SUPPLEMENTAL MATERIAL

Data S1. Supplemental Methods

Specific procedure hierarchy and groupings

Within the NCHDA dataset, each procedure is described by up to 8 individual procedural International Paediatric and Congenital Cardiac Codes (IPCCCs) [1]. An algorithm developed by the NCHDA Steering Committee links the individual IPCCCs for a given record to 1 of 56 *specific procedures,* i.e. reported surgical operations or transcatheter procedures. Note that the hierarchical system is shown here in its entirety for reference purposes. It is designed for children of any age and many procedures listed would be rarely if ever performed in infancy.

The algorithm imposes a hierarchy with the record assigned the most complex specific procedure consistent with the collection of codes recorded. Approximately 85% of procedures fall into one of these 56 specific procedures. For children that had more than one procedure during their index admission, their index intervention was chosen to be the most complex according to the NCHDA specific procedure hierarchy.

For reasons of model reliability and validity of predictive discrimination, the index specific procedures were aggregated into three procedural groups considered clinically meaningful to the focus of the study: definitive, staged and ungrouped. A definitive procedure would be expected to be the final, often only, operation in achieving a biventricular or functionally univentricular circulation, although acknowledging that later procedures may be required in an individual's lifetime, such as conduit or valve replacement. A staged procedure would be undertaken in the expectation that further operations would be expected to achieve either a definitive biventricular circulation or definitive univentricular repair with a Fontan-type operation in early childhood.

Specific procedure	**NCHDA hierarchy**	**Procedure group**
Norwood	1	Staged
Heart Transplant	*2*	*Excluded*
Totally anomalous pulmonary venous connection (TAPVC) Repair + Arterial Shunt	3	Staged
Fontan procedure †	4	Staged
Bidirectional cavopulmonary shunt	5	Staged
Senning or Mustard procedure	6	Staged
Truncus and interruption repair	7	Definitive
Truncus arteriosus repair	8	Definitive
Tricuspid valve replacement	9	Ungrouped
Interrupted aortic arch repair	10	Definitive
Multiple ventricular septal defect (VSD) closure	11	Definitive
Mitral valve replacement	12	Definitive
Repair of TAPVC	13	Definitive
Atrioventricular septal defect and tetralogy repair	14	Definitive
Atrioventricular septal defect (complete) repair	15	Definitive
Atrioventricular septal defect (partial) repair	16	Definitive
Aortic valvotomy (surgical)	17	Definitive
Aortic valvoplasty	18	Definitive

Anomalous coronary artery repair	19	Definitive
Cor triatriatum repair	20	Definitive
Arterial switch + VSD closure	21	Definitive
Arterial switch (for isolated transposition)	22	Definitive
Pulmonary atresia & VSD repair	23	Definitive
Pulmonary valve replacement	24	Definitive
Tetralogy with absent pulmonary valve repair	25	Definitive
Tetralogy repair	26	Definitive
Isolated coarctation repair	27	Definitive
Aortic Valve Replacement - non Ross	28	Definitive
Supravalvar aortic stenosis repair	29	Definitive
Rastelli procedure	30	Definitive
Aortic valve replacement - Ross	31	Definitive
Aortic root replacement (not Ross)	32	Definitive
Subvalvar aortic stenosis repair	33	Definitive
Aortopulmonary window repair	34	Definitive
Atrial septal defect (ASD) repair	35	Definitive
VSD Repair	36	Definitive
Arterial shunt	37	Staged
Isolated Pulmonary artery band	38	Staged
Patent ductus arteriosus (PDA) ligation (surgical)	39	Definitive
Transcatheter pulmonary valve replacement *	40	*Excluded*
VSD closure (catheter) *	41	*Excluded*
Aortic balloon valvotomy	42	Definitive
Coarctation angioplasty	43	Definitive
Pulmonary artery stenting *	44	*Excluded*
ASD closure (catheter) *	45	*Excluded*
PDA closure (catheter)	46	Definitive
Recoarctation angioplasty *	47	*Excluded*
Pulmonary balloon valvoplasty	48	Definitive
Blade atrial septostomy *	49	*Excluded*
Coarctation stenting	50	Definitive
PFO closure (catheter) *	51	*Excluded*
Pulmonary valvotomy (radiofrequency)	52	Definitive
Duct Stenting	53	Staged
RVOT Stenting	54	Staged
Radiofrequency ablation for supraventricular tachycardia *	*55*	*Excluded*
Implantable Cardioverter Defibrillator *	*56*	*Excluded*
Minor and Excluded Procedures *	*57*	*Excluded*
Not a specific procedure: surgical **	58	Ungrouped
Not a specific procedure: catheter *	*59*	*Excluded*

* Catheter procedure excluded from analysis

** Note that n=53 out of 231 children with a cardiac diagnosis of aortic arch obstruction +/- VSD/ASD and no index specific procedure had either a banding of pulmonary trunk or pulmonary trunk band removal and were therefore classified as a "staged" procedure group rather than "ungrouped".

† Only one patient in our infant cohort had a Fontan as their index procedure.

Candidate patient risk factors

Potential non-medical, pre-procedure or post- procedure risk factors available in the patient-based analysis dataset that would be known at the point of discharge were pre-specified (Supplemental Table 1). Some variables were simplified prior to the statistical analyses in order to reduce the number of values (degrees of freedom) in the model and hence the risk of overfitting (see Harrell [2]). An appropriate power calculation was performed. The origin of each risk factor (either the PICANet or NCHDA dataset) is noted in Supplemental Table 1. Where both audits contained information on a particular risk factor, the most complete source was used or, in the case of ethnicity, a combination of the two sources (see Supplemental Table 1).

