ORIGINAL RESEARCH

Death and Emergency Readmission of Infants Discharged After Interventions for Congenital Heart Disease: A National Study of 7643 Infants to Inform Service Improvement

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***Background*—**Improvements in hospital-based care have reduced early mortality in congenital heart disease. Later adverse outcomes may be reducible by focusing on care at or after discharge. We aimed to identify risk factors for such events within 1 year of discharge after intervention in infancy and, separately, to identify subgroups that might benefit from different forms of intervention.

***Methods and Results*—**Cardiac procedures performed in infants between 2005 and 2010 in England and Wales from the UK National Congenital Heart Disease Audit were linked to intensive care records. Among 7976 infants, 333 (4.2%) died before discharge. Of 7643 infants discharged alive, 246 (3.2%) died outside the hospital or after an unplanned readmission to intensive care (risk factors were age, weight-for-age, cardiac procedure, cardiac diagnosis, congenital anomaly, preprocedural clinical deterioration, prematurity, ethnicity, and duration of initial admission; c-statistic 0.78 [0.75–0.82]). Of the 7643, 514 (6.7%) died outside the hospital or had an unplanned intensive care readmission (same risk factors but with neurodevelopmental condition and acquired cardiac diagnosis and without preprocedural deterioration; c-statistic 0.78 [0.75–0.80]). Classification and regression tree analysis were used to identify 6 subgroups stratified by the level (3–24%) and nature of risk for death outside the hospital or unplanned intensive care readmission based on neurodevelopmental condition, cardiac diagnosis, congenital anomaly, and duration of initial admission. An additional 115 patients died after planned intensive care admission (typically following elective surgery).

***Conclusions*—**Adverse outcomes in the year after discharge are of similar magnitude to in-hospital mortality, warrant service improvements, and are not confined to diagnostic groups currently targeted with enhanced monitoring. **(*J Am Heart Assoc*. 2016;5:e003369 doi: 10.1161/JAHA.116.003369)**

Key Words: congenital heart defects • health policy and outcomes research • pediatrics • risk model • risk stratification

The main focus in the audit of pediatric cardiac surgery has been operative mortality, expressed as either 30-day mortality[1] or mortality at hospital discharge.[2] These very early outcomes have improved significantly over time,[3,4] but while relevant to quality assurance, they cannot inform service improvements outside the hospital setting. There remains a significant risk of death or clinical deterioration following discharge after "successful" surgery. For instance, "interstage mortality" for infants with hypoplastic left heart syndrome (HLHS) was 12% within a recent multicenter trial.[5] Single-center reports indicate that home monitoring programs of enhanced postdischarge surveillance for HLHS reduce interstage mortality,[6–9] but this practice is not universally implemented[5] and local protocols vary.[10] Studies of postdischarge outcomes for congenital heart disease (CHD) other than HLHS are sparse,[11] and a greater understanding of the risk of adverse

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Accompanying Data S1, Tables S1 through S4, and Data S2 are available at http://jaha.ahajournals.org/content/5/5/e003369/DC1/embed/inline-supplementary-material-1.pdf

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outcomes after discharge among the broader patient population could usefully inform quality improvement efforts.

To this end, we undertook a national study of outcomes in the first year after discharge from hospital among infants undergoing intervention for CHD. Our first aim was to measure the rates of adverse outcomes at 1 year among this population and then identify patient-level factors independently associated with these outcomes. Our second, complementary aim was to identify groups of patients who might benefit from different interventions because of the differing nature and scale of risk that they face. The adverse events of interest to us were deaths in the community and any unplanned readmissions to intensive care, regardless of outcome, in the first year after discharge, because these are potentially avoidable through improved care at or after discharge. Deaths in the first year postdischarge that occurred after a planned readmission to intensive care (typically for elective surgery as part of a prospectively planned, staged treatment pathway) were not a focus of this work because they are less likely to be remediable through improvements to care at or after discharge.

This national study was possible because of the United Kingdom's unique combination of mandatory national audit data sets for pediatric cardiac procedures (the National Congenital Heart Disease Audit [NCHDA][12]) and pediatric intensive care unit (PICU) admissions (the Paediatric Intensive Care Audit Network [PICANet][13]), which is augmented in England and Wales with independently ascertained life status tracking.

Methods

Ethics

Approval was obtained from the London Central Research Ethics Committee (reference No. 12/LO/1398) and the National Health Service (NHS) Health Research Authority Confidentiality Advisory Group (reference No. ECC 6-02 (FT5)/2012). Requirement for consent was waived.

Constructing the Data Set for Analyses

Data sources and patient population

Two national audit data sets were used: NCHDA[12] and PICANet.[13] Data submission to each audit is mandatory, subject to external data validation,[14,15] and each audit has approval from the relevant regulatory authorities for use of patient identifiable data. The survival status of patients in NCHDA is independently verified for patients of English and Welsh centers by the UK Health and Social Care Information Centre by using their patients' unique identifier (NHS number).

