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Ethnic-specific mortality of infants undergoing congenital heart surgery in England and Wales.

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ABSTRACT

Purpose: To investigate ethnic differences in mortality for infants with congenital heart defects (CHDs) undergoing cardiac surgery or interventional catheterisation.

Design: Observational study of survival to age one year using linked records from routine national paediatric cardiac surgery and intensive care audits. Mortality risk was investigated using multivariable Poisson models with multiple imputation. Predictors included sex, ethnicity, preterm birth, deprivation, comorbidities, prenatal diagnosis, age and weight at surgery, pre-operative deterioration and cardiac diagnosis.

Setting: All paediatric cardiac surgery centres in England and Wales.

Patients: 5350 infants with CHDs born 2006 to 2009.

Main outcome measure: Survival at age one year.

Results: Mortality was 83.9 (95%CI 76.3, 92.1) per 1000 infants, with variation by ethnic group. Compared with those of White ethnicity, infants in British Asian (Indian, Pakistani, Bangladeshi) and 'All Other' (Chinese, Mixed, Other) categories experienced significantly higher mortality by age one year (relative risk [RR] 1.52 [95%CI 1.19, 1.95]; 1.62 [95%CI 1.20, 2.20] respectively), specifically during index hospital admission (RR 1.55 [95% CI 1.07, 2.26]; 1.64 [95%CI 1.05, 2.57] respectively). Further predictors of mortality included non-cardiac comorbidities, prenatal diagnosis, older age at surgery, pre-procedure deterioration and cardiac diagnosis. British Asian infants had higher mortality risk during elective hospital readmission (RR 1.86 [95%CI 1.02, 3.39]).

Conclusions: Infants of British Asian and 'All Other' non-white ethnicity experienced higher post-operative mortality risk, which was only partly explained by socio-economic deprivation and access to care. Further investigation of case-mix and timing of risk may provide important insights into potential mechanisms underlying ethnic disparities.

INTRODUCTION

Congenital heart defects (CHDs) contribute 10% of all infant mortality[1], and represent one-third of deaths in the first year of life attributable to congenital anomalies.[2 3] Several authors have reported higher mortality rates in infants from non-white ethnic groups with congenital anomalies compared to those of white ethnicity.[1 4-10] Analysis of UK audit data relating to paediatric cardiac surgery demonstrated increased postoperative 30-day mortality associated with British Asian ethnicity[11] while, in north America, longer in-patient stays and higher mortality after cardiac surgery have been reported for Black and Non-White Hispanic children.[12-14] These variations in survival with CHDs persist into adulthood.[1 15]

Despite a growing number of studies, it remains unclear whether ethnicity independently predicts mortality or if observed differences are related to associated factors, such as socio-economic deprivation[4 16], immaturity-related conditions[17], maternal age and health[10 17], health-related behaviors[18], or ethnic differences in the birth prevalence of complex CHDs.[6 19-21] In the US, access to health services is influenced by ability to pay which may contribute to ethnic and socio-economic disparities in survival with CHDs.[4 10 22 23] Pre-procedure clinical deterioration, older age at surgery and failure to achieve a prenatal diagnosis have been proposed as markers of poor access to care, and non-white ethnicity has been associated with delayed diagnosis and access to healthcare.[28 30-32] Despite non-white ethnic groups being over-represented within deprived communities in the UK[18], healthcare provision is universal, nevertheless other factors may represent barriers to care that differentially affect ethnic groups.

We linked routinely-collected national audit data from the National Congenital Heart Disease Audit (NCHDA) and Paediatric Intensive Care Audit Network (PICANet) to investigate ethnicity as a predictor of mortality for infants with significant structural CHDs who underwent a cardiac procedure, either cardiac surgery or interventional cardiac catheterisation, before age one year in England and Wales.[21 24] The primary outcome was mortality by age one year. To further investigate associations and potential mechanisms of mortality, we explored different periods of risk including early post-procedure mortality during the index hospital admission, unexpected out-of-hospital death and death during a subsequent planned readmission.

PATIENTS AND METHODS

The Infant Heart Study[21 24] linked NCHDA infant cardiac intervention records with PICANet paediatric intensive care unit (PICU) admission records to create an individual patient-level dataset. Babies who only had ligation for isolated patent ductus arteriosus or cardiac transplant were excluded. Infants without a linked PICANet record (n=1780) were also excluded; these were predominantly infants with mild CHDs and no, or few, PICU admissions.[21 24]

Children born with a significant structural CHD between 01/01/2006 and 31/12/2009 in England and Wales and who received their first interventional cardiac procedure while aged under one year, were identified in NCHDA.[21 24] NCHDA hierarchical classification algorithms defined one primary cardiac diagnosis per child.[24] Survival status on 13/12/2012 was independently verified using death registrations.[24] This paper focuses on mortality occurring between the index (or primary) cardiac surgery or interventional catheterisation, which was either a (i) definitive or (ii) palliative staging procedure, and one year of age, and excludes deaths prior to the procedure.[24]

The final analysis dataset comprised 5350 infants. Linked data was essential as NCHDA records included cardiac-related clinical and procedure details, while PICANet provided comorbidity, ethnicity and PICU admission details.