Non-medical variables

Deprivation was based on the residential address at admission and defined using quintiles of the English Index of Multiple Deprivation 2010 (IMD), which is calculated at the level of small (~ 1,500 people) geographic areas covering England [3].

Ethnicity information is recorded in both audits, with NCHDA using a bespoke classification scheme and PICANet using the Census 2001 classification used by the Office for National Statistics (ONS) [4]. PICANet was the primary source for our ethnicity variable due to its comparability with population statistics and was collapsed into seven groups to improve model stability: white, mixed, Asian, black, Chinese, other, and not stated. Where ethnic group was not available from PICANet, the NCHDA ethnic code was used to assign white, Asian or black ethnicity (which showed strong concordance across the two audits) but not to assign Chinese, other or mixed ethnicity (which showed poorer concordance) [5]. The most frequently recorded ethnic group was assigned to the child if they had multiple admission records.

Pre-procedure variables

Cardiac diagnoses and procedure information

Within the NCHDA dataset, each record (interventional procedure) can be described by up to 6 individual diagnostic International Paediatric and Congenital Cardiac Codes (IPCCCs). The combination of these can be mapped to 1 of 24 primary cardiac diagnoses using a hierarchical scheme developed by Brown *et al.* [6]. For the purposes of this study, this mapping scheme was implemented with two minor adjustments (see Supplemental Table 2): a new category of 'arrhythmia' was created (ranked 24th in the modified hierarchy) and the "miscellaneous congenital" diagnostic category was split into "major miscellaneous diagnoses" (ranked 9th in the modified hierarchy) and "minor miscellaneous diagnoses" (ranked 25th in the modified hierarchy).

To reduce the risk of overfitting in the model, we grouped the diagnostic categories into four cardiac diagnosis groups (see Supplemental Table 2): Hypoplastic left heart syndrome (HLHS); Functionally univentricular heart (UVH) or pulmonary atresia (PA) with an intact ventricular septum (IVS); Ventricular septal defect (VSD) and; "Other" (the remaining 22 diagnosis categories).
The choice of diagnosis group 'HLHS' reflects the body of literature related to 'inter-stage' deaths in this population. A separate group of 'UVH or PA+IVS' was chosen due to the high-risk nature of these conditions, which are often systemic-to-pulmonary arterial shunt dependent, with a view to distinguishing these from HLHS patients. Of the remaining cardiac diagnosis groups, we elected to review the VSD group separately as a recognizable bi-ventricular comparator group in order for us to evaluate the face validity of comparisons between HLHS or UVH/PA+IVS and the much larger, less homogeneous group of mainly biventricular diagnoses.

In addition to their overall primary cardiac diagnosis, each child was identified as having an acquired cardiac diagnosis if any of their records included an IPCCC diagnostic code mapping to this category, for example, ventricular dysfunction and ventricular hypoplasia. Some non-cardiac IPCCC diagnostic codes were identified as post-procedural morbidities (see below and Supplemental Table 4 for details).

The index (specific) procedures were aggregated into three groups (see above for mappings): Palliative (e.g. Norwood, bidirectional cavopulmonary shunt, arterial shunt), Corrective (e.g. truncus arteriosus repair, atrioventricular septal defect complete repair, tetralogy repair) or "Ungrouped" (if no specific procedure was assigned).

Non-cardiac diagnosis and co-morbidity information

Non-cardiac diagnosis and co-morbidity information was primarily sourced from PICANet, in which any given PICU admission can record up to 24 clinical Read codes [7]. As 3,325 discrete Read codes were present in the dataset, we developed a new scheme linking each code to 1 of 16 system-based categories (see Supplemental Table 3).

Congenital anomaly: If any PICU admission within the index admission contained a Read code for a congenital anomaly then the child was assigned this attribute. Many of these children had Downs syndrome, however other syndromes that are often associated with cardiac defects were also often represented, including DiGeorge syndrome (22q11 deletion). Non-syndromic congenital anomalies were also described, including urogenital/renal malformations, tracheal/trachea-oesophageal malformations, vision/hearing deficits and exomphalos/gastrointestinal malformations. These are major anomalies, some requiring neonatal surgery, and their impact is likely to be life-long.

Neurodevelopmental condition: If any Read code within the index admission was linked to the neurodevelopmental category then the child was assigned this attribute. These comprised a range acquired and congenital conditions most with global effects on the central nervous system and likely to have lifelong impact, the most common examples being (in order of decreasing frequency): epilepsy/seizures, developmental delay, sleep apnoea, hydrocephalus, retinopathy of prematurity, stroke, hemiparesis/hemiplegia, anoxic encephalopathy, cerebral venous sinus thrombosis and cerebral palsy. Within the analysis dataset, n= 95 children were coded as having developmental delay, of which n=64 had no other neurodevelopmental problem coded. On closer inspection of these n=64 children, 41% had a congenital anomaly or syndrome (e.g. Down's syndrome, DiGeorge syndrome, craniosynostosis, microcephaly) or a comorbidity (e.g. meningitis, preterm birth, brain injury) that could be associated with developmental delay. The remaining 59% had no record of a comorbidity associated with developmental delay but since coding is not comprehensive (e.g. preterm children were not always recorded as such), it is possible that these are nonetheless correct and were used where a degree of neurodevelopmental delay was evident even within infancy.

Prematurity: Finally, a child was assigned the attribute of prematurity (<37 completed weeks gestation) if they had a Read code for this in any admission.

Additional pre-procedure factors

Additional pre-procedure factors considered on the basis of potential clinical relevance were: Gender; Age at procedure; Weight-for-age at procedure (calculated using WHO reference standards [7]); Antenatal diagnosis, Clinical deterioration prior to the index intervention (assigned if the index admission or any prior PICU admissions were urgent and unplanned).

