Technical Information

The technical information in this document accompanies the National Child Mortality Database (NCMD) thematic report entitled 'Infection related deaths in children and young people in England' and aims to present the methodology and limitations of the report. The report analyses data on child (0-17 years) deaths in England between 1 April 2019 and 31 March 2022 where infection may have contributed to death, or where infection provided a complete and sufficient explanation of death.

Cohort identification and exclusions

All child (0 – 17 years) deaths where the CDOP in England were planning to, or had already, reviewed the death were captured. This included a small number of deaths that occurred abroad, and of children not usually resident in England.

For Section 1, deaths between 1 April 2019 and 31 March 2023 were included where the death was coded as 'infection' at notification (48 hours) by two or more of the NCMD clinical team. This means that the numbers presented are lower than in Section 2 (which also includes deaths where infection was evident at the review but not at notification) and it is likely to be an underestimate, but is consistent throughout the period and with previous work, and is designed to show changes over time.

For Section 2, all deaths between 1 April 2019 and 31 March 2022 where infection may have contributed to or caused the death were identified, where the death was coded as 'infection' at notification by two or more of the NCMD clinical team, or where, after full review, the CDOP allocated the primary or secondary category of death as ‘infection’ or ‘perinatal infection’. This included any deaths where the initial notification was coded as infection but the CDOP did not categorise the death as infection, and vice versa.

Section 3 included completed child death reviews by CDOPs where the child died between 1 April 2019 and 31 March 2022 and the review had been finalised by 3 May 2023. The reviews in this section included those where 'infection' or 'perinatal infection' was the primary category of death (i.e., the likely cause), and also reviews where either of these categories were selected as a secondary category of death. Of the infection related deaths included in Section 2 (n=1507), 87% (n=1315) had been reviewed by a CDOP; however only 843 of these were included in Section 3. On review of some cases not included, this was often because all relevant categories had not been selected by the CDOP (e.g., infection had not been selected as a secondary category of death). However, we restricted the analysis of Section 3 to deaths that were categorised as 'infection' or 'perinatal infection' by the CDOP, to fully ensure learning reported by CDOPs was relevant to infection deaths.

Identification of pathogens and clinical conditions

Pathogens and clinical conditions were identified using a combination of free text searching of information recorded within NCMD, followed by confirmation by the NCMD team. Information recorded in the notification form (including notification details, suspected cause of death, and alert details), infection supplementary reporting form, contributory factors recorded by the CDOP, and the cause of death (both medical certificate and cause of death determined by the CDOP), was reviewed.

A table of pathogens and clinical conditions, along with the search terms used to look for them, is available in Table B. The list was not exhaustive but aimed to capture the majority of the main pathogens and conditions, therefore some pathogens may not be reported. A set of all records where a pathogen/condition was found was validated by the NCMD team, to confirm that the detected free text referred to evidence of the expected pathogen/condition; any incorrect matches picked up in error were removed. Pathogens/conditions were confirmed where there was information within the fields confirming the pathogen/condition (e.g., it was listed within the cause of death), or where there was confirmation of the pathogen/condition in the preceding events or hospital care leading to death. Pathogens were confirmed and included regardless of whether it was thought that this may have contributed to or caused the death, and included invasive and non-invasive infections. For the purposes of this report, deaths where 'septicaemia' was recorded were included under 'Sepsis'.

At least one pathogen was identified in 56% (n=841) of deaths and a clinical condition was identified in 52% of deaths (n=785) (Table A). A total of 80% (n=1209) had either a pathogen or clinical condition identified.

Table A: Number of infection related child deaths between 1 April 2019 and 31 March 2022, by the number of pathogens/clinical conditions identified

	Infection related deaths
	1507
Any pathogen identified	**841 (56%)**
1 pathogen identified	521
2 pathogens identified	255
3+ pathogens identified	65
Any clinical condition identified	**785 (52%)**
1 clinical condition identified	694
2 clinical conditions identified	87
3+ clinical conditions identified	4

Table B: Search terms used to identify potential matches for pathogens and clinical conditions

	Search terms
Pathogens	
Streptococcus (group A)	'% gas %', '% igas %' , '%group a strep%', '%strep a%', '%streptococcus A%', '%strep%pyog%'
Streptococcus (group B)	'% gbs %', '% igbs %', '%group b strep%', '%strep b%', '%streptococcus b%'
Streptococcus pneumoniae (pneumococcal)	'%pneumococcal%', '%pneumoccocal%', '%strep%pneum%', '%s_pneum%', '%s__pneum%'
Streptococcus (Other or unspecified)	'%streptococcus%'
E. coli	'%e_coli%', '%e__coli%', '%ecoli%', '%escherichia coli%'
Pseudomonas	'%pseudomonas%', '%p_aeruginosa%', '%p__aeruginosa%', '%p___aeruginosa%'
Haemophilus influenzae	'%hib%', '%haemoph%flu%', '%hemoph%flu%', '%h_influ%', '%h__influ%'
Other gram negative bacteria	%gram_negative%', '%gram -ve%', '%salmonella%', '%shigella%', '%enterobacter%', '%moraxella%', '%stenotrophomonas%', '%citrobac%',