Outcomes and definitions

The primary outcome was death within the first year of life (Figure 1). Secondary outcomes were (1) death during index hospital admission (for the index procedure), (2) unexpected death following hospital discharge (death outside hospital or after urgent readmission to intensive care), and (3) death during elective readmission. These last two groups included inter-stage deaths.

Children were grouped into four ethnic categories (UK Census): White (n=3968; 78%), British Asian (n=604; 12%), Black British (n=240; 5%); 'All Other' (n=320; 6%; comprising Chinese, Mixed and Other); 218 (4.1%) children without ethnicity data were excluded.[21 24]

Weights were converted to age- and sex-standardised z-scores. Area-based socioeconomic deprivation scores (Index of Multiple Deprivation [IMD]) were derived from residential postcode and subdivided into quintiles.[21] Age at surgery was in weeks from birth. Read

codes in PICAnet defined whether children had a congenital anomaly, acquired comorbidity or neurodevelopmental problem.[24] Children had 'pre-procedure deterioration' if their admission was 'urgent' or 'unplanned'.[24]

Statistical analyses

Descriptive statistics are presented as numbers and percentages; 95% confidence intervals (CI) were estimated using binomial exact method. We fitted a Poisson regression model with robust variance estimates[25] to determine the relative risk (RR) for the primary mortality outcome using White ethnicity as the reference. Potential predictors (Supplementary Table S2) were explored in univariable analyses and a multivariable model constructed to determine joint associations.[24] Pearson goodness-of-fit test confirmed that the multivariable model including all predictors was a good fit for our data and the inclusion of interaction terms did not improve the model.

Missing data were imputed for IMD, weight z-score, gestation, prenatal diagnosis (Supplementary Table S2) using Markov-chain imputation and assuming data were missing at random. Imputation was conditioned on variables associated with missingness, including non-cardiac congenital anomalies, acquired comorbidities, pre-procedure deterioration, age at surgery, and primary cardiac diagnosis. Results using 20 imputed datasets generated using 2000 iterations (n=5131 infants) were compared with those excluding infants with missing data (n=3011 'complete cases').

We investigated secondary outcomes using the multivariable Poisson model for the primary outcome. All analyses were undertaken using Stata SE 14 (Timberlake Consulting).

Ethics approval

Approved by London-Central Research Ethics Committee (12/LO/1398) and the Confidentiality Advisory Group (ECC6-02(FT5)/2012).

RESULTS

Mortality

Of 5350 infants with CHD undergoing a cardiac procedure, 449 died before age one year, representing an infant mortality rate of 83.9 (95% CI 76.3, 92.1) per 1000 infants (Table 1). Of these deaths, half occurred during the index admission and half after discharge home (Figure 1; Table 1). Compared with children of White ethnicity, the relative mortality risk was significantly higher for British Asian (RR 1.6 [95% CI 1.2, 2.1]) and 'All Other' (RR 1.7 [95% CI 1.2, 2.4]) ethnic groups.

Table 1: Mortality rates per 1000 infants undergoing a cardiac procedure aged under 1 year, born between 2006 and 2009 (n=5350)

	Primary Outcome		Secondary outcomes		
	Deaths in first year of life	Effect size	Deaths during index hospital admission	Death following index discharge	
				Unexpected death* following discharge	Death during planned readmission
	N; rate per 1000 (95% CI)	**OR** (95%CI)	**N;** rate per 1000 (95% CI)	**N;** rate per 1000 (95% CI)	**N;** rate per 1000 (95% CI)
Total infants (N=5350)	**449;** 83.9 (76.3, 92.1)	-	**227;** 42.4 (37.1, 48.3)	**146;** 27.3 (23.0, 32.1)	**76;** 14.2 (11.2, 17.8)
White (N=3968)	**287;** 72.3 (64.5, 80.8)	-	**144;** 36.3 (30.7, 42.6)	**94;** 23.7 (19.2, 28.9)	**49;** 12.3 (9.1, 16.3)
British Asian (N=604)	**72;** 119.2 **(**94.4, 147.8)	**1.7** (1.3, 2.3)	**35;** 57.9 (40.7, 79.7)	**22;** 36.4 (23.0, 54.6)	**15;** 24.8 (14.0, 40.6)
Black British (N=240)	**25;** 104.2 (68.6, 149.9)	**1.5** (1.0, 2.3)	**14;** 58.3 (32.3, 95.9)	**7;** 29.2 (11.8, 59.2)	**4;** 16.7 (4.6, 42.1)
All Other (N=320)	**40;** 125.0 (90.8, 166.3)	**1.8** (1.3, 2.6)	**20;** 62.5 (38.6, 94.9)	**14;** 43.8 (24.1, 72.3)	**6;** 18.7 (6.9, 40.4)
Not stated (N=218)†	**25**	**1.7** (1.1, 2.6)	**14**	**9**	**2**

Notes: * Deaths in the community, at home or after urgent readmission; † Ethnic-specific mortality rates have not been calculated for children whose ethnicity was not stated; **N** = number; **OR** = Odds Ratio (Odds of death in first year for each group compared with White ethnic group)

