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Review Article

Unexpected deaths and unplanned re-admissions in infants discharged home after cardiac surgery: a systematic review of potential risk factors

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Abstract *Background:* Babies with CHDs are a particularly vulnerable population with significant mortality in their 1st year. Although most deaths occur in the hospital within the early postoperative period, around one-fifth of postoperative deaths in the 1st year of life may occur after hospital discharge in infants who have undergone apparently successful cardiac surgery. *Aim:* To systematically review the published literature and identify risk factors for adverse outcomes, specifically deaths and unplanned re-admissions, following hospital discharge after infant surgery for life-threatening CHDs. *Methods:* A systematic search was conducted in MEDLINE, EMBASE, CINAHL, Cochrane Library, Web of Knowledge, and PsycINFO electronic databases, supplemented by manual searching of conference abstracts. *Results:* A total of 15 studies were eligible for inclusion. Almost exclusively, studies were conducted in single US centres and focussed on children with complex single ventricle diagnoses. A wide range of risk factors were evaluated, and those more frequently identified as having a significant association with higher mortality or unplanned re-admission risk were non-Caucasian ethnicity, lower socio-economic status, co-morbid conditions, age at surgery, operative complexity and procedure type, and post-operative feeding difficulties. *Conclusions:* Studies investigating risk factors for adverse outcomes post-discharge following diverse congenital heart operations in infants are lacking. Further research is needed to systematically identify higher risk groups, and to develop interventions targeted at supporting the most vulnerable infants within an integrated primary and secondary care pathway.

Keywords: Congenital heart disease; systematic review; surgical outcomes; mortality

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MAJOR TECHNOLOGICAL ADVANCES IN PAEDIATRIC surgical and intensive care in recent decades, particularly for neonates, have resulted in the survival of children with previously life-threatening CHD;[1] yet, CHDs remain the most common cause of infant death in the United Kingdom.[2,3] Although many deaths are associated with surgery, national cardiac audit data suggest that significant numbers of deaths occur more than 30 days after neonatal cardiac surgery but within the first postoperative year.[4] Moreover, analysis of 1018 neonates undergoing cardiac surgery in two London hospitals from 2000 to 2009 found that of 176 deaths during the 1st year of life, 116 (66%) occurred during the initial post-surgical hospital stay and 37 (21%) were unexpected late deaths in infants who had been discharged home

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after apparently successful cardiac surgery.[5] Thus, infants with cardiac disease remain vulnerable even after surgery, particularly if the cardiac intervention involves a series of staged procedures within the first few months of life.[6] Nevertheless, it is well-recognised that babies with CHDs who survive past their first birthday are subsequently at lower mortality risk during childhood.[3,7] Although considerable emphasis has been placed on quantifying and exploring the risk factors for early postoperative and in-hospital mortality,[8–11] far less attention has been paid to later adverse outcomes, particularly those occurring after discharge home, such as deaths in the community or emergency re-admissions.

Guidance on hospital discharge for high-risk neonates from the American Academy of Pediatrics is informed by a robust evidence base describing the specific needs of vulnerable newborns at the time of hospital discharge.[12] Although neonates with complex congenital anomalies are highlighted as a vulnerable population, specific guidance for the post-discharge care of neonates with CHDs is not provided.

Developing effective interventions to address late adverse outcomes through integrated networks of care, involving specialist hospitals and community provision, is a great challenge for health services, but would be timely in the light of the new review of congenital heart services, led by NHS England,[13] which aims to improve standards across the whole patient care pathway. Nevertheless, to achieve optimal outcomes post-discharge in these babies and offer targeted support to vulnerable infants and their families at home in the community, it is also important to understand the risk factors for these late outcomes. We, therefore, undertook a systematic review of the published literature on infants with CHDs to identify the key risk factors, identifiable at the time of discharge home after apparently successful cardiac surgery, which are associated with unexpected death in the community or unplanned re-admission to the hospital.

Methods

In order to ensure a comprehensive review of the evidence and to capture any pertinent risk factors that may not yet have been identified in studies with CHD patients, we used a broad search strategy that included other life-threatening congenital malformations requiring major surgery in the 1st year of life – for example, gastroschisis or diaphragmatic hernia. We used key terms relating to children, congenital abnormalities, surgical procedures, hospital discharge, and adverse outcomes to electronically search MEDLINE (1980 to 1February, 2013), EMBASE (1980 to 1 February, 2013), CINAHL (1981 to 1 February, 2013), Cochrane Library, Web of Knowledge (1980 to 1 February, 2013), and PsycINFO (1980 to 1 February, 2013). Conference abstracts from the Association for European Paediatric Cardiology, the American Heart Association, and the European Surveillance of Congenital Anomalies symposia were searched for the period 2008–2012. A forward citation search was carried out on the reference lists of all the selected studies to identify additional published studies for review.

