoma of other specified skin site	42153
3	B32y0 00	Overlapping malignant melanoma of skin	96585
3	B32z.0 0	Malignant melanoma of skin NOS	28556
3	BBE..0 0	[M]Malignant melanoma in junctional naevus	63574
3	BBE1. 00	[M]Malignant melanoma NOS	579
3	BBE1. 11	[M]Melanocarcinoma	24551
3	BBE1. 12	[M]Melanoma NOS	7483
3	BBE1. 13	[M]Melanosarcoma NOS	44157

3	BBE1.14	[M]NAEVOCARCINOMA	67966
3	BBE1000	[M]Malignant melanoma, regressing	51353
3	BBE1100	[M]Desmoplastic melanoma, malignant	58835
3	BBE2.00	[M]Nodular melanoma	20982
3	BBE4.00	[M]Balloon cell melanoma	68889
3	BBEA.00	[M]Amelanotic melanoma	17232
3	BBEC.00	[M]MALIGNANT MELANOMA IN JUNCTIONAL NAEVUS	63574
3	BBEF.00	[M]Hutchinson's melanotic freckle	20709
3	BBEF.11	[M]Lentigo maligna	2705
3	BBEG.00	[M]Malignant melanoma in Hutchinson's melanotic freckle	62088
3	BBEG.11	[M]Lentigo maligna melanoma	11922
3	BBEG000	[M]Acral lentiginous melanoma, malignant	22692
3	BBEH.00	[M]Superficial spreading melanoma	24208
3	BBEM.00	[M]Malignant melanoma in giant pigmented naevus	73251
3	BBEN.11	[M]Juvenila melanoma	4871
3	BBEP.00	[M]Epithelioid cell melanoma	23085
3	BBEQ.00	[M]Spindle cell melanoma NOS	44061
3	BBES.00	[M]Spindle cell melanoma, type B	92293
3	BBET.00	[M]Mixed epithelioid and spindle melanoma	40303
3	BBEz.00	[X]Malignant melanoma of other+unspecified parts of face	56925
3	Byu4.00	[X] Melanoma and other malignant neoplasms of skin	19144
3	Byu4000	[X]MALIGNANT MELANOMA OF OTHER+UNSPECIFIED PARTS OF FACE	56925
3	Byu4100	[X]Malignant melanoma of skin, unspecified	19444

Non-melanoma, skin

metadata	category	readcode	readterm	medcode
Name: nonmelskin_cprd	3	B33z100	Naevoid basal cell carcinoma syndrome	54182
Version: 1	3	B33z111	Basal cell naevus syndrome	21156
Source: CPRD	3	BB3..00	[M]Basal cell neoplasms	3516
Author: C McKenna	3	BB3C.00	[M]Superficial basal cell carcinoma	102417
Date: 19th October 2018	3	BB5A.00	[M]Basal cell adenoma	34291
Categories:	3	BB3F.00	[M]Basal cell carcinoma, infiltrative	103178
1 = H/O	3	B33..16	Epithelioma basal cell	3445
2= Probable	3	B33..11	Basal cell carcinoma	876

3 = Definite	3	7G05D00	Excision biopsy of basal cell carcinoma	93402
	3	BB32.00	[M]Multicentric basal cell carcinoma	59919
	3	BB30.00	[M]Basal cell tumour	29282
	3	BB34.00	[M]Basal cell carcinoma, fibroepithelial type	29524
	3	BB3D.00	[M]Basal cell carcinoma, nodular	102547
	3	BB3z.00	[M]Basal cell neoplasm NOS	30853
	3	BB33.00	[M]Basal cell carcinoma, morphoea type	9885
	3	BB31.00	[M]Basal cell carcinoma NOS	3028
	3	BB3G.00	[M]Pigmented basal cell carcinoma	103066
	3	BB3E.00	[M]Basal cell carcinoma, micronodular	103440
	3	BB5y000	[M]Basal cell adenocarcinoma	16902
	3	BB26.00	[M]Papillary squamous cell carcinoma	20807
	3	BB2C.00	[M]Squamous cell carcinoma, keratinising type NOS	29787
	3	BB2F.00	[M]Squamous cell carcinoma, spindle cell type	45458
	3	BB2..00	[M]Papillary and squamous cell neoplasms	40494
	3	BB2J.00	[M]Squamous cell carcinoma, microinvasive	33497
	3	BB2D.00	[M]Squamous cell carcinoma, large cell, non-keratinising	59143
	3	B33z.11	Squamous cell carcinoma of skin NOS	93490
	3	BB2B.00	[M]Squamous cell carcinoma, metastatic NOS	24293
	3	BB2H.00	[M]Squamous cell ca-in-situ, questionable stromal invasion	61928
	3	BB25.00	[M]Squamous cell papilloma	155
	3	4K29000	Cervical smear - borderline change in squamous cells	107261
	3	BB24.12	[M]Verrucous squamous cell carcinoma	4852
	3	44a4.00	Squamous cell carcinoma antigen level	32351
	3	BB2E.00	[M]Squamous cell carcinoma, small cell, non-keratinising	41816
	3	BB2A.13	[M]Squamous cell carcinoma of skin NOS	94873
	3	BB29.13	[M]Intraepithelial squamous cell carcinoma	19678
	3	BB2G.00	[M]Adenoid squamous cell carcinoma	31004
	3	BB2A.00	[M]Squamous cell carcinoma NOS	1624
	3	B338.00	Squamous cell carcinoma of skin	93352
	3	BB2z.00	[M]Papillary or squamous cell neoplasm NOS	49399
	3	BB29.00	[M]Squamous cell carcinoma in situ NOS	10134
	3	BB2..12	[M]Squamous cell neoplasms	7967
	2	1J0G.00	Suspected skin cancer	11541
	2	9Np9.00	Seen in fast track suspected skin cancer clinic	106004
	2	8Hn0.00	Fast track referral for suspected skin cancer	85844
	2	B763z00	Benign neoplasm of skin of face NOS	54863
	2	B765z00	Benign neoplasm of skin of trunk, excluding scrotum, NOS	64399
	3	B335000	Malignant neoplasm of skin of axillary fold	70380
	3	B337z00	Malignant neoplasm of skin of lower limb or hip NOS	61194

3	B335z00	Malignant neoplasm of skin of trunk, excluding scrotum, NOS	15868
2	B760.00	Benign neoplasm of skin of lip	33787
2	B762100	Benign neoplasm of skin of external auditory meatus	4066
3	B336200	Malignant neoplasm of skin of fore-arm	30577
2	B767400	Benign neoplasm of skin of foot	27288
2	B765300	Benign neoplasm of skin of abdomen	17688
3	B332100	Malignant neoplasm of skin of external auditory meatus	62080
3	B335700	Malignant neoplasm of skin of back	45077
3	B330.00	Malignant neoplasm of skin of lip	18245
3	B336.00	Malignant neoplasm of skin of upper limb and shoulder	30747
3	B333100	Malignant neoplasm of skin of chin	49403
2	B763000	Benign neoplasm of skin of forehead	12758
3	B582600	Secondary malignant neoplasm of skin of breast	9505
3	B336300	Malignant neoplasm of skin of hand	54352
2	B765900	Benign neoplasm of skin of back	11514
2	B765000	Benign neoplasm of skin of axilla	27531
3	B337300	Malignant neoplasm of skin of popliteal fossa area	68197
3	B582500	Secondary malignant neoplasm of skin of hip and leg	48828
2	B765400	Benign neoplasm of skin of umbilicus	20213
3	B336z00	Malignant neoplasm of skin of upper limb or shoulder NOS	60526
2	B766z00	Benign neoplasm of skin of upper limb or shoulder NOS	69856
3	B335600	Malignant neoplasm of skin of perineum	46458
3	B336000	Malignant neoplasm of skin of shoulder	43122
2	B763100	Benign neoplasm of skin of nose	30623
2	B762.00	Benign neoplasm of skin of ear and external auditory meatus	37741
3	Byu4300	[X]Malignant neoplasm of skin, unspecified	56121
3	B333000	Malignant neoplasm of skin of cheek, external	30645
2	B765700	Benign neoplasm of skin of buttock	42483
3	B335800	Malignant neoplasm of skin of buttock	62305
2	B763200	Benign neoplasm of skin of cheek	21074
3	B337500	Malignant neoplasm of skin of ankle	64270
3	B336100	Malignant neoplasm of skin of upper arm	42707
2	B765600	Benign neoplasm of skin of perineum	38374
3	B335500	Malignant neoplasm of skin of groin	66319
2	B765100	Benign neoplasm of skin of breast	28143
3	B582z00	Secondary malignant neoplasm of skin NOS	55096
3	B337900	Malignant neoplasm of skin of great toe	67914
3	B337200	Malignant neoplasm of skin of knee	56954
3	B33z.00	Malignant neoplasm of skin NOS	2492
2	B766300	Benign neoplasm of skin of hand	53360
3	B335A00	Malignant neoplasm of skin of scapular region	66447
2	B762000	Benign neoplasm of skin of auricle	37148
2	B767.11	Benign neoplasm of skin of leg	69450

3	B337400	Malignant neoplasm of skin of lower leg	33682
2	B767000	Benign neoplasm of skin of hip	62872
3	B335300	Malignant neoplasm of skin of abdominal wall	18618
2	B766.00	Benign neoplasm of skin of upper limb and shoulder	45135
3	B337800	Malignant neoplasm of skin of toe	65782
3	B335400	Malignant neoplasm of skin of umbilicus	67748
2	B763400	Benign neoplasm of skin of temple	38348
2	B763.00	Benign neoplasm of skin of face NEC	28089
3	B337100	Malignant neoplasm of skin of thigh	58601
2	B763300	Benign neoplasm of skin of eyebrow	59422
3	B333500	Malignant neoplasm of skin of temple	21327
3	B582300	Secondary malignant neoplasm of skin of trunk	41144
2	B766200	Benign neoplasm of skin of fore-arm	41862
2	B764100	Benign neoplasm of skin of neck	23901
3	B582400	Secondary malignant neoplasm of skin of shoulder and arm	63896
2	B76z.00	Benign neoplasm of skin NOS	27618
3	B337.00	Malignant neoplasm of skin of lower limb and hip	57442
3	B337700	Malignant neoplasm of skin of foot	70587
2	B767100	Benign neoplasm of skin of thigh	30304
3	B335200	Malignant neoplasm of skin of breast	30543
2	B765.00	Benign neoplasm of skin of trunk, excluding scrotum	42081
3	B333300	Malignant neoplasm of skin of forehead	30576
2	B767.00	Benign neoplasm of skin of hip and lower limb	45884
2	B763500	Benign neoplasm of skin of chin	43692
3	B337000	Malignant neoplasm of skin of hip	70988
3	B333400	Malignant neoplasm of skin of nose (external)	16202
3	B582100	Secondary malignant neoplasm of skin of face	100296
2	B766.11	Benign neoplasm of skin of arm	63295
3	B334100	Malignant neoplasm of skin of neck	43619
2	B766100	Benign neoplasm of skin of upper arm	53313
3	B336400	Malignant neoplasm of skin of finger	25245
2	B765500	Benign neoplasm of skin of groin	16637
3	B33..00	Other malignant neoplasm of skin	4632
3	B582.00	Secondary malignant neoplasm of skin	19945
3	B337600	Malignant neoplasm of skin of heel	104025
2	B767z00	Benign neoplasm of skin of hip or lower limb NOS	68998
2	B76..00	Benign neoplasm of skin	5329
3	ZV7660 0	[V]Screening for malignant neoplasm of skin	33259
2	B767200	Benign neoplasm of skin of knee	57302
3	B335100	Malignant neoplasm of skin of chest, excluding breast	37969
3	B582200	Secondary malignant neoplasm of skin of neck	35999
3	B333200	Malignant neoplasm of skin of eyebrow	55670
2	B766000	Benign neoplasm of skin of shoulder	19160

1	ZV10y14	[V]Personal history of malignant neoplasm of skin	47669
3	B582000	Secondary malignant neoplasm of skin of head	43930
3	B336500	Malignant neoplasm of skin of thumb	64406
2	B767300	Benign neoplasm of skin of lower leg	41802
3	B335.00	Malignant neoplasm of skin of trunk, excluding scrotum	57446
2	B765200	Benign neoplasm of skin of chest	24474
3	B332000	Malignant neoplasm of skin of auricle (ear)	33997
3	B33..14	Malignant neoplasm of sebaceous gland	37016
3	B33..15	Malignant neoplasm of sweat gland	40443
3	B331.00	Malignant neoplasm of eyelid including canthus	43087
3	B332.00	Malignant neoplasm skin of ear and external auricular canal	53515
3	B332z00	Malig neop skin of ear and external auricular canal NOS	62399
3	B333.00	Malignant neoplasm skin of other and unspecified parts face	27370
3	B333z00	Malignant neoplasm skin other and unspec part of face NOS	46008
3	B334.00	Malignant neoplasm of scalp and skin of neck	54234
3	B334000	Malignant neoplasm of scalp	37165
3	B334z00	Malignant neoplasm of scalp or skin of neck NOS	73760
3	B335900	Malignant neoplasm of perianal skin	23480
3	B33X.00	Malignant neoplasm overlapping lesion of skin	42429
3	B33y.00	Malignant neoplasm of other specified skin sites	18354
3	Byu4200	[X]Oth malignant neoplasm/skin of oth+unspecfd parts of face	57184
3	Byu5A00	[X]Malignant neoplasm overlapping lesion of skin	60162
3	B33..13	Rodent ulcer	1940

Myeloma

metadata	category	readcode	readterm	medcode
Name: myeloma_cprd	3	N330900	Osteoporosis in multiple myelomatosis	60433
Version: 1	3	B936.11	Myeloma - solitary	43312
Source: CPRD	3	B63z.00	Immunoproliferative neoplasm or myeloma NOS	43450
Author: C McKenna	3	B63..00	Multiple myeloma and immunoproliferative neoplasms	37182
Date: 19th October 2018	3	BBn2.11	[M]Monostotic myeloma	102164
Categories:	3	B630300	Lambda light chain myeloma	46042
1 = H/O	3	B630.00	Multiple myeloma	4944
2= Probable	3	BBn0.11	[M]Multiple myeloma	18744
3 = Definite	3	BBn0.12	[M]Myeloma NOS	3672
	3	BBn0.13	[M]Myelomatosis	53647
	3	BBn0.14	[M]Plasmacytic myeloma	39490
	3	BBn2.12	[M]Solitary myeloma	73135
	3	B630.12	Myelomatosis	15211
	3	4C53.00	Bone marrow: myeloma cells	52946
	3	BBn0.00	[M]Plasma cell myeloma	31671
	3	B630100	Solitary myeloma	19028

Neuroblastoma

metadata	category	readcode	readterm	medcode
Name: neuroblastoma_cprd	3	BBc1.00	[M]Neuroblastoma NOS	2123
Version: 1	3	BBcC.00	[M]Aesthesioneuroblastoma	51878
Source: CPRD	2	1J05.00	Suspected neuroblastoma	11297
Author: C McKenna	3	BBc0100	[M]Ganglioneuroblastoma	39121
Date: 19th October 2018	3	B546.00	Neuroblastoma	100083
Categories:	3	BBcC.11	[M]Olfactory neuroblastoma	39388
1 = H/O				
2= Probable				
3 = Definite				

Ovarian

metadata	category	readcode	readterm	medcode
Name: ovarian_cprd	3	B912.00	Neoplasm of uncertain behaviour of ovary	1918
Version: 1	3	B440.11	Cancer of ovary	1986
Source: CPRD	3	B440.00	Malignant neoplasm of ovary	7805
Author: C McKenna	2	B7A2.00	Benign teratoma of ovary	11937
Date: 19th October 2018	3	B833000	Carcinoma in situ of ovary	17137
Categories:	3	BB81.11	[M]Ovarian cystadenoma or carcinoma	17151
1 = H/O	3	BB81.12	[M]Ovarian mucinous tumour	18638
2= Probable	3	B44..00	Malignant neoplasm of ovary and other uterine adnexa	19141
3 = Definite	3	BBC0.12	[M]Ovarian stromal tumour	21435
	3	BB81.14	[M]Ovarian serous tumour	30541
	3	BB81.13	[M]Ovarian papillary tumour	39007
	3	BB81z00	[M]Ovarian cystic, mucinous or serous neoplasm NOS	40033
	3	B586.00	Secondary malignant neoplasm of ovary	44615
	3	D212000	Anaemia in ovarian carcinoma	48145
	1	ZV10414	[V]Personal history of malignant neoplasm of ovary	52141
	3	BB80200	[M]Borderline mucinous cystadenoma of the ovary	69978
	3	BBQA100	[M]Struma ovarii, malignant	71301
	3	BB81.00	Ovarian cystic, mucinous and serous neoplasms	260885
	3	BB81.11	Ovarian cystadenoma or carcinoma	297606
	3	BB81z00	Ovarian cystic, mucinous or serous neoplasm NOS	206336

