NEURODEVELOPMENTAL STATUS AND FOLLOW-UP IN PRE-SCHOOL CHILDREN WITH HEART DISEASE IN LONDON UK

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Abstract

Objective: To describe neurodevelopment and follow-up services in pre-school children with heart disease (HD).

Design: Secondary analysis of a prospectively collected multi-centre dataset.

Setting: Three London tertiary cardiac centres.

Patients: Pre-school children <5 years of age: both inpatients and outpatients.

Methods: We analysed results of Mullen Scales of Early Learning (MSEL) and parental report of follow-up services in a representative convenience sample evaluated between January 2014 and July 2015 within a previous study.

Results: Of 971 pre-school children: 577 (59.4%) had ≥1 heart operation, 236 (24.3%) had a known diagnosis linked to developmental delay (DD) ('known group') and 130 (13.4%) had previous history of clinical event linked to DD. On MSEL assessment, 643 (66.2%) had normal development, 181 (18.6%) had borderline scores and 147 (15.1%) had scores indicative of DD. Of 971 children, 609 (62.7%) were not receiving follow-up linked to child development; and were more likely to be under these services with a known group diagnosis, previous history of clinical event linked to DD and DD (defined by MSEL). Of 236 in known group, parents of 77 (32.6%) and of 48 children not in a known group but with DD 29 (60.4%), reported no child development related follow-up. DD defined by MSEL assessment was more likely with a known group and older age at assessment.

Conclusions: Our findings indicate that a structured neurodevelopmental follow-up pathway in pre-school children with HD should be considered for development and evaluation as they get older, with particular focus on those at higher risk.

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Introduction

Several longitudinal studies (1-7) and systematic reviews (8-10), including a scientific statement from the American Heart Association (AHA) (11), have reported that children with congenital and/or acquired heart disease (HD) are at risk of developmental delay (DD). A recent Centers for Disease Control and Prevention report identified that up to 60% of children with HD have one or more special healthcare needs as compared to 18.7% of the general population (12). Risk factors for DD are multifactorial, and range from cardiac diagnosis (13-17) and underlying syndromes to access to healthcare (4, 18, 19). Therefore, the importance of appropriate timely interventions has been highlighted (20) and several leading programmes in the USA and Europe have advocated for a multidisciplinary neurodevelopmental follow-up programme (2, 18, 21, 22). The absence of structured neurodevelopmental follow-up, variable access to healthcare, added stresses of frequent hospitalisations, and presence of other co-morbidities compound the problems faced by these families (23). Therefore, data on the development of children with HD in the UK could have important implications on planning and service provision for this vulnerable group.

As part of a wider NIHR-funded research project to explore morbidities following paediatric cardiac surgery (24), we undertook a study to validate an early recognition tool – brief developmental assessment (BDA) – for child development in pre-school children with HD. This study entailed assessment of neurodevelopmental status using validated measures in a representative convenience sample of pre-school children with HD in 3 tertiary cardiac programmes in London, UK (25). This dataset provided an opportunity for a secondary analysis that aimed to: ascertain the prevalence of neurodevelopment issues, explore service provision and associations between patient factors and DD in order to identify a high-risk group for targeted follow-up.

Methods

This study is a secondary analysis of a prospectively collected multicentre cross-sectional dataset. The age structure and sub-groups within the sample reflect the primary study objective of developing and

validating the BDA (25, 26). The study protocol was approved by the London City Road Research Ethics Committee (study number 14-LO-1442).

Study population

Parents of children with HD at a corrected age of at least term (37 weeks) and a calendar age of up to 5 years were invited to participate, in inpatient or outpatient setting, between January 2014 and July 2015 at three tertiary paediatric cardiac centres in London, UK. Children who were unwell, those with a normal heart, and those where no carer could speak English, were excluded. We recruited 200 children (number so chosen as was powered to validate the BDA) within each of five different age bands: 0-16.9 weeks, 17-34.9 weeks, 35-60 weeks, 15 months-2.9 years and 3.0-4.9 years, recruiting until the target number (within age band) was achieved (25). All participating children were assessed with the Mullen Scales of Early Learning (MSEL) (27) by a small team of trained psychology assistants under the supervision of a single senior psychology researcher (JW) and a medical lead (AH).