<u>Post-procedure variables</u>

Post-procedure patient variables known at hospital discharge were: Length of stay for the index admission; Requirement for renal support (including dialysis and haemofiltration) or extracorporeal

membrane oxygenation support (ECMO) during the index admission; Any adverse ICU events during the index admission (assigned if any PICU admission contained a Read code for: collapse or cardiac arrest, acquired injury or complications, or a non-cardiac operation (categories 9-11 in Supplemental Table 3)); Whether the index admission was associated with any acquired co-morbidities (categories 1-8 in Supplemental Table 3); Whether the index admission was associated with any post-procedural morbidity (Supplemental Table 4); Any catheter or surgical procedures performed during the index admission in addition to the index procedure (either before or after the index procedure).

Table S1: Summary of candidate patient risk factors

Descriptions of the pre-specified potential risk factors considered in the analysis, including whether a given variable relates to the index procedure, index admission or is a characteristic of the child, its possible values and the source dataset (PICANet or NCHDA). All variables would be known at the point of discharge and are grouped according to whether they are a non-medical, pre-procedure or post- procedure factor.

Pre-specified candidate risk factor	Description	Variable level	Values	Source dataset
Non-medical				
Deprivation	Quintiles of the English Index of Multiple Deprivation 2010 [2] as recorded for the index procedure.	Child	1-5 (1 most deprived, 5 least deprived)	NCHDA
Ethnicity	Census 2001 classification used by ONS [3], collapsed into seven groups. Most frequently recorded ethnic group if child had multiple records.	Child	White, Mixed, Asian, Black, Chinese, Other, Not stated	PICANet[†]
Pre-procedure				
Cardiac diagnosis group	Aggregated groupings of the cardiac diagnosis categories assigned through application of a modified version of the hierarchical mapping scheme developed by Brown *et al.*[5] across all cardiac records for a child (see Table A2).	Child	VSD, HLHS, UVH/PA+IVS, Other	NCHDA
Acquired cardiac diagnosis	Assigned if any cardiac record in the index admission had an IPCCC diagnostic code corresponding to the acquired cardiac diagnosis category (see Table A2).	Index admission	Yes, No	NCHDA
Specific procedure group	Aggregated groupings of the index specific procedures assigned through application of the NCHDA specific procedure hierarchy across all interventions within the index admission (see Appendix 1).	Index procedure	Corrective, palliative, ungrouped	NCHDA
Congenital anomaly	Assigned if any PICU record during the index admission contained a Read code corresponding to the congenital anomaly category.	Index admission	Yes, No,	PICANet
Neurodevelopment condition	Assigned if any PICU record during the index admission contained a Read code corresponding to the neurodevelopmental category.	Index admission	Yes, No	PICANet
Prematurity	Assigned if any PICU record for the child contained a Read code corresponding to prematurity or preterm birth (see Table A3).	Child	Yes, No, Missing	PICANet
Gender	Most frequently occurring gender across all cardiac records for a patient (or gender at index procedure if tied).	Child	Male, Female	NCHDA
Age at index procedure	Age recorded in cardiac record for the index procedure.	Index procedure	Continuous variable	NCHDA

Weight-for-age z-score	Standardised weight-for-age at index procedure, calculated from index procedure weight and age using WHO reference standards [6].	Index procedure	Continuous variable	NCHDA
Antenatal diagnosis	Assigned if coded in any cardiac record for the child.	Child	Yes, No, Missing	NCHDA
Clinical deterioration	Assigned if any PICU admissions prior to discharge from the index admission were urgent and unplanned.	Index admission	Yes, No	PICANet
Post-procedure				
Length of stay	The length in days of the continuous period as in-patient within a specialist paediatric cardiac hospital or PICU that surrounds a child's first interventional cardiac procedure in infancy.	Index admission	Continuous variable	NCHDA & PICANet
Need for renal support	Assigned if any PICU record within the index admission indicated renal support was required (including dialysis and haemofiltration).	Index admission	Yes, No, Missing	PICANet
Need for ECMO	Assigned if any PICU record within the index admission indicated ECMO support was required.	Index admission	Yes, No, Missing	PICANet
Acquired comorbidity	Assigned if any PICU record during the index admission contained a Read code identified an acquired condition (categories 1-8 in Table A3).	Index admission	Yes, No, Missing	PICANet
Adverse event in PICU	Assigned if any PICU record during the index admission contained a Read code corresponding to collapse or cardiac arrest, acquired injury or complications, or a non-cardiac operation in PICU (categories 9-11 in Table A3).	Index admission	Yes, No, Missing	PICANet
Post-procedural morbidity	Assigned if any cardiac record during the index admission contained an IPCCC code identified as a post-procedural morbidity (see Table A4).	Index admission	Yes, No	NCHDA
Additional surgical procedures	Assigned if any surgical procedures were performed during the index admission in addition to the index procedure (before or after).	Index admission	Yes, No	NCHDA
Additional catheter procedures	Assigned if any catheter procedures were performed during the index admission in addition to the index procedure (before or after).	Index admission	Yes, No	NCHDA

ONS = Office for National Statistics; PICU = paediatric intensive care unit; NCHDA = National Congenital Heart Disease Audit; PICANet = Paediatric Intensive Care Audit Network; IPCCC = International Paediatric and Congenital Cardiac Code; ECMO = extracorporeal membrane oxygenation; HLHS = hypoplastic left heart syndrome; UVH = functionally univentricular heart; PA+IVS = pulmonary atresia with intact ventricular septum; VSD = Ventricular septal defect.