Pancreas

metadata	category	readcode	readterm	medcode
Name: pancreas_cprd	3	B170.00	Malignant neoplasm of head of pancreas	8771
Version: 2	3	B171.00	Malignant neoplasm of body of pancreas	40810
Source: CPRD	3	B172.00	Malignant neoplasm of tail of pancreas	39870
Author: C McKenna/C Parisinos/ V Kuan	3	B173.00	Malignant neoplasm of pancreatic duct	35535

Date: 19th October 2018	3	B174.00	Malignant neoplasm of Islets of Langerhans	35795
Categories:	3	B175.00	Malignant neoplasm, overlapping lesion of pancreas	97875
1 = H/O	3	B17..00	Malignant neoplasm of pancreas	8166
2= Probable	3	B17y000	Malignant neoplasm of ectopic pancreatic tissue	96635
3 = Definite	3	B17y.00	Malignant neoplasm of other specified sites of pancreas	48537
	3	B17yz00	Malignant neoplasm of specified site of pancreas NOS	95783
	3	B17z.00	Malignant neoplasm of pancreas NOS	34388
	3	BB5B100	[M]Islet cell carcinoma	63102
	3	BB5B300	[M]Insulinoma, malignant	95609
	3	BB5B500	[M]Glucagonoma, malignant	32294
	3	BB5B600	[M]Mixed islet cell and exocrine adenocarcinoma	98825
	3	BB5C100	[M]Gastrinoma, malignant	49629

Prostate

metadata	category	readcode	readterm	medcode
Name: prostate_cprd	1	1427000	H/O: prostate cancer	102314
Version: 2	1	ZV10415	[V]Personal history of malignant neoplasm of prostate	37306
Source: CPRD	3	7B20000	Radical cystoprostatourethrectomy	9541
Author: C McKenna/C Parisinos/ V Kuan	3	7B20200	Radical cystoprostatectomy	10633
Date: 19th October 2018	3	7B36000	Radical prostatectomy - unspecified excision of pelvic nodes	4997
Categories:	3	7B36500	Radical prostatectomy without pelvic node excision	12593
1 = H/O	3	7B36600	Radical prostatectomy with pelvic node sampling	11492
2= Probable	3	7B36700	Radical prostatectomy with pelvic lymphadenectomy	9533
3 = Definite	3	4M00.00	Gleason prostate grade 2-4 (low)	18503
	3	4M01.00	Gleason prostate grade 5-7 (medium)	18612
	3	4M02.00	Gleason prostate grade 8-10 (high)	26081
	3	4M0..00	Gleason grading of prostate cancer	10178
	3	B46..00	Malignant neoplasm of prostate	780

Renal

metadata	category	readcode	readterm	medcode
Name: renal_cprd	3	B4A1.00	Malignant neoplasm of renal pelvis	12389
Version: 2	3	B4A1000	Malignant neoplasm of renal calyces	27540

		B4A1z0		
Source: CPRD	3	0	Malignant neoplasm of renal pelvis NOS	54184
Author: C McKenna/C Parisinos/		BB5a00		
V Kuan	3	0	[M]Renal cell carcinoma	10668
		B4A..1		
Date: 19th October 2018	3	1	Renal malignant neoplasm	18712
		B4A..0	Malig neop of kidney and other unspecified urinary	
Categories:	3	0	organs	13559
		B4A0.0		
1 = H/O	3	0	Malignant neoplasm of kidney parenchyma	1599
		B4A00		
2= Probable	3	00	Hypernephroma	7978
		B4A11		
3 = Definite	3	00	Malignant neoplasm of ureteropelvic junction	101608
		B91z10		
	3	0	Neoplasm of uncertain behaviour of kidney	18749
		B91z11		
	3	1	Renal neoplasm of uncertain behaviour	25940
		B91z30	Neoplasm of uncertain or unknown behaviour of	
	3	0	renal pelvis	43804
		BBLJ.0		
	3	0	[M]Clear cell sarcoma of kidney	18771
		BB5Y.0		
	3	0	[M]Hypernephroid tumour	27697
		BB5a.0		
	3	0	[M]Renal adenoma and carcinoma	8101
		BB5a01		
	3	1	[M]Grawitz tumour	52266
		BB5a01		
	3	2	[M]Hypernephroma	15419
		BB5az0		
	3	0	[M]Renal adenoma or carcinoma NOS	35467
		BBL7.0		
	3	0	[M]Mixed and stromal renal neoplasms	71161
		BBL7.1		
	3	1	[M]Nephromas and nephroblastomas	43703
		BBL70		
	3	00	[M]Mesoblastic nephroma	54594
		BBL71		
	3	00	[M]Nephroblastoma NOS	21681
		BBL71		
	3	12	[M]Wilms' tumour	17314
		BBL72		
	3	00	[M]Epithelial nephroblastoma	100371
		BBL73		
	3	00	[M]Mesenchymal nephroblastoma	105862
		B4A2.0		
	3	0	Malignant neoplasm of ureter	15223
		B4Ay0	Malignant neoplasm of overlapping lesion of	
	3	00	urinary organs	59286
		B4Az.0	Malignant neoplasm of kidney or urinary organs	
	3	0	NOS	29462

Rentinoblastoma

metadata	category	readcode	readterm	medcode
Name: retinoblastoma_cprd	3	BBc9.00	[M]Retinoblastomas	28836
Version: 1	3	BBc9100	[M]Retinoblastoma, undifferentiated type	103883
Source: CPRD	3	BBc9z00	[M]Retinoblastoma NOS	48952
Author: C McKenna	3	B505.00	Malignant neoplasm of retina	28069
Date: 19th October 2018				

Categories:

1 = H/O

2= Probable

3 = Definite

Testicular

metadata	category	readcode	readterm	medcode
Name: testicular_cprd	2	1J0C.00	Suspected testicular cancer	26878
Version: 1	3	B47..00	Malignant neoplasm of testis	15148
Source: CPRD	3	B470.00	Malignant neoplasm of undescended testis	64602
Author: C McKenna	3	B470200	Seminoma of undescended testis	7740
Date: 19th October 2018	3	B470300	Teratoma of undescended testis	36325
Categories:	3	B470z00	Malignant neoplasm of undescended testis NOS	96429
1 = H/O	3	B471.00	Malignant neoplasm of descended testis	19475
2= Probable	3	B471000	Seminoma of descended testis	21786
3 = Definite	3	B471100	Teratoma of descended testis	9476
	3	B471z00	Malignant neoplasm of descended testis NOS	91509
	3	B47z.00	Malignant neoplasm of testis NOS	38510
	3	B47z.11	Seminoma of testis	2961
	3	B47z.12	Teratoma of testis	15989
	3	B58y600	Secondary malignant neoplasm of testis	34145
	3	B836000	Carcinoma in situ of testis	8177
	3	B914.00	Neoplasm of uncertain behaviour of testis	29479
	3	BBC0.13	[M]Testicular stromal tumour	21319
	3	BBC9.14	[M]Testicular adenoma	40954
	1	ZV10416	[V]Personal history of malignant neoplasm of testis	48808

Thyroid/ Parathyroid

metadata	category	readcode	readterm	medcode
Name: thyroidParathy_cprd	1	ZV10y15	[V]Personal history of malignant neoplasm of thyroid	35771
Version: 1	3	B213300	Malignant neoplasm of thyroid cartilage	47862
Source: CPRD	3	B53..00	Malignant neoplasm of thyroid gland	5637
Author: C McKenna	3	B541.00	Malignant neoplasm of parathyroid gland	4218
Date: 19th October 2018	3	BB5c.00	[M]Parathyroid adenomas and adenocarcinomas	4217
Categories:	3	BB5cz00	[M]Parathyroid adenoma or adenocarcinoma NOS	42169
1 = H/O	3	BB5f.00	[M]Thyroid adenoma and adenocarcinoma	19263
2= Probable	3	BB5fz00	[M]Thyroid adenoma or adenocarcinoma NOS	38685
3 = Definite	3	ByuB.00	[X]Malignant neoplasm of thyroid and other endocrine glands	40608
	3	5A12.00	Thyroid tumour/metast irradiat	67248
	3	B924000	Neoplasm of uncertain behaviour of thyroid gland	17415

3	B906000	Neoplasm of uncertain behaviour of thyroid cartilage	72959
3	B8yy000	Carcinoma in situ of thyroid gland	8958
3	B8yy200	Carcinoma in situ of parathyroid gland	58016
3	B7G..11	Adenoma of thyroid gland	2610
3	B924100	Neoplasm of uncertain behaviour of parathyroid gland	46892
3	B810000	Carcinoma in situ of thyroid cartilage	35772
3	BB5f100	M]Follicular adenocarcinoma NOS""	21741
3	BB5f111	[M]Follicular carcinoma""	21847
3	BB5f200	M]Follicular adenocarcinoma well differentiated type""	59918
3	BB5f300	M]Follicular adenocarcinoma trabecular type""	61467
3	BB5f600	[M]Papillary and follicular adenocarcinoma""	46761
3	BB5f700	[M]Nonencapsulated sclerosing carcinoma""	68757
3	BB19.00	M]Carcinoma anaplastic type NOS	12609
3	BB5W111	[M]Hurthle cell adenocarcinoma""	29008

Uterus

metadata	category	readcode	readterm	medcode
Name: uterus_cprd	1	ZV10417	[V]Personal history of malignant neoplasm of uterine body	46779
Version: 1	3	B40..00	Malignant neoplasm of uterus, part unspecified	2744
Source: CPRD	3	B43..00	Malignant neoplasm of body of uterus	7046
Author: C McKenna	3	B430.00	Malignant neoplasm of corpus uteri, excluding isthmus	3213
Date: 19th October 2018	3	B430000	Malignant neoplasm of cornu of corpus uteri	72723
Categories:	3	B430100	Malignant neoplasm of fundus of corpus uteri	68155
1 = H/O	3	B430200	Malignant neoplasm of endometrium of corpus uteri	2890
2= Probable	3	B430300	Malignant neoplasm of myometrium of corpus uteri	45793
3 = Definite	3	B430z00	Malignant neoplasm of corpus uteri NOS	45490
	3	B431.00	Malignant neoplasm of isthmus of uterine body	43940
	3	B431000	Malignant neoplasm of lower uterine segment	59097
	3	B431z00	Malignant neoplasm of isthmus of uterine body NOS	70729
	3	B432.00	Malignant neoplasm of overlapping lesion of corpus uteri	16967
	3	B43y.00	Malignant neoplasm of other site of uterine body	31608
	3	B43z.00	Malignant neoplasm of body of uterus NOS	33617
	3	B44..00	Malignant neoplasm of ovary and other uterine adnexa	19141
	3	B44y.00	Malignant neoplasm of other site of uterine adnexa	97996
	3	B44z.00	Malignant neoplasm of uterine adnexa NOS	65106
	3	Byu7000	[X]Malignant neoplasm of uterine adnexa, unspecified	64497
	3	B58y100	Secondary malignant neoplasm of uterus	55090

	3	B430211	Malignant neoplasm of endometrium	49400

Wilm's

metadata	category	readcode	readterm	medcode
Name: Wilms_cprd	3	BBL7112	[M]Wilms' tumour	17314
Version: 1	3	K01w112	Wilms' tumour + nephrotic syndrome + pseudohermaphroditism	108922
Source: CPRD	3	BBL7300	[M]Mesenchymal nephroblastoma	105862
Author: C McKenna	3	BBL7200	[M]Epithelial nephroblastoma	100371
Date: 19th October 2018	3	BBL7.11	[M]Nephromas and nephroblastomas	43703
Categories:	3	BBL7100	[M]Nephroblastoma NOS	21681
1 = H/O				
2= Probable				
3 = Definite				

CANCER CODE LISTS, ICD-10 CODES

Bladder

metadata	icd_term	icd_code	Category
Name: bladder_HES	Malignant neoplasm of bladder	C67	3
Version: 1	Overlapping lesion of urinary organs	C68.8	3
Source: HES	Urinary organ, unspecified	C68.9	3
Author: C McKenna	Carcinoma in situ of other and unspecified sites: bladder	D09.0	3
Date: 19th October 2018	Neoplasm of uncertain or unknown behaviour of brain and central nervous system: bladder	D41.4	3
Categories:	Benign neoplasm of urinary organs: bladder	D30.3	2
1 = H/O			
2= Probable			
3 = Definite			

Bone

metadata	icd_term	icd_code	Category
Name:bone_HES	Malignant neoplasm of bone and articular cartilage of limbs	C40	3
Version: 1	Malignant neoplasm of bone and articular cartilage of other and unspecified sites	C41	3
Source: HES	Neoplasm of uncertain or unknown behaviour of other and unspecified sites: bone and cartilage	D48.0	3

Author: C McKenna
Date: 19th October 2018
Categories:
1 = H/O
2= Probable
3 = Definite

Brain/ CNS

metadata	icd_term	icd_code	Category
Name:brainCNS_HES	Malignant neoplasm of meninges	C70	3
Version: 1	Malignant neoplasm of brain	C71	3
Source: HES	Malignant neoplasm of spinal cord, cranial nerves and other parts of central nervous system	C72	3
Author: C McKenna	Neoplasm of uncertain or unknown behaviour of brain and central nervous system	D43	3
Date: 19th October 2018	Benign neoplasm of brain and other parts of central nervous system	D33	2
Categories:	Benign neoplasm of meninges	D32	2
1 = H/O	Secondary malignant neoplasm of brain and cerebral meninges	C79.3	3
2= Probable	Peripheral nerves and autonomic nervous system: peripheral nerves and autonomic nervous system	D36.1	3
3 = Definite			

Breast

metadata	icd_term	icd_code	Category
Name:breast_HES	Malignant neoplasm of breast	C50	3
Version: 2	Carcinoma in situ of breast	D05	3
Source: HES	Benign neoplasm of breast	D24	2
Author: C McKenna/C Parisinos/ V Kuan			
Date: 19th October 2018			
Categories:			
1 = H/O			
2= Probable			
3 = Definite			

Cervix

metadata	icd_term	icd_code	Category
Name:cervix_HES	Malignant neoplasm of cervix uteri	C53	3
Version: 1	Carcinoma in situ of cervix uteri	D06	3
Source: HES	Dysplasia of cervix uteri	N87	3
Author: C McKenna			
Date: 19th October 2018			

Categories:

1 = H/O

2= Probable

3 = Definite

Colorectal

metadata	icd_term	icd_code	Category
Name:colorectal_HES	Malignant neoplasm of colon	C18	3
Version: 2	Malignant neoplasm of rectosigmoid junction	C19	3
Source: HES	Malignant neoplasm of rectum	C20	3
Author: C McKenna/C Parisinos/ V Kuan	Malignant neoplasm of anus and anal canal	C21	3
Date: 19th October 2018	Benign neoplasm of colon, rectum, anus and anal canal	D12	2

Categories:

1 = H/O

2= Probable

3 = Definite

Hepatobiliary

metadata	icd_term	icd_code	Category
Name:liverbiliary_HES	Liver cell carcinoma	C22.0	3
Version: 2	Hepatoblastoma	C22.2	3
Source: HES	Angiosarcoma of liver	C22.3	3
Author: C McKenna/C Parisinos/ V Kuan	Other sarcomas of liver	C22.4	3
Date: 19th October 2018	Other specified carcinomas of liver	C22.7	3
Categories:	Liver unspecified	C22.9	3
1 = H/O	Malignant neoplasm of gallbladder	C23	3
2= Probable	Malignant neoplasm of other and unspecified parts of biliary tract	C24	3
3 = Definite	Intrahepatic bile duct carcinoma	C22.1	3
	Neoplasm of uncertain or unknown behaviour of oral cavity and digestive organs: Liver, gallbladder and bile ducts	D37.6	3
	Carcinoma in situ of other and unspecified digestive organs: Liver, gallbladder and bile ducts	D01.5	3
	Benign neoplasm of other and ill-defined parts of digestive system: liver	D13.4	2
	Benign neoplasm of other and ill-defined parts of digestive system: liver Extrahepatic bile ducts	D13.5	2

Gastroesophageal

metadata	icd_term	icd_code	Category
Name: gastricoesoph_HES	Malignant neoplasm of stomach	C16	3
Version: 2	Malignant neoplasm of oesophagus	C15	3
Source: HES	Carcinoma in situ of oral cavity, oesophagus and stomach: oesophagus	D00.1	3
Author: C McKenna/C Parisinos/ V Kuan	Carcinoma in situ of oral cavity, oesophagus and stomach: stomach	D00.2	3
Date: 19th October 2018	Benign neoplasm of other and ill-defined parts of digestive system: oesophagus	D13.0	2
Categories:	Benign neoplasm of other and ill-defined parts of digestive system: stomach	D13.1	2
1 = H/O			
2= Probable			
3 = Definite			