Patient descriptors

Children with a non-cardiac known current diagnosis of a condition that is definitely linked to DD were identified from their medical records on the basis of any of the following 1) identified genetic syndrome, 2) DD of unknown cause including undefined dysmorphism and multiple congenital anomalies, 3) any acquired brain injury and 4) combination of these groups; and were classified as being in a 'known group'.

The presence of a previous history of a clinical event linked to DD over and above these 'known groups' was identified based on any of the following: prematurity (<37 weeks of gestation), history of cardiac arrest, history of Extracorporeal Life Support (ECLS) and any combination of these factors. Out of the many risk factors that are identified for neurodevelopmental impairment (28, 29), these risk factors were chosen as they are objective criteria that can be reliably obtained. In addition, they are applicable across the range of HD including children who have not had cardiac surgery. The following psychosocial characteristics were recorded: ethnicity, index of multiple deprivations (2015) (30), primary language spoken and maternal educational level. The cardiac case mix complexity was categorised as: 1) congenital HD (functionally univentricular heart with/without arch obstruction, biventricular heart

with/without arch obstruction), and 2) acquired or medical HD (31, 32). The number of pre-assessment interventions - cardiac surgery and cardiac catheter procedures - was recorded.

Neurodevelopmental outcome

Outcome was assessed using MSEL as it is a validated measure for early developmental assessment of children (birth-5 years), with scoring undertaken based on the Manual (27). MSEL was the gold standard measure selected for BDA validation as elucidated in our related papers (25, 26). Children under 33 months of age were scored on two domains - cognitive and motor, and those over 33 months of age were scored only on the cognitive domain. The scores were categorised as: within the normal range (within 1 SD of the normative mean), borderline (between 1-2 SD below the normative mean) and low (more than 2 SD below the normative mean). The 4 cognitive scales (visual reception, fine motor, receptive language and expressive language) were combined to generate a composite score, which within the general population has a mean of 100 with SD 15, and a score between 70-84 was classified borderline, and score <70 was classified as low. The gross motor score was analysed separately as it is only applicable for children <33 months of age. The scale has a mean 50 with SD of 10, and a score between 30-39 was classified as borderline, and that <39 was classified low. MSEL-cognitive and MSEL-motor results were used to generate a child developmental outcome defined as: 'normal' (all scores normal), 'borderline development' (any 'borderline' but no low score) or 'developmental delay (DD)' (any 'low' score).

Follow-up services

As part of the research assessment on direct questioning by the research assistants, the families of participating children were asked to list any current follow-up from healthcare providers over and above their paediatric cardiologist and general practitioner (all children were under the care of these last two). If the parent did not report any additional services, then none were recorded. At analysis stage, these were grouped based on qualitative review by two researchers, with final allocation reviewed by a senior clinician: service type one - child development or neurology, general paediatrics, service type two - special senses (examples - audiology, ophthalmology), service type three - tertiary specialists not linked to child development (examples - general surgery, ear nose and throat) and 4) service type four - dietetics. Our goal was to retrospectively ascertain, as a measure of service performance, whether or not

the child was under a health care professional likely to have checked the child's development. We assumed that a child under a professional listed in service type one would certainly have had a developmental assessment (whether or not the parent was aware of this). Our inference was that a child under a professional in service type two was likely to have had a developmental assessment at some stage either by the professional listed or at the time of referral to these professionals. We did not draw any inference as to the likelihood of a child's development having been assessed based on follow-up from service types three and four.

Data analysis

Stata version 15 was used for statistical analysis.

Neurodevelopmental outcome

Data are presented as number (%) for all the clinical and demographic variables. MSEL scores and MSEL outcome categories were calculated for each clinical and demographic group.

Follow-up services

We hypothesised that there might be differential provision of services by age with older children more likely to be under the care of appropriate health professionals (service types one and two), and this was explored using a non-parametric test for trend (33). The mean age for each age band was used to reflect the ordering of the groups, to account for unequal spacing between age bands. We also explored whether children in a known group, with previous history of clinical event linked to DD or presence of DD were more likely to be under service types one and two, using chi square test.