Studies were eligible for inclusion only if they separately reported outcomes for children discharged from hospital and in-hospital surgical mortality. To ensure relevance to infant survival, only studies involving children up to the age of 5 years were included in the review, and major surgery was defined as requiring intensive or high-dependency care in the postoperative period. Inclusion criteria for the studies included in the review are summarised in Table 1. Titles and abstracts for all studies were independently reviewed by two reviewers, J.T. and

Table 1. Summary of the eligibility criteria for inclusion in the review.

Inclusion criteria
Studies including children
• aged from birth up to and including 5 years of age
• with a life-threatening congenital abnormality
• who have undergone major surgery (involving intensive care) for potentially life-threatening congenital disease
• who were discharged home from the hospital following their successful surgery
Exclusion criteria
Studies that
• refer exclusively to adults, children over the age of 5 years, or where the age group of interest is not clearly defined
• include previously healthy children who had major surgery as a consequence of traumatic injury
• do not refer to specified adverse outcomes – for example, death and unplanned hospital re-admission
• do not present post-discharge events and risk factors separately from in-hospital events
• included children discharged home for palliative medical care
• where case series of fewer than 20 cases, personal communications, letters, and commentaries
• have no available English language abstract

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J.W., and then full-text papers of the selected studies were assessed by three reviewers, J.T., K.B., and R.K., to determine whether they met the inclusion criteria. Any discrepancies between the reviewers were resolved through discussion with a fourth reviewer – J.W.

Data extraction was independently completed by two reviewers, J.T.and R.K., using a standard proforma that included information on study design, population, diagnosis, comparison groups, outcomes, and risk factors. Studies were assessed for methodological quality of study design using levels of evidence rated from "one" for most rigorous trials – for example, randomised controlled trial – to "four" for least rigorous trials – for example, retrospective uncontrolled case series.[14] Within each evidence level, studies were assessed as "A" for high quality to "C" for the lowest quality, using predetermined criteria such as confounding, completeness of follow-up, and objective measurement of outcomes.

The outcomes of interest were unexpected death or unplanned re-admission to the hospital in the 1st year of life after discharge following cardiac surgery. Factors associated with increased mortality or re-admission risk are presented in a narrative synthesis.

The protocol and search strategy are registered (PROSPERO; CRD42013003483).[15]

Results

Study selection

There were 17 studies identified through systematic searches and further six studies through forward citations. Of 23 full-text papers reviewed, eight studies failed to meet the inclusion criteria, resulting in 15 studies eligible for review (Fig 1). Despite our inclusive search strategy, no studies of post-surgical outcomes for children with non-cardiac congenital anomalies met the inclusion criteria.

The review included eight retrospective reviews of surgical cases,[16–23] four retrospective cohort studies,[24–27] two case–control studies,[28,29] and one randomised controlled trial that was reported in two papers.[19,30] Only three studies[22,29,30] included a prospective element. Although study designs differed, all studies were rated as good quality (Table 2). Studies assigned a lower rating failed to address some potential confounding factors. In total, 10 reports were of patients with functional single ventricle diagnosis,[16,17,19–21,23,26,28–30] which was most often hypoplastic left heart syndrome. A total of 14 papers involved patients who underwent cardiac surgery during the 1st year of life, and the remaining study[24] included cardiac patients operated up to the age of 18 years with results provided separately for each