All children who underwent their first interventional catheterization or cardiac surgery when younger than 1 year in the United Kingdom between January 1, 2005 and December 31, 2010 were identified in NCHDA (overseas patients without an NHS number were removed at this stage; patients treated in Northern Ireland and Scotland were later identified and excluded). Records within PICANet for these patients were then identified by a trusted third party using patient NHS number, and patients with record(s) in NHCDA but not in PICANet were removed and analyzed separately. Separate data extracts from each audit were provided to the study team, each with the same patient-level identifier (pseudonymized NHS number). A single patient potentially had multiple procedure-based records in the NCHDA extract and multiple admission-based records in the PICANet extract. The study team constructed a single patient-based analysis data set by linking events for the same patient using the patient-level identifier, including cardiac-related details and life status (NCHDA) and rich comorbidity and emergency PICU admission information (PICANet).

Defining the index admission and index procedure

The index admission for each child was defined as the continuous period as an inpatient within the pediatric cardiac center, including admission(s) to PICU, that included their first surgical procedure or their first definitive or initial staging interventional catheter procedure (see Data S1 for included catheterizations). This period defined the index length of stay (LOS). Within the NCHDA data set, each procedure is described based on up to 8 individual procedural International Paediatric and Congenital Cardiac Codes (IPCCCs).[16] An algorithm developed by the NCHDA Steering Committee defines the specific procedure undertaken, based on the combinations of IPCCCs recorded. These defined "specific procedures" are listed in hierarchical order with the Norwood operation at the top and, for surgery, ligation of patent ductus arteriosus (PDA) at the bottom, with interventional catheter procedures appearing below surgeries in the hierarchy (see Data S1 for further details). For children who underwent >1 procedure during their index admission, their index intervention was chosen to be the most complex according to this hierarchy.

Exclusions

Children who underwent only catheter procedure(s) listed as exclusions in Data S1, premature babies who had ligation of PDA only, and cardiac transplant patients were excluded from our analysis because they have their own discharge and follow-up care pathways. Patients treated in Northern Ireland and Scotland were also removed because they do not have verified life status.

Candidate Patient Risk Factors

Candidate nonmedical, preoperative and postoperative risk factors available in the patient-based analysis data set that would be known at the point of discharge were identified: these are provided in Table 1 (with further details regarding the definitions in Data S1 and Tables S1–S4). Each child's primary cardiac diagnosis was identified based on a hierarchical IPCCC coding map,[21] which also identified records where there was a concurrent acquired cardiac diagnosis. Other clinical information, including the presence of comorbid conditions and postoperative complications, was based on a mapping of Read codes.[22] Where both audits contained information on a particular risk factor, the most complete source was used. Clinical variables with multiple parameters were necessarily collapsed into broad groups before statistical analyses to reduce the degrees of freedom and, hence, the risk of overfitting.[23] Table 2 lists the diagnostic categories within each of the 4 primary cardiac groups used in the analyses.

Missing data

Where ethnic group was not available from PICANet, the NCHDA ethnic code was used to assign White, Asian, or Black

Table 1. Candidate Patient Risk Factors

Candidate Factors	Categories (or Examples)
Nonmedical factors	
Deprivation	English index of multiple deprivation[17]
Ethnicity	White, Mixed, Asian, Black, Chinese, "Other", not stated[18,19]
Preprocedural risk factors	
Primary cardiac diagnosis group	Hypoplastic left heart syndrome (HLHS), functionally univentricular heart (UVH) or pulmonary atresia with intact ventricular septum (PA+IVS), isolated ventricular septal defect (VSD) (a recognizable biventricular comparator group), "other" (all remaining primary diagnoses consisting of a broad range of biventricular conditions)
Presence of an acquired cardiac diagnosis	For example, acquired atrioventricular block, cardiomyopathy, myocardial ischemia, endocardial fibroelastosis
Index procedure group	Initial staged, definitive repair, "ungrouped"
Presence of a congenital anomaly	For example, Downs syndrome, DiGeorge syndrome (22q11 deletion), urogenital/renal malformations, tracheal/tracheaoesophageal malformations, vision/hearing deficits and exomphalos/gastrointestinal malformations
Presence of a neurodevelopmental condition	For example, epilepsy/seizures, developmental delay, sleep apnea, hydrocephalus, retinopathy of prematurity, stroke, hemiparesis/hemiplegia, anoxic encephalopathy, cerebral venous sinus thrombosis and cerebral palsy
Prematurity	<37 completed weeks' gestation
Sex	Male, female
Age at procedure	Age at index procedure
Weight-for-age at procedure	Calculated using World Health Organization reference standards[20]
Antenatal diagnosis	Antenatal diagnosis of congenital heart defect
Clinical deterioration prior to index intervention	Emergency admission to intensive care involving retrieval by specialist team
Postprocedural risk factors	
Index admission length of stay	Continuous period as an inpatient within a specialist paediatric cardiac hospital or PICU that surrounds a child's first interventional cardiac procedure in infancy
Receipt of renal support or extracorporeal life support during index admission	Including dialysis and hemofiltration
Any adverse PICU events during index admission	For example, collapse or cardiac arrest, acquired injury or complications, a noncardiac operation
Postprocedural morbidity during index admission	For example, postprocedural pneumothorax, mediastinitis, chylothorax, cardiac arrest after procedure
Acquired comorbidities during index admission	For example, meconium aspiration syndrome, gastritis, liver failure, pneumonia, *Clostridium difficile* infection
Any catheter or surgical procedures performed in addition to index procedure	Either before or after the index procedure and within the index admission

The candidate nonmedical, preoperative, and postoperative risk factors used in the analyses. These were all available in the patient-based analysis data set and would be known at the point of discharge. See Data S1 and Tables S1–S4 for further details. PICU indicates pediatric intensive care unit.