Risk factors for outcome of developmental delay

A full multivariable logistic regression analysis (34) was used to explore the importance of pre-specified risk factors on DD (any low score on MSEL-cognitive or MSEL-motor) versus a combined normal and borderline score. Risk factors were age, functionally univentricular heart, multiple surgeries, multiple catheter interventions, known group, previous history of clinical event linked to DD, ethnicity, IMD, primary language and maternal education. Multiple imputation, assuming data was missing at random was used to account for missing data. The imputation model included outcome measures and all pre-specified risk factors, which we assume includes all predictors of missingness. We generated 20 date

sets and ran the full logistic model on all imputed data sets and estimates were combined using Rubin's rules (35).

Results

Study sample

Of the 992 children recruited, 21 were excluded due to incomplete data – child refused/shy to speak (n=8), child fell asleep (n=4), first language not English (n=4), child distracted (n=3), and family had to leave early (n=2) leaving 971 children with complete MSEL assessment.

The distribution of the patient sample by age group, clinical and demographic variables is presented in Table 1 alongside the relevant MSEL data. The predominant cardiac physiology was biventricular and 92 (9.5%) had single ventricle circulation, 577 (59.4%) had one or more cardiac surgeries and 212 (21.8%) had a cardiac catheter intervention. Of 971, 236 (24.3%) were in a 'known group', the most common being a congenital syndrome in 162 (16.7%), 130 (13.4%) had a previous history of a clinical event linked to DD, the most common being prematurity (n=98, 10.1%). The ethnic origin was predominantly 'White' in 618 (66.0%), and 852 (91.4%) had English as the primary language. Majority of the mothers (n=603, 74.5%) were educated beyond secondary school, and 448 (55.4%) attended university. Despite the fact that the study design implied voluntary participation, there was no pattern recognised in IMD rating and 469 (51.5%) reported to be in quintiles 1 and 2 (where 1 is most deprived).

Neurodevelopmental outcome

The MSEL scores (a cognitive score for all participants and a motor score for participants under the age of 33 months) are reported by important clinical groups in Table 1.

Whole study population

For the 971 children, MSEL-cognitive score was normal in 762 (78.5%), borderline in 119 (12%) and low in 90 (9.3%) children. The MSEL-motor score in 753 children under 33 months was normal in 540 (71.7%), borderline in 124 (16.5%) and low in 89 (11.8%). Child developmental outcome (as defined above) was normal in 643 (66.2%), borderline in 181 (18.7%) and DD in 147 (15.1%).

Cognitive versus Motor

In the 753 children <33 months of age with both MSEL-cognitive and MSEL-motor scores, the proportion scoring in the borderline and low ranges was higher on the motor scale versus the cognitive scale - borderline scores: motor n=124 (16.5%), cognitive n=97 (12.9%); low scores: motor n=89, (11.8%), cognitive n=47 (6.2%).

Known group versus non-known group

Of the 236 children in a known group, the developmental outcome was normal in 76 (32.2%), borderline in 61 (25.8%) and DD in 99 (42.0%). Amongst 735 children not in a known group, as expected, the proportion with a child developmental outcome of normal was higher at 567 (77.1%); leaving 120 (16.3%) with borderline outcome and 48 (6.6%) with DD.

Follow-up services

The proportion of parents that reported each follow-up service is presented by age band in Table 2. This shows that there was an increased in the proportion of children under services two and three for children that were assessed at older ages ($p<0.001$ for both), whereas services one and four showed no trend with age. Of note, only services one and two were relevant to child development (see methods). Table 3 shows that the percentages of children under services linked to child development (service types one and two) was significantly higher for children in a known group, those with previous history of clinical event linked to DD and those with DD ($p<0.001$ for all). We note that for children in a known group, surprisingly 77/236 (32.6%) did not report any services types one and two. Of 735 children not in any known group, the majority 627 (85.3%) did not report service type one or service type two. Importantly, of the 48 children with no known group who had DD, 29 (60.4%) did not report service type one or service type two.