	'%klebsiella%', '%proteus%', '%serratia%', '%typhus%', '%typhi%', '%acinetobacter%'
Listeria	'%listeria%', '%listeriosis%', '%l_monocytogenes%', '%l__monocytogenes%', '%l___monocytogenes%'
Meningococcal sp.	'%meningococcal%'
Staphylococcus sp.	'%staphylococcus%'
Enterococcus sp.	'%enterococcus%', '%enterococcal%', '%enteroccocus%', '%enteroccocal%'
Tuberculosis (TB)	'% tb %', '%tuberculosis%'
Herpes simplex virus (HSV)	'%hsv%', '%herpes%', '%neonatal herpes%', '%herpes simplex virus%'
Influenzae	'%flu%' AND NOT LIKE ("Haemoph%"/"Hemophi%"/"H. Influ%")
Varicella zoster virus (VZV)	'%vzv%', '%varicella%', '%chickenpox%'
Coronavirus	'%coronavirus%', '%covid%', '%sars%', or linked to a positive SARS-CoV-2 test result within 28 days of death
Metapneumovirus	'%metapneumovirus%'
Cytomegalovirus (CMV)	'%cmv%', '%cytomeg%'
Respiratory syncytial virus (RSV)	'%rsv%', '%respiratory syncytial virus%'
Enterovirus	'%enterovirus%'
Adenovirus	'%adenovirus%'
Human immunodeficiency virus (HIV)	'%hiv%', '%human immunodeficiency virus%'
Fungal	'%fungal%', '%aspergi%', '%candid%', '%fungaemia%'
Clinical conditions	
Gastroenteritis	'%gastroenteritis%'
Meningitis/encephalitis	'%meningitis%', '%encephalitis%', '%encephalomyelitis%'
Myocarditis	'%myocarditis%'
Pneumonia/lower respiratory tract infection (LRTI)	'%pneumonia%', '%lrti%', '%lower respiratory tract infection%', '%bronchiolitis%', '%chest infection%', '%lower respiratory infection%', '%tracheobronchitis%', '%respiratory tract infection %'
Upper respiratory tract infection (URTI)/pharyngitis/tonsilitis	'%urti%', '%pharyngitis%', '%tonsilitis%', '%upper respiratory tract infection%'
Urinary tract infection (UTI)	'%uti%', '%urinary tract Infection%', '%cystitis%', '%pyelonephritis%'
Sepsis	
Septicaemia/sepsis	'%septic%', '%sepsis%'

Data extraction

The dataset used within this report was extracted on 3 May 2023 and pathogens/clinical conditions were coded with information available in the system.

Data sources

ONS census data (2021) for 0-17 year olds (or adjusted to represent the appropriate age group) were used as denominators to calculate risk of death, including ethnicity data. Risks of death were calculated per 100,000 children, per year, and are presented alongside their appropriate 95% confidence intervals. The data was assumed to follow a Poisson distribution for calculation of confidence intervals and error bars.

Data reported by CDOPs in the statutory child death data collection forms was used for this analysis. The child's postcode of residence was linked to the Index of Multiple Deprivation

for a measure of local deprivation, with a lower value suggesting greater deprivation, and was also linked to determine the urban/rural classification of the child's residence.

Identification of underlying health conditions

Underlying health conditions were identified using a combination of data recorded in NCMD and through linked Hospital Episode Statistics (HES) data.

Life-limiting conditions for each child were identified through linking to ICD-10 diagnosis codes recorded within HES data, or where the life-limiting condition or oncology supplementary form was completed during the child death review. ICD-10 codes used were kept consistent with those identified in previous research on children with life-limiting conditions. This list includes life-threatening conditions (those for which curative treatment may be feasible but can fail, for example, cancer) and can be found in Table C.

Contributory factors

Whilst completeness of at least one factor graded at a 2 or above was generally good (93%), numbers and proportions should be interpreted as a minimum. On some occasions, the factor could have been recorded with a relevance of 1 (i.e., factors identified but are unlikely to have contributed to the death), and therefore not included within this report, or the factor may not have been recorded at all on the analysis form. The denominator used to calculate proportions of contributory factors present was the total number of reviews completed.