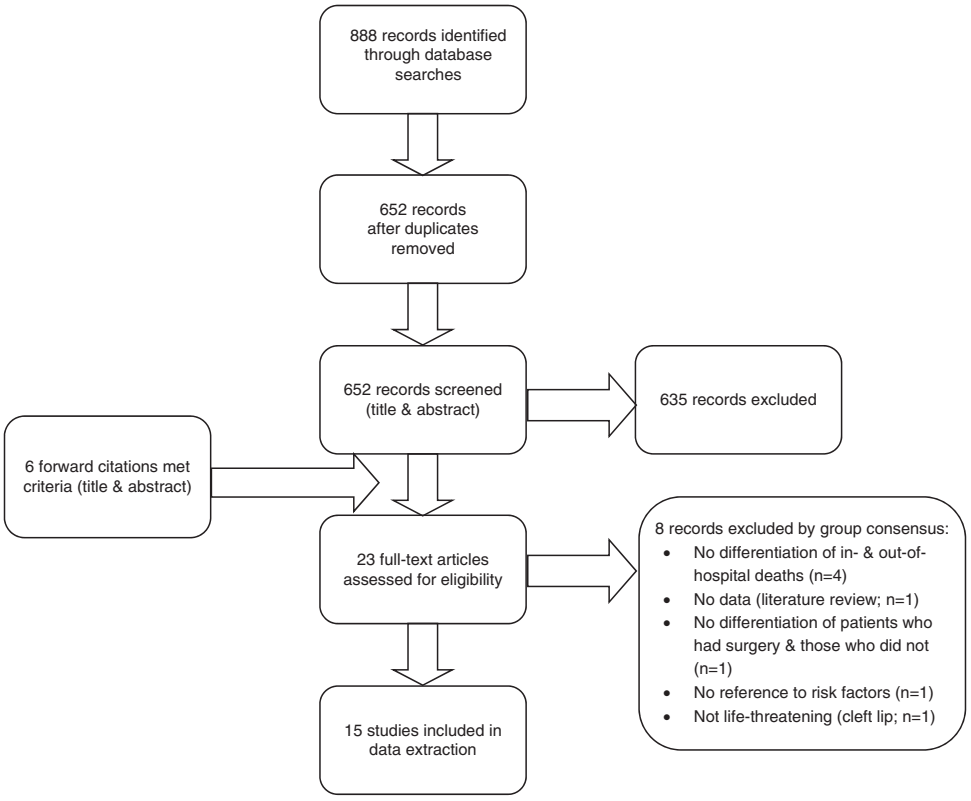

Figure 1.
PRISMA flowchart showing study selection process.

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Table 2. Summary of study quality by levels of evidence.

References	Levels of Evidence (LOE)[1]											
	LOE 1: Prospective cohort study, RCT, or meta-analysis			LOE 2: Prospective case-control study (including records-based)			LOE 3: Retrospective cohort or case-control study (including records-based)			LOE 4: Retrospective review of cases without controls		
Study quality	A	B	C	A	B	C	A	B	C	A	B	C
Ashburn et al[16]										■		
Carlo et al[17]										■		
Chang et al[24]							■					
Edwards et al[18]										■		
Fixler et al[25]							■					
Ghanayem et al[19]							■					
Hansen et al[20]										■		
Hebson et al[26]							■					
Hehir et al[28]							■					
Kogon et al[27]								■				
Mackie et al[29]					■							
Mahle et al[21]								■				
Ohye et al[30]		■										
Pinto et al[22]										■		
Simsic et al[23]											■	

LOE = levels of evidence; RCT = randomised controlled trial
Rated A (high quality) to C (low quality)

age group. Only two studies were not conducted in the United States.[16,20] In total, 29,019 patients were followed-up for mortality outcomes, of whom 1113 (4%) died; 452 (12%) of 3672 children died after single ventricle surgery compared with 661 (3%) of 25,347 children who underwent other types of cardiac surgery. Of 1639 children who were observed in three studies of unplanned re-admission, 173 (11%) were re-admitted to the hospital during the study follow-up period. Table 3 summarises the included papers.

Adverse outcomes

Reported mortality varied markedly and was influenced by the study population at risk as well as the duration of follow-up. A total of five studies[16,19,23,26,28] involved children with single ventricle diagnoses undergoing staged palliative surgery and reported "inter-stage" mortality between first and second stage surgery that ranged from 8 to 16%, with follow-up ending at around 1 year after surgery in most studies. In addition, two studies focussed on "unexpected" inter-stage deaths, defined as acute events or sudden cardiovascular collapse, and reported 4–5% unexpected deaths in neonates discharged home between stages 1 and 2.[21,30] Carlo et al[17] and Hansen et al[20] reported inter-stage mortality of 9% for children discharged home between second – superior cavopulmonary anastomosis or bi-directional Glenn surgery – and third stage – Fontan surgery. Two studies investigated post-discharge mortality after all types of cardiac surgery: Chang et al[24] reported a low mortality of 0.62% at 1 year after any cardiac surgery undertaken in children up to 18 years of age,[24] whereas Pinto et al[22] found a higher mortality of 8% in the 2 years following discharge after neonatal congenital heart surgery. Mortality over 10% was reported in studies focussing on specific higher-risk cardiac defect subgroups[25] or patients discharged home on mechanical ventilation.[18]

In total, two studies evaluated unplanned hospital re-admissions distinct from mortality,[22,27] and one further study[29] reported unplanned re-admissions as part of a combined outcome measure of mortality and re-admission. Re-admission rates within 30 days of hospital discharge ranged from 10[27] to 30%[29] and at 2 years post-discharge were 45%.[22] Variations were influenced by duration of follow-up and differences in data collection methods that included hospital records review[27,29] and telephone survey.[22]

Risk factors associated with adverse outcomes

Although many different factors were investigated (Table 4), the findings relating to individual factors were inconsistent; this may reflect the heterogeneity of participant characteristics and study designs. Table 4 summarises the factors investigated by different studies and indicates whether these were found to increase mortality risk.

Individual and family factors. Ethnicity,[19,22,25,27] socio-economic status,[19,25,29] and non-cardiac malformations or genetic syndromes[25,27,29] were the most frequently evaluated individual factors. Socio-economic deprivation, assessed through measures

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Table 3. Studies meeting criteria for review (n = 15) examining risk factors for post-discharge mortality and/or unplanned hospital re-admission.