Table 2. Primary Cardiac Diagnosis Categories

Cardiac Diagnosis Group	Primary Cardiac Diagnosis Category
Hypoplastic left heart syndrome (HLHS)	HLHS
Functionally univentricular heart (UVH) or pulmonary atresia (PA) with an intact ventricular septum (IVS)	UVH; PA+IVS
Isolated ventricular septal defect (VSD)	Isolated VSD±interatrial communication (atrioventricular septal defect [ASD])±patent ductus arteriosus (PDA)
Other	Common arterial trunk (truncus arteriosus); transposition of the great arteries (TGA)+VSD/double outlet right ventricle (DORV)-TGA type; interrupted aortic arch; TGA (concordant atrioventricular and discordant ventriculoatrial connections) and intact ventricular septum; PA+VSD (including Fallot type); miscellaneous congenital primary diagnoses; ASD; Fallot/DORV-Fallot type; aortic valve stenosis (isolated); tricuspid valve abnormality (including Ebstein); mitral valve abnormality (including supravalvar, subvalvar); totally anomalous pulmonary venous connection; aortic arch obstruction±VSD/ASD; pulmonary stenosis; subaortic stenosis (isolated); aortic regurgitation; interatrial communication (ASD); PDA; acquired noncongenital heart disease; arrhythmia; miscellaneous congenital terms; noncardiac or uncoded diagnosis

The 4 primary cardiac diagnosis groups used in the analyses, which aggregate a set of 26 primary cardiac diagnosis categories, thereby reducing the degrees of freedom and, hence, the risk of overfitting.[23] The primary cardiac diagnosis categories themselves are based on a hierarchical IPCCC coding map[21] (see Table S2).

ethnicity (which showed strong concordance across the 2 audits); sensitivity analyses were performed excluding records without PICANet-derived ethnicity. Weight-for-age outside the range ±5 *z*-scores was assumed to be erroneous and treated as missing.

Outcomes

For the majority of our analyses, an *adverse event* was defined as either death outside a PICU admission (ie, "in the community") or any emergency unplanned readmission to PICU, regardless of outcome, within 1 year after discharge from the index admission. We note the inclusion of nonfatal unplanned readmissions to PICU as these were considered "near misses" of relevance to informing service improvement. However, for the purposes of comparison with in-hospital mortality rates and risk modeling, some analyses were restricted to fatal adverse events only (deaths outside a planned admission)—where this was the case, we state this clearly in the text. Note that this research was designed to inform improvements in services at discharge and in the community; therefore, we did not consider death within 1 year of discharge from the index admission that occurred during a planned readmission to intensive care (typically for elective surgery as part of a staged treatment pathway) as an adverse outcome. Such patients were important to include in the analysis, however, as the period before the second elective surgery in a staged treatment pathway is known to be particularly high risk for many patients.[5] Age at death (if applicable) and life status were available in NCHDA, while emergency unplanned admissions to PICU were extracted from PICANet.

Statistical Methods

Descriptive and univariate analyses

Descriptive analyses were performed to characterize the data set, and univariate logistic regression analysis on complete case data was used to assess the relation of each candidate predictor with each outcome by using fractional polynomials to investigate departure from linearity. This informed which variables were considered in two additional, complementary strands of analysis: first, the development of a risk model for adverse event and, separately, for fatal adverse events only, to generate generalizable knowledge about the individual underlying risk factors; and second, the identification of patient groups differentiated by risk of adverse event to inform potential interventions that might benefit certain subgroups of the population.

Developing risk models for adverse events and for fatal adverse events only

The significant variables from the univariate analysis ($P<0.10$) were investigated in a multivariable model for each outcome in turn. Initially, models were developed in which the continuous predictors were used and, where appropriate, suitable transformations were included. For the final model presentation, continuous predictors were categorized based on considerations of model interpretability as well as statistical performance.

Multiple imputation (assuming data were missing at random) was used to account for missing data when fitting the multivariable models. The imputation models included all risk factors considered in the univariate analysis (which we assume includes all predictors of missingness). We generated

20 data sets and ran a full logistic regression, using the whole data set and implementing a bootstrap (200 samples) for each imputed data set to correct for overfitting. Significant predictors were selected based on the inclusion frequency of each predictor over the imputed data sets (ie, the proportion of times that the factor appeared in the model[24]; see Data S2 for further details). The final models were derived by fitting a logistic regression model for all significant predictors, and estimates were combined by using Rubin rules.[25] Model performance was assessed in terms of discrimination and calibration. The c-statistic (area under the receiver operator curve), corrected for overfitting by using the bootstrap, was used to summarize the discrimination of the models.[26] The Hosmer–Lemeshow statistic was used to test calibration (goodness-of-fit), and the range of *P*-values obtained over the 20 imputed data sets is presented.

Sensitivity of the results to adjustment for clustering at both the hospital level and the regional level (English Primary Care Trusts[27]) was assessed for each model by using the complete case data. All analyses were performed in Stata 13,[28] and a value of $P<0.05$ was considered statistically significant unless otherwise stated.