Risk factors for outcome of developmental delay

As outlined above, the multivariable regression model was run incorporating the pre-defined risk factors. The two younger age brackets (0-16.9 weeks and 17-34.9 weeks) were grouped together for this analysis because the sensitivity of MSEL is lower in the very early age band of 0-16 weeks and the number of events were low (n=3, 1.48%). The regression model showed that children in the 3 oldest age groups at testing were significantly more likely to have the DD outcome, compared with the 0-34.9 week group

(see Table 4, $p<0.001$ for all). Similarly, those in a known group were also significantly more likely to have DD ($p<0.001$). While there was a suggestion that a history of cardiac surgery had an increased odds of DD, at 1.43 (95% CI 0.86, 2.37), the relationship was not significant. A previous history of a clinical event related to DD, ethnicity, IMD, primary language and maternal education had no significant relationship with occurrence of DD in this study cohort. A subsequent post-hoc analysis conducted to investigate the interaction between the known groups and cardiac surgery found a significant effect ($p=0.02$), demonstrating an increase in the risk of DD for children with previous cardiac surgery (9.1%) versus those with no surgery (3.2%), in the 'no known group'. For the children in a known group, this was not the case and those who had previous cardiac surgery had a lower risk of DD (40.8%), compared with those with no prior cardiac surgery (44.3%).

Discussion

Our study findings

To our knowledge, this is the first report addressing neurodevelopment and developmental follow-up services within a large sample of pre-school children with HD from paediatric cardiac centres in the UK. Within a large representative convenience sample, 15% of pre-school children with HD had DD defined by MSEL assessment. A notable proportion of children, despite being in the high-risk category did not appear to be under appropriate services for their developmental needs. An exploratory analysis in this large cohort identified that a higher proportion of children in the older age brackets and those in a known group had greater risk of DD.

Our sample and outcomes

In contrast to some previous studies, only 59.4% of children had experienced cardiac intervention, reflecting the recruitment from outpatient and inpatient settings, and the young median age of 11.3 months (some awaiting or not requiring an operation). In terms of patient complexity and conditions linked to DD, one-quarter of children (24.3%) had a 'known condition' which is similar to UK audit data (36) but the proportion of those with more complex HD such as functionally univentricular heart was lower (37, 38). Also, our sample is reasonably representative of the UK national congenital heart diseases audit data which shows ethnic and socioeconomic variation in the incidence of congenital heart disease (CHD) (39). In our dataset, the percentage of families in the more deprived quintiles was higher

than the national average, and 66% of families had a White ethnic background with the rest belonging to Black Minority Ethnic (BME) backgrounds, reflecting the population of London where the BME population is larger than the national average. Overall, the outcomes of children in our study, including the higher proportion of children with motor delay, are comparable (reassuringly so) to reported studies worldwide (4, 40, 41). The risk factors for outcome were consistent with previous reports (3, 4, 11, 16, 18, 37, 42).

Findings in context and interpretation

In line with our findings, a multi-institutional study of neurodevelopmental outcomes after cardiac surgery in infancy by Gaynor et al. showed that the presence of extracardiac anomaly, lower birth weight, male sex and lower level of maternal education were important risk factors for DD (4). In the multivariable model, maternal education was not found to be significant, however the direction of the effect indicated that lower maternal education was associated with higher DD. There is a possibility that this effect of maternal education was attenuated by other factors such as IMD and ethnicity. Cardiac condition complexity was not significant in our analyses as noted by some authors (4, 43, 44), whereas the presence of being in a known group condition was significantly associated with DD regardless of whether they had cardiac surgery or not. The prevalence and severity of DD and the association with complexity of congenital HD in children with identified and non-identified genetic syndromes is well-described (4, 18, 19) and is the basis for identification of specific sub-populations for targeted surveillance (4, 11). For those not in a known group, the impact of previous cardiac surgery on DD was noted to be significant in the post-hoc analysis, compared with the impact of cardiac surgery for those in a known group, most likely reflecting more severe HD necessitating earlier surgery with attendant peri-operative risks to neurodevelopment (3, 40).