References	Participants	Setting and study design	Quality rating	Follow-up period	Primary outcome measure	Mortality (post-hospital discharge)	Factors associated with mortality/hospital re-admission
Ashburn et al[16]	710 HLHS with critical aortic stenosis or aortic valve atresia who underwent Norwood stage 1 procedure (512 infants discharged alive after stage 1 surgery)	Canadian multicentre study; retrospective records review of surgical cases; risk analysis for outcomes including death, further surgery	4A	Follow-up at 1 month, 6 months, 1 year, and 5 years after stage 1 procedure	Time of transition to death, further planned surgery, transplantation or other outcomes	12% of 512 infants died between stage 1 and stage 2 surgery. Survival after stage 1 surgery for the entire cohort: 72% at 1 month; 62% at 6 months; 60% at 1 year; and 54% at 5 years	*Patient-specific*: low birth weight, smaller ascending aorta, older age at Norwood. *Institutional*: institutions enrolling ⩽10 neonates had higher risk than institutions enrolling ⩾40 neonates. *Procedural*: shunt originating from the aorta, longer circulatory arrest time, management of ascending aorta
Carlo et al[17]	85 HLHS (65% male) who underwent Norwood stage 1 followed by bi-directional Glenn procedure (BDG; stage 2)	Single US centre; retrospective records review of surgical cases; comparison between survivors and deceased	4A	From BDG (stage 2) until Fontan (stage 3) procedure, cardiac transplant or death. Follow-up for mean 3.4 (range 1.6–5.8) years after stage 2 procedure	Inter-stage attrition (death or cardiac transplantation) after hospital discharge from BDG (stage 2 procedure) and before Fontan (stage 3 procedure)	8 died unexpectedly at home (9.4% mortality) and 3 underwent cardiac transplantation (13% overall attrition)	Attrition group had longer intubation periods (median 2 days versus 1 day, $p < 0.01$) and hospital length of stay (median 19 days versus 6 days, $p < 0.01$). *Multivariable analysis*: lower weight z-score at BDG and moderate-to-severe tricuspid regurgitation were associated with attrition. *Inter-stage attrition not associated with*: sex, anatomic subtype in HLHS, use of antegrade cerebral perfusion, restrictive atrial septum at birth, age, or weight at stage 1 palliation, stage 1 operative characteristics, age at BDG, haemodynamic data obtained at cardiac catheterisation, aortic arch obstruction, right ventricular dysfunction

Table 3. *Continued*

References	Participants	Setting and study design	Quality rating	Follow-up period	Primary outcome measure	Mortality (post-hospital discharge)	Factors associated with mortality/hospital re-admission
Chang et al[24]	23,897 children <18 years (55% male) with ICD-9-CM procedure codes indicating any cardiac surgery; includes cardiac surgery for non-congenital diagnoses	All US California state hospitals; retrospective cohort follow-up using state-wide database; multivariate analysis of risk factors	3A	Up to 365 days post-discharge	Postoperative deaths within 1 year of surgery (included in-hospital death). "Late deaths" (occurring 31–365 days after hospital discharge) were reported separately	23, 987 "alive" hospital discharges, 148 deaths (0.62%) occurred within 365 days after discharge (37 deaths within 30 days; 44 deaths at 31–90 days; 67 deaths at 91–365 days)	Predictors of post-discharge death included younger age and procedure type. Neonates and infants undergoing Norwood procedure, aortopulmonary shunt with atrial septostomy, total anomalous pulmonary veins or truncus arteriosus repair, thoracic vessel procedures, and open valvotomy are at high risk of late post-discharge death. *Factors not associated with late death included*: ethnicity, sex, income, and hospital care volume
Edwards et al[18]	35 CHD (various) (46% male) who underwent any CHD surgery and were under home mechanical ventilation programme	Single US centre; retrospective review using hospital records; survival analysis	4A	2–168 months after starting home mechanical ventilation	Mortality	12 (34%) died	*Higher mortality risk was associated with:* multivariable analysis: adjusted RACHS[8] score ⩾4. *Univariable analysis*: broncho-pulmonary dysplasia, neurological disorder
Fixler et al[25]	1213 CHD diagnosis associated with >25% mortality	US state (Texas) registry; observational cohort follow-up using linked records; multivariate analysis of risk factors	3A	Up to 1 year after birth	1st year mortality	Overall 1st year survival was 59.9%	Overall ethnicity did not influence survival, but Hispanic infants *with HLHS* had decreased survival. *Predictors of worse survival after adjustment for defect type:* living on Mexican border (proxy for deprivation); low birth weight (<2500kg) and gestational age, extra-cardiac defects. *Factors not associated with 1st year mortality included* distance to cardiac centre, parental birthplace, sex, maternal education, and marital status