Identifying patient groups differentiated by risk of adverse event

Classification and regression tree (CART) analysis was used to identify patient groups with different "profiles of risk" that could usefully inform the development of interventions targeted at different groups. For other examples of CART applications in health care, see references 29–31. The CART algorithm recursively partitioned the data into subsets that were as homogeneous as possible with respect to adverse event (ie, into subsets of increasing "purity").[32] All variables significantly associated with adverse event in univariate analysis were included in the CART analysis, with continuous variables entered in their categorized form as per final risk model development. To prevent overfitting, the CART groups were developed in a random 60% of the data and, for reasons of statistical robustness and potential usability, we restricted the tree depth to 4 and required a minimum of 100 cases for branching to continue, with at least 50 cases in either branch. The resulting classification tree was applied to the remaining 40% of the data set and the occurrence of adverse events among patients at each node was compared with the corresponding group in the development set to assess model stability. For both data sets, the c-statistic was calculated by assessing the final group characterizations obtained in the derivation data set as a predictor for adverse event. All analysis was performed in SPSS 22.[33]

Results

Data Set

A total of 12 390 infants meeting the inclusion criteria and with a valid patient identifier were identified in NCHDA, of whom 9385 (76%) were linked to ≥1 record in PICANet. Of these, 115 children who had an excluded catheter procedure only, 765 premature babies who had ligation of PDA only, 24 cardiac transplant patients, and 505 patients from Scotland or Northern Ireland were removed. Of 3005 patients who had no linked PICANet record, 1225 would not have been included in our study as they were either from Scotland or Northern Ireland or were premature and undergoing a PDA procedure only. The remaining 1780 demonstrated a greater prevalence of minor forms of CHD than did patients in the study data set.

Of the 7976 patients included in our study, 333 (4.2%) died during their index admission and were excluded from our analyses, leaving a final analysis data set of 7643 infants who were discharged alive from their index admission. Of these, 246 (3.2%) died within 1 year after discharge from the index admission and not during a planned admission (fatal adverse events), and 514 (6.7%) either died or had an emergency unplanned readmission to PICU within 1 year (all adverse events). Finally, 115 (1.5%) children died during a planned admission to PICU within 1 year after discharge from the index admission (not considered an outcome in our analysis), giving an overall mortality within the year after discharge from index admission of 4.7%.

Descriptive and Univariate Analyses

A summary of the descriptive and univariate logistic regression analyses is presented in the Data S2. There was no association identified with either outcome (fatal adverse events or all adverse events) and with either sex or the performance of additional cardiac catheterizations during the index procedure.

Developing Risk Models for Adverse Events and for Fatal Adverse Events Only

In the multivariable analysis in which continuous variables were treated as such, the significant risk factors for both outcomes were age at procedure, weight-for-age *z*-score, index procedure group, cardiac diagnosis group, noncardiac congenital anomaly, prematurity, ethnicity, and LOS in a specialist center. Preprocedural clinical deterioration was additionally significant to fatal adverse events only, while neurodevelopmental condition and acquired cardiac diagnoses were additionally significant to all adverse events.

Details of these continuous regression models are presented in the Data S2. In the final model development, the continuous predictors were categorized as follows: age at index procedure (>3 months old, 1–2 months old, 10–30 days, 0–10 days old); weight-for-age *z*-score (>−2 SDs, −2 to −4 SDs, <−4 SDs); and length of stay (0–7 days, 7–30 days, >1 month). Details of the final regression models for fatal adverse events and all adverse events are shown in Tables 3 and 4. For all models, adjusting for clustering at either the hospital or regional level had no statistically significant impact on results when comparing models using Akaike criteria (we present the unadjusted results).

The c-statistic of the final (categorical) model for fatal adverse events was 0.78 (95% CI 0.75–0.82), indicating good discrimination (and only marginally less discriminative than the continuous model, c-statistic 0.80). The final (categorical) model for all adverse events also showed good discrimination with a combined c-statistic of 0.78 (0.75–0.80) compared with 0.78 for the continuous model. Calibration of the final categorical and continuous models for both outcomes was also good, with Hosmer–Lemeshow *P*-values ranging from 0.10 to 0.75 across the models fitted on the 20 imputed data sets, indicating no statistically significant differences between observed and expected number of deaths when calculated in deciles of predicted risk for each of the imputed data sets.

Identifying Patient Groups Differentiated by Risk of Adverse Event

The Figure depicts the final tree generated with the CART analysis including the rate of adverse events and number of patients within each of the 6 discrete patient groups that were generated (further details presented in Table 5). Of the 18 candidate risk factors entered in the analysis, CART identified presence/absence of a neurodevelopmental condition (24% risk among 307 patients) as the best single discriminator between patients experiencing an adverse event or not. For those without a neurodevelopmental condition, the next best discriminator was whether the cardiac diagnosis was HLHS or (functionally univentricular heart/pulmonary atresia with an intact ventricular septum) (15.2% risk among 868 patients). For patients with neither of the first 2 risk factors, the next best discriminator was presence/absence of a congenital anomaly followed by the LOS (threshold 1 month) (8.6% risk in patients with a congenital anomaly and LOS of <1 month, 24% in patients with congenital anomaly and LOS of >1 month, and 9.3% in patients with no congenital anomaly and LOS of >1 month). The remaining 4778 low-risk patients with none of the above factors had an adverse event rate of 2.8%. The development and test sets had c-statistics of 0.73 and 0.74, respectively.