[†] Where ethnic group was not available from PICANet, the NCHDA ethnic code was used to assign white, Asian or black ethnicity (which showed strong concordance across the two audits) but not to assign Chinese, other or mixed ethnicity (which showed poorer concordance).

Table S2: Primary cardiac diagnosis hierarchy and collapsed groupings
The hierarchy used to assign a primary cardiac diagnosis category to each child in the analysis dataset (modified from scheme developed by Brown *et al.*[5]), along with the mappings from diagnosis category to cardiac diagnosis group (the candidate patient risk factor used in the analyses).

Primary cardiac diagnosis category	**Hierarchy rank**[†]	**Cardiac diagnosis group**[††]
Hypoplastic left heart syndrome	1	HLHS
Functionally univentricular heart	2	UVH or PA+IVS
Common arterial trunk (truncus arteriosus)	3	Other
TGA + VSD/DORV-TGA type	4	Other
Interrupted aortic arch	5	Other
TGA (concordant AV and discordant VA connections) and intact ventricular septum	6	Other
PA with an intact ventricular septum	7	UVH or PA+IVS
Pulmonary atresia + VSD (including Fallot type)	8	Other
Miscellaneous congenital primary diagnoses	9	Other
Atrioventricular septal defect	10	Other
Fallot/DORV-Fallot type	11	Other
Aortic valve stenosis (isolated)	12	Other
Tricuspid valve abnormality (including Ebstein's)	13	Other
Mitral valve abnormality (including supravalvar, subvalvar)	14	Other
Totally anomalous pulmonary venous connection	15	Other
Aortic arch obstruction +/- VSD/ASD	16	Other
Pulmonary stenosis	17	Other
Subaortic stenosis (isolated)	18	Other
Aortic regurgitation	19	Other
Isolated VSD +/- ASD +/- PDA	20	VSD
Interatrial communication (ASD)	21	Other
Patent ductus arteriosus (PDA)	22	Other
Acquired non-congenital heart disease	23	Other
Arrhythmia	24	Other
Miscellaneous congenital terms	25	Other
Noncardiac or uncoded diagnosis	26	Other

TGA = transposition of the great arteries; VSD = ventricular septal defect; DORV = double outlet right ventricle; AV = atrioventricular; VA = ventriculoarterial; ASD = atrial septal defect.
[†] The hierarchical scheme developed by Brown *et al.*[5], modified for the purposes of this study with two minor adjustments: creating a new category of 'arrhythmia' and splitting the original "miscellaneous congenital" diagnostic category into "major miscellaneous diagnoses" and "minor miscellaneous diagnoses".
[††] For reasons of model reliability and validity of predictive discrimination, we grouped the diagnostic categories into four cardiac diagnosis groups considered clinically meaningful to the study focus: Hypoplastic left heart syndrome (HLHS); Functionally univentricular heart (UVH) or pulmonary atresia with an intact ventricular septum (PA+IVS); Ventricular septal defect (VSD); "Other".

Table S3: Coding scheme for non-cardiac diagnoses and comorbidities

A new scheme developed and implemented in this work to link each Read code [6] to at most 1 of 16 system-based categories. Given the large number of codes, we present exemplars within each of categories rather than the extensive list: further details are available from authors on request. We note that **c**ongenital heart disease/cardiac procedure Read codes in PICANet were not included as a category as they were inconsistently recorded. Cardiac diagnostic and procedure codes for the analysis were derived from the NCHDA dataset only.

	Category	**Number of codes**	**Examples of included clinical conditions**
1	Acquired endocrine, nutritional and metabolic conditions	82	Diabetes mellitus; alpha-1-antitrypsin disorder; rickets; failure to thrive
2	Acquired gastrointestinal (digestive system) conditions	166	Gastritis; constipation; liver failure; hernia; jaundice; perianal fistula
3	Acquired infections (in any system except respiratory infections which are included within the category for acquired respiratory system conditions)	144	Cytomegalovirus; E coli infection; MRSA; meningitis; otitis media; wound abscess
4	Conditions related to haematology, oncology or immunology, which may be acquired or congenital.	97	Acute myeloid leukaemia; Factor VIII deficiency; teratoma; sickle cell anaemia
5	Acquired musculoskeletal, connective tissue or skin conditions	29	Atopic dermatitis; scoliosis; systemic onset juvenile chronic arthritis
6	Acquired genitourinary system conditions	42	Acute renal failure; hydronephrosis; rectovaginal fistula
7	Acquired respiratory system conditions	229	Stridor; asthma; bronchiolitis; pulmonary oedema; pneumonia; haemothorax
8	Conditions originating in or specific to the perinatal period	109	Birth asphyxia; gestational diabetes; meconium ileus; shoulder dystocia
9	Non-cardiac intervention or operation, excluding procedures that are part of routine intensive care	478	Adenoidectomy; bone marrow transplant; splenectomy; plication of diaphragm
10	Collapse or cardiac arrest	14	Cardiac arrest; hypovolaemic shock; fainting; respiratory arrest
11	Acquired injury or complication of surgery/other condition	145	Brain injury; anaesthetic shock; closed rib fracture; vocal cord palsy; limb ischaemia
12	Congenital anomalies (all severity)	342	Trisomy 18; Pierre-Robin syndrome; cleft palate; club foot; oesophageal atresia
13	Neurological or neurodevelopmental conditions – may be congenital or acquired	126	Cataract, cerebral palsy; autistic spectrum disorder; epilepsy; optic atrophy
14	Additional codes which are non-specific or do not have standardised coding	429	e.g. family history of hypothyroidism; child in foster care; central line feeding;
15	Premature birth (<37 completed weeks gestation)	11	Baby born premature/very premature
16	Supportive procedures	7	Extracorporeal membrane oxygenation (ECMO); ventricular assist device

Table S4: Post-procedural morbidities

Some non-cardiac diagnostic International Paediatric and Congenital Cardiac Codes (IPCCC) were identified as post-procedural morbidities as set out in the table below. If any NCHDA record during the index admission period for a child contained an IPCCC corresponding to a post-procedural morbidity then their index admission was flagged as having a post-procedural morbidity.