Table 3. *Continued*

References	Participants	Setting and study design	Quality rating	Follow-up period	Primary outcome measure	Mortality (post-hospital discharge)	Factors associated with mortality/hospital re-admission
Ghanayem et al[19]	426 single ventricle diagnosis; survived to hospital discharge after Norwood stage 1 surgery	US multicentre; retrospective case records analysis within a controlled trial; multivariate risk factor analysis	3A	Until stage 2 surgery or death (up to 14 months after stage 1 surgery)	Inter-stage mortality post-hospital discharge	50 (12%) died	*Predictors of worse survival included* preterm delivery; Hispanic ethnicity; aortic/mitral atresia; higher number of postoperative complications; % below poverty line (US census data); shunt type (MBTS predicted worse survival than RVPAS).
Hansen et al[20]	115 HLHS (67% male); underwent superior cavo-pulmonary anastomosis (stage 2) surgery	Single centre, Germany; retrospective surgical case series; multivariate analysis of risk factors	4A	Follow-up over a 14-year period – minimum follow-up of 2 years	Death/cardiac transplant; postoperative complication and adverse events	Late adverse outcome in 10 (8.7%) patients (death n = 8; cardiac transplant n = 2)	*Risk factors for death/cardiac transplant:* longer cardiopulmonary bypass time; ⩾moderate tricuspid regurgitation on postoperative echocardiogram (odds ratio [OR] 16.5 (4.4–62.6, $p < 0.001$). Patients with ⩾moderate tricuspid valve regurgitation had higher risk of adverse outcomes than those with less severe tricuspid regurgitation. Age <4 months at surgery did not increase the risk for adverse outcome (death or transplant) (OR 1.2 (0.4–3.6), $p = 0.78$)
Hebson et al. (2012)[26]	334 neonates aged <30 days at surgery; single ventricle diagnosis (varied); underwent Norwood stage 1 (n = 165), pulmonary artery band (n = 17), or MBTS (n = 152) procedures	Single US centre; retrospective cohort study; analysis of different feeding modalities post-discharge	3A	Until stage 2 surgery (follow-up ranged from 1 to 8 years overall, but was not specified for individual patients)	Inter-stage mortality	26 (7.8%) inter-stage deaths. 9 deaths with Nissen fundoplication (NF) or gastrostomy tube (GT); 17 without NF/GT. 7 died in hospital and 19 died at home/local facilities	*Findings from multivariate analysis (adjusted for age, weight, genetic syndromes; prematurity; heterotaxy; postoperative arrhythmia; and ventricular function at discharge):* feeding with gastrostomy tube (GT) with/without Nissen fundoplication (NF) was associated with higher risk of inter-stage mortality (relative risk 2.38 (1.05–5.40), $p = 0.04$)

Table 3. *Continued*

References	Participants	Setting and study design	Quality rating	Follow-up period	Primary outcome measure	Mortality (post-hospital discharge)	Factors associated with mortality/hospital re-admission
Hehir et al. (2008)[28]	313 "hospital survivors" with HLHS (and variants); underwent Norwood stage 1 procedure	Single US centre; retrospective nested case–control study; multivariate analysis of risk factors	3A	Follow-up was for 1 year after stage 1 surgery or until stage 2 surgery or death, if earlier	Inter-stage mortality (post-discharge and before stage 2 procedure)	33 inter-stage deaths (10.5%)	*Risk factors for death:* restrictive atrial septum, older age at operation, post-operative arrhythmias and respiratory complications. *Multivariate logistic regression:* highly restrictive atrial septum (OR 7.6[1.9–29.6]), age at operation >7 days (OR 3.8 [1.3–11.2]). *Factors not associated with inter-stage morality included* intra-operative factors, cardiac status at discharge, sex, birth weight, gestation, prenatal diagnosis, distance from centre, feeding at discharge, non-cardiac anomalies, oxygen at discharge, re-operation, discharge on >3 medications, seizures, postoperative ECMO, or cardiac arrest
Kogon et al[27]	685 any CHD diagnosis requiring surgery (57% male)	Single US centre; retrospective observational cohort study; multivariate analysis of risk factors	3B	Until 30 days after hospital discharge	Unplanned re-admissions within 30 days of hospital discharge	70 patients (10.2%) were re-admitted (total 74 re-admissions in 70 patients)	*Re-admission more likely if univariable analysis* – younger age; lower weight at surgery; Hispanic; genetic syndrome; failure to thrive; pre-operative ventilation; higher RACHS-1 score; nasogastric feeding at discharge; palliative surgery; longer length of stay in ICU/ hospital. *Multivariable analysis* – Hispanic ethnicity; failure to thrive; hospital length of stay >10 days. *Factors not associated with unplanned re-admission* – arrhythmia, gastro-oesophageal reflux, and developmental delay