Discussion

Outcomes and Risk Factors

The causes of attrition after hospital discharge are poorly understood compared with adverse events occurring in hospital, yet as in-hospital care improves, these postdischarge deaths are becoming increasingly numerically significant. Of 7976 patients who had undergone an intervention for CHD in infancy, representing the caseload for England and Wales over a 6-year period, 333 (4.2%) died during their index admission. Of those discharged alive, 246 (3.2%) died either outside the specialist hospital or after an emergency unplanned PICU readmission within 1 year (fatal adverse events). An additional 268 patients (3.6%) experienced unplanned urgent readmission to an intensive care unit but subsequently survived ("near misses"), giving a combined total of 514 (6.7%) adverse events. The data set was generated by linking 2 national audits, each documenting variables potentially associated with these postdischarge outcomes.

The following risk factors have previously been linked to adverse postdischarge outcomes: primary diagnosis (in particular, HLHS and other diagnoses requiring an initial palliative [staged] procedure[34,35]), noncardiac congenital anomalies[35,36], prematurity[37], prolonged LOS[35,36] (indicating greater complexity and perhaps a surrogate for postprocedural complications[38]), and ethnicity.[5] The risk models in our study further identified lower weight-for-age at procedure (which may correlate with feeding difficulties in infancy, a known risk factor[39]); additional acquired cardiac diagnoses and preoperative clinical deterioration (which may relate to studies indicating that severer forms of a given type of CHD are at risk of poor postdischarge outcome[5,40]); neurodevelopmental conditions (which may overlap with noncardiac anomalies); and younger age at surgery (which, in contrast to studies specifically relating to HLHS that indicate older age at surgery increases risk of interstage death,[41,42] may reflect a broader effect such as young neonates being at higher risk than older infants[34,35]).

Informing Quality Improvement

The data presented reflect outcomes within the context of recent historical provision of services for infants with major CHD and are potentially insightful for ongoing quality improvement initiatives. To this end, we used CART analysis to identify patient groups with different "profiles of risk" (ie, defined by both their *level* of risk and the nature of that risk) who might benefit from specific interventions. The 6 groups that were identified have levels of risk of adverse event between 3% and 24%, which is informative when considering which groups may be a priority for intervention, while the clinical characteristics underlying the risk of each patient

Table 3. Final Logistic Regression Model for Fatal Adverse Events Only

Patient Variable	Overall No. (%)	No. of (%) Fatal Adverse Events	Odds Ratio	SE	95% CI
Ethnicity					
White	5728 (75.0)	166 (2.9)	Reference category		
Mixed	196 (2.6)	4 (2.0)	0.68	0.35	0.25–1.88
Asian	867 (11.3)	38 (4.4)	1.38	0.26	0.95–2.01
Black	345 (4.5)	12 (3.5)	1.00	0.31	0.54–1.85
Chinese	28 (0.4)	3 (3.6)	1.46	1.53	0.19–11.43
Other	133 (1.7)	12 (9.0)	2.82	0.94	1.46–5.44
Not stated	346 (4.5)	13 (3.8)	1.53	0.47	0.85–2.78
Cardiac diagnosis group					
VSD	1348 (17.6)	25 (1.9)	Reference category		
HLHS	390 (5.1)	48 (12.3)	3.07	0.97	1.65–5.71
UVH or PA+IVS	531 (7.0)	41 (7.7)	2.31	0.69	1.29–4.15
Other	5374 (70.3)	132 (2.5)	1.12	0.26	0.70–1.77
Specific procedure group					
Corrective	4973 (65.1)	86 (1.7)	Reference category		
Palliative	1629 (21.3)	119 (7.3)	2.14	0.38	1.50–3.04
Ungrouped	1041 (13.6)	41 (3.9)	1.77	0.36	1.20–2.63
Congenital anomaly					
No	6035 (79.0)	156 (2.6)	Reference category		
Yes	1608 (21.0)	90 (5.6)	2.43	0.37	1.81–3.27
Prematurity					
No	4714 (61.7)	161 (3.4)	Reference category		
Yes	828 (10.8)	44 (5.3)	1.64	0.30	1.16–2.34
Clinical deterioration					
No	6174 (80.8)	161 (2.6)	Reference category		
Yes	1469 (19.2)	85 (5.8)	1.66	0.24	1.25–2.22
Age at index procedure					
>3 mo	3202 (41.9)	55 (1.7)	Reference category		
1–2 mo	1427 (18.7)	45 (3.2)	1.32	0.28	0.87–2.01
10–30 d	1114 (14.6)	43 (3.9)	1.89	0.45	1.19–3.02
0–10 d	1900 (24.9)	103 (5.4)	2.54	0.60	1.61–4.03
Weight-for-age *z*-score					
>−2 SDs	4064 (53.2)	128 (3.1)	Reference category		
−2 to −4 SDs	2467 (32.3)	71 (2.9)	1.59	0.28	1.12–2.26
<−4 SDs	584 (7.6)	19 (3.3)	2.28	0.61	1.34–3.87
Index length of stay					
0–7 d	2564 (33.5)	35 (1.4)	Reference category		
7–30 d	4327 (56.6)	146 (3.4)	1.56	0.31	1.06–2.31
>1 mo	752 (9.8)	65 (8.6)	2.70	0.63	1.71–4.26

Details of the final regression model for fatal adverse events (death within a year after discharge from the index admission and not during a planned admission). 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 indicates hypoplastic left heart syndrome; PA+IVS, pulmonary atresia with an intact ventricular septum; PICU, pediatric intensive care unit; UVH, functionally univentricular heart; VSD, ventricular septal defect.