IPCCC identified as post-procedural morbidities
160101. Pneumothorax
160104. Pleural effusion
160107. Chylothorax
100811. Postpericardiotomy syndrome
110412. Junctional ectopic tachycardia (His bundle): post-op
110617. Postprocedural complete AV block
110632. Procedure related complete AV block requiring temporary pacing
110633. Procedure related complete AV block requiring permanent pacemaker system
150001. Cardiac arrest during procedure
150002. Cardiac arrest following procedure
150003. Postprocedural low cardiac output
150005. Myocardial infarction following procedure
150009. Postprocedural requirement for mechanical circulatory support
150030. Postprocedural hypovolaemia
150200. Postprocedural haemorrhage
150203. Postprocedural coagulopathy
150207. Postprocedural haemolysis
150265. Postprocedural haemorrhage requiring reoperation
150300. Median sternotomy complication
150303. Infection of median sternotomy wound
150308. Dehiscence of median sternotomy wound
150315. Keloid-hypertrophic scar of median sternotomy wound
150330. Lateral thoracotomy complication
150332. Infection of lateral thoracotomy wound
150350. Wound infection
150351. Wound dehiscence
150352. Mediastinitis
152420. Postprocedural femoral arterial complication
154306. Unplanned reoperation during current admission
155000. Cardiac catheterisation complication
155001. Intramyocardial injection of contrast medium
155003. Perforation of cardiac chamber-vessel during cardiac catheterisation
155011. Lost pulse after cardiac catheterisation
155030. Equipment problem during cardiac catheterisation
155037. Embolisation of catheter introduced device
155040. Failed attempt to implant coil-device during transcatheter intervention
155060. Complication involving device implantation
155070. Complication involving stent
155702. Extracorporeal Membrane Oxygenation (ECMO) circuit complication
155703. Ventricular assist device complication
155721. Intraaortic balloon pump (IABP) complication
155801. Complication related to echocardiographic procedure
155900. Medication related complication or error
156002. Arrhythmia following procedure
156738. Wound related complication
157700. Cardiopulmonary bypass complication
158000. General systemic complication of cardiac procedure
158001. Postprocedural metabolic derangement

158005. Postprocedural septicaemia
158006. Capillary leak syndrome
158015. Postprocedural acidosis
158016. Multiple organ dysfunction syndrome (MODS)
158019. Systemic inflammatory response syndrome (SIRS)
158020. Respiratory complication after cardiac procedure
158021. Postprocedural pulmonary infection
158022. Postprocedural pulmonary hypertensive crises
158029. Postprocedural Acute Respiratory Distress Syndrome (ARDS)
158031. Postprocedural lung collapse (atelectasis)
158032. Postprocedural requirement for mechanical respiratory support > 7 days
158033. Postprocedural requirement for reintubation
158050. Postprocedural pleural effusion
158051. Postprocedural right pleural effusion
158052. Postprocedural left pleural effusion
158055. Postprocedural chylothorax
158056. Postprocedural haemothorax
158061. Pleural effusion requiring drainage
158062. Postprocedural pneumothorax
158070. Postprocedural complication involving tracheo-bronchial tree
158086. Postprocedural requirement for tracheostomy
158087. Postprocedural bronchial compression
158090. Intraprocedural phrenic nerve injury (paralysed diaphragm)
158093. Intraprocedural recurrent laryngeal nerve injury (palsy)
158094. Postprocedural Horner’s syndrome
158200. Postprocedural renal failure
158206. Renal failure requiring temporary dialysis
158207. Renal failure requiring permanent dialysis
158221. Postprocedural gastrointestinal bleeding
158223. Postprocedural inability to sustain gastric feeding
158228. Postprocedural intestinal obstruction
158229. Postprocedural peritonitis
158230. Postprocedural necrotising enterocolitis
158232. Pseudomembranous colitis
158233. Postprocedural protein losing enteropathy
158238. Postprocedural feeding difficulties
158243. Postprocedural hepatic impairment
158247. Postprocedural acute pancreatitis
158250. Neurological complication after cardiac procedure
158251. Postprocedural generalised seizures
158253. Postprocedural temporary neurological impairment
158257. Postprocedural permanent neurological impairment
158264. Postprocedural brain death
158266. Postprocedural cerebral abscess
158267. Postprocedural new onset seizures
158268. Postprocedural neurological impairment persisting at discharge
158281. Postprocedural cerebral abnormality on imaging
158800. Vascular line (access) related complication
159001. Postprocedural complication
159014. Procedure related complication
159020. Complication during period of anaesthetic care
165020. Complication following respiratory tract stent implantation
101824. Postmyocardial infarction complication

Data S2. Supplemental Results

Summary of results from descriptive and univariate analyses

Ethnic group was not available from PICANet for 1,703 children in the final dataset. Of these, the NCHDA ethnic code was used to assign white (n=1,001), Asian (n=243) or black (n=113). Excluding records without PICANet-derived ethnicity from the analyses did not significantly affect the results. A total of 528 children had missing or anomalous weight-for-age (assumed erroneous and treated as missing). The variable with the markedly highest level of missing data (n=2,101 (27.5%)) was prematurity (yes/no): sensitivity analysis comparing models with and without prematurity showed a marginally better fit if it was included and very little difference in the odds ratio coefficients for all other factors.