Leukaemia

metadata	icd_term	icd_code	Category
Name: leukaemia_HES	Plasma cell leukaemia	C90.1	3
Version: 1	Lymphoid leukaemia	C91	3
Source: HES	Myeloid leukaemia	C92	3
Author: C McKenna	Monocytic leukaemia	C93	3
Date: 19th October 2018	Other leukaemias of specified cell type	C94	3
Categories:	Leukemia of unspecified cell typE	C95	3
1 = H/O	Chronic eosinophilic leukaemia [hypereosinophilic syndrome]	D47.5	3
2= Probable			
3 = Definite			

Lung

metadata	icd_term	icd_code	Category
Name: lung_HES	Malignant neoplasm of the bronchus and lung	C34	3
Version: 2	Carcinoma in situ of middle ear and respiratory system	D02	3
Source: HES	Benign neoplasm of middle ear and respiratory system: lung	D14.3	2
Author: C McKenna/C Parisinos/ V Kuan			
Date: 19th October 2018			
Categories:			
1 = H/O			
2= Probable			
3 = Definite			

Lymphoma

Source: HES	Non-follicular lymphoma	C83	3
Author: C McKenna	Mature T/NK-cell lymphomas	C84	3
Date: 19th October 2018	Other and unspecified types of non-Hodgkin lymphoma	C85	3
Categories:	Other specified types of T/NK-cell lymphoma	C86	3
1 = H/O	Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue [MALT-lymphoma]	C88.4	3
2= Probable	Adult T-cell lymphoma/leukaemia (HTLV-1-associated)	C91.5	3
3 = Definite	Malignant neoplasm of lymphoid, haematopoietic and related tissue, unspecified	C96.9	3

Melanoma

metadata	icd_term	icd_code	Category
Name: melanoma_HES	Melanoma	C43	3
Version: 2	Melanoma in situ	D03	3
Source: HES			
Author: C McKenna/C Parisinos/ V Kuan			
Date: 19th October 2018			
Categories:			
1 = H/O			
2= Probable			
3 = Definite			

Non-melanoma, skin

metadata	icd_term	icd_code	Category
Name: nonmelskin_HES	Other malignant neoplasms of skin	C44	3
Version: 1	Carcinoma in situ of skin	D04	3
Source: HES			
Author: C McKenna			
Date: 19th October 2018			
Categories:			
1 = H/O			
2= Probable			
3 = Definite			

Myeloma

metadata	icd_term	icd_code	Category
Name: myeloma_HES	Multiple myeloma	C900	3
Version: 1			
Source: HES			
Author: C McKenna			
Date: 19th October 2018			
Categories:			

1 = H/O

2= Probable

3 = Definite

Neuroblastoma

metadata	icd_term	icd_code	Category
Name: neuroblastoma_HES	Adrenal gland, unspecified	C74.9	3
Version: 1			
Source: HES			
Author: C McKenna			
Date: 19th October 2018			
Categories:			
1 = H/O			
2= Probable			
3 = Definite			

Ovarian

metadata	icd_term	icd_code	Category
Name: ovarian_HES	Malignant neoplasm of ovary	C56	3
Version: 1	Overlapping lesion of female genital organs	C57.8	3
Source: HES	Benign neoplasm of ovary	D27	2
Author: C McKenna			
Date: 19th October 2018			
Categories:			
1 = H/O			
2= Probable			
3 = Definite			

Pancreas

metadata	icd_term	icd_code	Category
Name: pancreas_HES	Malignant neoplasm of pancreas	C25	3
Version: 2	Benign neoplasm of other and ill-defined parts of digestive system: pancreas	D13.6	2
Source: HES			
Author: C McKenna/C Parisinos/ V Kuan			
Date: 19th October 2018			
Categories:			
1 = H/O			
2= Probable			
3 = Definite			

Prostate

metadata	icd_term	icd_code	Category
Name: prostate_HES	Malignant neoplasm of the prostate	C61	3
Version: 2	Carcinoma in situ of other and unspecified genital organs: prostate	D07.5	3
Source: HES	Benign neoplasm of male genital organs: prostate	D29.1	2
Author: C McKenna/C Parisinos/ V Kuan			
Date: 19th October 2018			
Categories:			
1 = H/O			
2= Probable			
3 = Definite			

Renal

metadata	icd_term	icd_code	Category
Name: renal_HES	Malignant neoplasm of renal pelvis	C65	3
Version: 2	Malignant neoplasm of kidney, except renal pelvis	C64	3
Source: HES	Benign neoplasm of urinary organs: kidney	D30.0	2
Author: C McKenna/C Parisinos/ V Kuan	Benign neoplasm of urinary organs: renal pelvis	D30.1	2
Date: 19th October 2018			
Categories:			
1 = H/O			
2= Probable			
3 = Definite			

Rentinoblastoma

metadata	icd_term	icd_code	Category
Name: retinoblastoma_HES	Malignant neoplasm of eye and adnexa: retina	C69.2	3
Version: 1			
Source: HES			
Author: C McKenna			
Date: 19th October 2018			
Categories:			
1 = H/O			
2= Probable			
3 = Definite			

Testicular

metadata	icd_term	icd_code	Category
Name: testicular_HES	Neoplasm of uncertain or unknown behaviour of male genital organs: testis	D40.1	3

Version: 1	Malignant neoplasm of testis	C62	3
Source: HES	Benign neoplasm of male genital organs: testicles	D29.2	2
Author: C McKenna Date: 19th October 2018	Other male genital organs: seminal vesicle, spermatic cord, tunica vaginalis	D29.7	3
Categories:			
1 = H/O			
2= Probable			
3 = Definite			

Thyroid/ Parathyroid

metadata	icd_term	icd_code	Category
Name: thyroidParathyroid_HES	Malignant neoplasm of thyroid gland	C73	3
Version: 1	Neoplasm of uncertain or unknown behaviour of endocrine glands: THYROID	D44.0	3
Source: HES	Carcinoma in situ of other and unspecified sites: THYROID	D09.3	3
Author: C McKenna	Neoplasm of uncertain or unknown behaviour of endocrine glands: PARATHYROID	D44.2	3
Date: 19th October 2018	Malignant neoplasm of other endocrine glands and related structures: Parathyroid gland	C75.0	3
Categories:	Carcinoma in situ of other and unspecified sites: thyroid	D09.3	3
1 = H/O	Benign neoplasm of thyroid gland	D34	2
2= Probable	Benign neoplasm of other and unspecified endocrine glands	D35.1	2
3 = Definite			

Uterus

metadata	icd_term	icd_code	Category
Name: Uterus_HES	Malignant neoplasm of corpus uteri	C54	3
Version: 1	Malignant neoplasm of uterus, part unspecified	C55	3
Source: HES	Leiomyoma of uterus	D25	3
Author: C McKenna	Other benign neoplasms of uterus	D26	2
Date: 19th October 2018			
Categories:			
1 = H/O			
2= Probable			
3 = Definite			

Wilm's

metadata	icd_term	icd_code	Category
Name: Wilms_HES	Malignant neoplasm of kidney, except renal pelvis	C64	3

Version: 1
Source: HES
Author: C McKenna
Date: 19th October 2018
Categories:
1 = H/O
2= Probable
3 = Definite

DEVELOPMENT OF CANCER CODE LISTS, READ CODES

Bladder

FINAL	18
Code browser	18
Peer reviewed publications	0
Caliber portal	19
Duplicates	18
Inappropriate	1
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, infiltrating, malignancy of bladder, urinary organs

Bone

FINAL	24
Code browser	55
Peer reviewed publications	0
Caliber portal	64
Duplicates	55
Inappropriate	40
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, infiltrating, malignancy of bone, osteosarcoma, osteoma, sarcoma, chondrosarcoma, chordoma

Brain/ CNS

FINAL	29
Code browser	29
Peer reviewed publications	60
Caliber portal	33

Duplicates	62
Inappropriate	31
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, infiltrating, malignancy of brain, cerebrum, basal ganglia, globus pallidus, thalamus, lobe, ventricles, choroid plexus, brain strem, medulla, midbrain, corpus callosum, meninges, cranial nerves, central nervous system

Bannon, F. J., et al. "Non-steroidal anti-inflammatory drug use and brain tumour risk: a case–control study within the Clinical Practice Research Datalink." Cancer Causes & Control 24.11 (2013): 2027-2034.

Breast

FINAL	45
Code browser	72
Peer reviewed publications	60
Caliber portal	43
Duplicates	103
Inappropriate	27
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, infiltrating, malignancy of breast, paget's, ductal, nipple, areola

Peeters, Paul JHL, et al. "Insulin glargine use and breast cancer risk: associations with cumulative exposure." Acta Oncologica 55.7 (2016): 851-858.
Meier, Christoph R., Stephen Schmitz, and Hershel Jick. "Association between acetaminophen or nonsteroidal antiinflammatory drugs and risk of developing ovarian, breast, or colon cancer." Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy 22.3 (2002): 303-309.
Parisinos, Constantinos et al. 2019 (Unpublished)

Cervix

FINAL	26
Code browser	26
Peer reviewed publications	20
Caliber portal	12
Duplicates	32
Inappropriate	0
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, infiltrating, malignancy, dysplasia of cervix, cervical

Walker, S., and W. Hamilton. "Risk of cervical cancer in symptomatic women aged≥ 40 in primary care: A case–control study using electronic records." European journal of cancer care 26.3 (2017): e12706.

Colorectal

FINAL	32

Code browser	33
Peer reviewed publications	32
Caliber portal	33
Duplicates	65
Inappropriate	1
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, infiltrating, malignancy of bowel, colon, intestine, anus, anal, rectum, rectal, appendix, caecum, sigmoid.

Parisinos, Constantinos et al. 2019 (Unpublished)
Birks, J., Bankhead, C., Holt, T. A., Fuller, A., & Patnick, J. (2017). Evaluation of a prediction model for colorectal cancer: retrospective analysis of 2.5 million patient records. Cancer medicine, 6(10), 2453-2460.
Meier, Christoph R., Stephen Schmitz, and Hershel Jick. "Association between acetaminophen or nonsteroidal antiinflammatory drugs and risk of developing ovarian, breast, or colon cancer." Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy 22.3 (2002): 303-309.

Hepatobiliary

FINAL	32

Code browser	55
Peer reviewed publications	30
Caliber portal	28
Duplicates	58
Inappropriate	23
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, infiltrating, malignancy of liver, bile duct, ampulla of vater, biliary, hepatoma, hepatocellular, gallbladder, cholangiocarcinoma

Parisinos, Constantinos et al. 2019 (Unpublished)
McGlynn, Katherine A., et al. "Menopausal hormone therapy use and risk of primary liver cancer in the clinical practice research datalink." International journal of cancer 138.9 (2016): 2146-2153.

Gastroesophageal

FINAL	44

Code browser	50
Peer reviewed publications	42
Caliber portal	36
Duplicates	78
Inappropriate	6
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, infiltrating, malignancy of oesophag, stomach, gastric

Parisinos, Constantinos et al. 2019 (Unpublished)

Krishnamoorthi, Rajesh, et al. "Rates and predictors of progression to esophageal carcinoma in a large population-based Barrett's esophagus cohort." Gastrointestinal endoscopy 84.1 (2016): 40-46.
Busby, John, et al. "The effect of medications which cause inflammation of the gastro-oesophageal tract on cancer risk: a nested case–control study of routine Scottish data." International journal of cancer 140.8 (2017): 1828-1835.

Leukaemia

FINAL	123
Code browser	125
Peer reviewed publications	0
Caliber portal	95
Duplicates	95
Inappropriate	2
Search terms	Leukaemia

Lung

FINAL	44
Code browser	90
Peer reviewed publications	80
Caliber portal	53
Duplicates	133
Inappropriate	46
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, infiltrating, malignancy of lung, respiratory, pulmonary, bronchus, trachea, alevolar, bronchio, pneomoblastoma, mesothelioma

Walker, A. J., Baldwin, D. R., Card, T. R., Powell, H. A., Hubbard, R. B., & Grainge, M. J. (2016). Risk of venous thromboembolism in people with lung cancer: a cohort study using linked UK healthcare data. British journal of cancer, 115(1), 115.

Parisinos, Constantinos et al. 2019 (Unpublished)

Lymphoma

FINAL	178
Code browser	150
Peer reviewed publications	75
Caliber portal	233
Duplicates	225
Inappropriate	55
Search terms	Lymphoma, lymphoproliferative, lymphoid, lymphoblastic, Burkitt, Hodgkin, lymphomatoid, lymphatic, lymphosarcoma

Gelfand, Joel M., et al. "The risk of lymphoma in patients with psoriasis." Journal of investigative dermatology 126.10 (2006): 2194-2201.

Melanoma

FINAL	89
Code browser	89
Peer reviewed publications	86
Caliber portal	53
Duplicates	139
Inappropriate	0
Search terms	Melanoma

Parisinos, Constantinos et al. 2019 (Unpublished)

Non-melanoma, skin

FINAL	157
Code browser	158
Peer reviewed publications	79
Caliber portal	79
Duplicates	158
Inappropriate	1
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, malignancy of skin, scalp, basal cell, squamous cell, rodent ulcer

Reinau, D., Surber, C., Jick, S. S., & Meier, C. R. (2015). Nonsteroidal anti-inflammatory drugs and the risk of nonmelanoma skin cancer. International journal of cancer, 137(1), 144-153.

Myeloma

FINAL	16
Code browser	17
Peer reviewed publications	0
Caliber portal	14
Duplicates	14
Inappropriate	1
Search terms	Myeloma, myelomatosis

Neuroblastoma

FINAL	6
Code browser	6

Peer reviewed publications	0
Caliber portal	2
Duplicates	2
Inappropriate	0
Search terms	Neuroblastoma

Ovarian

FINAL	20
Code browser	184
Peer reviewed publications	50
Caliber portal	7
Duplicates	57
Inappropriate	164
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, infiltrating, malignancy of ovary, ovarii, ovarian, mucinous, serous

Bodmer, Michael, et al. "Use of metformin and the risk of ovarian cancer: a case–control analysis." Gynecologic oncology 123.2 (2011): 200-204.
Meier, Christoph R., Stephen Schmitz, and Hershel Jick. "Association between acetaminophen or nonsteroidal antiinflammatory drugs and risk of developing ovarian, breast, or colon cancer." Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy 22.3 (2002): 303-309.

Pancreas

FINAL	16
Code browser	32
Peer reviewed publications	16
Caliber portal	11
Duplicates	27
Inappropriate	16
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, infiltrating, malignancy of pancreas, pancreatic, islet, gastrinoma

Parisinos, Constantinos et al. 2019 (Unpublished)

Prostate

FINAL	13
Code browser	13
Peer reviewed publications	13
Caliber portal	7

Duplicates	20
Inappropriate	0
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, infiltrating, malignancy of prostate

Parisinos, Constantinos et al. 2019 (Unpublished)

Renal

FINAL	28
Code browser	23
Peer reviewed publications	5
Caliber portal	15
Duplicates	15
Inappropriate	0
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, infiltrating, malignancy of kidney, renal, ureter, nephroma, nephroblastoma

Parisinos, Constantinos et al. 2019 (Unpublished)

Rentinoblastoma

FINAL	4
Code browser	4
Peer reviewed publications	0
Caliber portal	2
Duplicates	2
Inappropriate	0
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, infiltrating, malignancy of retina, retinoblastoma

Testicular

FINAL	19
Code browser	146
Peer reviewed publications	0
Caliber portal	32
Duplicates	32
Inappropriate	127
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, infiltrating, malignancy of testi

Thyroid/ Parathyroid

FINAL	25
Code browser	30
Peer reviewed publications	20
Caliber portal	16
Duplicates	36
Inappropriate	5
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, infiltrating, malignancy of thyroid, parathyroid, papillary, follicular

Becker, Claudia, et al. "No evidence for a decreased risk of thyroid cancer in association with use of metformin or other antidiabetic drugs: a case-control study." BMC cancer 15.1 (2015): 719.

Uterus

FINAL	21
Code browser	28
Peer reviewed publications	0
Caliber portal	28
Duplicates	0
Inappropriate	7
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, infiltrating, malignancy of uterus, uteri, uterine

Wilm's

FINAL	6
Code browser	6
Peer reviewed publications	0
Caliber portal	0
Duplicates	0
Inappropriate	0
Search terms	Wilm, nephroblastoma

DEVELOPMENT OF CANCER CODE LISTS, ICD-10

Bladder

FINAL	6
Code browser	6

Peer reviewed publications	1
Caliber portal	1
Duplicates	2
Inappropriate	0
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, infiltrating, malignancy of bladder, urinary organs

Hasle, H., Friedman, J. M., Olsen, J. H., & Rasmussen, S. A. (2016). Low risk of solid tumors in persons with Down syndrome. Genetics in Medicine, 18(11), 1151.

Bone

FINAL	3
Code browser	3
Peer reviewed publications	2
Caliber portal	2
Duplicates	4
Inappropriate	0
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, infiltrating, malignancy of bone, osteosarcoma, osteoma, sarcoma, chondrosarcoma, chordoma

Hasle, H., Friedman, J. M., Olsen, J. H., & Rasmussen, S. A. (2016). Low risk of solid tumors in persons with Down syndrome. Genetics in Medicine, 18(11), 1151.