Other limitations

The NCMD is reliant on accurate data being inputted by professionals involved in submitting information for the child death review.

Deaths were only included within the cohort if there was information in the record at notification of infection, or if after full review, the CDOP categorised the death as infection or perinatal infection, at the point of data extraction. 82% of the total number of deaths during the time period had been reviewed at the time of extraction, therefore the numbers presented may be an underestimate of the true incidence over the 3 years. Some deaths where there was no evidence of infection at notification, and the review had not completed, may turn out to be caused by an infection. However, this is unlikely to affect the patterns in characteristics presented.

The time period within this report (1 April 2019 – 31 March 2022) includes the COVID-19 pandemic, where during this time the absolute rates of many other infections were also affected, as measures were put into place to stop the spread of COVID-19. Therefore, this was not a typical period for many infections, and may have impacted the number presented within this report.

Category of death assigned by the CDOP

The NCMD is reliant on accurate categorisation of death by the CDOP. 87% (n=1315/1507) of the infection related deaths had been reviewed by a CDOP (Figure A). Of those, 482 (37%) reviews were categorised as infection (n=345) or perinatal infection (n=137) as the primary category of death by the CDOP. Of the remaining reviews (n=833) where infection may have been contributory, 361 reviews were assigned infection or perinatal infection as a secondary cause of death by the CDOP, whereas 472 reviews did not have infection selected as any category of death by the CDOP. These 472 deaths were included in section 2 as there was sufficient evidence of infection that may have contributed at notification, however, they were not included in section 3 which focusses on child death reviews. It is important that CDOPs should follow the categorisation of death hierarchy as described in the statutory analysis form; all relevant categories should be ticked if more than one category could reasonably be applied. The uppermost ticked category will be recorded as the primary category and others as secondary categories.

Of the deaths where infection may have been contributory (n=833), the most common primary category of death was Chromosomal, genetic and congenital anomalies (n=248), followed by Perinatal or neonatal event (excluding infection) (n=239), Chronic medical condition (n=158) and Acute medical or surgical condition (n=110).

Figure A: Number of infection related deaths identified and proportion reviewed by a CDOP

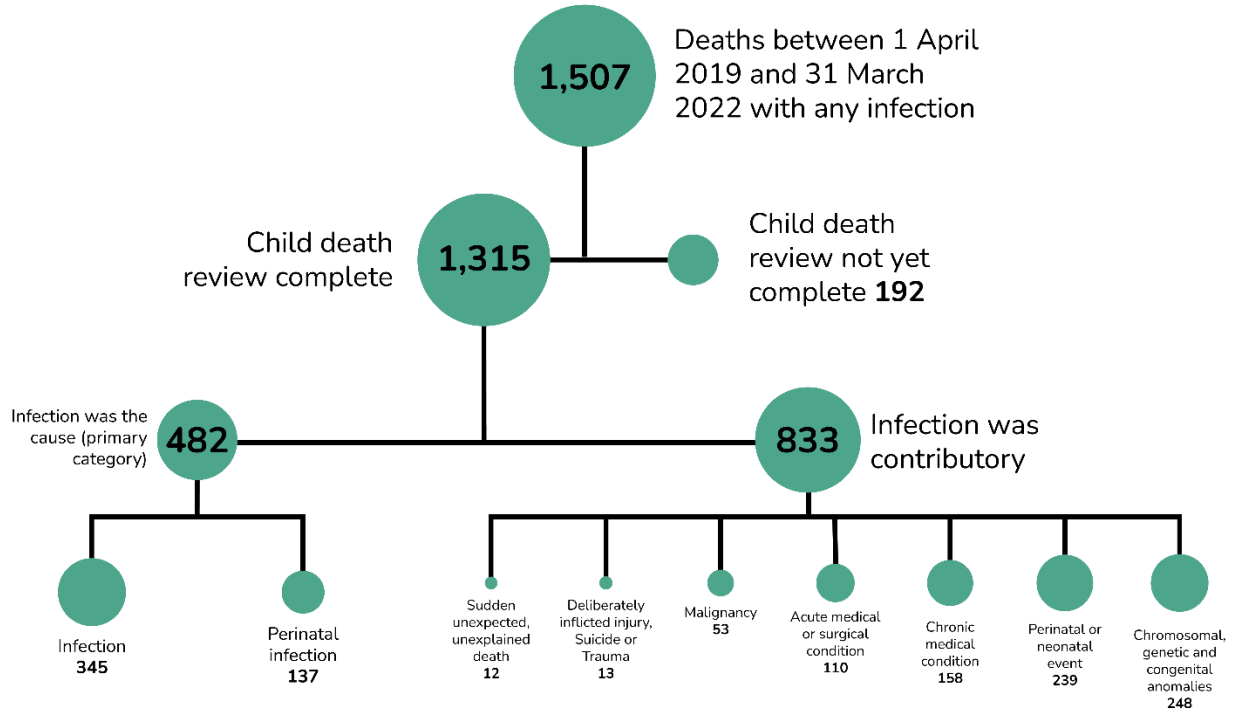

Table C: ICD-10 codes used to identify life-limiting conditions within Hospital Episode Statistics data