In a systematic review, Snookes et al. found that infants undergoing cardiac surgery under 6 months of age had lower developmental scores at all ages studied (8). Hovels-Gurich et al. reported that developmental impairment in one or more domains doubled from 26% at 5.4 years of age to 55% at 8-14 years in children with Transposition of the Great Arteries (44). We conclude that the greater likelihood of DD in the older age bands reflects the emergence of delay as children get older. We also accept that the instruments to test may become more sensitive as the children get older but the

phenomenon of 'growing into deficits' is well-recognised in longitudinal studies of children critically unwell in early childhood (45, 46).

Children with HD are a unique population vulnerable to risks that compromise neurodevelopment throughout their childhood and adolescence, including frequent hospitalisations, repeated operations and associated comorbid conditions (19, 47). Given that this can be a progression, neurodevelopmental issues may become more apparent as children grow (48, 49) and this may explain why older children were more likely to be under follow-up. This concept of 'emerging' difficulties is being increasingly recognised as challenges increase as they grow older. We note that the training for cardiac specialists entails little exposure to child development and their focus is highly specialised, hence contributing to the gaps in follow-up services for patients in our study. Further, we note that whilst other comparable high-risk groups such as ex-premature infants below 33 weeks undergo standardised neurodevelopmental follow-up based on NICE Quality Standard (50), there is no UK guidance applicable to children with HD unlike in the USA (11). We believe our data suggest that some children have unmet needs, and healthcare delivery might be enhanced by the introduction of structured neurodevelopmental follow-up for pre-school children with HD.

Limitations

As a secondary analysis within a cross-sectional convenience sample, (25) our study has some limitations. Although we studied a large group of almost 1000 children, the case mix was heterogeneous and was skewed towards younger children by the age bands, whereas most studies report on neurodevelopmental status at a defined age or time period (5, 6, 9, 13, 29). Certain risk factors (head circumference, postoperative seizures, length of hospital stay, or neuro-imaging) were not included in our analysis as our study focussed on all-comers to the tertiary hospitals (operated and non-operated, age range from 0-4.9 years) with a pragmatic approach to identify the prevalence of DD and explore DD-related service provision and identify a high-risk groups rather than developing a comprehensive prognostic model incorporating multiple factors linked to DD in children with HD. Our review of services was based on parental memory/report, which clearly has human limits and may have led to

under reporting of services (missing data). It is possible that some under-reporting of paediatric follow-up could have resulted from parents believing that a PEC is a cardiologist.

Conclusions

The rates of DD and the risk factors for lower scores in this UK cohort of children with heart disease are comparable to published literature. However, a significant proportion of children with HD under 5 years of age despite having certain developmental high-risk factors such as a 'known group' condition, a previous history of a clinical event related to DD, and those with identified DD were not universally under follow-up of services related to child development. Although there are no UK based guidelines, we believe that all children in known groups, with DD and with risk factors for DD should be under developmental follow-up. Further research and planning is needed to determine the best approach to optimal assessment of development over time for children with HD within the UK National Health Service.

"What is already known on this topic" – followed by a maximum of 3 brief statements (no more than 25 words per statement)

1. Neurodevelopmental disabilities are an important morbidity in children with heart disease and are ranked as number one priority for all stakeholders involved, including parents.
2. Early identification and structured follow-up are essential to increase access to formal neurodevelopmental assessment and timely intervention in children with heart disease.
3. There is increased understanding that children with heart disease, as they grow up, face problems in academic attainments, executive function and social integration.

"What this study adds" – followed by a maximum of 3 brief statements (no more than 25 words per statement).

1. For the first time in the UK, we report the neurodevelopmental profile of a large representative sample of pre-school children with heart disease.
2. Parental report suggested that notable proportion of children with heart disease, even those with known conditions linked to developmental problems, were not under developmental services.
3. The study provides evidence of unmet need for child development service provision in children with heart disease, and an area for service improvement.