Risk factors

Risk factors (Supplementary Table S1) included individual characteristics (ethnicity, sex, birth gestation), non-cardiac clinical diagnoses (congenital anomalies, acquired comorbidities, neurodevelopmental problems), care-related factors (prenatal diagnosis, pre-procedure deterioration), primary cardiac diagnosis, socio-economic deprivation (IMD), weight z-score and age at index admission. Compared with the White ethnic group, more Black British infants were girls (Black British 52.9%, White 44.4%; difference 8.5% [95% CI 2.0, 14.9]), and older than three months at surgery (Black British 50.4%, White 41.1%; difference 9.3% [95% CI 2.8, 15.7]), and more British Asian children had neurodevelopmental problems (British Asian 7.1%, White 3.4%; difference 3.7% [95% CI 1.8, 6.1]). Between 44.2% and 53.4% of non-White infants lived in the most deprived areas compared with 24.7% of White infants. The incidence of individual cardiac diagnoses varied by ethnic group.

Unadjusted outcome models

Compared with White infants, children in British Asian and 'All Other' ethnic groups experienced significantly higher mortality risk before age one year (Supplementary Table S2; British Asian RR 1.65 [95% CI 1.29, 2.10]; 'All Other' RR 1.73 [95% CI 1.27, 2.36]), and during the index hospital admission (British Asian RR 1.60 [95% CI 1.11, 2.29]; 'All Other' RR 1.72 [95% CI 1.09, 2.71] respectively), while children of 'All Other' ethnicity had higher risk of unexpected post-discharge death (RR 1.85 [95%CI 1.07, 3.20]) and British Asian infants experienced higher mortality during planned readmissions (RR 2.01 [95%CI 1.14, 3.56]). With the exception of sex, birth gestation and weight z-score, all factors in univariable models were significant predictors at $p<0.05$ of the primary outcome.

Primary outcome

In the multivariable model using imputed data (Table 2; Figure 2), infants of British Asian and 'All Other' ethnicity had significantly higher relative mortality risk during the first year of life (RR 1.52 [95% CI 1.19, 1.95]; RR 1.62 [95% CI 1.20, 2.20] respectively). Other independent predictors of mortality were primary cardiac diagnosis, non-cardiac congenital anomalies, acquired comorbidities, pre-procedure deterioration and prenatal

CHD diagnosis (Table 2). Older age at procedure predicted lower infant mortality (RR 0.95 [95% CI 0.94, 0.97] per week increased age).

Table 2: Relative risk of mortality during the first year of life by ethnic group (n=5131; multivariable analysis with multiple imputation)

	Relative Risk[RR]; (95% CI)	p-value
Ethnicity (reference: White)		
British Asian	**1.52 (1.19, 1.95)**	<0.001
Black British	1.23 (0.85, 1.78)	0.273
All Other (non-White)	**1.62 (1.20, 2.20)**	0.002
Sex (reference: boys)		
Girls	1.04 (0.86, 1.24)	0.695
Area deprivation (IMD) quintile (reference: Quintile 5 = least deprived)		
Quintile 4	1.27 (0.90, 1.79)	0.181
Quintile 3	1.07 (0.75, 1.53)	0.700
Quintile 2	1.33 (0.97, 1.83)	0.079
Quintile 1: most deprived	1.08 (0.78, 1.49)	0.648
Birth gestation (reference: term birth ≥37 weeks gestation)		
Preterm (<37 weeks)	1.31 (0.90, 1.90)	0.151
Prenatal diagnosis (reference: not prenatally diagnosed)		
Prenatal diagnosis	**1.58 (1.28, 1.95)**	<0.001
Non-cardiac comorbidities/procedure-related clinical status (reference: no comorbidities)		
Congenital anomalies	**1.86 (1.49, 2.31)**	<0.001
Acquired comorbidities	**1.59 (1.19, 2.13)**	0.002
Neurodevelopmental problems	0.88 (0.60, 1.29)	0.523
Pre-procedure deterioration	**1.52 (1.24, 1.86)**	<0.001
Index admission		
Age (per week increase)	**0.95 (0.94, 0.97)**	<0.001
Weight z-score	0.93 (0.84, 1.03)	0.168
Primary cardiac diagnoses (reference: VSD)		
Hypoplastic left heart syndrome	**4.92 (3.03, 7.99)**	<0.001
Functionally univentricular heart	**3.99 (2.45, 6.47)**	<0.001
Common arterial trunk	**2.53 (1.33, 4.83)**	0.005
TGA with VSD/DORV-TGA type	0.93 (0.50, 1.73)	0.817
Interrupted aortic arch	**2.15 (1.03, 4.48)**	0.041
TGA + IVS	0.78 (0.34, 1.78)	0.554
Pulmonary atresia + IVS	**2.96 (1.71, 5.15)**	<0.001
Pulmonary atresia + VSD	**2.56 (1.46, 4.47)**	<0.001
Miscellaneous primary cardiac diagnoses	**1.92 (1.12, 3.31)**	0.018
Complete AVSD	1.56 (0.94, 2.59)	0.087
Fallot's tetralogy/ DORV-Fallot type	1.23 (0.68, 2.21)	0.495
Aortic valve stenosis (isolated)	**3.60 (1.99, 6.52)**	<0.001
Tricuspid valve abnormality	**2.84 (1.19, 6.77)**	0.019
Mitral valve abnormality	**4.80 (2.46, 9.37)**	<0.001
TAPVC	0.92 (0.36, 2.36)	0.857
Aortic arch obstruction	0.86 (0.48, 1.53)	0.600
Pulmonary stenosis	0.53 (0.16, 1.71)	0.289
ASD	**2.93 (1.28, 6.71)**	0.011
PDA	1.39 (0.57, 3.38)	0.466
Miscellaneous congenital terms	0.83 (0.20, 3.42)	0.801