Table 4. Final Logistic Regression Model for Adverse Event

Patient Variable	Overall Number (%)	Number (%) Adverse Events	OR	SE	95% CI
Ethnicity					
White	5728 (75.0)	348 (6.1)	Reference category		
Mixed	196 (2.6)	9 (4.6)	0.63	0.23	0.31–1.29
Asian	867 (11.3)	73 (8.4)	1.21	0.17	0.92–1.61
Black	345 (4.5)	34 (9.9)	1.43	0.29	0.96–2.12
Chinese	28 (0.4)	1 (3.6)	0.65	0.68	0.09–5.02
Other	133 (1.7)	19 (14.3)	2.39	0.65	1.40–4.08
Not stated	346 (4.5)	30 (8.7)	1.76	0.37	1.16–2.65
Cardiac diagnosis group					
VSD	1348 (17.6)	60 (4.5)	Reference category		
HLHS	390 (5.1)	70 (18.0)	2.46	0.58	1.55–3.90
UVH or PA+IVS	531 (7.0)	73 (13.8)	2.15	0.46	1.41–3.28
Other	5374 (70.3)	311 (5.8)	1.20	0.19	0.88–1.64
Specific procedure group					
Corrective	4973 (65.1)	219 (4.4)	Reference category		
Palliative	1629 (21.3)	205 (12.6)	1.65	0.21	1.28–2.13
Ungrouped	1041 (13.6)	90 (8.7)	1.61	0.22	1.23–2.11
Congenital anomaly					
No	6035 (79.0)	305 (5.1)	Reference category		
Yes	1608 (21.0)	209 (13.0)	2.71	0.29	2.19–3.35
Neurodevelopment condition					
No	7336 (96.0)	439 (6.0)	Reference category		
Yes	307 (4.0)	75 (24.4)	2.81	0.44	2.06–3.82
Prematurity					
No	4714 (61.7)	340 (7.2)	Reference category		
Yes	828 (10.8)	93 (11.2)	1.59	0.21	1.22–2.06
Acquired diagnosis					
No	7164 (93.7)	457 (6.4)	Reference category		
Yes	479 (6.3)	57 (11.9)	1.85	0.30	1.35–2.53
Age at index procedure					
>3 months old	3202 (41.9)	129 (4.0)	Reference category		
1–2 months old	1427 (18.7)	110 (7.7)	1.59	0.23	1.20–2.10
10–30 days	1114 (14.6)	90 (8.1)	2.21	0.37	1.59–3.06
0–10 days old	1900 (24.9)	185 (9.7)	2.93	0.48	2.12–4.04
Weight-for-age *z*-score					
>−2SD	4064 (53.2)	243 (6.0)	Reference category		
−2 to −4 SD	2467 (32.3)	168 (6.8)	1.72	0.22	1.34–2.21
<−4SD	584 (7.6)	50 (8.6)	2.60	0.48	1.81 to 3.75
Index length of stay					
0–7 days	2564 (33.5)	84 (3.3)	Reference category		
7–30 days	4327 (56.6)	302 (7.0)	1.54	0.21	1.19–2.00
>1 month	752 (9.8)	128 (17.0)	2.73	0.44	1.99–3.75

Details of the final regression model for adverse event (either death or an emergency unplanned readmission to PICU within 1 year after discharge from the index admission). For each patient variable, the number (percentage) of adverse events, the multivariable odds ratios, SEs, and 95% CIs 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 indicates hypoplastic left heart syndrome; PA+IVS, pulmonary atresia with an intact ventricular septum; PICU, pediatric intensive care unit; UVH, functionally univentricular heart; VSD, ventricular septal defect.