The observed numbers of patients and rate of adverse events and fatal adverse events only for all candidate risk factors are shown below along with the results of the univariate analysis.

The relationship between length of stay and both outcomes was non-linear and the fractional polynomial transformation was used in the subsequent risk model development analyses, whilst for age we used a log transformation. The relationship between weight-for-age and each outcome did not depart significantly from linearity. We used a multi-degree of freedom test for ethnicity, with results for fatal adverse events and all adverse events of p = 0.003 and p = 0.0001 respectively.

Patient variable		Num. (%) overall	Fatal adverse events only		All adverse events	
			Num. (%)	Univariate OR (p-value)	Num. (%)	Univariate OR (p-value)
Non-medical						
Deprivation						
	1 – most	2,205 (28.9)	79 (3.6)	1	157 (7.1)	1
	2	1,563 (20.5)	51 (3.3)	0.91 (0.60)	104 (6.7)	0.93 (0.58)
	3	1,242 (16.3)	41 (3.3)	0.92 (0.66)	77 (6.2)	0.86 (0.30)
	4	1,078 (14.1)	38 (3.5)	0.98 (0.93)	79 (7.3)	1.03 (0.83)
	5 – least	1,085 (14.2)	23 (2.1)	0.58 (0.02)	64 (5.9)	0.82 (0.19)
	Missing	470 (6.2)	-	-	-	-
Ethnicity						
	White	5,728 (75.0)	166 (2.9)	1	348 (6.1)	1
	Mixed	196 (2.6)	4 (2.0)	0.70 (0.48)	9 (4.6)	0.74 (0.39)
	Asian	867 (11.3)	38 (4.4)	1.54 (0.02)	73 (8.4)	1.42 (< 0.01)
	Black	345 (4.5)	12 (3.5)	1.21 (0.54)	34 (9.9)	1.69 (< 0.01)
	Chinese	28 (0.4)	3 (3.6)	1.24 (0.83)	1 (3.6)	0.57 (0.59)
	Other	133 (1.7)	12 (9.0)	3.32 (< 0.001)	19 (14.3)	2.58 (< 0.001)
	Not stated	346 (4.5)	13 (3.8)	1.31 (0.36)	30 (8.7)	1.47 (0.05)
Pre-operative						
Cardiac diagnosis group						
	VSD	1348 (17.6)	25 (1.9)	1	60 (4.5)	1
	HLHS	390 (5.1)	48 (12.3)	7.43 (< 0.001)	70 (18.0)	4.70 (< 0.001)
	UVH/PA	531 (7.0)	41 (7.7)	4.43 (< 0.001)	73 (13.8)	3.42 (< 0.001)
	Other	5374 (70.3)	132 (2.5)	1.33 (0.19)	311 (5.8)	1.32 (0.06)
Acquired diagnosis						
	Yes	479 (6.3)	25 (5.2)	1.73 (0.01)	57 (11.9)	1.98 (< 0.001)
	No	7164 (93.7)	221 (3.1)	1	457 (6.4)	1
Specific procedure group						

Corrective	4973 (65.1)	86 (1.7)	1	219 (4.4)	1
Palliative	1629 (21.3)	119 (7.3)	4.48 (< 0.001)	205 (12.6)	3.13 (< 0.001)
Ungrouped	1041 (13.6)	41 (3.9)	2.33 (< 0.001)	90 (8.7)	2.05 (< 0.001)
Congenital anomaly					
Yes	1608 (21.0)	90 (5.6)	2.23 (< 0.001)	209 (13.0)	2.81 (< 0.001)
No	6035 (79.0)	156 (2.6)	1	305 (5.1)	1
Neurodevelopment condition					
Yes	307 (4.0)	27 (8.8)	3.13 (< 0.001)	75 (24.4)	5.08 (< 0.001)
No	7336 (96.0)	219 (3.0)	1	439 (6.0)	1
Prematurity					
Yes	828 (10.8)	44 (5.3)	1.59 (< 0.01)	93 (11.2)	1.63 (< 0.001)
No	4714 (61.7)	161 (3.4)	1	340 (7.2)	1
Missing	2101 (27.5)	-	-	-	-
Gender					
Male	4232 (55.4)	114 (3.4)	1	302 (7.1)	1
Female	3410 (44.6)	102 (3.0)	0.88 (0.31)	212 (6.2)	0.86 (0.11)
Not known	1 (0.0)	-	-	-	-
Age at index procedure (continuous)	Med. 64 days IQR (11,153) Missing = 0	Not shown	0.99 (< 0.001)	Not shown	0.99 (< 0.001)
Weight-for-age Z-score (continuous)	Med. -1.7 IQR (-2.8,-0.6) Missing = 528	Not shown	1.02 (0.69) *	Not shown	0.95 (0.13) *
Antenatal diagnosis					
Yes	2146 (8.1)	105 (4.9)	2.04 (< 0.001)	219 (10.2)	2.03 (< 0.001)
No	5046 (66.0)	124 (2.5)	1	268 (5.3)	1
Missing	451 (5.9)	-	-	-	-
Clinical deterioration					
Yes	1469 (19.2)	85 (5.8)	2.29 (< 0.001)	154 (10.5)	1.89 (< 0.001)
No	6174 (80.8)	161 (2.6)	1	36 (0.8)	1
Post-operative					
Length of stay (continuous)	Med. 10 days IQR (7, 17) Missing = 0	Not shown	(< 0.001)	Not shown	(< 0.001)
Additional surgical procedures					
Yes	414 (5.4)	23 (5.6)	1.85 (< 0.01)	54 (13.0)	2.21 (< 0.001)
No	7229 (94.6)	223 (3.1)	1	460 (6.4)	1
Additional catheter procedures					
Yes	577 (7.6)	16 (2.8)	0.85 (0.53)	32 (5.6)	0.80 (0.24)
No	7066 (92.4)	230 (3.3)	1	482 (6.8)	1
Need for renal support					
Yes	522 (6.8)	31 (5.9)	1.99 (<0.01)	57 (10.9)	1.82 (< 0.001)
No	6721 (87.9)	207 (3.1)	1	425 (6.3)	1
Missing	400 (5.2)	-	-	-	-
Need for ECMO					
Yes	64 (0.8)	5 (7.8)	2.53 (0.05)	9 (14.1)	2.32 (0.02)
No	7290 (95.4)	236 (3.2)	1	480 (6.6)	1
Missing	289 (3.8)	-	-	-	-
Acquired comorbidity					
Yes	1481 (19.4)	84 (5.7)	2.19 (< 0.001)	165 (11.1)	2.15 (< 0.001)
No	5918 (77.4)	158 (2.7)	1	326 (5.5)	1
Missing	244 (3.2)	-	-	-	-