Brain/ CNS

FINAL	8
Code browser	8
Peer reviewed publications	6
Caliber portal	3
Duplicates	9
Inappropriate	0
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, infiltrating, malignancy of brain, cerebrum, basal ganglia, globus pallidus, thalamus, lobe, ventricles, choroid plexus, brain strem, medulla, midbrain, corpus callosum, meninges, cranial nerves, central nervous system

Hasle, H., Friedman, J. M., Olsen, J. H., & Rasmussen, S. A. (2016). Low risk of solid tumors in persons with Down syndrome. Genetics in Medicine, 18(11), 1151.

Breast

FINAL	3
Code browser	3
Peer reviewed publications	2
Caliber portal	1
Duplicates	3
Inappropriate	0
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, infiltrating, malignancy of breast, paget's, ductal, nipple, areola

Hasle, H., Friedman, J. M., Olsen, J. H., & Rasmussen, S. A. (2016). Low risk of solid tumors in persons with Down syndrome. Genetics in Medicine, 18(11), 1151.

Parisinos, Constantinos et al. 2019 (Unpublished)

Cervix

FINAL	3
Code browser	3
Peer reviewed publications	1
Caliber portal	1
Duplicates	2
Inappropriate	0
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, infiltrating, malignancy, dysplasia of cervix, cervical

Hasle, H., Friedman, J. M., Olsen, J. H., & Rasmussen, S. A. (2016). Low risk of solid tumors in persons with Down syndrome. Genetics in Medicine, 18(11), 1151.

Colorectal

FINAL	5
Code browser	5
Peer reviewed publications	8
Caliber portal	5
Duplicates	13
Inappropriate	0
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, infiltrating, malignancy of bowel, colon, intestine, anus, anal, rectum, rectal, appendix, caecum, sigmoid.

Hasle, H., Friedman, J. M., Olsen, J. H., & Rasmussen, S. A. (2016). Low risk of solid tumors in persons with Down syndrome. Genetics in Medicine, 18(11), 1151.

Parisinos, Constantinos et al. 2019 (Unpublished)

Hepatobiliary

FINAL	13
Code browser	13
Peer reviewed publications	12
Caliber portal	3
Duplicates	15
Inappropriate	0
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, infiltrating, malignancy of liver, bile duct, ampulla of vater, biliary, hepatoma, hepatocellular, gallbladder, cholangiocarcinoma

Hasle, H., Friedman, J. M., Olsen, J. H., & Rasmussen, S. A. (2016). Low risk of solid tumors in persons with Down syndrome. Genetics in Medicine, 18(11), 1151.

Parisinos, Constantinos et al. 2019 (Unpublished)

Gastroesophageal

FINAL	6
Code browser	6
Peer reviewed publications	4
Caliber portal	2
Duplicates	6
Inappropriate	0
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, infiltrating, malignancy of oesophag, stomach, gastric

Hasle, H., Friedman, J. M., Olsen, J. H., & Rasmussen, S. A. (2016). Low risk of solid tumors in persons with Down syndrome. Genetics in Medicine, 18(11), 1151.

Parisinos, Constantinos et al. 2019 (Unpublished)

Leukaemia

FINAL	7
Code browser	7
Peer reviewed publications	6
Caliber portal	16
Duplicates	13
Inappropriate	9
Search terms	Leukaemia

Hasle, H., Friedman, J. M., Olsen, J. H., & Rasmussen, S. A. (2016). Low risk of solid tumors in persons with Down syndrome. Genetics in Medicine, 18(11), 1151.

Cardwell, C. R., et al. "Infections in early life and childhood leukaemia risk: a UK case–control study of general practitioner records." British journal of cancer 99.9 (2008): 1529.

Lung

FINAL	3
Code browser	3
Peer reviewed publications	4
Caliber portal	2
Duplicates	6
Inappropriate	0
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, infiltrating, malignancy of lung, respiratory, pulmonary, bronchus, trachea, alevolar, bronchio, pneomoblastoma, mesothelioma

Hasle, H., Friedman, J. M., Olsen, J. H., & Rasmussen, S. A. (2016). Low risk of solid tumors in persons with Down syndrome. Genetics in Medicine, 18(11), 1151.

Parisinos, Constantinos et al. 2019 (Unpublished)

Lymphoma

FINAL	9
Code browser	9
Peer reviewed publications	6
Caliber portal	11
Duplicates	15
Inappropriate	2
Search terms	Lymphoma, lymphoproliferative, lymphoid, lymphoblastic, Burkitt, Hodgkin, lymphomatoid, lymphatic, lymphosarcoma

Hasle, H., Friedman, J. M., Olsen, J. H., & Rasmussen, S. A. (2016). Low risk of solid tumors in persons with Down syndrome. Genetics in Medicine, 18(11), 1151.

Melanoma

FINAL	2
Code browser	2
Peer reviewed publications	2
Caliber portal	2
Duplicates	4
Inappropriate	0
Search terms	Melanoma

Hasle, H., Friedman, J. M., Olsen, J. H., & Rasmussen, S. A. (2016). Low risk of solid tumors in persons with Down syndrome. Genetics in Medicine, 18(11), 1151.

Parisinos, Constantinos et al. 2019 (Unpublished)

Non-melanoma, skin

FINAL	2
Code browser	2
Peer reviewed publications	1
Caliber portal	1
Duplicates	2
Inappropriate	0
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, malignancy of skin, scalp, basal cell, squamous cell, rodent ulcer

Hasle, H., Friedman, J. M., Olsen, J. H., & Rasmussen, S. A. (2016). Low risk of solid tumors in persons with Down syndrome. Genetics in Medicine, 18(11), 1151.

Myeloma

FINAL	1
Code browser	1
Peer reviewed publications	2
Caliber portal	1
Duplicates	2
Inappropriate	1
Search terms	Myeloma, myelomatosis

Hasle, H., Friedman, J. M., Olsen, J. H., & Rasmussen, S. A. (2016). Low risk of solid tumors in persons with Down syndrome. Genetics in Medicine, 18(11), 1151.

Neuroblastoma

FINAL	1
Code browser	1
Peer reviewed publications	0
Caliber portal	0
Duplicates	0
Inappropriate	0
Search terms	Neuroblastoma

Ovarian

FINAL	3
Code browser	3
Peer reviewed publications	2
Caliber portal	1
Duplicates	3

Inappropriate	0
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, infiltrating, malignancy of ovary

Hasle, H., Friedman, J. M., Olsen, J. H., & Rasmussen, S. A. (2016). Low risk of solid tumors in persons with Down syndrome. Genetics in Medicine, 18(11), 1151.

Pancreas

FINAL	2
Code browser	2
Peer reviewed publications	2
Caliber portal	1
Duplicates	3
Inappropriate	0
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, infiltrating, malignancy of pancreas, pancreatic, islet, gastrinoma

Hasle, H., Friedman, J. M., Olsen, J. H., & Rasmussen, S. A. (2016). Low risk of solid tumors in persons with Down syndrome. Genetics in Medicine, 18(11), 1151.

Parisinos, Constantinos et al. 2019 (Unpublished)

Prostate

FINAL	3
Code browser	3
Peer reviewed publications	2
Caliber portal	1
Duplicates	3
Inappropriate	0
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, infiltrating, malignancy of prostate

Hasle, H., Friedman, J. M., Olsen, J. H., & Rasmussen, S. A. (2016). Low risk of solid tumors in persons with Down syndrome. Genetics in Medicine, 18(11), 1151.

Parisinos, Constantinos et al. 2019 (Unpublished)

Renal

FINAL	4
Code browser	4
Peer reviewed publications	5
Caliber portal	3
Duplicates	7

Inappropriate	1
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, infiltrating, malignancy of kidney, renal, ureter, nephroma, nephroblastoma

Hasle, H., Friedman, J. M., Olsen, J. H., & Rasmussen, S. A. (2016). Low risk of solid tumors in persons with Down syndrome. Genetics in Medicine, 18(11), 1151.

Parisinos, Constantinos et al. 2019 (Unpublished)

Rentinoblastoma

FINAL	1
Code browser	1
Peer reviewed publications	0
Caliber portal	0
Duplicates	0
Inappropriate	0
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, infiltrating, malignancy of retina, retinoblastoma

Testicular

FINAL	4
Code browser	4
Peer reviewed publications	1
Caliber portal	2
Duplicates	3
Inappropriate	0
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, infiltrating, malignancy of testi

Hasle, H., Friedman, J. M., Olsen, J. H., & Rasmussen, S. A. (2016). Low risk of solid tumors in persons with Down syndrome. Genetics in Medicine, 18(11), 1151.

Thyroid/ Parathyroid

FINAL	8
Code browser	8
Peer reviewed publications	0
Caliber portal	1
Duplicates	1
Inappropriate	0
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, infiltrating, malignancy of thyroid, parathyroid, papillary, follicular

Uterus

FINAL	4
Code browser	4
Peer reviewed publications	3
Caliber portal	2
Duplicates	5
Inappropriate	0
Search terms	Cancer, carcinoma, neoplasm, tumor, malignant, infiltrating, malignancy of uterus, uteri, uterine

Hasle, H., Friedman, J. M., Olsen, J. H., & Rasmussen, S. A. (2016). Low risk of solid tumors in persons with Down syndrome. Genetics in Medicine, 18(11), 1151.

Wilm's

FINAL	1
Code browser	1
Peer reviewed publications	0
Caliber portal	0
Duplicates	0
Inappropriate	0
Search terms	Wilm, nephroblastoma