Notes: Results from a multivariable Poisson model with 20 imputed datasets. **Bold** text indicates significant result at p<0.05.

Abbreviations: TAPVC = Totally Anomalous Pulmonary Venous Connection; **IVS** = intact ventricular septum; **TGA** = transposition of the great arteries; **DORV** = double outlet right ventricle; **ASD** = atrial septal defect; **VSD** = ventricular septal defect; **AVSD** = atrioventricular septal defect; **PDA** = persistent ductus arteriosus.

Secondary outcomes

In multivariable secondary outcomes models using imputed data, infants of British Asian and 'All Other' ethnicity experienced significantly higher mortality during index admission (RR 1.55 [95% CI 1.07, 2.26]; 1.64 [95% CI 1.05, 2.57] respectively; Table 3; Figure 2). Further predictors of higher mortality during the index admission, included acquired comorbidities and congenital anomalies, pre-procedure deterioration and primary cardiac diagnosis.

Higher mortality risk for British Asian infants during planned readmissions (Supplementary Table S3) persisted in multivariable models (RR 1.86 [95%CI 1.02, 3.39]) after adjustment, whereas higher risk of unexpected post-discharge death in the 'All Other' ethnic group was attenuated (RR 1.63 [0.93, 2.85]). Independent predictors of unexpected post-discharge death (Supplementary Table S4) were non-cardiac acquired comorbidities, congenital anomalies, pre-procedure deterioration and hypoplastic left heart syndrome (HLH). Factors independently predicting death during planned readmission were prenatal CHD diagnosis, younger age at surgery, non-cardiac congenital anomalies and primary cardiac diagnosis.

Complete case models demonstrated similar direction of effect.

Table 3. Mortality during the index hospital admission (n=5131; multivariable analysis with multiple imputation)

	Relative Risk [RR]; (95%CI)	p-value
Ethnicity (reference: White)		
British Asian	**1.55 (1.07, 2.26)**	**0.020**
Black British	1.39 (0.81, 2.38)	0.233
All Other	**1.64 (1.05, 2.57)**	**0.031**
Sex (reference: boys)		
Girls	1.06 (0.81, 1.40)	0.675
Area deprivation (IMD) quintile (reference: Quintile 5 = least deprived)		
Quintile 4	1.04 (0.63, 1.71)	0.879
Quintile 3	0.87 (0.52,1.46)	0.610
Quintile 2	1.33 (0.86, 2.06)	0.203
Quintile 1: most deprived	0.94 (0.60, 1.48)	0.796
Birth gestation (reference: term birth ≥37 weeks gestation)		
Preterm (<37 weeks)	1.25 (0.57, 2.77)	0.569
Prenatal diagnosis (reference: not prenatally diagnosed)		
Prenatal diagnosis	**1.92 (1.41, 2.64)**	**<0.001**
Non-cardiac comorbidities/procedure-related clinical status (reference: no comorbidities)		
Congenital anomalies	**1.58 (1.12, 2.24)**	**0.010**
Acquired comorbidities	**1.58 (1.04, 2.41)**	**0.033**
Neurodevelopmental problems	**0.41 (0.18, 0.94)**	**0.035**
Pre-procedure deterioration	**1.52 (1.12, 2.06)**	**0.008**
Index admission		
Age (per week increase)	**0.98 (0.96, 0.99**	**0.020**
Weight z-score	0.97 (0.80, 1.19)	0.769
Primary cardiac diagnoses (reference: VSD)		
Hypoplastic left heart syndrome	**8.27 (3.61, 18.96)**	**<0.001**
Functionally univentricular heart	**6.34 (2.79, 14.43)**	**<0.001**
Common arterial trunk	**6.74 (2.62, 17.35)**	**<0.001**
TGA with VSD/DORV-TGA type	1.96 (0.75, 5.08)	0.168
Interrupted aortic arch	**6.71 (2.42, 8.58)**	**<0.001**
TGA + IVS	0.81 (0.17, 3.83)	0.790
Pulmonary atresia + IVS	**6.45 (2.71, 15.36)**	**<0.001**
Pulmonary atresia + VSD	**6.32 (2.68, 14.94)**	**<0.001**
Miscellaneous primary cardiac diagnoses	**2.88 (1.14, 7.25)**	**0.025**
Complete AVSD	1.96 (0.80, 4.85)	0.143
Fallot's tetralogy/ DORV-Fallot type	2.25 (0.91, 5.57)	0.078
Aortic valve stenosis (isolated)	**7.18 (2.80, 18.42)**	**<0.001**
Tricuspid valve abnormality	**5.99 (1.84, 19.50)**	**0.003**
Mitral valve abnormality	**8.01 (2.81, 22.77)**	**<0.001**
TAPVC	0.71 (0.09, 5.75)	0.752
Aortic arch obstruction	1.14 (0.42, 3.09)	0.794
Pulmonary stenosis	1.11 (0.24, 5.09)	0.892
ASD	**5.89 (1.81, 19.16)**	**0.003**
PDA	0.93 (0.13, 6.92)	0.945
Miscellaneous congenital terms	*Too few events*	