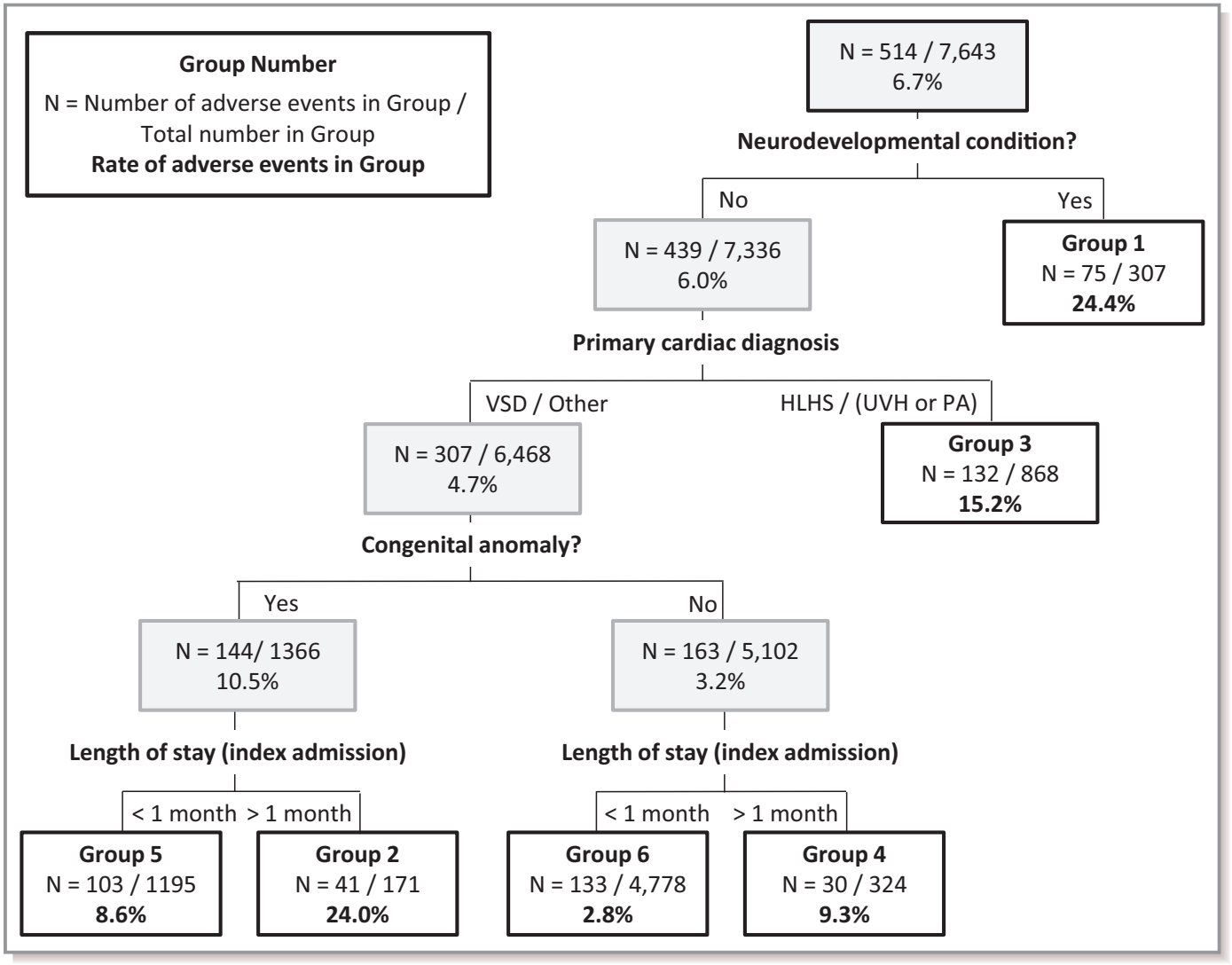

Figure. Classification and regression tree (CART) analysis. The stratification tree generated by the CART analysis and evaluated across the entire data set (see Table 5 for a breakdown by development and test set). The number and rate of adverse events and the total number of patients are given for each node. HLHS indicates hypoplastic left heart syndrome; PA, pulmonary atresia; UVH, functionally univentricular heart; VSD, ventricular septal defect.

group (defined in terms of neurodevelopmental conditions; cardiac diagnosis of HLHS, functionally univentricular heart, or pulmonary atresia with an intact ventricular septum; congenital anomalies; LOS >1 month) can inform the type of intervention that might be most appropriate. For example, group 3 consists of those patients most widely recognized as vulnerable to late death and offered enhanced surveillance, namely patients with cardiac diagnoses of HLHS and other functionally univentricular heart conditions.[43] For example, single-center studies from the United States[7,8,43] and Germany[9] suggest that postdischarge packages for HLHS (home monitoring programs) reduce interstage mortality. However, groups 1 and 2 have a higher occurrence of adverse events, suggesting that it may also be important to mitigate risks arising from patient factors beyond cardiac diagnosis, in particular clinically significant neurodevelopmental conditions and congenital anomalies. The type of intervention appropriate for these typically complex and lifelong comorbidities may be very different from those currently aimed at mitigating the cardiac risk of functionally single-ventricle and shunt-dependent infants.

Strengths and Weaknesses

The national audit data underpinning this study offer a unique opportunity for a population-based analysis of surgically treated infants with CHD. First, the data are of high quality as demonstrated by the results of a regular systematic independent validation process.[14,15] Second, the NHS number enabled late deaths outside treatment centers to be reliably ascertained by using life status tracking and enabled linkage between the two national audit data sets allowing their

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Table 5. Patient Groups Identified by Using CART Analysis