Appendix 6: Syntax used for analyses in Project 2. Stata 16.

```
use "S:\CALIBER_17_009R\Raw Data\Data\indicators.dta"
gen casesafe = cases
tab casesafe
label define caseslabel 1"DS" 0"Control"
label values cases caseslabel
tab cases
replace cases=. if EXCLUDE==1
tab cases
drop if cases ==.

**********PERSON YEARS**********
*TOTAL PERSON YEARS
total person_yrs, over(cases)
tab cases, sum(person_yrs)

*MEAN PERSON YEARS WITH CI
mean person_yrs, over(cases)
*COMPARISON OF MEANS
ttest person_yrs, by(cases)

*MEDIAN PERSON YEARS WITH CI
*histogram person_yrs
bysort cases: centile person_yrs
*COMPARISON OF MEDIANS
median person_yrs, by(cases)

**********GENDER**********
*GENDER TOTAL, %, DS V. CONTROLS
tab cases gender, row

*COMPARSION OF PROPORTIONS
*tab cases gender, chi2 - doesn't give seperate values cases v controls)
gen male=1 if gender==1
recode male (.=0)
tab male
gen female=1 if gender==2
recode female (.=0)
```

```
tab female

tab male cases, chi2
tab female cases, chi2
proportion male, over(cases)
proportion female, over(cases)

**********AGE**********
gen age_start = year(date_start) - yob
sum age_start
*gen age_end = year(date_end) - yob (Arturo already created)
sum age_end

*MEDIANS WITH CI
by cases: centile age_start
by cases: centile age_end
*COMPARSION OF MEDIANS
median age_start, by(cases)
median age_end, by(cases)

*age ranges DS
gen DSage_start = age_start if cases ==1
sum DSage_start
gen DSage_end = age_end if cases ==1
sum DSage_end

*age ranges CONTROLS
gen Cage_start = age_start if cases ==0
sum Cage_start
gen Cage_end = age_end if cases ==0
sum Cage_end

tab age_end cases if age_end<=18
tab age_start if age_start>=30

**********DATA EXIT**********
gen death_ind = 0
replace death_ind = 1 if death_date != .
```

```
tab death_ind cases, col
tab death_ind cases, chi2
proportion death_ind, over(cases)

gen deathage = year(death_date) - yob
tab deathage

bysort cases: centile deathage
median deathage, by(cases)

histogram deathage if cases==1
histogram deathage if cases==0

**********NUMBER AGE RANGE @START**********
histogram age_start if cases==1
histogram age_start if cases==0

gen zerofiveS = 0
replace zerofiveS = 1 if age_start <=5
tab zerofiveS

gen sixtenS=0
replace sixtenS = 1 if age_start>=6 & age_start<=10
tab sixtenS

gen eleveneighteenS=0
replace eleveneighteenS = 1 if age_start>=11 & age_start<=18
tab eleveneighteenS

gen nineteenthirtyS=0
replace nineteenthirtyS = 1 if age_start>=19 & age_start<=30
tab nineteenthirtyS

gen thirtyonesixtyS=0
replace thirtyonesixtyS = 1 if age_start>=31 & age_start<=60
tab thirtyonesixtyS

gen oversixtyS=0
replace oversixtyS = 1 if age_start>60
```

```
tab oversixtyS

**********COMPARISON DS V. CONTROLS FOR AGE RANGES START**********
tab cases zerofiveS, row
tab cases zerofiveS, chi2
proportion zerofiveS, over(cases)

tab cases sixtenS, row
tab cases sixtenS, chi2
proportion sixtenS, over(cases)

tab cases eleveneighteenS , row
tab cases eleveneighteenS, chi2
proportion eleveneighteenS, over(cases)

tab cases nineteenthirtyS, row
tab cases nineteenthirtyS, chi2
proportion nineteenthirtyS, over(cases)

tab cases thirtyonesixtyS, row
tab cases thirtyonesixtyS, chi2
proportion thirtyonesixtyS, over(cases)

tab cases oversixtyS, row
tab cases oversixtyS, chi2
proportion oversixtyS, over(cases)

**********NUMBER AGE RANGE @END**********
*histogram age_end if cases==1
*histogram age_end if cases==0

gen zerofiveE = 0
replace zerofiveE = 1 if age_end <=5
tab zerofiveE

gen sixtenE=0
replace sixtenE = 1 if age_end>=6 & age_end<=10
tab sixtenE
```

```
gen eleveneighteenE=0
replace eleveneighteenE = 1 if age_end>=11 & age_end<=18
tab eleveneighteenE

gen nineteenthirtyE=0
replace nineteenthirtyE = 1 if age_end>=19 & age_end<=30
tab nineteenthirtyE

gen thirtyonesixtyE=0
replace thirtyonesixtyE = 1 if age_end>=31 & age_end<=60
tab thirtyonesixtyE

gen oversixtyE=0
replace oversixtyE = 1 if age_end>60
tab oversixtyE

**********COMPARISON DS V. CONTROLS FOR AGE RANGES END**********
tab cases zerofiveE, row
tab cases zerofiveE, chi2
proportion zerofiveE, over(cases)

tab cases sixtenE, row
tab cases sixtenE, chi2
proportion sixtenE, over(cases)

tab cases eleveneighteenE, row
tab cases eleveneighteenE, chi2
proportion eleveneighteenE, over(cases)

tab cases nineteenthirtyE, row
tab cases nineteenthirtyE, chi2
proportion nineteenthirtyE, over(cases)

tab cases thirtyonesixtyE, row
tab cases thirtyonesixtyE, chi2
proportion thirtyonesixtyE, over(cases)

tab cases oversixtyE, row
tab cases oversixtyE, chi2
```

```
proportion oversixtyE, over(cases)

**********PERSON YEARS PER AGE GROUP**********
gen DSzerofiveS = 1 if zerofiveS==1&cases==1
recode DSzerofiveS .=0 if cases==1
tab DSzerofiveS

gen DSsixtenS = 1 if sixtenS==1&cases==1
recode DSsixtenS .=0 if cases==1
tab DSsixtenS

gen DSeleveneighteenS = 1 if eleveneighteenS==1&cases==1
recode DSeleveneighteenS .=0 if cases==1
tab DSeleveneighteenS

gen DSnineteenthirtyS = 1 if nineteenthirtyS==1&cases==1
recode DSnineteenthirtyS .=0 if cases==1
tab DSnineteenthirtyS

gen DSthirtyonesixtyS = 1 if thirtyonesixtyS==1&cases==1
recode DSthirtyonesixtyS .=0 if cases==1
tab DSthirtyonesixtyS

gen DSoversixtyS = 1 if oversixtyS==1&cases==1
recode DSoversixtyS .=0 if cases==1
tab DSoversixtyS

total person_yrs, over(DSzerofiveS)
total person_yrs, over(DSsixtenS)
total person_yrs, over(DSeleveneighteenS)
total person_yrs, over(DSnineteenthirtyS)
total person_yrs, over(DSthirtyonesixtyS)
total person_yrs, over(DSoversixtyS)

*person years per control age group
*this would have been a quicker way for cases
gen CSperson_yrs = person_yrs if cases==0
gen CSstartcomb = 1 if zerofiveS==1 & cases==0
replace CSstartcomb = 2 if sixtenS==1 & cases==0
```

```
replace CSstartcomb = 3 if eleveneighteenS ==1 & cases==0
replace CSstartcomb = 4 if nineteenthirtyS ==1 & cases==0
replace CSstartcomb = 5 if thirtyonesixtyS ==1 & cases==0
replace CSstartcomb = 6 if oversixtyS ==1 & cases==0
tab CSstartcomb
total person_yrs, over(CSstartcomb)

**********ETHNICITY**********
*ETHNICITY TOTAL, %, DS V. CONTROLS
tab gen_ethnicity cases, col
tab gen_ethnicity cases, col mi
*tab gen_ethnicity if cases==0, mi
*tab gen_ethnicity if cases==1, mi

*CHANGING TO A STRING
gen ethn = 0
replace ethn = 1 if gen_ethnicity == "White"
replace ethn = 2 if gen_ethnicity == "Bangladesi"
replace ethn = 2 if gen_ethnicity == "Pakistani"
replace ethn = 2 if gen_ethnicity == "Chinese"
replace ethn = 2 if gen_ethnicity == "Indian"
replace ethn = 2 if gen_ethnicity == "Oth_Asian"
replace ethn = 3 if gen_ethnicity == "Bl_Afric"
replace ethn = 3 if gen_ethnicity == "Bl_Carib"
replace ethn = 3 if gen_ethnicity == "Bl_Other"
replace ethn = 4 if gen_ethnicity == "Mixed"
replace ethn = 4 if gen_ethnicity == "Other"
replace ethn = 4 if gen_ethnicity == "Unknown"
tab ethn

label define ethnlabel 0"Missing" 1"White" 2"Asian" 3"Black" 4"Other"
label values ethn ethnlabel
tab ethn
*PROPORTIONS FOR EACH GROUP, EXCLUDING MISSING
gen ethnprev = ethn
recode ethnprev (0=.)
label values ethnprev ethnlabel
tab ethnprev
tab ethnprev cases, col
```

```
*COMPARING PROPORTIONS FOR EACH ETHN, MUST TAKE ACCOUNT OF MISSING
gen ethnabsent =1 if ethn==0
tab ethn
tab ethnabsent
*WHITE
gen white=1 if ethn==1
recode white (.=0)
tab white
tab white cases, chi2
tab white cases if ethnabsent!=1, chi2
proportion white if ethnabsent!=1,over(cases)
*ASIAN
gen asian=1 if ethn==2
recode asian (.=0)
tab asian
tab asian cases if ethnabsent!=1, chi2
proportion asian if ethnabsent!=1,over(cases)
*BLACK
gen black=1 if ethn==3
recode black (.=0)
tab black
tab black cases if ethnabsent!=1, chi2
proportion black if ethnabsent!=1,over(cases)
*OTHER
gen other=1 if ethn==4
recode other (.=0)
tab other
tab other cases if ethnabsent!=1, chi2
proportion other if ethnabsent!=1,over(cases)

**********SOCIOECONOMIC STATUS**********
*SOCIOECONOMIC STATUS
tab e2015_imd_5 cases, col
*creating a variable for each imd category
gen imd1=1 if e2015_imd_5==1
recode imd1 (.=0)
tab imd1
gen imd2=1 if e2015_imd_5==2
```

```
recode imd2 (.=0)
tab imd2
gen imd3=1 if e2015_imd_5==3
recode imd3 (.=0)
tab imd3
gen imd4=1 if e2015_imd_5==4
recode imd4 (.=0)
tab imd4
gen imd5=1 if e2015_imd_5==5
recode imd5 (.=0)
tab imd5
*IMD1
tab imd1 cases, chi2
proportion imd1,over(cases)
*IMD2
tab imd2 cases, chi2
proportion imd2,over(cases)
*IMD3
tab imd3 cases, chi2
proportion imd3,over(cases)
*IMD4
tab imd4 cases, chi2
proportion imd4,over(cases)
*IMD5
tab imd5 cases, chi2
proportion imd5,over(cases)

**********BMI**********
*AVERAGE BMI
gen nbmi = bmi
destring nbmi, replace ignore(NULL)
tab nbmi if cases==1, mi
tab nbmi if cases==0, mi
*COMPARSION OF MEANS
ttest nbmi, by(cases)

**********SMOKING**********
*SMOKING STATUS (3 categories of smoking status, ALSO STRING VARIABLE)
tab smoking_status
```

```
*gen one smoking variable
gen smok = 0
replace smok = 1 if smoking_status =="2"
replace smok = 1 if smoking_status =="4"
tab smok
* Now 1 = smoker or ex-smoker, 0=nonsmokers AND MISSING

*TAKE ACCOUNT OF MISSING FOR CHI SQUARED
gen smok_data_avail = .
replace smok_data_avail = 1 if smoking_status =="1"
replace smok_data_avail = 1 if smok==1
tab smok_data_avail
*COMPARSION OF PROPORTIONS, CHI2, TAKING ACCOUNT OF MISSING
tab smok cases if smok_data_avail==1, chi2

*PREVALENCE TAKING ACCOUNT OF MISSING
tab smok cases if smok_data_avail==1, col
*MISSINGNESS CASES V. CONTROLS
tab smoking_status cases, col

*for odds ratio Am sure I made this difficult
gen ORsmok =.
replace ORsmok = 1 if smoking_status =="2"
replace ORsmok = 1 if smoking_status =="4"
replace ORsmok = 0 if smoking_status=="NULL"
tab ORsmok, mi

proportion smok if smok_data_avail==1, over(cases)

**********GEOGRAPHICAL**********
*GEOGRAPHICAL REGION
tab region cases, col

*COMPARSION, CHI2
*reg 1
gen reg1=1 if region==1
recode reg1 (.=0)
tab reg1
tab reg1 cases, chi2
```

```
proportion reg1, over(cases)
*reg 2
gen reg2=1 if region==2
recode reg2 (.=0)
tab reg2
tab reg2 cases, chi2
proportion reg2, over(cases)
*reg3
gen reg3=1 if region==3
recode reg3 (.=0)
tab reg3
tab reg3 cases, chi2
proportion reg3, over(cases)
*reg4
gen reg4=1 if region==4
recode reg4 (.=0)
tab reg4
tab reg4 cases, chi2
proportion reg4, over(cases)
*reg5
gen reg5=1 if region==5
recode reg5 (.=0)
tab reg5
tab reg5 cases, chi2
proportion reg5, over(cases)
*reg6
gen reg6=1 if region==6
recode reg6 (.=0)
tab reg6
tab reg6 cases, chi2
proportion reg6, over(cases)
*reg7
gen reg7=1 if region==7
recode reg7 (.=0)
tab reg7
tab reg7 cases, chi2
proportion reg7, over(cases)
*reg8
gen reg8=1 if region==8
```

```
recode reg8 (.=0)
tab reg8
tab reg8 cases, chi2
proportion reg8, over(cases)
*reg9
gen reg9=1 if region==9
recode reg9 (.=0)
tab reg9
tab reg9 cases, chi2
proportion reg9, over(cases)
*reg10
gen reg10=1 if region==10
recode reg10 (.=0)
tab reg10
tab reg10 cases, chi2
proportion reg10, over(cases)

**********PRIMARY ANALYSIS, PREVALENCE OF MORBIDITIES**********
*ADHD
tab1 flag_adhd_cprd flag_adhd_hes
gen adhd = 1 if (flag_adhd_cprd==1)|(flag_adhd_hes==1)
recode adhd .=0
tab cases adhd, row
tab cases adhd, chi2
proportion adhd, over(cases)

*ANXIETY
tab1 flag_anxietydepression_cprd flag_anxietydepression_hes
gen anx = 1 if (flag_anxietydepression_cprd==1)|(flag_anxietydepression_hes==1)
recode anx .=0
tab cases anx, row
tab cases anx, chi2
proportion anx, over(cases)

*ARTHRITIS
tab1 flag_arthritiscomb_cprd flag_arthritiscomb_hes
gen arth = 1 if (flag_arthritiscomb_cprd==1)|( flag_arthritiscomb_hes==1)
recode arth .=0
tab cases arth, row
```

```
tab cases arth, chi2
proportion arth, over(cases)

*Atlantoaxial instability
tab1 flag_atlantoaxialinstab_cprd flag_atlantoaxialinstab_hes
gen atlanto = 1 if (flag_atlantoaxialinstab_cprd==1)|(flag_atlantoaxialinstab_hes==1)
recode atlanto .=0
tab cases atlanto, row
tab cases atlanto, chi2
proportion atlanto, over(cases)

*AUTISM
tab1 flag_autism_cprd flag_autism_hes
gen aut = 1 if ( flag_autism_hes==1)|(flag_autism_cprd==1)
recode aut .=0
tab cases aut, row
tab cases aut, chi2
proportion aut, over(cases)

*CATARACT
tab1 flag_cataract_cprd flag_cataract_hes
gen cata = 1 if (flag_cataract_cprd==1)|(flag_cataract_hes==1)
recode cata .=0
tab cases cata, row
tab cases cata, chi2
proportion cata, over(cases)

*CKD
tab1 flag_chronickidneydisease_cprd flag_chronickidneydisease_hes
gen ckd = 1 if (flag_chronickidneydisease_cprd ==1)|(flag_chronickidneydisease_hes==1)
recode ckd  .=0
tab cases ckd, row
tab cases ckd, chi2
proportion ckd, over(cases)

*COELIAC
tab1 flag_coeliac_cprd flag_coeliac_hes
gen coel = 1 if (flag_coeliac_cprd==1)|(flag_coeliac_hes==1)
recode coel  .=0
```

```
tab cases coel, row
tab cases coel, chi2
proportion coel, over(cases)

*CHD
tab1 flag_congencardiac_cprd flag_congencardiac_hes
gen chd = 1 if (flag_congencardiac_hes==1)|(flag_congencardiac_cprd==1)
recode chd .=0
tab cases chd, row
tab cases chd, chi2
proportion chd, over(cases)

*CONGEN GASTRO
tab1 flag_congengastro_cprd flag_congengastro_hes
gen gastro = 1 if (flag_congengastro_hes==1)|(flag_congengastro_cprd ==1)
recode gastro .=0
tab cases gastro, row
tab cases gastro, chi2
proportion gastro, over(cases)

*DEMENTIA
tab1 flag_dementia_cprd_3 flag_dementia_hes
gen dem= 1 if (flag_dementia_cprd_3==1)|(flag_dementia_hes==1)
recode dem .=0
tab cases dem, row
tab cases dem, chi2
proportion dem, over(cases)

tab cases dem if age_start>=30, row
tab cases dem if age_start>=30, chi2
proportion dem if age_start>=30, over(cases)

*DM COMB
tab1 flag_dmcombined_cprd_3 flag_dmcombined_hes
gen dmcomb = 1 if (flag_dmcombined_cprd_3==1)|(flag_dmcombined_hes==1)
recode dmcomb .=0
tab cases dmcomb, row
tab cases dmcomb, chi2
proportion dmcomb, over(cases)
```

```
*DM1
tab1 flag_dmt1_cprd_3
gen dm1 = 1 if (flag_dmt1_cprd_3==1)
recode dm1 .=0
tab cases dm1, row
tab cases dm1, chi2
proportion dm1, over(cases)

*DM2
tab1 flag_dmt2_cprd_3
gen dm2 = 1 if (flag_dmt2_cprd_3==1)
recode dm2 .=0
tab cases dm2, row
tab cases dm2, chi2
proportion dm2, over(cases)

*DUCHENNE
tab1 flag_duchennemyop_cprd flag_duchennemyop_hes
gen duch = 1 if (flag_duchennemyop_cprd==1)|(flag_duchennemyop_hes==1)
recode duch .=0
tab cases duch, row
tab cases duch, chi2
tab cases duch, exact chi2
proportion duch, over(cases)

*ECZEMA
tab1 flag_eczema_cprd flag_eczema_hes
gen ecz = 1 if (flag_eczema_cprd==1)|(flag_eczema_hes==1)
recode ecz .=0
tab cases ecz, row
tab cases ecz, chi2
proportion ecz, over(cases)

*SKIN OTHER
tab1 flag_skinother_cprd flag_skinother_hes
gen skin = 1 if (flag_skinother_cprd==1)|(flag_skinother_hes==1)
recode skin .=0
tab cases skin, row
```

```
tab cases skin, chi2
proportion skin, over(cases)

*EPILEPSY
tab1 flag_epilepsy_cprd flag_epilepsy_hes
gen epi = 1 if (flag_epilepsy_cprd==1)|( flag_epilepsy_hes==1)
recode epi .=0
tab cases epi, row
tab cases epi, chi2
proportion epi, over(cases)

*GORD
tab1 flag_gord_hes flag_reflux_cprd
gen gord = 1 if (flag_gord_hes==1)|(flag_reflux_cprd==1)
recode gord .=0
tab cases gord, row
tab cases gord, chi2
proportion gord, over(cases)

*GLAUCOMA
tab1 flag_glaucoma_cprd flag_glaucoma_hes
gen glau = 1 if (flag_glaucoma_cprd==1)|(flag_glaucoma_hes==1)
recode glau .=0
tab cases glau, row
tab cases glau, chi2
proportion glau, over(cases)

*HEARING IMPAIR
tab1 flag_hearingimpairment_cprd flag_hearingimpairment_hes
gen hear= 1 if (flag_hearingimpairment_cprd==1)|(flag_hearingimpairment_hes==1)
recode hear .=0
tab cases hear, row
tab cases hear, chi2
proportion hear, over(cases)

*HYPERTHYROID
tab1 flag_hyperthyroidism_cprd flag_hyperthyroidism_hes
gen hypert = 1 if (flag_hyperthyroidism_cprd==1)|(flag_hyperthyroidism_hes==1)
recode hypert .=0
```

```
tab cases hypert, row
tab cases hypert, chi2
proportion hypert, over(cases)

*HYPOTHYROID
tab1 flag_hypothyroidism_cprd flag_hypothyroidism_hes
gen hypot = 1 if (flag_hypothyroidism_cprd==1)|(flag_hypothyroidism_hes==1)
recode hypot .=0
tab cases hypot, row
tab cases hypot, chi2
proportion hypot, over(cases)

*IBD
tab1 flag_ibd_cprd flag_ibd_hes
gen ibd = 1 if (flag_ibd_cprd==1)|(flag_ibd_hes==1)
recode ibd .=0
tab cases ibd, row
tab cases ibd, chi2
proportion ibd, over(cases)

*IRON DEFIC
tab1 flag_irondefic_hes flag_irondefic_cprd
gen iron = 1 if (flag_irondefic_hes==1)|(flag_irondefic_cprd==1)
recode iron .=0
tab cases iron, row
tab cases iron, chi2
proportion iron, over(cases)

*IHD
tab1 flag_ichaemiaheartdisease_cprd flag_ischaemiaheartdisease_hes
gen ihd = 1 if (flag_ichaemiaheartdisease_cprd==1)|(flag_ischaemiaheartdisease_hes==1)
recode ihd .=0
tab cases ihd, row
tab cases ihd, chi2
proportion ihd, over(cases)

tab cases ihd if age_start>=40, row
tab cases ihd if age_start>=40, chi2
proportion ihd if age_start>=40, over(cases)
```

```
*NAI
tab1 flag_naichildabuse_cprd flag_naichildabuse_hes
gen nai = 1 if (flag_naichildabuse_cprd==1)|(flag_naichildabuse_hes==1)
recode nai .=0
tab cases nai, row
tab cases nai, chi2
proportion nai, over(cases)

*SCHIZOPHRENIA
tab1 flag_schizophrenia_cprd flag_schizophrenia_hes
gen schiz = 1 if (flag_schizophrenia_cprd==1)|(flag_schizophrenia_hes==1)
recode schiz .=0
tab cases schiz, row
tab cases schiz, chi2
proportion schiz, over(cases)

*SDB
tab1 flag_sdb_cprd flag_sdb_hes
gen sdb = 1 if (flag_sdb_hes==1)|(flag_sdb_cprd==1)
recode sdb .=0
tab cases sdb, row
tab cases sdb, chi2
proportion sdb, over(cases)

*STROKE
tab1 flag_stroke_cprd flag_stroke_hes
gen stroke = 1 if (flag_stroke_cprd==1)|(flag_stroke_hes==1)
recode stroke .=0
tab cases stroke, row
tab cases stroke, chi2
proportion stroke, over(cases)

*UNDESCENDED TESTIS
tab1 flag_undescendedtestis_cprd flag_undescendedtestis_hes
gen undes = 1 if (flag_undescendedtestis_cprd==1)|(flag_undescendedtestis_hes==1)
recode undes .=0
tab cases undes, row
tab cases undes, chi2
```

```
proportion undes, over(cases)

*VITD DEFIC
tab1 flag_vitddefic_cprd flag_vitddefic_hes
gen vitd = 1 if (flag_vitddefic_cprd==1)|(flag_vitddefic_hes==1)
recode vitd .=0
tab cases vitd, row
tab cases vitd, chi2
proportion vitd, over(cases)

**********ODDS RATIOS, MORBIDITIES**********
*CONFOUNDERS
tab1 ethnprev ORsmok
sum person_yrs

* ADJUTSED AND UNADJUSTED odd ratios
logit adhd cases, or
logit adhd cases ethnprev ORsmok, or
logit adhd cases ethnprev ORsmok person_yrs, or

logit anx cases, or
logit anx cases ethnprev ORsmok, or
logit anx cases ethnprev ORsmok person_yrs, or

logit arth cases, or
logit arth cases ethnprev ORsmok, or
logit arth cases ethnprev ORsmok person_yrs, or

logit atlanto cases, or
logit atlanto cases ethnprev ORsmok, or
logit atlanto cases ethnprev ORsmok person_yrs, or

logit aut cases, or
logit aut cases ethnprev ORsmok, or
logit aut cases ethnprev ORsmok person_yrs, or

logit cata cases, or
logit cata cases ethnprev ORsmok, or
logit cata cases ethnprev ORsmok person_yrs, or
```

```
logit ckd cases, or
logit ckd cases ethnprev ORsmok, or
logit ckd cases ethnprev ORsmok person_yrs, or

logit coel cases, or
logit coel cases ethnprev ORsmok, or
logit coel cases ethnprev ORsmok person_yrs, or

logit chd cases, or
logit chd cases ethnprev ORsmok, or
logit chd cases ethnprev ORsmok person_yrs, or

logit gastro cases, or
logit gastro cases ethnprev ORsmok, or
logit gastro cases ethnprev ORsmok person_yrs, or

logit dem cases, or
logit dem cases ethnprev ORsmok, or
logit dem cases ethnprev ORsmok person_yrs, or

logit dem cases if age_start>=30, or
logit dem cases ethnprev ORsmok if age_start>=30, or
logit dem cases ethnprev ORsmok person_yrs if age_start>=30, or

logit dmcomb cases, or
logit dmcomb cases ethnprev ORsmok, or
logit dmcomb cases ethnprev ORsmok person_yrs, or

logit dm1 cases, or
logit dm1 cases ethnprev ORsmok, or
logit dm1 cases ethnprev ORsmok person_yrs, or

logit dm2 cases, or
logit dm2 cases ethnprev ORsmok, or
logit dm2 cases ethnprev ORsmok person_yrs, or

logit duch cases, or
logit duch cases ethnprev ORsmok, or
```