Notes: Results from a multivariable Poisson model with 20 imputed datasets. **Bold** text indicates significant result at p<0.05.

Abbreviations: TAPVC = Totally Anomalous Pulmonary Venous Connection; **IVS** = intact ventricular septum; **TGA** = transposition of the great arteries; **DORV** = double outlet right ventricle; **ASD** = atrial septal defect; **VSD** = ventricular septal defect; **AVSD** = atrioventricular septal defect; **PDA** = persistent ductus arteriosus.

DISCUSSION

Key findings

Compared with White infants, mortality was 53% higher for British Asians and 63% higher for 'All Other' ethnicity by age one year. Independent predictors of higher mortality were non-cardiac congenital anomalies or comorbidities, prenatal CHD diagnosis, pre-procedure clinical deterioration, younger age at surgery and presence of complex cardiac diagnoses. During index admission, infants of British Asian and 'All Other' ethnicity experienced significantly higher mortality than White infants. Following hospital discharge, the British Asian group had higher mortality risk during planned readmissions for staged care. Potential causes for these differences include case-mix severity, socio-economic deprivation, access to maternity and child health services[19] and maternal early life experience, such as undernutrition[17] These could not be fully explored using routinely-collected audit data and further research into the mediators of ethnic variation is needed.

Ethnicity

Our finding of higher CHD mortality for British Asian ethnic groups is consistent with previous UK[26 27] and US studies.[1 5 10 12 13 15 22 28 29] We identified that higher mortality risk experienced by British Asian infants was related to the index hospital admission and planned readmissions. This increased risk may be explained by case-mix factors that are not currently captured in routinely coded audit data, including cardiac defects that increase severity, such as isomerism, or associated comorbidities. Targeting healthcare initiatives at more severely affected infants, and co-ordinating specialist cardiac with general paediatric care to address multiple comorbidities and neurodevelopmental problems, could disproportionately benefit British Asian infants.

In our adjusted analysis, the 'All Other' (Chinese, Mixed and Other) ethnic group was at higher risk during the index admission but not of unexpected post-discharge death. In a previous study[24], children in the 'Other' but not those of Chinese or Mixed) ethnicity did experience higher rates of out-of-hospital death. The small numbers in our study prevented further exploration of differences between infants of Chinese, Mixed and Other ethnicity comprising the 'All Other' group, however this would be important for future larger studies.

Although Black British infants experienced 23% higher mortality than White infants, this was not significant. This could be due to differences in the spectrum of primary cardiac diagnoses in Black British infants which were dominated by septal defects.

Our analysis suggests key differences in the predictors and timing of risk for different ethnic groups; further investigation would provide important insights into the causative mechanisms underlying ethnic disparities.[10]

Access to care and deprivation

Delayed access to care has been proposed as an underlying reason for ethnic differences in mortality in the US, and higher risk of post-operative complications and mortality in Non-White Hispanic and Black US infants has been attributed to hospital referral and treatment approaches.[33] In our study prenatal diagnosis and pre-procedure deterioration, potential markers of delayed healthcare access, independently predicted first-year mortality but only partly explained ethnic variations. Despite similar rates of prenatal diagnosis, there were higher rates of complex defects (e.g. HLH, UVH) at birth in British Asian and Black British compared with White ethnic groups. This discrepancy could indicate failure to detect the most complex defects due to poorer access to prenatal diagnosis or ethnic differences in the acceptability of pregnancy termination. The higher rate of pre-procedure deterioration observed in Black British infants may also indicate delayed access to care however other influences, such as the spectrum of cardiac diagnoses, cannot be excluded.

We found no evidence that deprivation influenced CHD mortality within the UK healthcare system. However non-White infants were highly clustered in more deprived areas[21] and our reliance on this single measure of socio-economic status may have limited our ability to detect a difference. Other authors have reported an association between higher area deprivation and adverse CHD outcomes[34 35] but no evidence for ethnic

differences by household income or health insurance.[5 12 14] It is unclear which socio-economic measures best reflect individual experience[16], particularly within non-White communities. British Asian children have higher prevalence of complex CHDs[21] and are more likely to live in deprived areas, so may experience multiple barriers to accessing specialist care, as well as stressors related to socio-economic disadvantage.

The existing literature suggests multiple causes for ethnic variation in access to care, even within a universal healthcare system. Moreover deprivation, language, biological and cultural differences are likely to have differing impact; for example, while recent migrants may experience language as a barrier, this is less likely to affect those who have been born in the UK. Understanding the differences in experience within ethnic groups is fundamental to developing appropriate interventions.