Table 3. *Continued*

References	Participants	Setting and study design	Quality rating	Follow-up period	Primary outcome measure	Mortality (post-hospital discharge)	Factors associated with mortality/hospital re-admission
Mackie et al[29]	162 (54 cases; 108 controls) HLHS, other single ventricle or transposition of the great arteries; underwent Norwood stage 1 or arterial switch procedure	Single US centre; case–control study; multivariate analysis of risk factors	2B	Until 30 days after hospital discharge	Unplanned re-admission or death (combined outcome used to explore risk factors)	54 cases (from 752 operated children) included 48 re-admissions (29.6% of 752); 6 deaths (3.7% of 752)	Risk factors for death or re-admission residual haemodynamic problems (OR 4.10), ICU stay >7 days (OR 5.17), establishment of full oral intake <2 days before. Combining with the control group, living in a low income areas was associated with a lower likelihood of re-admission (OR 0.25 [0.07, 0.85], p = 0.027)
Mahle et al[21]	536 HLHS and variants; underwent stage 1 surgery for single ventricle reconstruction	Single US centre; retrospective records-based identification of cohort with prospective confirmation of outcomes; multivariate analysis of risk	3B	Deaths within the 1st year after stage 1 (range 25–227 days post-surgery)	"Unexpected" death (defined as cardiovascular collapse without regaining consciousness)	22 unexpected deaths (4.1%) and 63 non-surgery-related deaths (11.8%) from 536 infants discharged home after stage 1 surgery. Median age at unexpected death was 79 (25–227) days	Perioperative arrhythmia and earlier year of surgery were associated with higher mortality risk. Factors not associated with mortality risk included prenatal diagnosis, aortic atresia, age at admission, age at each surgical stage, peri-operative seizure, ventricular function measures and feeding difficulties
Ohye et al[30]	549 single ventricle; underwent Norwood stage 1 (randomised to two shunt types)	United States; multicentre; prospective RCT comparing two types of single ventricle surgery; multivariate analysis of risk factors	1B	Until 12 months after stage 1 surgery	Deaths (including "unexpected" death) in the 12 months following Norwood stage 1 surgery	164 died: 88 in- hospital at stage 1; 54 between stages 1 and 2; 16 in-hospital at stage 2; and 6 within 12 months of stage 2 discharge. 29 deaths were "unexpected"	Shunt type: MBTS associated with higher mortality than RVPAS. 12 (41%) of the 29 "unexpected" (post-discharge) deaths had prodromal illness including poor feeding/vomiting, fussiness, diarrhoea, cyanosis, fever, increased work of breathing

Table 3. *Continued*

References	Participants	Setting and study design	Quality rating	Follow-up period	Primary outcome measure	Mortality (post-hospital discharge)	Factors associated with mortality/hospital re-admission
Pinto et al[22]	202 any CHD requiring surgery (51.5% male); underwent neonatal congenital heart surgery (not minor surgery)	Single US centre; retrospective records review and follow-up survey; multivariate analysis of risk factors	4A	23.9 (±3.4) months post-discharge after neonatal congenital heart surgery	Mortality + "adverse events" (unplanned re-admissions and cardiac re-interventions)	16 deaths (8%). Post-discharge adverse events were reported for surviving patients by telephone survey (contact rate 59%). Of those, 49 (45%) had an unplanned re-admission	Patients residing 90–300 minutes from the surgical centre were less likely to experience an adverse event than those living <90 minutes away but there was a non-significant trend towards higher mortality in this same group when compared with those living <90 minutes and >30 minutes away. Residence >300 minutes from the hospital not associated with higher risk of post-discharge death
Simsic et al[23]	50 HLHS/single ventricle diagnosis; underwent Norwood stage 1 procedure	Single US centre; retrospective review of surgical cases and outcomes; multivariable analysis of risk factors	4B	For 1 year after stage 1 surgery (until stage 2 surgery or death)	Inter-stage mortality between Norwood stage 1 discharge and stage 2 surgery	8 deaths (16%) within 1 year after Norwood procedure	Increased risk if, at discharge after Norwood, postoperative arrhythmias decreased ventricular function. Factors not associated with increased risk of inter-stage mortality included duration of cardiopulmonary bypass, cross-clamp or circulatory arrest; moderate valve regurgitation; postoperative epinephrine, length of mechanical ventilation; length of hospital stay; discharge medication

ECMO = extracorporeal membrane oxygenation; HLHS = hypoplastic left heart syndrome; MBTS = Modified Blalock–Taussig Shunt; RACHS = Risk Adjustment in Congenital Heart Surgery; RVPAS = right ventricle to pulmonary artery shunt

Table 4. Summary of factors examined in the 15 studies.