Adverse event in PICU						
	Yes	634 (8.3)	47 (7.4)	2.70 (< 0.001)	89 (14.0)	2.58 (< 0.001)
	No	6765 (88.5)	195 (2.9)	1	402 (5.9)	1
	Missing	244 (3.2)	-	-	-	-
Post-op morbidity						
	Yes	113 (1.5)	9 (8.0)	2.66 (< 0.01)	17 (15.0)	2.51 (< 0.01)
	No	7530 (98.5)	237 (3.2)	1	497 (6.6)	1

PICU = paediatric intensive care unit; IQR = interquartile range; ECMO = extracorporeal membrane oxygenation; HLHS = hypoplastic left heart syndrome; UVH = functionally univentricular heart; PA = pulmonary atresia; VSD = Ventricular septal defect.
* Weight-for-age z-score (continuous) showed no univariate association with either outcome but was nonetheless taken forward to the multivariable analyses.

Details regarding the categorization of age at procedure, weight-for-age z-score and length of stay are presented below: these were initially continuous variables that were categorised due to considerations of potential model usability and clinical face validity. The observed numbers of patients and rate of fatal adverse events and all adverse events in the dataset in each category are shown for each categorized variable.

	Num. (%) overall	**Num. (%) Fatal adverse events only**	**Num. (%) All adverse events**
Age at index procedure			
> 3 months old	3202 (41.9)	55 (1.7)	129 (4.0)
1-2 months old	1427 (18.7)	45 (3.2)	110 (7.7)
10-30 days	1114 (14.6)	43 (3.9)	90 (8.1)
0-10 days old	1900 (24.9)	103 (5.4)	185 (9.7)
Weight-for-age z-score			
>-2SD	4064 (53.2)	128 (3.1)	243 (6.0)
-2 to -4 SD	2467 (32.3)	71 (2.9)	168 (6.8)
<-4SD	584 (7.6)	19 (3.3)	50 (8.6)
Missing	528 (6.9)	28 (5.3)	53 (10.0)
Length of stay			
0-7 days	2564 (33.5)	35 (1.4)	84 (3.3)
7-30 days	4327 (56.6)	146 (3.4)	302 (7.0)
> 1 month	752 (9.8)	65 (8.6)	128 (17.0)

Multiple imputation results

For both outcomes there was very little difference in the significance of risk factors between the imputed data sets; there was a clear set of significant factors ($p < 0.01$) with an inclusion frequency of 100% and a clear set of factors that did not reach statistical significance with an inclusion frequency of 0%. For fatal adverse events only there were two factors (prematurity and acquired diagnosis) and for all adverse events three factors (prematurity, antenatal diagnosis and clinical deterioration) that were borderline significant, with an inclusion frequency of approximately 50%. These borderline risk factors were investigated further along with the set of significant risk factors and only prematurity remained statistically significant. The Multiple Imputation suite of programs in Stata was used to conduct the imputation analysis.

Continuous logistic regression models

Details of the continuous regression model for fatal adverse events only (death within 1-year following discharge from the index admission and not during a planned admission) are shown below. For each patient variable the number (percentage) of fatal adverse events, multivariable odds ratios, standard errors and 95% confidence intervals are presented and the reference category indicated. The overall number (percentage) of patients within each category for a given patient variable is also noted. HLHS = hypoplastic left heart syndrome; UVH = functionally univentricular heart; PA+IVS = pulmonary atresia with an intact ventricular septum; VSD = ventricular septal defect.
† Log transformation ‡Fractional polynomial transformation.