All	ICD10_Description
A17	Tuberculosis of nervous system
A810	Creutzfeldt-Jakob disease
A811	Subacute sclerosing panencephalitis
B20-B24	Human immunodeficiency virus [HIV] disease
C00-C97	Malignant neoplasms
D33	Benign neoplasm of brain and other parts of central nervous system
D43	Neoplasm of uncertain or unknown behaviour of brain and central nervous
D444	Neoplasm of uncertain behavior of craniopharyngeal duct
D48	Neoplasm of uncertain or unknown behaviour of other and unspecified
D561	Beta thalassemia
D610	Constitutional aplastic anaemia
D619	Aplastic anemia, unspecified
D70	Agranulocytosis
D761	Hemophagocytic lymphohistiocytosis
D81	Combined immunodeficiencies
D821	Di George's syndrome
D83	Common variable immunodeficiency
D891	Cryoglobulinemia
E310	Autoimmune polyglandular failure
E348	Other specified endocrine disorders
E702	Disorders of tyrosine metabolism
E71	Disorders of branched-chain amino-acid metabolism and fatty-acid
E72	Other disorders of amino-acid metabolism
E74	Other disorders of carbohydrate metabolism
E75	Disorders of sphingolipid metabolism and other lipid storage disorders
E76	Disorders of glycosaminoglycan metabolism
E77	Disorders of glycoprotein metabolism
E791	Lesch-Nyhan syndrome
E830	Disorders of copper metabolism
E84	Cystic fibrosis
E880	Disorders of plasma-protein metabolism, not elsewhere classified
E881	Lipodystrophy, not elsewhere classified
F803	Acquired aphasia with epilepsy [Landau-Kleffner]
F842	Rett's syndrome
G10	Huntington's disease
G111	Early-onset cerebellar ataxia
G113	Cerebellar ataxia with defective DNA repair
G12	Spinal muscular atrophy and related syndromes
G20	Parkinson's disease
G230	Hallervorden-Spatz disease
G238	Other specified degenerative diseases of basal ganglia
G318	Other specified degenerative diseases of nervous system
G319	Degenerative disease of nervous system, unspecified
G35	Multiple sclerosis
G404	Other generalized epilepsy and epileptic syndromes
G405	Special epileptic syndromes
G600	Hereditary motor and sensory neuropathy
G601	Refsum's disease
G702	Congenital and developmental myasthenia
G709	Myoneural disorder, unspecified
G710	Muscular dystrophy
G711	Myotonic disorders
G712	Congenital myopathies
G713	Mitochondrial myopathy, not elsewhere classified

G800	Spastic quadriplegic cerebral palsy
G808	Other cerebral palsy
G823	Flaccid tetraplegia
G824	Spastic tetraplegia
G825	Tetraplegia, unspecified
G934	Encephalopathy, unspecified
G936	Cerebral edema
G937	Reye's syndrome
H111	Conjunctival degenerations and deposits
H355	Hereditary retinal dystrophy
H498	Other paralytic strabismus
I21	Acute myocardial infarction
I270	Primary pulmonary hypertension
I42	Cardiomyopathy
I613	Nontraumatic intracerebral hemorrhage in brain stem
I81	Portal vein thrombosis
J841	Other interstitial pulmonary diseases with fibrosis
J96	Respiratory failure, not elsewhere classified
J984	Other disorders of lung
K550	Acute vascular disorders of intestine
K559	Vascular disorder of intestine, unspecified
K72	Hepatic failure, not elsewhere classified
K74	Fibrosis and cirrhosis of liver
K765	Hepatic veno-occlusive disease
K868	Other specified diseases of pancreas
M313	Wegener granulomatosis
M321	Systemic lupus erythematosus with organ or system involvement
M895	Osteolysis
N17	Acute renal failure
N18	Chronic kidney disease
N19	Unspecified kidney failure
N258	Other disorders resulting from impaired renal tubular function
P101	Cerebral hemorrhage due to birth injury
P112	Unspecified brain damage due to birth injury
P210	Severe birth asphyxia
P285	Respiratory failure of newborn
P290	Neonatal cardiac failure
P293	Persistent fetal circulation
P350	Congenital rubella syndrome
P351	Congenital cytomegalovirus infection
P358	Other congenital viral diseases
P371	Congenital toxoplasmosis
P524	Intracerebral (nontraumatic) hemorrhage of newborn
P525	Subarachnoid (nontraumatic) hemorrhage of newborn
P529	Intracranial (nontraumatic) hemorrhage of newborn, unspecified
P832	Hydrops fetalis not due to hemolytic disease
P912	Neonatal cerebral leukomalacia
P916	Hypoxic ischaemic encephalopathy of newborn
P960	Congenital renal failure
Q000	Anencephaly
Q01	Encephalocele
Q031	Atresia of foramina of Magendie and Luschka
Q039	Congenital hydrocephalus, unspecified
Q040	Congenital malformations of corpus callosum
Q042	Holoprosencephaly
Q043	Other reduction deformities of brain
Q044	Septo-optic dysplasia of brain
Q046	Congenital cerebral cysts
Q049	Congenital malformation of brain, unspecified
Q070	Arnold-Chiari syndrome
Q200	Common arterial trunk