logit duch cases ethnprev ORsmok person_yrs, or

logit ecz cases, or
logit ecz cases ethnprev ORsmok, or
logit ecz cases ethnprev ORsmok person_yrs, or

logit skin cases, or
logit skin cases ethnprev ORsmok, or
logit skin cases ethnprev ORsmok person_yrs, or

logit epi cases, or
logit epi cases ethnprev ORsmok, or
logit epi cases ethnprev ORsmok person_yrs, or

logit gord cases, or
logit gord cases ethnprev ORsmok, or
logit gord cases ethnprev ORsmok person_yrs, or

logit glau cases, or
logit glau cases ethnprev ORsmok, or
logit glau cases ethnprev ORsmok person_yrs, or

logit hear cases, or
logit hear cases ethnprev ORsmok, or
logit hear cases ethnprev ORsmok person_yrs, or

logit hypert cases, or
logit hypert cases ethnprev ORsmok, or
logit hypert cases ethnprev ORsmok person_yrs, or

logit hypot cases, or
logit hypot cases ethnprev ORsmok, or
logit hypot cases ethnprev ORsmok person_yrs, or

logit ibd cases, or
logit ibd cases ethnprev ORsmok, or
logit ibd cases ethnprev ORsmok person_yrs, or

logit iron cases, or

```
logit iron cases ethnprev ORsmok, or
logit iron cases ethnprev ORsmok person_yrs, or

logit ihd cases, or
logit ihd cases ethnprev ORsmok, or
logit ihd cases ethnprev ORsmok person_yrs, or

logit ihd cases if age_start>=40, or
logit ihd cases ethnprev ORsmok if age_start>=40, or
logit ihd cases ethnprev ORsmok person_yrs if age_start>=40, or

logit nai cases, or
logit nai cases ethnprev ORsmok, or
logit nai cases ethnprev ORsmok person_yrs, or

logit schiz cases, or
logit schiz cases ethnprev ORsmok, or
logit schiz cases ethnprev ORsmok person_yrs, or

logit sdb cases, or
logit sdb cases ethnprev ORsmok, or
logit sdb cases ethnprev ORsmok person_yrs, or

logit stroke cases, or
logit stroke cases ethnprev ORsmok, or
logit stroke cases ethnprev ORsmok person_yrs, or

logit undes cases, or
logit undes cases ethnprev ORsmok, or
logit undes cases ethnprev ORsmok person_yrs, or

logit vitd cases, or
logit vitd cases ethnprev ORsmok, or
logit vitd cases ethnprev ORsmok person_yrs, or

**********CANCER PREVALENCE**********
*BLADDER
gen bladder=1 if (flag_bladder_cprd==1)|(flag_bladder_hes==1)|(flag_bladder_cr_hes==1)
recode bladder (.=0)
```

```
tab bladder
tab cases bladder, row
tab cases bladder, chi2
proportion bladder, over(cases)

*BONE
gen bone=1 if (flag_bone_cprd==1)|(flag_bone_hes==1)|(flag_bone_cr_hes==1)
recode bone (.=0)
tab bone
tab cases bone, row
tab cases bone, chi2
proportion bone, over(cases)

*BRAINCNS*
gen braincns=1 if (flag_braincns_cprd==1)|(flag_braincns_hes==1)|(flag_braincns_cr_hes==1)
recode braincns (.=0)
tab braincns
tab cases braincns, row
tab cases braincns, chi2
proportion braincns, over(cases)

*BREAST
gen breast=1 if (flag_breast_cprd==1)|(flag_breast_hes==1)|(flag_breast_cr_hes==1)
recode breast (.=0)
tab breast
tab cases breast, row
tab cases breast, chi2
proportion breast, over(cases)

*CERVIX
gen cervix=1 if (flag_cervix_cprd==1)|(flag_cervix_hes==1)|(flag_cervix_cr_hes==1)
recode cervix (.=0)
tab cervix
tab cases cervix, row
tab cases cervix, chi2
proportion cervix, over(cases)

*COLORECTAL
gen colorectal=1 if (flag_colorectal_cprd==1)|(flag_colorectal_hes==1)|(flag_colorectal_cr_hes==1)
```

```
recode colorectal (.=0)
tab colorectal
tab cases colorectal, row
tab cases colorectal, chi2
proportion colorectal, over(cases)

*GATRICOESOPHAGEAL
gen gastricoesoph=1 if(flag_gastricoesoph_hes==1)|(flag_gastricoesoph_cr_hes==1)
recode gastricoesoph (.=0)
tab gastricoesoph
tab cases gastricoesoph, row
tab cases gastricoesoph, chi2
proportion gastricoesoph, over(cases)

*LEUKAEMIA
gen leukaemia=1 if (flag_leukaemia_cprd==1)|(flag_leukaemia_hes==1)|(flag_leukaemia_cr_hes==1)
recode leukaemia (.=0)
tab leukaemia
tab cases leukaemia, row
tab cases leukaemia, chi2
proportion leukaemia, over(cases)

tab cases leukaemia if age_end<=18, row
tab cases leukaemia if age_end<=18, chi2
proportion leukaemia if age_end<=18, over(cases)

*LIVERBILIARY
gen liverbiliary=1 if (flag_liverbiliary_cprd==1)|(flag_liverbiliary_cr_hes==1)
recode liverbiliary (.=0)
tab liverbiliary
tab cases liverbiliary, row
tab cases liverbiliary, chi2
proportion liverbiliary, over(cases)

*LUNG
gen lung=1 if (flag_lung_cprd==1)|(flag_lungs_hes==1)|(flag_lungs_cr_hes==1)
recode lung (.=0)
tab lung
tab cases lung, row
```

```
tab cases lung, chi2
proportion lung, over(cases)

*LYMPHOMA
gen lymphoma=1 if (flag_lymphoma_cprd==1)|(flag_lymphoma_hes==1)|(flag_lymphoma_cr_hes==1)
recode lymphoma (.=0)
tab lymphoma
tab cases lymphoma, row
tab cases lymphoma, chi2
proportion lymphoma, over(cases)

*MELANOMA
gen melanoma=1 if (flag_melanoma_cprd==1)|(flag_melanoma_hes==1)|(flag_melanoma_cr_hes==1)
recode melanoma (.=0)
tab melanoma
tab cases melanoma, row
tab cases melanoma, chi2
proportion melanoma, over(cases)

*NONMELSKIN
gen nonmelskin=1 if (flag_nonmelskin_cprd==1)|(flag_nonmelskin_hes==1)|(flag_nonmelskin_cr_hes==1)
recode nonmelskin (.=0)
tab nonmelskin
tab cases nonmelskin, row
tab cases nonmelskin, chi2
proportion nonmelskin, over(cases)

*MYELOMA
gen myeloma=1 if
(flag_neuroblastoma_cprd==1)|(flag_neuroblastoma_hes==1)|(flag_neuroblastoma_cr_hes==1)
recode myeloma (.=0)
tab myeloma
tab cases myeloma, row
tab cases myeloma, chi2
proportion myeloma, over(cases)

*NEUROBLASTOMA
gen neuroblastoma=1 if
(flag_neuroblastoma_cprd==1)|(flag_neuroblastoma_hes==1)|(flag_neuroblastoma_cr_hes==1)
```

```
recode neuroblastoma (.=0)
tab neuroblastoma
tab cases neuroblastoma, row
tab cases neuroblastoma, chi2
proportion neuroblastoma, over(cases)

*OVARIAN
gen ovarian=1 if (flag_ovarian_cprd==1)|(flag_ovarian_hes==1)|(flag_ovarian_cr_hes==1)
recode ovarian (.=0)
tab ovarian
tab cases ovarian, row
tab cases ovarian, chi2
proportion ovarian, over(cases)

*PANCREAS
gen pancreas=1 if (flag_pancreas_cprd==1)|(flag_pancreas_hes==1)|(flag_pancreas_cr_hes==1)
recode pancreas (.=0)
tab pancreas
tab cases pancreas, row
tab cases pancreas, chi2
proportion pancreas, over(cases)

*PROSTATE
gen prostate=1 if (flag_prostate_cprd==1)|(flag_prostate_hes==1)|(flag_prostate_cr_hes==1)
recode prostate (.=0)
tab prostate
tab cases prostate, row
tab cases prostate, chi2
proportion prostate, over(cases)

*RENAL
gen renal=1 if (flag_renal_cprd==1)|(flag_renal_hes==1)|(flag_renal_cr_hes==1)
recode renal (.=0)
tab renal
tab cases renal, row
tab cases renal, chi2
proportion renal, over(cases)

*RETINOBLASTOMA
```

```
gen retinoblastoma=1 if
(flag_retinoblastoma_cprd==1)|(flag_retinoblastoma_hes==1)|(flag_retinoblastoma_cr_hes==1)
recode retinoblastoma (.=0)
tab retinoblastoma
tab cases retinoblastoma, row
tab cases retinoblastoma, chi2
proportion retinoblastoma, over(cases)

*TESTICULAR
gen testi=1 if (flag_testicular_cprd==1)|(flag_testicular_hes==1)|(flag_testicular_cr_hes==1)
recode testi (.=0)
tab testi
tab cases testi, row
tab cases testi, chi2
proportion testi, over(cases)

*THYROIDPARARTHY
gen thypara=1 if
(flag_thyroidparathy_cprd==1)|(flag_thyroidparathyroid_hes==1)|(flag_thyroidparathyroid_cr_hes==1)
recode thypara (.=0)
tab thypara
tab cases thypara, row
tab cases thypara, chi2
proportion thypara, over(cases)

*UTERUS
gen uterus=1 if (flag_uterus_cprd==1)|(flag_uterus_hes==1)|(flag_uterus_cr_hes==1)
recode uterus (.=0)
tab uterus
tab cases uterus, row
tab cases uterus, chi2
proportion uterus, over(cases)

*WILMS
gen wilms=1 if (flag_wilms_cprd==1)|(flag_wilms_hes==1)|(flag_wilms_cr_hes==1)
recode wilms (.=0)
tab wilms
tab cases wilms, row
tab cases wilms, chi2
```

```
proportion wilms, over(cases)

*ANY TUMOR
gen anytumor=1 if
(bladder==1)|(bone==1)|(braincns==1)|(breast==1)|(cervix==1)|(colorectal==1)|(gastricoesoph==1)|(liverbiliary
==1)|(leukaemia==1)|(lung==1)|(lymphoma==1)|(melanoma==1)|(nonmelskin==1)|(myeloma==1)|(neuroblasto
ma==1)|(ovarian==1)|(pancreas==1)|(prostate==1)|(renal==1)|(retinoblastoma==1)|(testi==1)|(thypara==1)|(uter
us==1)|(wilms==1)
recode anytumor(.=0)
tab anytumor
tab cases anytumor, row
tab cases anytumor, chi2
proportion anytumor, over(cases)

**********CANCER ODDS RATIOS**********

*CONFOUNDERS
tab1 ethnprev ORsmok
sum person_yrs

logit bladder cases, or
logit bladder cases ethnprev ORsmok, or
logit bladder cases ethnprev ORsmok person_yrs, or

logit bone cases, or
logit bone cases ethnprev ORsmok, or
logit bone cases ethnprev ORsmok person_yrs, or

logit braincns cases, or
logit braincns cases ethnprev ORsmok, or
logit braincns cases ethnprev ORsmok person_yrs, or

logit breast cases, or
logit breast cases ethnprev ORsmok, or
logit breast cases ethnprev ORsmok person_yrs, or

logit cervix cases, or
logit cervix cases ethnprev ORsmok, or
logit cervix cases ethnprev ORsmok person_yrs, or
```

```
logit colorectal cases, or
logit colorectal cases ethnprev ORsmok, or
logit colorectal cases ethnprev ORsmok person_yrs, or

logit gastricoesoph cases, or
logit gastricoesoph cases ethnprev ORsmok, or
logit gastricoesoph cases ethnprev ORsmok person_yrs, or

logit leukaemia cases, or
logit leukaemia cases ethnprev ORsmok, or
logit leukaemia cases ethnprev ORsmok person_yrs, or

logit leukaemia cases if age_end<=18, or
logit leukaemia cases ethnprev ORsmok if age_end<=18, or
logit leukaemia cases ethnprev ORsmok person_yrs if age_end<=18, or

logit liverbiliary cases, or
logit liverbiliary cases ethnprev ORsmok, or
logit liverbiliary cases ethnprev ORsmok person_yrs, or

logit lung cases, or
logit lung cases ethnprev ORsmok, or
logit lung cases ethnprev ORsmok person_yrs, or

logit lymphoma cases, or
logit lymphoma cases ethnprev ORsmok, or
logit lymphoma cases ethnprev ORsmok person_yrs, or

logit melanoma cases, or
logit melanoma cases ethnprev ORsmok, or
logit melanoma cases ethnprev ORsmok person_yrs, or

logit nonmelskin cases, or
logit nonmelskin cases ethnprev ORsmok, or
logit nonmelskin cases ethnprev ORsmok person_yrs, or

logit myeloma cases, or
logit myeloma cases ethnprev ORsmok, or
```

logit myeloma cases ethnprev ORsmok person_yrs, or

logit neuroblastoma cases, or
logit neuroblastoma cases ethnprev ORsmok, or
logit neuroblastoma cases ethnprev ORsmok person_yrs, or

logit ovarian cases, or
logit ovarian cases ethnprev ORsmok, or
logit ovarian cases ethnprev ORsmok person_yrs, or

logit pancreas cases, or
logit pancreas cases ethnprev ORsmok, or
logit pancreas cases ethnprev ORsmok person_yrs, or

logit prostate cases, or
logit prostate cases ethnprev ORsmok, or
logit prostate cases ethnprev ORsmok person_yrs, or

logit renal cases, or
logit renal cases ethnprev ORsmok, or
logit renal cases ethnprev ORsmok person_yrs, or

logit retinoblastoma cases, or
logit retinoblastoma cases ethnprev ORsmok, or
logit retinoblastoma cases ethnprev ORsmok person_yrs, or

logit testi cases, or
logit testi cases ethnprev ORsmok, or
logit testi cases ethnprev ORsmok person_yrs, or

logit thypara cases, or
logit thypara cases ethnprev ORsmok, or
logit thypara cases ethnprev ORsmok person_yrs, or

logit uterus cases, or
logit uterus cases ethnprev ORsmok, or
logit uterus cases ethnprev ORsmok person_yrs, or