Patient variable	Overall number (%)	Number (%) fatal adverse events	OR	S.E.	95% CI	
Ethnicity						
White	5,728 (75.0)	166 (2.9)	Reference category			
Mixed	196 (2.6)	4 (2.0)	0.69	0.36	0.25	1.91
Asian	867 (11.3)	38 (4.4)	1.38	0.26	0.95	2.01
Black	345 (4.5)	12 (3.5)	0.98	0.31	0.53	1.83
Chinese	28 (0.4)	3 (3.6)	1.61	1.68	0.21	12.46
Other	133 (1.7)	12 (9.0)	2.97	0.99	1.54	5.73
Not stated	346 (4.5)	13 (3.8)	1.49	0.46	0.82	2.71
Cardiac diagnosis group						
VSD	1348 (17.6)	25 (1.9)	Reference category			
HLHS	390 (5.1)	48 (12.3)	2.70	0.86	1.45	5.04
UVH or PA+IVS	531 (7.0)	41 (7.7)	2.29	0.68	1.28	4.11
Other	5374 (70.3)	132 (2.5)	1.14	0.27	0.72	1.80
Specific procedure group						
Corrective	4973 (65.1)	86 (1.7)	Reference category			
Palliative	1629 (21.3)	119 (7.3)	2.15	0.39	1.51	3.06
Ungrouped	1041 (13.6)	41 (3.9)	1.78	0.36	1.20	2.64
Congenital anomaly						
No	6035 (79.0)	156 (2.6)	Reference category			
Yes	1608 (21.0)	90 (5.6)	2.29	0.35	1.70	3.09
Prematurity						
No	4714 (61.7)	161 (3.4)	Reference category			
Yes	828 (10.8)	44 (5.3)	1.55	0.28	1.09	2.20
Clinical deterioration						
No	6174 (80.8)	161 (2.6)	Reference category			
Yes	1469 (19.2)	85 (5.8)	1.59	0.23	1.19	2.12
Age at index procedure†	-	-	0.77	0.05	0.68	0.87
Weight-for-age z-score	-	-	0.83	0.05	0.74	0.92
Index length of stay‡						
First degree of polynomial	-	-	3239	4361	231	45332
Second degree of polynomial	-	-	0.00	0.00	0.00	0.00

Details of the continuous regression model for all adverse events (either death or an emergency unplanned readmission to PICU within 1-year following discharge from the index admission) are shown below. For each patient variable the number (percentage) of adverse events, the multivariable odds ratios, standard errors and 95% confidence intervals are presented and the reference category indicated. The overall number (percentage) of patients within each category for a given patient variable is also noted.
HLHS = hypoplastic left heart syndrome; UVH = functionally univentricular heart; PA+IVS = pulmonary atresia with an intact ventricular septum; VSD = ventricular septal defect.
† Log transformation ‡Fractional polynomial transformation.

Patient variable	Overall number (%)	Number (%) adverse events	OR	S.E.	95% CI	
Ethnicity						
White	5,728 (75.0)	348 (6.1)	Reference category			
Mixed	196 (2.6)	9 (4.6)	0.64	0.23	0.32	1.31
Asian	867 (11.3)	73 (8.4)	1.22	0.18	0.92	1.62
Black	345 (4.5)	34 (9.9)	1.40	0.29	0.94	2.09
Chinese	28 (0.4)	1 (3.6)	0.70	0.72	0.09	5.32
Other	133 (1.7)	19 (14.3)	2.52	0.68	1.48	4.29
Not stated	346 (4.5)	30 (8.7)	1.71	0.36	1.13	2.58
Cardiac diagnosis group						
VSD	1348 (17.6)	60 (4.5)	Reference category			
HLHS	390 (5.1)	70 (18.0)	2.08	0.49	1.31	3.30
UVH or PA+IVS	531 (7.0)	73 (13.8)	2.06	0.44	1.35	3.14
Other	5374 (70.3)	311 (5.8)	1.18	0.19	0.87	1.61
Specific procedure group						
Corrective	4973 (65.1)	219 (4.4)	Reference category			
Palliative	1629 (21.3)	205 (12.6)	1.72	0.22	1.34	2.22
Ungrouped	1041 (13.6)	90 (8.7)	1.62	0.22	1.24	2.13
Congenital anomaly						
No	6035 (79.0)	305 (5.1)	Reference category			
Yes	1608 (21.0)	209 (13.0)	2.62	0.28	2.12	3.24
Neurodevelopment condition						
No	7336 (96.0)	439 (6.0)	Reference category			
Yes	307 (4.0)	75 (24.4)	2.71	0.43	1.99	3.69
Prematurity						
No	4714 (61.7)	340 (7.2)	Reference category			
Yes	828 (10.8)	93 (11.2)	1.50	0.20	1.15	1.95
Acquired diagnosis						
No	7164 (93.7)	457 (6.4)	Reference category			
Yes	479 (6.3)	57 (11.9)	1.76	0.28	1.28	2.41
Age at index procedure†						
	-	-	0.77	0.03	0.70	0.83
Weight-for-age z-score						
	-	-	0.83	0.03	0.77	0.90
Index length of stay‡						
First degree of polynomial	-	-	2254	2151	347	14633
Second degree of polynomial	-	-	0.00	0.00	0.00	0.00

Supplemental References

1. IPCCC (2012) International Paediatric and Congenital Cardiac Code (IPCCC) Home Page. Available:www.ipccc.net. Accessed 12 April 2012. 2. Harrell FE, Lee KL, Califf RM, Pryor DB, Rosati RA (1984) Regression modelling strategies for improved prognostic prediction. Stat Med 3: 143–152.

3. LHO (2011) English Indices of Deprivation 2010 - deprivation category lookups and average scores for higher geographies. Available:http://www.apho.org.uk/resource/view.aspx?RID=111277. Accessed 13 February 2015.

4. Office for National Statistics (2011) Guidance and methodology: Ethnic group. Available:http://ons.gov.uk/ons/guide-method/measuring-equality/equality/ethnic-nat-identity-religion/ethnic-group/index.html#1. Accessed 13 February 2015.

5. Brown K, Wray J, Knowles R, Crowe S, Tregay J, et al. (2015) Project grant report: Infant deaths in the UK community following successful cardiac surgery - building the evidence base for optimal surveillance.

6. Brown KL, Crowe S, Pagel C, Bull C, Muthialu N, et al. (2013) Use of diagnostic information submitted to the United Kingdom Central Cardiac Audit Database: development of categorisation and allocation algorithms. Cardiol Young 23: 491–498. doi:10.1017/S1047951112001369.

7. Health and Social Care Information Centre (n.d.) Read codes. Available:https://isd.hscic.gov.uk/trud3/user/guest/group/0/home. Accessed 18 December 2014.