Factors reported (by category)	Reference numbers for studies reporting on each factor	
	Studies reporting "Not a risk factor"	Studies reporting "Significant risk factor"
Individual and family factors	24 28 17 25	
Sex	24	19 27 22 25
Race/ethnicity	24	19 29 25
SES/home income	25	
Parent factors e.g. maternal education	28 25	22
Distance to cardiac centre	28	19 25
Prematurity/gestational age <37 weeks	28	16 25
Low birth weight	24	27
Failure to thrive	28	27 25 29
Extra-cardiac/genetic syndromes		
Cardiac diagnostic factors	21 17	19
Anatomic subtype in HLHS		17 20
Tricuspid regurgitation† (⩾moderate)	17	28
Intact/highly restrictive atrial septum		16
Smaller ascending aorta	21 28	22
Prenatal diagnosis	27	
Pre-operative arrhythmia		
Procedural and operative factors	17	
Operative characteristics at stage I surgery	21 17 20	24 16 28 27
Age at surgery	17	27
Weight at initial surgery		21
Surgical era	24	16
Hospital case volume		27
Pre-op ventilation	27	
Pre-op developmental delay	27	
Pre-op reflux		27 22 18
Operative complexity (RACHS⩾4)		
Procedure type*	21	24 16 19 30 27
Bypass type	17	
Bypass time	23	20
Cross-clamp time	23	
Circulatory arrest time	23	16
Unspecified operative factors	28	
Post-operative symptoms/complications	23	28 17
Intubation time/airway complication	28	
O2 at discharge	28 23	22
Medications at discharge	21 28	
Peri/post-operative seizure		21 23
Peri/post-operative arrhythmia	28	16 19
Post-op complications/re-op/revision	21 23	27 29
Longer ICU/hospital stay	17	29
Residual hemodynamic problems	23	
Moderate AV valvar regurgitation (in HLHS)	17	
Aortic arch obstruction (in HLHS)		
Ventricular dysfunction	21 17	23
Unspecified cardiac status at discharge	28	
Feeding difficulties	21 28	26 27 29

Complexity of cardiac anatomy

AV = atrioventricular; HLHS = hypoplastic left heart syndrome.

*Cardiac surgical procedures defined in these studies were as follows: palliative procedures, Norwood stage 1, bi-directional Glenn, shunt construction, thoracic vessel procedures, truncus arteriosus repair, total anomalous pulmonary venous return (TAPVR) repair, open valvotomy

such as household income,[29] family income below the national poverty threshold,[19] and deprivation index of the residential area,[25] and Hispanic ethnicity[14,19,22] were highlighted as risk factors for mortality and unplanned hospital re-admission in US studies. Preterm birth[19,25] and low birth weight[16,25] were risk factors for mortality, but patient gender was not significantly associated with adverse outcomes.[17,24,25,28] Children living 90–300 minutes from the cardiac centre were at significantly lower risk of unplanned re-admission[22] compared with families living under 90 minutes away, but there was no association with mortality.[22,25] Family factors including maternal education, marital status, and country of birth were not associated with adverse outcomes.[25]

Cardiac diagnosis and procedural factors. Infants with more complex hypoplastic left heart variants[16,17,19,20,28]

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were at higher risk of mortality or re-admission. Children undergoing more complex operations, based on the Risk Adjustment in Congenital Heart Surgery 1 system,[8,31] were at greater risk.[18,22,27] Several studies reported that Norwood procedures,[24] specific shunt operations,[16,19,24,30] total anomalous pulmonary venous connection repair,[24] and truncus arteriosus repair[24] were associated with significantly higher mortality, whereas palliative operations[27] increased the risk of unplanned re-admission. There was insufficient evidence to suggest that intra-operative characteristics such as cardiopulmonary bypass or circulatory arrest time had a negative impact on outcome.[16,23,28]

In children undergoing staged palliative operations, older age at first procedure was associated with higher mortality risk,[16,28] whereas younger age, under 4 months, at the second stage Glenn procedure increased the risk of postoperative complications.[20] Futhermore, two papers[19,30] reporting findings from the Single Ventricle Reconstruction trial, in which patients with hypoplastic left heart syndrome were randomised to receive different surgical interventions, higher mortality after hospital discharge was observed within the group receiving a modified Blalock–Taussig shunt compared with a right ventricle-to-pulmonary artery conduit; this difference was no longer significant after adjustment for severity of postoperative atrioventricular valvar regurgitation.

Postoperative symptoms/complications. A total of five studies explored postoperative feeding difficulties;[21,26–29] three of these identified feeding difficulties, including the need for gastrostomy tube placement,[26] as a risk factor for mortality or unplanned re-admission. Peri- and postoperative arrhythmias were also a significant risk factor for mortality in two studies,[21,23] whereas airway complications, prolonged postoperative hospital length of stay, postoperative complications, and medications at discharge were not found to influence outcomes post-discharge.