logit wilms cases, or

```
logit wilms cases ethnprev ORsmok, or
logit wilms cases ethnprev ORsmok person_yrs, or

logit anytumor cases, or
logit anytumor cases ethnprev ORsmok, or
logit anytumor cases ethnprev ORsmok person_yrs, or


**********SUB-ANALYSIS, CHILDREN ONLY**********
gen child = cases
replace child=. if age_end>=19
drop if child==.
tab child

label define childlabel 1"DS" 0"Control"
label values child childlabel

**********PERSON YEARS**********
*TOTAL PERSON YEARS
total person_yrs, over(child)
tab child, sum(person_yrs)

*MEAN PERSON YEARS WITH CI
mean person_yrs, over(child)
*COMPARISON OF MEANS
ttest person_yrs, by(child)


*MEDIAN PERSON YEARS WITH CI
*histogram person_yrs
bysort child: centile person_yrs
*COMPARISON OF MEDIANS
median person_yrs, by(child)

**********GENDER**********
*GENDER TOTAL, %, DS V. CONTROLS
tab child gender, row

*COMPARSION OF PROPORTIONS
```

```
*tab cases gender, chi2 - doesn't give seperate values cases v controls)
gen male=1 if gender==1
recode male (.=0)
tab male
gen female=1 if gender==2
recode female (.=0)
tab female

tab male child, chi2
tab female child, chi2
proportion male, over(child)
proportion female, over(child)

**********AGE**********
gen age_start = year(date_start) - yob
sum age_start
*gen age_end = year(date_end) - yob (Arturo already created)
sum age_end

*MEDIANS WITH CI
by child: centile age_start
by child: centile age_end
*COMPARSION OF MEDIANS
median age_start, by(child)
median age_end, by(child)

*age ranges DS
gen DSage_startB = age_start if child ==1
sum DSage_startB
gen DSage_endB = age_end if child ==1
sum DSage_endB

*age ranges CONTROLS
gen Cage_startB = age_start if child ==0
sum Cage_startB
gen Cage_endB = age_end if child ==0
sum Cage_endB

**********DATA EXIT**********
```

```
gen death_ind = 0
replace death_ind = 1 if death_date != .

tab death_ind child, col
tab death_ind child, chi2
proportion death_ind, over(child)

gen deathage = year(death_date) - yob
tab deathage

bysort child: centile deathage
median deathage, by(child)

histogram deathage if child==1
histogram deathage if child==0

**********NUMBER AGE RANGE @START**********
histogram age_start if child==1
histogram age_start if child==0

gen zerofiveS = 0
replace zerofiveS = 1 if age_start <=5
tab zerofiveS

gen sixtenS=0
replace sixtenS = 1 if age_start>=6 & age_start<=10
tab sixtenS

gen eleveneighteenS=0
replace eleveneighteenS = 1 if age_start>=11 & age_start<=18
tab eleveneighteenS

*COMPARISON DS V. CONTROLS FOR AGE RANGESS START

tab child zerofiveS, row
tab child zerofiveS, chi2
proportion zerofiveS, over(child)
```

```
tab child sixtenS, row
tab child sixtenS, chi2
proportion sixtenS, over(child)

tab child eleveneighteenS , row
tab child eleveneighteenS, chi2
proportion eleveneighteenS, over(child)

**********NUMBER AGE RANGE @END**********
gen zerofiveE = 0
replace zerofiveE = 1 if age_end <=5
tab zerofiveE

gen sixtenE=0
replace sixtenE = 1 if age_end>=6 & age_end<=10
tab sixtenE

gen eleveneighteenE=0
replace eleveneighteenE = 1 if age_end>=11 & age_end<=18
tab eleveneighteenE

*COMPARISON DS V. CONTROLS FOR AGE RANGES END
tab child zerofiveE, row
tab child zerofiveE, chi2
proportion zerofiveE, over(child)

tab child sixtenE, row
tab child sixtenE, chi2
proportion sixtenE, over(child)

tab child eleveneighteenE, row
tab child eleveneighteenE, chi2
proportion eleveneighteenE, over(child)

*******PERSON YEARS PER AGE GROUP*****
gen DSzerofiveS = 1 if zerofiveS==1&child==1
recode DSzerofiveS .=0 if child==1
tab DSzerofiveS
```

```
gen DSsixtenS = 1 if sixtenS==1&child==1
recode DSsixtenS .=0 if child==1
tab DSsixtenS

gen DSeleveneighteenS = 1 if eleveneighteenS==1&child==1
recode DSeleveneighteenS .=0 if child==1
tab DSeleveneighteenS

total person_yrs, over(DSzerofiveS)
total person_yrs, over(DSsixtenS)
total person_yrs, over(DSeleveneighteenS)

*person years per control age group
*this would have been a quicker way for cases
gen CSperson_yrs = person_yrs if child==0
gen CSstartcomb = 1 if zerofiveS==1 & child==0
replace CSstartcomb = 2 if sixtenS==1 & child==0
replace CSstartcomb = 3 if eleveneighteenS ==1 & child==0
tab CSstartcomb
total person_yrs, over(CSstartcomb)

**********ETHNICITY**********
*ETHNICITY TOTAL, %, DS V. CONTROLS
tab gen_ethnicity child, col
tab gen_ethnicity child, col mi

*CHANGING TO A STRING
gen ethn = 0
replace ethn = 1 if gen_ethnicity == "White"
replace ethn = 2 if gen_ethnicity == "Bangladesi"
replace ethn = 2 if gen_ethnicity == "Pakistani"
replace ethn = 2 if gen_ethnicity == "Chinese"
replace ethn = 2 if gen_ethnicity == "Indian"
replace ethn = 2 if gen_ethnicity == "Oth_Asian"
replace ethn = 3 if gen_ethnicity == "Bl_Afric"
replace ethn = 3 if gen_ethnicity == "Bl_Carib"
replace ethn = 3 if gen_ethnicity == "Bl_Other"
replace ethn = 4 if gen_ethnicity == "Mixed"
replace ethn = 4 if gen_ethnicity == "Other"
```

```
replace ethn = 4 if gen_ethnicity == "Unknown"
tab ethn

label define ethnlabel 0"Missing" 1"White" 2"Asian" 3"Black" 4"Other"
label values ethn ethnlabel
tab ethn

*PROPORTIONS FOR EACH GROUP, EXCLUDING MISSING
gen ethnprev = ethn
recode ethnprev (0=.)
label values ethnprev ethnlabel
tab ethnprev
tab ethnprev child, col

*COMPARING PROPORTIONS FOR EACH ETHN, MUST TAKE ACCOUNT OF MISSING
gen ethnabsent =1 if ethn==0
tab ethn
tab ethnabsent
*WHITE
gen white=1 if ethn==1
recode white (.=0)
tab white
tab white child if ethnabsent!=1, chi2
proportion white if ethnabsent!=1,over(child)
*ASIAN
gen asian=1 if ethn==2
recode asian (.=0)
tab asian
tab asian child if ethnabsent!=1, chi2
proportion asian if ethnabsent!=1,over(child)
*BLACK
gen black=1 if ethn==3
recode black (.=0)
tab black
tab black child if ethnabsent!=1, chi2
proportion black if ethnabsent!=1,over(child)
*OTHER
gen other=1 if ethn==4
recode other (.=0)
```

```
tab other
tab other child if ethnabsent!=1, chi2
proportion other if ethnabsent!=1,over(child)

**********SOCIOECONOMIC STATUS**********
*SOCIOECONOMIC STATUS
tab e2015_imd_5 child, col
*creating a variable for each imd category
gen imd1=1 if e2015_imd_5==1
recode imd1 (.=0)
tab imd1
gen imd2=1 if e2015_imd_5==2
recode imd2 (.=0)
tab imd2
gen imd3=1 if e2015_imd_5==3
recode imd3 (.=0)
tab imd3
gen imd4=1 if e2015_imd_5==4
recode imd4 (.=0)
tab imd4
gen imd5=1 if e2015_imd_5==5
recode imd5 (.=0)
tab imd5
*IMD1
tab imd1 cases, chi2
proportion imd1,over(child)
*IMD2
tab imd2 cases, chi2
proportion imd2,over(child)
*IMD3
tab imd3 cases, chi2
proportion imd3,over(child)
*IMD4
tab imd4 cases, chi2
proportion imd4,over(child)
*IMD5
tab imd5 cases, chi2
proportion imd5,over(child)
```

```
**********BMI**********
*AVERAGE BMI
gen nbmi = bmi
destring nbmi, replace ignore(NULL)

tab nbmi if child==1, mi
tab nbmi if child==0, mi

ttest nbmi, by(child)

**********GEOGRAPHICAL**********
*GEOGRAPHICAL REGION
tab region child, col

*COMPARSION, CHI2
*reg 1
gen reg1=1 if region==1
recode reg1 (.=0)
tab reg1
tab reg1 child, chi2
proportion reg1, over(child)
*reg 2
gen reg2=1 if region==2
recode reg2 (.=0)
tab reg2
tab reg2 child, chi2
proportion reg2, over(child)
*reg3
gen reg3=1 if region==3
recode reg3 (.=0)
tab reg3
tab reg3 child, chi2
proportion reg3, over(child)
*reg4
gen reg4=1 if region==4
recode reg4 (.=0)
tab reg4
tab reg4 child, chi2
proportion reg4, over(child)
```

```
*reg5
gen reg5=1 if region==5
recode reg5 (.=0)
tab reg5
tab reg5 child, chi2
proportion reg5, over(child)
*reg6
gen reg6=1 if region==6
recode reg6 (.=0)
tab reg6
tab reg6 child, chi2
proportion reg6, over(child)
*reg7
gen reg7=1 if region==7
recode reg7 (.=0)
tab reg7
tab reg7 child, chi2
proportion reg7, over(child)
*reg8
gen reg8=1 if region==8
recode reg8 (.=0)
tab reg8
tab reg8 child, chi2
proportion reg8, over(child)
*reg9
gen reg9=1 if region==9
recode reg9 (.=0)
tab reg9
tab reg9 child, chi2
proportion reg9, over(child)
*reg10
gen reg10=1 if region==10
recode reg10 (.=0)
tab reg10
tab reg10 child, chi2
proportion reg10, over(child)

*******************************************************************************
*ADHD
```

```
tab1 flag_adhd_cprd flag_adhd_hes
gen adhd = 1 if (flag_adhd_cprd==1)|(flag_adhd_hes==1)
recode adhd .=0
tab child adhd, row
tab child adhd, chi2
proportion adhd, over(child)

*ANXIETY
tab1 flag_anxietydepression_cprd flag_anxietydepression_hes
gen anx = 1 if (flag_anxietydepression_cprd==1)|(flag_anxietydepression_hes==1)
recode anx .=0
tab child anx, row
tab child anx, chi2
proportion anx, over(child)

*ARTHRITIS
tab1 flag_arthritiscomb_cprd flag_arthritiscomb_hes
gen arth = 1 if (flag_arthritiscomb_cprd==1)|( flag_arthritiscomb_hes==1)
recode arth .=0
tab child arth, row
tab child arth, chi2
proportion arth, over(child)

*Atlantoaxial instability
tab1 flag_atlantoaxialinstab_cprd flag_atlantoaxialinstab_hes
gen atlanto = 1 if (flag_atlantoaxialinstab_cprd==1)|(flag_atlantoaxialinstab_hes==1)
recode atlanto .=0
tab child atlanto, row
tab child atlanto, chi2
proportion atlanto, over(child)

*AUTISM
tab1 flag_autism_cprd flag_autism_hes
gen aut = 1 if ( flag_autism_hes==1)|(flag_autism_cprd==1)
recode aut .=0
tab child aut, row
tab child aut, chi2
proportion aut, over(child)
```

```
*CATARACT
tab1 flag_cataract_cprd flag_cataract_hes
gen cata = 1 if (flag_cataract_cprd==1)|(flag_cataract_hes==1)
recode cata .=0
tab child cata, row
tab child cata, chi2
proportion cata, over(child)

*CKD
tab1 flag_chronickidneydisease_cprd flag_chronickidneydisease_hes
gen ckd = 1 if (flag_chronickidneydisease_cprd ==1)|(flag_chronickidneydisease_hes==1)
recode ckd  .=0
tab child ckd, row
tab child ckd, chi2
proportion ckd, over(child)

*COELIAC
tab1 flag_coeliac_cprd flag_coeliac_hes
gen coel = 1 if (flag_coeliac_cprd==1)|(flag_coeliac_hes==1)
recode coel  .=0
tab child coel, row
tab child coel, chi2
proportion coel, over(child)

*CHD
tab1 flag_congencardiac_cprd flag_congencardiac_hes
gen chd = 1 if (flag_congencardiac_hes==1)|(flag_congencardiac_cprd==1)
recode chd .=0
tab child chd, row
tab child chd, chi2
proportion chd, over(child)

*CONGEN GASTRO
tab1 flag_congengastro_cprd flag_congengastro_hes
gen gastro = 1 if (flag_congengastro_hes==1)|(flag_congengastro_cprd ==1)
recode gastro .=0
tab child gastro, row
tab child gastro, chi2
proportion gastro, over(child)
```

```
*DM COMB
tab1 flag_dmcombined_cprd_3 flag_dmcombined_hes
gen dmcomb = 1 if (flag_dmcombined_cprd_3==1)|(flag_dmcombined_hes==1)
recode dmcomb .=0
tab child dmcomb, row
tab child dmcomb, chi2
proportion dmcomb, over(child)

*DM1
tab1 flag_dmt1_cprd_3
gen dm1 = 1 if (flag_dmt1_cprd_3==1)
recode dm1 .=0
tab child dm1, row
tab child dm1, chi2
proportion dm1, over(child)

*DUCHENNE
tab1 flag_duchennemyop_cprd flag_duchennemyop_hes
gen duch = 1 if (flag_duchennemyop_cprd==1)|(flag_duchennemyop_hes==1)
recode duch .=0
tab child duch, row
tab child duch, chi2
tab child duch, exact chi2
proportion duch, over(child)

*ECZEMA
tab1 flag_eczema_cprd flag_eczema_hes
gen ecz = 1 if (flag_eczema_cprd==1)|(flag_eczema_hes==1)
recode ecz .=0
tab child ecz, row
tab child ecz, chi2
proportion ecz, over(child)

*SKIN OTHER
tab1 flag_skinother_cprd flag_skinother_hes
gen skin = 1 if (flag_skinother_cprd==1)|(flag_skinother_hes==1)
recode skin .=0
tab child skin, row
```

```
tab child skin, chi2
proportion skin, over(child)

*EPILEPSY
tab1 flag_epilepsy_cprd flag_epilepsy_hes
gen epi = 1 if (flag_epilepsy_cprd==1)|( flag_epilepsy_hes==1)
recode epi .=0
tab child epi, row
tab child epi, chi2
proportion epi, over(child)

*GORD
tab1 flag_gord_hes flag_reflux_cprd
gen gord = 1 if (flag_gord_hes==1)|(flag_reflux_cprd==1)
recode gord .=0
tab child gord, row
tab child gord, chi2
proportion gord, over(child)

*GLAUCOMA
tab1 flag_glaucoma_cprd flag_glaucoma_hes
gen glau = 1 if (flag_glaucoma_cprd==1)|(flag_glaucoma_hes==1)
recode glau .=0
tab child glau, row
tab child glau, chi2
proportion glau, over(child)

*HEARING IMPAIR
tab1 flag_hearingimpairment_cprd flag_hearingimpairment_hes
gen hear= 1 if (flag_hearingimpairment_cprd==1)|(flag_hearingimpairment_hes==1)
recode hear .=0
tab child hear, row
tab child hear, chi2
proportion hear, over(child)

*HYPERTHYROID
tab1 flag_hyperthyroidism_cprd flag_hyperthyroidism_hes
gen hypert = 1 if (flag_hyperthyroidism_cprd==1)|(flag_hyperthyroidism_hes==1)
recode hypert .=0
```

```
tab child hypert, row
tab child hypert, chi2
proportion hypert, over(child)

*HYPOTHYROID
tab1 flag_hypothyroidism_cprd flag_hypothyroidism_hes
gen hypot = 1 if (flag_hypothyroidism_cprd==1)|(flag_hypothyroidism_hes==1)
recode hypot .=0
tab child hypot, row
tab child hypot, chi2
proportion hypot, over(child)

*IBD
tab1 flag_ibd_cprd flag_ibd_hes
gen ibd = 1 if (flag_ibd_cprd==1)|(flag_ibd_hes==1)
recode ibd .=0
tab child ibd, row
tab child ibd, chi2
proportion ibd, over(child)

*IRON DEFIC
tab1 flag_irondefic_hes flag_irondefic_cprd
gen iron = 1 if (flag_irondefic_hes==1)|(flag_irondefic_cprd==1)
recode iron .=0
tab child iron, row
tab child iron, chi2
proportion iron, over(child)

*NAI
tab1 flag_naichildabuse_cprd flag_naichildabuse_hes
gen nai = 1 if (flag_naichildabuse_cprd==1)|(flag_naichildabuse_hes==1)
recode nai .=0
tab child nai, row
tab child nai, chi2
proportion nai, over(child)

*OBESITY ??DROP
tab1  flag_obesity_cprd flag_obesity_hes
gen obs = 1 if (flag_obesity_cprd==1)|(flag_obesity_hes==1)
```

```
recode obs .=0
tab child obs, row
tab child obs, chi2
proportion obs, over(child)

*SCHIZOPHRENIA
tab1 flag_schizophrenia_cprd flag_schizophrenia_hes
gen schiz = 1 if (flag_schizophrenia_cprd==1)|(flag_schizophrenia_hes==1)
recode schiz .=0
tab child schiz, row
tab child schiz, chi2
proportion schiz, over(child)

*SDB
tab1 flag_sdb_cprd flag_sdb_hes
gen sdb = 1 if (flag_sdb_hes==1)|(flag_sdb_cprd==1)
recode sdb .=0
tab child sdb, row
tab child sdb, chi2
proportion sdb, over(child)

*STROKE
tab1 flag_stroke_cprd flag_stroke_hes
gen stroke = 1 if (flag_stroke_cprd==1)|(flag_stroke_hes==1)
recode stroke .=0
tab child stroke, row
tab child stroke, chi2
proportion stroke, over(child)

*UNDESCENDED TESTIS
tab1 flag_undescendedtestis_cprd flag_undescendedtestis_hes
gen undes = 1 if (flag_undescendedtestis_cprd==1)|(flag_undescendedtestis_hes==1)
recode undes .=0
tab child undes, row
tab child undes, chi2
proportion undes, over(child)

*VITD DEFIC
tab1 flag_vitddefic_cprd flag_vitddefic_hes
```

```
gen vitd = 1 if (flag_vitddefic_cprd==1)|(flag_vitddefic_hes==1)
recode vitd .=0
tab child vitd, row
tab child vitd, chi2
proportion vitd, over(child)


*********************************************************************************
*CONFOUNDERS
tab1 ethnprev
sum person_yrs

* ADJUTSED AND UNADJUSTED odd ratios
logit adhd child, or
logit adhd child ethnprev , or
logit adhd child ethnprev  person_yrs, or

logit anx child, or
logit anx child ethnprev , or
logit anx child ethnprev  person_yrs, or

logit arth child, or
logit arth child ethnprev , or
logit arth child ethnprev  person_yrs, or

logit atlanto child, or
logit atlanto child ethnprev , or
logit atlanto child ethnprev  person_yrs, or

logit aut child, or
logit aut child ethnprev , or
logit aut child ethnprev  person_yrs, or

logit cata child, or
logit cata child ethnprev , or
logit cata child ethnprev  person_yrs, or

logit ckd child, or
logit ckd child ethnprev , or
```

```
logit ckd child ethnprev  person_yrs, or

logit coel child, or
logit coel child ethnprev , or
logit coel child ethnprev  person_yrs, or

logit chd child, or
logit chd child ethnprev , or
logit chd child ethnprev  person_yrs, or

logit gastro child, or
logit gastro child ethnprev , or
logit gastro child ethnprev  person_yrs, or

logit dmcomb child, or
logit dmcomb child ethnprev , or
logit dmcomb child ethnprev  person_yrs, or

logit dm1 child, or
logit dm1 child ethnprev , or
logit dm1 child ethnprev  person_yrs, or

logit duch child, or
logit duch child ethnprev , or
logit duch child ethnprev  person_yrs, or

logit ecz child, or
logit ecz child ethnprev , or
logit ecz child ethnprev  person_yrs, or

logit skin child, or
logit skin child ethnprev , or
logit skin child ethnprev  person_yrs, or

logit epi child, or
logit epi child ethnprev , or
logit epi child ethnprev  person_yrs, or

logit gord child, or
```

```
logit gord child ethnprev , or
logit gord child ethnprev  person_yrs, or

logit glau child, or
logit glau child ethnprev , or
logit glau child ethnprev  person_yrs, or

logit hear child, or
logit hear child ethnprev , or
logit hear child ethnprev  person_yrs, or

logit hypert child, or
logit hypert child ethnprev , or
logit hypert child ethnprev  person_yrs, or

logit hypot child, or
logit hypot child ethnprev , or
logit hypot child ethnprev  person_yrs, or

logit ibd child, or
logit ibd child ethnprev , or
logit ibd child ethnprev  person_yrs, or

logit iron child, or
logit iron child ethnprev , or
logit iron child ethnprev  person_yrs, or

logit nai child, or
logit nai child ethnprev , or
logit nai child ethnprev  person_yrs, or

logit schiz child, or
logit schiz child ethnprev , or
logit schiz child ethnprev  person_yrs, or

logit sdb child, or
logit sdb child ethnprev , or
logit sdb child ethnprev  person_yrs, or
```

```
logit stroke child, or
logit stroke child ethnprev , or
logit stroke child ethnprev  person_yrs, or

logit undes child, or
logit undes child ethnprev , or
logit undes child ethnprev  person_yrs, or

logit vitd child, or
logit vitd child ethnprev , or
logit vitd child ethnprev  person_yrs, or

*LEUKAEMIA
gen leukaemia=1 if (flag_leukaemia_cprd==1)|(flag_leukaemia_hes==1)|(flag_leukaemia_cr_hes==1)
recode leukaemia (.=0)
tab leukaemia
tab child leukaemia, row
tab child leukaemia, chi2
proportion leukaemia, over(child)

*LYMPHOMA
gen lymphoma=1 if (flag_lymphoma_cprd==1)|(flag_lymphoma_hes==1)|(flag_lymphoma_cr_hes==1)
recode lymphoma (.=0)
tab lymphoma
tab child lymphoma, row
tab child lymphoma, chi2
proportion lymphoma, over(child)

*NEUROBLASTOMA
gen neuroblastoma=1 if
(flag_neuroblastoma_cprd==1)|(flag_neuroblastoma_hes==1)|(flag_neuroblastoma_cr_hes==1)
recode neuroblastoma (.=0)
tab neuroblastoma
tab child neuroblastoma, row
tab child neuroblastoma, chi2
proportion neuroblastoma, over(child)

*ANY TUMOR
```

```
gen anytumor=1 if
(bladder==1)|(bone==1)|(braincns==1)|(breast==1)|(cervix==1)|(colorectal==1)|(gastricoesoph==1)|(liverbiliary
==1)|(leukaemia==1)|(lung==1)|(lymphoma==1)|(melanoma==1)|(nonmelskin==1)|(myeloma==1)|(neuroblasto
ma==1)|(ovarian==1)|(pancreas==1)|(prostate==1)|(renal==1)|(retinoblastoma==1)|(testi==1)|(thypara==1)|(uter
us==1)|(wilms==1)
recode anytumor(.=0)
tab anytumor
tab child anytumor, row
tab child anytumor, chi2
proportion anytumor, over(child)

*************************************************************************
*CONFOUNDERS
tab1 ethnprev
sum person_yrs

logit leukaemia child, or
logit leukaemia child ethnprev , or
logit leukaemia child ethnprev  person_yrs, or

logit lymphoma child, or
logit lymphoma child ethnprev , or
logit lymphoma child ethnprev  person_yrs, or

logit neuroblastoma child, or
logit neuroblastoma child ethnprev , or
logit neuroblastoma child ethnprev  person_yrs, or

logit anytumor child, or
logit anytumor child ethnprev , or
logit anytumor child ethnprev  person_yrs, or
```