Strengths and limitations

An important strength of our study was the linked national audit dataset representative of the multi-ethnic UK population. However routinely-collected audit data also has limitations with some variables incomplete; we could not account for deaths before surgery, comprising 5% of affected births[36], and 14% of NCHDA records were not matched to PICANet. Audit data did not fully capture some variables important to case-mix severity or unexpected collapse. Collection of these additional factors is improving, particularly in terms of case-mix, and future analyses are likely to provide greater insight. Nevertheless, the audits are nationwide, mandatory, externally validated, have high case ascertainment, and death registrations provide a robust record of outcome, therefore contribute important evidence to the limited literature on ethnic variation in CHD deaths.

CONCLUSION

CHDs are an important contributor to infant mortality and significant ethnic differences have been reported. Although we were unable to fully explore all potential mediators of ethnic variation using routine data, we identified higher mortality and differences in the timing of risk for UK infants from British Asian and 'All Other' non-White ethnic groups compared with those of White ethnicity. It is important to understand how and why

ethnicity influences mortality as there may be potential to ameliorate this by enhancing healthcare approaches that improve equity. For example where access is restricted by language, cultural beliefs or lack of familiarity with healthcare systems, additional support or innovative approaches to providing care may reduce ethnic variation. Further research should explore the relative impact of case-mix complexity, cultural beliefs and health-seeking behaviours, and other potential barriers to care that influence ethnic variation. This would inform the development of targeted interventions that address these ethnic-specific risk factors, improve health equity and result in better CHD outcomes overall within a multi-ethnic population.

KEY POINTS

What is already known on this topic?

- Congenital heart defects (CHDs) contribute to 10% of all infant mortality and represent one-third of infant deaths with congenital anomalies.
- Higher mortality has been reported for children with CHDs of non-white compared to white ethnicity in North America and the UK.
- The contribution of socio-economic disadvantage and healthcare access to ethnic variations in mortality remains unclear.

What this study adds

- In the UK, infants of British Asian and 'All Other' non-white ethnicity experience higher first-year mortality after 'successful' cardiac procedures than white infants.
- Differences in socio-economic deprivation and healthcare access only partly explain ethnic variations in mortality.
- Interventions should mitigate ethnic differences, including facilitating access to healthcare and targeting infants with complex diagnoses or multiple comorbidities.

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Author's Contributions

RK conceived the analysis and drafted the paper. RK, DR and KB designed the study. RK and DR performed the statistical analysis. RK, DR, KB, SC, CB, JW, JT, RF, DB and RP contributed to the interpretation of the data. All authors revised the work critically for important intellectual content and approved the manuscript for submission.

RK had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Competing Interests

All authors confirm that they have no competing interest to disclose.

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Data-sharing

Data were obtained from the NCHDA (12-CONG-07; 15-CONG-03) and PICANet (HQIP012) under data-sharing agreements that do not permit further sharing. All original audit data used in this study are available from NCHDA and PICANet.

Ethical approval

The study was approved by London-Central Research Ethics Committee (12/LO/1398) and given Section 251 support after review by the Health Research Authority Confidentiality Advisory Group (ECC6-02(FT5)/2012).

REFERENCES

1. Boneva RS, Botto LD, Moore CA, et al. Mortality associated with congenital heart defects in the United States: trends and racial disparities, 1979-1997. *Circulation* 2001;103(19):2376-81.

2. Kurinczuk JJ, Hollowell J, Boyd PA, et al. The contribution of congenital anomalies to infant mortality. *Inequalities in Infant Mortality Project: Briefing Paper 4.*National Perinatal Epidemiology Unit, University of Oxford, 2010. Available at: https://www.npeu.ox.ac.uk/downloads/files/infant-mortality/Infant-Mortality-Briefing-paper-4.pdf; Accessed 21 April 2018.

3. Lee K, Khoshnood B, Chen L, et al. Infant mortality from congenital malformations in the United States, 1970-1997. *Obstet Gynecol* 2001;98(4):620-7.

4. Fixler DE, Pastor P, Sigman E, et al. Ethnicity and socioeconomic status: impact on the diagnosis of congenital heart disease. *J Am Coll Cardiol* 1993;21(7):1722-6.

5. Benavidez OJ, Gauvreau K, Jenkins KJ. Racial and ethnic disparities in mortality following congenital heart surgery. *Pediatr Cardiol* 2006;27(3):321-8.

6. Balarajan R, Soni Raleigh V, Botting B. Mortality from congenital malformations in England and Wales: variations by mother's country of birth. *Arch Dis Child* 1989;64(10):1457-62.

7. Office for National Statistics. *Pregnancy and ethnic factors influencing births and infant mortality: 2013*. ONS Statistical Bulletin, 2015. Available at: https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/causesofdeath/bulletins/pregnancyandethnicfactorsinfluencingbirthsandinfantmortality/2015-10-14; Accessed 21 April 2018.

8. Nembhard WN, Salemi JL, Ethen MK, et al. Racial/Ethnic disparities in risk of early childhood mortality among children with congenital heart defects. *Pediatrics* 2011;127(5):e1128-38.