Q203	Discordant ventriculoarterial connection
Q204	Double inlet ventricle
Q206	Isomerism of atrial appendages
Q208	Other congenital malformations of cardiac chambers and connections
Q213	Tetralogy of Fallot
Q218	Other congenital malformations of cardiac septa
Q220	Pulmonary valve atresia
Q221	Congenital pulmonary valve stenosis
Q224	Congenital tricuspid stenosis
Q225	Ebstein's anomaly
Q226	Hypoplastic right heart syndrome
Q230	Congenital stenosis of aortic valve
Q232	Congenital mitral stenosis
Q234	Hypoplastic left heart syndrome
Q239	Congenital malformation of aortic and mitral valves, unspecified
Q254	Other congenital malformations of aorta
Q256	Stenosis of pulmonary artery
Q262	Total anomalous pulmonary venous connection
Q264	Anomalous pulmonary venous connection, unspecified
Q268	Other congenital malformations of great veins
Q282	Arteriovenous malformation of cerebral vessels
Q321	Other congenital malformations of trachea
Q336	Congenital hypoplasia and dysplasia of lung
Q396	Congenital diverticulum of esophagus
Q410	Congenital absence, atresia and stenosis of duodenum
Q419	Congenital absence, atresia and stenosis of small intestine, part
Q437	Persistent cloaca
Q442	Atresia of bile ducts
Q445	Other congenital malformations of bile ducts
Q447	Other congenital malformations of liver
Q601	Renal agenesis, bilateral
Q606	Potter's syndrome
Q614	Renal dysplasia
Q619	Cystic kidney disease, unspecified
Q642	Congenital posterior urethral valves
Q743	Arthrogryposis multiplex congenita
Q748	Other specified congenital malformations of limb(s)
Q750	Craniosynostosis
Q772	Short rib syndrome
Q773	Chondrodysplasia punctata
Q774	Achondroplasia
Q780	Osteogenesis imperfecta
Q785	Metaphyseal dysplasia
Q792	Exomphalos
Q793	Gastroschisis
Q804	Harlequin fetus
Q81	Epidermolysis bullosa
Q821	Xeroderma pigmentosum
Q824	Ectodermal dysplasia (anhidrotic)
Q858	Other phakomatoses, not elsewhere classified
Q860	Fetal alcohol syndrome (dysmorphic)
Q870	Congenital malformation syndromes predominantly affecting facial
Q871	Congenital malformation syndromes predominantly associated with short
Q872	Congenital malformation syndromes predominantly involving limbs
Q878	Other specified congenital malformation syndromes, not elsewhere
Q91	Edwards syndrome and Patau syndrome
Q920	Whole chromosome trisomy, nonmosaicism (meiotic nondisjunction)
Q921	Whole chromosome trisomy, mosaicism (mitotic nondisjunction)
Q924	Duplications seen only at prometaphase
Q927	Triploidy and polyploidy
Q932	Chromosome replaced with ring, dicentric or isochromosome

Q933	Deletion of short arm of chromosome 4
Q934	Deletion of short arm of chromosome 5
Q935	Other deletions of part of a chromosome
Q938	Other deletions from the autosomes
Q952	Balanced autosomal rearrangement in abnormal individual
T860	Bone-marrow transplant rejection
T862	Heart transplant failure and rejection
Z515	Encounter for palliative care

Data source: https://pubmed.ncbi.nlm.nih.gov/33323043/