Discussion

We identified 15 studies that evaluated the potential risk factors associated with mortality or unplanned hospital re-admission in children successfully discharged from the hospital after cardiac surgery for serious CHDs. Factors identified most frequently by these studies as predicting significantly increased risk of adverse events were non-Caucasian ethnicity,[19,22,25,27] lower socio-economic status,[19,25,29] co-morbid conditions including non-cardiac malformations and syndromes,[25,27,29] age at surgery,[16,24,27,28] operative complexity or procedure type,[16,18,19,22,24,27,30] and postoperative feeding difficulties.[26,27,29] Patient sex, parental factors, intra-operative factors, and postoperative complications were also investigated, but were not found to be independent predictors of post-discharge outcomes.

Our review confirms the significant lack of research into adverse outcomes after hospital discharge following surgery, and highlights the fact that the evidence base to inform post-discharge clinical care and identify infants at high risk for focussed support is extremely limited. As many reports derive from North American studies, and the research population is often limited to infants who have severe and complex cardiac diagnoses requiring staged surgery, care must be taken in generalising the findings from these existing studies to the wider UK population of infants with CHDs.

Despite our broad search strategy that was intended to capture research into other life-threatening anomalies that require surgery during infancy, such as gastroschisis and diaphragmatic hernia,[32] the only studies of post-discharge outcomes that met the inclusion criteria concerned CHDs. CHDs, however, have the highest rate of infant deaths of all congenital anomaly subgroups, and this may account for the greater interest in monitoring outcomes after hospital discharge; however, it is also notable that post-discharge outcomes of infants with CHDs came to prominence with the introduction of staged palliative surgery for HLHS, which led to improved early in-hospital outcomes[33,34] and highlighted later inter-stage mortality as an important concern.[19,35]

In three US studies[19,25,27] within our review, patients of Hispanic ethnicity were found to be at risk of adverse outcomes relative to Caucasian patients post-hospital discharge. This confirms previous research, which has shown that US Hispanic communities are more likely to experience multiple barriers to healthcare, including language and immigration status, and financial barriers such as lack of health insurance or low family incomes.[36,37] On the other hand, the impact of ethnicity and socio-economic deprivation demonstrated in US studies may be influenced by an individual family's ability to pay for care,[36–43] and the relevance of these findings for the UK healthcare system is uncertain. Nevertheless, there is evidence that lower income families in the United Kingdom also experience a considerable financial burden when caring for their child with CHD and that this may affect care-seeking behaviours.[43] The results of our review, therefore, add to the growing body of evidence suggesting that patients from minority ethnic and lower socio-economic groups are more likely to experience barriers to timely and appropriate access to care, and underlines the relevance of these factors to the population of infants with CHDs following hospital discharge.

Postoperative feeding and growth were also significantly associated with adverse outcome in several studies[26,27,29] identified within the review, consistent with previous research;[44] however, the relationship between feeding difficulties and adverse outcomes post-discharge is likely to be complex, due to potential confounding with poorer cardiac status and other co-morbidities, and therefore requires further investigation.

A limitation of our review was the rigour of our eligibility criteria, which excluded any studies that did not clearly differentiate between deaths that occurred before and after hospital discharge, and thus may have removed from the review some studies that evaluated additional risk factors to those reported here. Nevertheless, the relative lack of studies reporting post-discharge surgical outcomes may also simply reflect the limited monitoring of late adverse events and specifically of events occurring in the community or primary-care setting.[24]

Re-admission to hospital will depend both on the child's clinical state and the response to this by parents and medical staff. It is possible that re-admission signified a timely response to a child's deteriorating clinical state in some cases, whereas in others it was a response to a child who became seriously unwell. In our review, we considered an unplanned re-admission to be an adverse event, indicating that a child's condition deteriorated unexpectedly at home, and thus did not experience a stable clinical course after discharge. Nevertheless, it is possible that the risk factors for re-admission may differ from those for deaths, and this may have contributed to the breadth of different risk factors identified.

We identified several key medical and social factors associated with a higher risk of mortality or unplanned hospital re-admission for children discharged from hospital after paediatric cardiac surgery. Some of these risk factors such as feeding difficulties would be amenable to modification through specific interventions, whereas others enable health professionals to identify children who are at greatest risk for adverse outcomes and to offer additional support, such as home monitoring programmes, targeted more effectively at vulnerable children and their families within the community setting. Although there were no studies of social and financial factors within the UK healthcare context, unequal access to care may disproportionately affect minority ethnic communities and low income families and should be a focus for future research in the United Kingdom. Crucially, this review highlights an evidence gap and important need for longer-term studies to investigate the risk factors for out-of-hospital outcomes after surgery separately from in-hospital outcomes. Such evidence would better inform post-discharge care and community-based interventions to improve long-term survival and the quality of life of infants with CHDs.

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Conflicts of Interest

None.

Ethical Standards

Not applicable (no human subjects).

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