9. Troe EJ, Bos V, Deerenberg IM, et al. Ethnic differences in total and cause-specific infant mortality in The Netherlands. *Paediatr Perinat Epidemiol* 2006;20(2):140-7.

10. Collins JWJ, Soskolne G, Rankin KM, et al. African-American:White Disparity in Infant Mortality due to Congenital Heart Disease. *J Pediatr* 2017;181:131-36.

11. Crowe S, Brown KL, Pagel C, et al. Development of a diagnosis- and procedure-based risk model for 30-day outcome after pediatric cardiac surgery. *J Thorac Cardiovasc Surg* 2013;145(5):1270-8.

12. Oster ME, Strickland MJ, Mahle WT. Racial and ethnic disparities in post-operative mortality following congenital heart surgery. *J Pediatr* 2011;159(2):222-6.

13. Lasa JJ, Cohen MS, Wernovsky G, et al. Is race associated with morbidity and mortality after hospital discharge among neonates undergoing heart surgery? *Pediatr Cardiol* 2013;34(2):415-23

14. Peterson JK, Chen Y, Nguyen DV, et al. Current trends in racial, ethnic, and healthcare disparities associated with pediatric cardiac surgery outcomes. *Congenit Heart Dis* 2017;12(4):520-32.

15. Nembhard WN, Xu P, Ethen MK, et al. Racial/ethnic disparities in timing of death during childhood among children with congenital heart defects. *Birth Defects Res A Clin Mol Teratol* 2013;97(10):628-40.

16. Kucik JE, Nembhard WN, Donohue P, et al. Community Socioeconomic Disadvantage and the Survival of Infants With Congenital Heart Defects. *Am J Public Health* 2014;104(11):e150-e57.

17. Collingwood Bakeo A. Investigating variations in infant mortality in England and Wales by mother's country of birth, 1983-2001. *Paediatr Perinat Epidemiol* 2006;20(2):127-39.

18. Sheikh A, Steiner MF, Cezard G, et al. Ethnic variations in asthma hospital admission, readmission and death: a retrospective, national cohort study of 4.62 million people in Scotland. *BMC Med* 2016;14:3.

19. Bundey S, Alam H, Kaur A, et al. Why do UK-born Pakistani babies have high perinatal and neonatal mortality rates? *Paediatr Perinat Epidemiol* 1991;5(1):101-14.

20. Sadiq M, Stumper O, Wright JG, et al. Influence of ethnic origin on the pattern of congenital heart defects in the first year of life. *Br Heart J* 1995;73(2):173-6.

21. Knowles RL, Ridout D, Crowe S, et al. Ethnic and socioeconomic variation in incidence of congenital heart defects. *Arch Dis Child* 2017;102(6):496-502.

22. Gonzalez PC, Gauvreau K, Demone JA, et al. Regional racial and ethnic differences in mortality for congenital heart surgery in children may reflect unequal access to care. *Pediatr Cardiol* 2003;24(2):103-8.

23. Flores G. Technical Report - Racial and Ethnic Disparities in the Health and Health Care of Children. *Pediatrics* 2010;125(4):e979-e1020.

24. Brown KL, Wray J, Knowles RL, et al. Infant deaths in the UK community following successful cardiac surgery: building the evidence base for optimal surveillance, a mixed-methods study. *NIHR Journals Library* 2016 (May). doi: 10.3310/hsdr04190

25. Zou G. A Modified Poisson Regression Approach to Prospective Studies with Binary Data. *Am J Epidemiol* 2004;159(7):702-06.

26. Parslow RC, Tasker RC, Draper ES, et al. Epidemiology of critically ill children in England and Wales: incidence, mortality, deprivation and ethnicity. *Arch Dis Child* 2009;94(3):210-5.

27. Nicholas O, Cunningham D, Brown KL, et al. *Analysis of candidate risk factors in paediatric cardiac surgery 30-day risk modelling: Ethnicity, deprivation, sex, year, volume, distance from home, weekday or weekend.* National Institute for Cardiac Outcomes Research (NICOR), London, 2015. Reported in: https://www.england.nhs.uk/wp-content/uploads/2015/07/Item-4-CHD-report.pdf (page 309); Accessed: 21 April 2018.

28. Chang RK, Rodriguez S, Lee M, et al. Risk factors for deaths occurring within 30 days and 1 year after hospital discharge for cardiac surgery among pediatric patients. *Am Heart J* 2006;152(2):386-93.

29. DiBardino DJ, Pasquali SK, Hirsch JC, et al. Effect of sex and race on outcome in patients undergoing congenital heart surgery: an analysis of the society of thoracic surgeons congenital heart surgery database. *Ann Thorac Surg* 2012;94(6):2054-9.

30. Brown KL, Ridout DA, Hoskote A, et al. Delayed diagnosis of congenital heart disease worsens preoperative condition and outcome of surgery in neonates. *Heart* 2006;92(9):1298-302.

31. Perlstein MA, Goldberg SJ, Meaney FJ, et al. Factors influencing age at referral of children with congenital heart disease. *Arch Pediatr Adol Med* 1997;151(9):892-7.