Patient Group	Group Characteristics	Possible Additional Risk Factors [% Patient Group]	No. of Patients			No. (%) of Adverse Events		
			Development Set	Test Set	Entire Dataset	Development Set	Test Set	Entire Dataset
1	Neurodevelopmental condition(s)	May also have: Congenital anomalies [52%] HLHS, UVH/PA+IVS [17%] LOS >1 mo [26%]	192	115	307	53 (28%)	22 (19%)	75 (24%)
2	No neurodev. conditions VSD/other Congenital anomalies LOS >1 mo	—	95	76	171	20 (21%)	21 (28%)	41 (24%)
3	No neurodev. conditions HLHS, UVH/PA+IVS	May also have: congenital anomalies [10%] LOS >1 mo [20%]	524 HLHS=219 UVH/PA+ IVS=305	344 HLHS=147 UVH/PA+IVS=197	868 HLHS=366 UVH/PA+ IVS=502	82 (16%) HLHS=37 (17%) UVH/PA+ IVS=45 (15%)	50 (15%) HLHS=28 (19%) UVH/PA+ IVS=22 (11%)	132 (15%) HLHS=65 (18%) UVH/PA+ IVS=67 (13%)
4	No neurodev. conditions VSD/other No congenital anomalies LOS >1 mo	—	189	135	324	20 (11%)	10 (7%)	30 (9%)
5	No neurodev. conditions VSD/other Congenital anomalies LOS <1 mo	—	701	494	1195	60 (9%)	43 (9%)	103 (9%)
6	No neurodev. conditions VSD/other No congenital anomalies LOS <1 mo	—	2898	1880	4778	88 (3%)	45 (2%)	133 (3%)

We list the patient characteristics that define each group in terms of combinations of ≥1 of the following: absence/presence of neurodevelopmental (neurodev.) condition; absence/presence of congenital anomaly; low-risk/high-risk primary cardiac diagnosis; index length of stay >1 or <1 month. For each group, the number of patients and occurrence of adverse events in the development, test, and overall data set are provided. For patient group 3, figures are also provided for the 2 subcategories of primary cardiac diagnosis within the high-risk group, namely hypoplastic left heart syndrome (HLHS) or functionally univentricular heart (UVH)/pulmonary atresia with intact ventricular septum (PA+IVS). CART indicates classification and regression tree; LOS, length of stay (index admission).

respective, and complementary, content to be used. Third, mandatory data submission means that all procedures for CHD are captured, the only exclusions being patients who traveled from overseas specifically for treatment (since these do not have an NHS number and would not form part of the follow-up program for UK specialist centers); patients in NCHDA who could not be linked to any records in PICANet (which includes those cared for only in neonatal units, those with a missing NHS number in PICANet, and those who did not require intensive care admission in either a neonatal unit or PICU for the procedure), and who represent predominantly more minor forms of CHD including a large proportion of PDA-only procedures and patients who are provided with follow-up by other specialist teams (eg, transplant recipients, premature infants without CHD). Our findings may therefore be considered more generalizable than those based on single-center studies or those from a more limited geographical area.

There are inherent limitations to using registry-based data, including the inevitable reliance on the data items that were routinely captured, which did not incorporate every potential variable of interest. Examples of important data that we could not access include the presence of residual lesions such as atrioventricular valve regurgitation, which is a known risk factor for late death in HLHS,[5] and information that is available later in the patient journey from outside the hospital such as weight gain, which is linked to late outcome.[39] There was a need to form tractable groupings from the vast range of diagnostic and procedure codes available to reduce the degrees of freedom for statistical analyses. Given our primary objective to inform quality improvement initiatives directed against late deterioration and death, we prioritized identification of diagnoses known to be high risk, namely HLHS and functionally single-ventricle patients.

Our study outcomes inevitably reflect recent health services specific to the United Kingdom as provided by the NHS and, further, relate to the English and Welsh populations in terms of ethnicity, which has known links to the distribution of congenital anomalies.[44] Evidence from North American studies suggests higher mortality for infants with CHD from Black and Hispanic ethnic groups, this being linked to reduced access to care[45–48]; however, these ethnic groupings are not representative of our study population. The ethnicity category "Other" in our data set was found to be at greater multivariable risk of adverse late outcome, whereas the more prevalent Asian and Black ethnic groups were not. Information from the UK Census suggests this category is largely comprised of individuals born in the Far East (Philippines, Japan, Thailand, and Vietnam), Middle East, and North Africa.[49] Infants with CHD from these ethnic groups could be in newly immigrant families where treatment may occur later in the disease process or access to care may be compromised for cultural or linguistic reasons. Interestingly, in our analysis, socioeconomic status (English index of multiple deprivation[17]) was not associated with outcome, in contrast to related data from North America.[5,37]

Conclusion

Our findings demonstrate that later unexpected deaths are comparable in scale to early deaths after major intervention for CHD and that, while further improvements in early mortality are possible and important, there may arguably be a diminishing return to improvement initiatives in the perioperative period compared with the postdischarge period because of the relative lack of attention to the latter to date. We note that guidelines for the entire discharge process in "high-risk infants" (not including CHD) have been proposed by the American Academy of Pediatrics with the aim of reducing variability and maintaining predetermined levels of care,[50] and our study suggests that something similar is warranted for CHD. This would require the development of appropriate intervention packages for patients with different needs, and our findings provide a valuable starting point in designing these. In particular, they show that adverse late outcomes are not confined to diagnostic groups currently targeted with enhanced monitoring in some services (ie, HLHS patients) and that subgroups of patients with neurodevelopmental conditions or congenital anomalies could also benefit from targeted intervention. Finally, to stimulate improvement initiatives aimed at reducing late adverse outcomes and to align activity across organizations responsible for the care of these patients, 1-year outcome after intervention for CHD in infancy may be a useful quality metric for pediatric cardiac surgery programs to complement the current focus on early mortality rates of surgery at 30 days or hospital discharge.

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Disclosures

None.

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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

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