Appendix 7: Further adjusted odds ratios (including person years contributed) for the occurrence of morbidities and cancers in the DS population v. controls.

Table 20: Primary analysis (adults & children): Further adjusted odds ratios (aOR) for the occurrence of DS associated morbidities in the DS cohort v. controls.

Morbidity	**aOR (CI)** (95% CI </>1)
ADHD	1.41(0.86-2.31)
Anxiety/depression	0.68(0.56-0.84)
Arthritis (combined)	1.31(1.03-1.66)
Atlantoaxial instability	10.31 (4.77-22.31)
Autism	5.06 (3.67-6.99)
Cataract	8.05 (6.32-10.26)
Chronic kidney disease	2.59 (1.89-3.55)
Coeliac disease	10.12 (6.33-16.19)
Congenital cardiac disease	57.01 (46.05-70.56)
Congenital gastrointestinal disease	12.93 (8.06-20.75)
Dementia	24.01 (17.81-32.35)
Dementia (≥30yrs at start of follow-up)"	30.18 (21.10-43.17)
Diabetes Mellitus (combined)	2.13 (1.68-2.70)
Diabetes Mellitus, Type 1^	3.01 (1.57-5.76)
Diabetes Mellitus, Type 2^	1.56 (1.04-2.35)
Duchenne muscular dystrophy	2.77 (0.82-9.30)
Eczema	0.97 (0.85-1.10)
Skin other	2.29 (1.85-2.83)
Epilepsy	7.66 (6.26-9.38)
Gastro-oesophageal reflux	2.63 (2.25-3.07)
Glaucoma	1.66 (0.87-3.16)
Hearing impairment	10.73 (8.98-12.82)
Hyperthyroidism	4.68 (3.11-7.05)
Hypothyroidism	14.75 (12.13-17.93)
Inflammatory bowel disease	2.39 (1.94-2.94)
Iron deficiency anaemia	1.84 (1.36-2.49)
Ischaemic heart disease	1.42 (1.07-1.89)
Ischaemic heart disease (≥40yrs at start of follow-up)'	0.45 (0.28-0.74)
Non-accidental injury/ maltreatment	1.29 (0.89-1.86)
Schizophrenia	1.59 (0.84-3.00)
Sleep disordered breathing	7.30 (5.97-8.92)
Stroke	1.97 (1.36-2.85)
Undescended testis	3.34 (2.41-4.62)
Vitamin D deficiency	3.33 (2.01-5.52)

Nb. Cases (individuals with DS) are matched with at least 4 controls (non-DS individuals) based on GP practice, practice level index of multiple deprivation, year of birth ± 1 year, sex and index date (the data at which a case is first labelled as having DS).
aOR = adjusted odds ratio; CI = 95% confidence intervals
Odds ratios are adjusted for ethnicity, smoking status and person years contributed..
Missing data: Ethnicity: DS=551, Control=6,068; Smoking status: DS=1,458 Controls=7,389
"DS N=2,163, Controls N=10,346
'DS N=1,501, Controls N=6,596
^The prevalence of type 1 and type 2 diabetes (separately) is based on CPRD data only. It is not possible to differentiate between the subtypes of diabetes using HES data.
ADHD: Attention Deficit Hyperactivity Disorder

Table 21: Primary analysis (adults & children): Further adjusted odds ratios (aOR) for the occurrence of cancers in the DS cohort v. controls.

Cancer site	aOR (CI) (95% CI </>1)
Bladder	0.62 (0.14-2.62)
Bone	2.22 (0.25-19.73)
Brain/Central Nervous System	1.05 (0.36-3.00)
Breast	0.33 (0.11-1.07)
Cervix	0.12 (0.03-0.49)
Colorectal	0.56 (0.27-1.15)
Gastro-oesophageal	-
Leukaemia	12.68 (6.22-25.83)
Liver/biliary	-
Lung	0.14 (0.02-1.00)
Lymphoma	0.65 (0.15-2.81)
Melanoma	-
Skin, non-melanoma	0.49 (0.22-1.12)
Myeloma	-
Neuroblastoma	-
Ovarian	1.55 (0.53-4.52)
Pancreas	1.73 (0.47-6.35)
Prostate	0.69 (0.21-2.22)
Renal	0.58 (0.08-4.54)
Retinoblastoma	-
Testicular	3.60 (1.15-11.21)
Thyroid/parathyroid	0.66 (0.08-5.16)
Uterus	0.53 (0.22-1.33)
Wilms' tumour	0.68 (0.09-5.35)
Any of the cancers above	0.83 (0.64-1.07)

Nb. Cases (individuals with DS) are matched with at least 4 controls (non-DS individuals) based on GP practice, practice level index of multiple deprivation, year of birth ± 1 year, sex and index date (the data at which a case is first labelled as having DS).
aOR = adjusted odds ratio; CI = 95% confidence intervals
Odds ratios are adjusted for ethnicity, smoking status and person years contributed..
Missing data: Ethnicity: DS=551, Control=6,068; Smoking status: DS=1,458 Controls=7,389
- = unable to calculate odd ratios due to absence of cancer in cases and/or controls, including after the inclusion of confounders in the model.

Table 22: Sub-analysis (children only): Further adjusted odds ratios (aOR) for the occurrence of DS associated morbidities and cancers in the DS cohort v. controls.

Morbidity	**aOR (CI)** (95% CI </>1)
ADHD	1.26 (0.74-2.13)
Anxiety/depression	0.67 (0.43-1.03)
Arthritis (combined)	2.32 (1.15-4.69)
Atlantoaxial instability	-
Autism	5.17 (3.76-7.09)
Cataract	19.25 (7.83-47.33)
Chronic kidney disease	3.69 (1.85-7.35)
Coeliac disease	11.18 (6.16-20.29)
Congenital cardiac disease	105.58 (81.18-137.33)
Congenital gastrointestinal disease	12.99 (7.93-21.28)
Diabetes Mellitus (combined)	3.93 (2.50-6.17)
Diabetes Mellitus, Type 1^	3.35 (1.37-8.20)
Duchenne muscular dystrophy	8.15 (1.46-45.39)
Eczema	0.77 (0.66-0.89)
Skin other	1.91 (1.40-2.62)
Epilepsy	3.86 (2.84-5.23)
Gastro-oesophageal reflux	4.49 (3.73-5.42)
Glaucoma	14.95 (2.98-75.01)
Hearing impairment	14.07 (11.33-17.48)
Hyperthyroidism	-
Hypothyroidism	36.36 (24.66-53.62)
Inflammatory bowel disease	3.15 (2.45-4.03)
Iron deficiency anaemia	2.21 (1.46-3.34)
Non-accidental injury/ maltreatment	1.72 (1.21-2.45)
Schizophrenia	0.92 (0.11-7.96)
Sleep disordered breathing	14.43 (11.29-18.44)
Stroke	12.28 (4.37-34.50)
Undescended testis	3.50 (2.55-4.81)
Vitamin D deficiency	3.30 (1.86-5.86)
Cancers	
Leukaemia	63.72 (15.08-269.33)
Lymphoma	2.29 (0.58-9.02)
Neuroblastoma	-

Nb. Cases (individuals with DS) are matched with at least 4 controls (non-DS individuals) based on GP practice, practice level index of multiple deprivation, year of birth ± 1 year, sex and index date (the data at which a case is first labelled as having DS).
aOR = adjusted odds ratio; CI = 95% confidence intervals
Odds ratios are adjusted for ethnicity, and person years contributed..
Missing data: Ethnicity: DS=68, Control=1,205
^The prevalence of type 1 and type 2 diabetes (separately) is based on CPRD data only. It is not possible to differentiate between the subtypes of diabetes using HES data.
- = unable to calculate odd ratios due to absence of cancer in cases and/or controls, including after the inclusion of confounders in the model.
ADHD: Attention Deficit Hyperactivity Disorder

Appendix 8: Letter sent to paediatric departments across the UK, requesting a copy of local health surveillance protocols.

LONDON'S GLOBAL UNIVERSITY

UCL

Population, Policy & Practice
UCL Great Ormond Street Institute of Child Health
30 Guilford Street, London, WC1N 1EH
ICH.DSprotocol@ucl.ac.uk
16th June 2017

Dear Sir/ Madam,

Apologies if you have already received a copy of this letter and responded.

We are writing to you **to request a copy of your local protocol(s) for the early recognition of associated co-morbidities ('health surveillance') in children with Down Syndrome.**

- We are undertaking a national research project at the Great Ormond Street Institute of Child Health.
- The aim of our research is to determine current practice in the early recognition of associated co-morbidities in children with Down Syndrome (commonly referred to as 'health surveillance' or 'health screening').
- We are requesting copies of local protocols from paediatric departments across the UK.
- We will compare practice across the UK to identify areas of consensus and diversity.
- In our final report, paediatric departments will **not** be mentioned individually.
- Our results will inform the development of national guidelines and policy with regards the early recognition of co-morbidities in children with Down Syndrome.
- Our findings will be disseminated to all paediatric departments and available online.
- The early recognition of associated co-morbidities is vital in optimising the health of those with Down Syndrome and reducing secondary morbidity.

Please return a copy of your local protocol in the free post return envelope or e-mail a copy to ICH.DSprotocol@ucl.ac.uk.

If you do not have a local protocol or instead follow published guidelines please complete and return the slip attached.

Yours Faithfully,

Prof Monica Lakhanpaul
Professor of Integrated Community Child Health
UCL Great Ormond Street Institute of Child Health

Prof Anne Schilder
NIHR Research Professor Director Evident, UCL Ear Institute
Royal National Throat, Nose and Ear Hospital

Dr Caoimhe McKenna
Clinical Academic Training Fellow
UCL Great Ormond Street Institute of Child Health

Appendix 9: 'Response slip' provided with the letter sent to paediatric departments across the UK, requesting a copy of local health surveillance protocols.

If you cannot provide a local protocol for the early recognition of associated co-morbidities ('health surveillance') in children with Down Syndrome, please tick one of the following:

☐ Our department does NOT have a local protocol for the early recognition of associated co-morbidities in children with Down Syndrome (e.g. practice varies according to clinician).

Our department uses guidance directly from:

☐ The Royal College of Paediatrics and Child Health

☐ The Department of Health

☐ The Down Syndrome Medical Interest Group

☐ Other (please state) _____

☐ Our department does NOT undertake routine health surveillance of children with Down Syndrome (e.g. this is undertaken by another department).

☐ Other (please explain):