32. Chang RK, Chen AY, Klitzner TS. Factors associated with age at operation for children with congenital heart disease. *Pediatrics* 2000;105(5):1073-81.

33. Chan T, Lion KC, Mangione-Smith R. Racial disparities in failure-to-rescue among children undergoing congenital heart surgery. *J Pediatr* 2015;166(4):812-8 e1-4.

34. Wang C, Guttmann A, To T, et al. Neighborhood income and health outcomes in infants: how do those with complex chronic conditions fare? *Arch Pediatr Adol Med* 2009;163(7):608-15.

35. Ko G, Shah P, Kovacs L, et al. Neighbourhood income level and outcomes of extremely preterm neonates: protection conferred by a universal health care system. *Can J Public Health* 2012;103(6):e443-7.

36. Knowles RL, Bull C, Wren C, et al. Modelling survival and mortality risk to 15 years of age for a national cohort of children with serious congenital heart defects diagnosed in infancy. *PloS One* 2014;9(8):e106806.

FIGURES

Figure 1: Flowchart presenting infant deaths (primary and secondary outcomes)

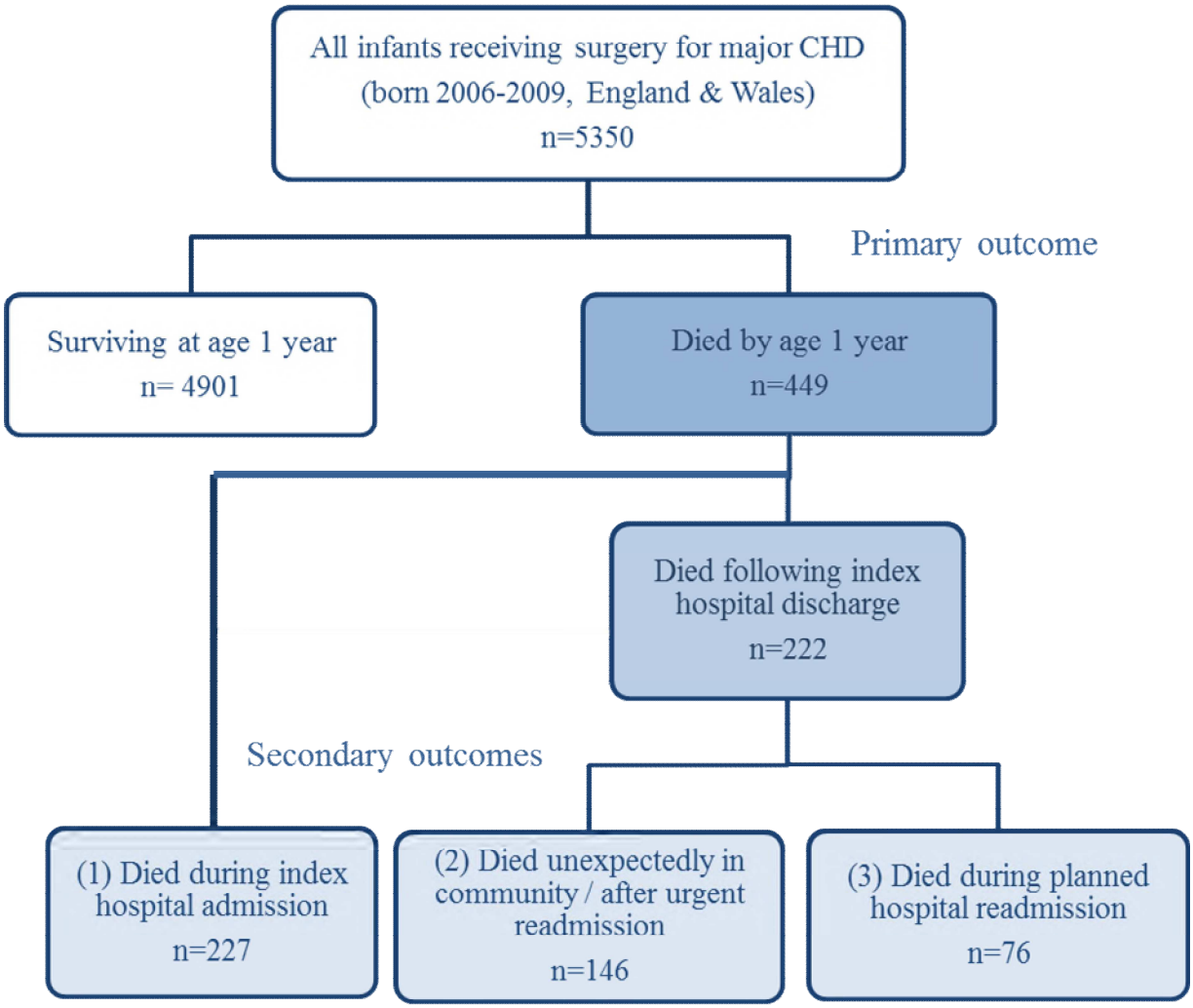

Figure 2: Relative risk of CHD mortality in first year of life by ethnic group