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Table 1: Demographics of children with heart disease who had neurodevelopmental assessment with Mullen Scales of Early Learning (MSEL)

Pre-specified Risk Factors	**Number (%) of children (N=971)**	**MSEL Cognitive score* Mean (SD) (N =971)**	**MSEL Motor score* Mean (SD) (N=753)**	**Number (%) of children with any MSEL score less than 1 SD below mean (normal)**	**Number (%) of children with any MSEL score 1-2 SD below mean (borderline)**	**Number (%) of children with any MSEL score more than 2 SD below mean (developmental delay)**
Male	497 (51.2)	99.6 (21.3)	45.6 (12.7)	328 (66.0)	93 (18.7)	76 (15.3)
Female	474 (48.8)	101.2 (21.7)	44.9 (11.9)	315 (66.5)	88 (18.5	71 (15.0)
Age group						
0 - 16 weeks	203 (20.9)	103.5 (15.4)	47.9 (7.9)	162 (79.8)	38 (18.7)	3 (1.5)
17 - 34 weeks	187 (19.3)	102.8 (16.7)	45.3 (11.5)	130 (69.5)	33 (17.7)	24 (12.8)
35 - 60 weeks	191 (19.7)	99.1 (16.9)	41.2 (13.7)	100 (52.4)	50 (26.2)	41 (21.4)
15 months - 2.9 years	194 (20.0)	92.9 (22.9)	46.6 (14.6)	111 (57.2)	42 (21.7)	41 (21.1)
3 years - 4.9 years	196 (20.2)	103.4 (30.2)	-	140 (71.4)	18 (9.2)	38 (19.4)
Diagnosis						
Functionally univentricular heart (UVH) – No	879 (90.5)	100.7 (21.5)	45.5 (12.4)	589 (67.0)	160 (18.2)	130 (14.8)
Yes	92 (9.5)	97.0 (21.5)	42.2 (10.7)	54 (58.7)	21 (22.8)	17 (18.5)
UVH + arch obstruction	53 (5.5)	96.8 (20.1)	42.6 (11.3)	31 (58.5)	13 (24.5)	9 (17.0)
UVH - arch obstruction	39 (4.0)	97.2 (23.6)	41.8 (10.1)	23 (59.0)	8 (20.5)	8 (20.5)
Biventricular + arch obstruction	87 (9.0)	101.1 (19.9)	47.6 (11.3)	62 (71.3)	14 (16.1)	11 (12.6)
Biventricular - arch obstruction	721 (74.3)	100.9 (22.2)	45.1 (12.6)	479 (66.5)	130 (18.0)	112 (15.5)
Acquired/Medical heart disease	71 (7.3)	98.4 (16.2)	47.0 (12.2)	48 (67.6)	16 (22.5)	7 (9.9)
Procedures						
Surgery – No	394 (40.6)	101.7 (20.6)	47.1 (12.3)	284 (72.1)	65 (16.5)	45 (11.4)
1 or more	577 (59.4)	99.4 (22.1)	43.9 (12.2)	359 (62.2)	116 (20.1)	102 (17.7)
Catheter intervention						
No	759 (78.2)	100.8 (21.2)	45.7 (12.0)	508 (66.9)	142 (18.7)	109 (14.4)
1 or more	212 (21.8)	98.8 (22.6)	43.4 (13.6)	135 (63.7)	39 (18.4)	38 (17.9)
Known factor						
None	735 (75.7)	105.5 (17.9)	47.9 (10.9)	567 (77.1)	120 (16.4)	48 (6.5)
Syndromes	162 (16.7)	83.5 (23.9)	36.5 (12.5)	54 (33.3)	37 (22.9)	71 (43.8)
Developmental delay of unknown cause	38 (3.9)	78.7 (22.9)	33.4 (12.8)	6 (15.8)	15 (39.5)	17 (44.7)
Acquired brain injury	32 (3.3)	96.1 (22.1)	40.9 (14.7)	16 (50.0)	8 (25.0)	8 (25.0)
Syndrome + brain injury	4 (0.4)	74.3 (28.1)	28.0 (2.8)	0 (0)	1 (25.0)	3 (75.0)
Previous history of clinical event linked to DD	841 (86.6)	101.2 (21.3)	45.5 (12.3)	567 (67.4)	150 (17.9)	124 (14.7)
None	98 (10.1)	99.3 (21.5)	45.1 (12.1)	67 (68.4)	17 (17.3)	14 (14.3)
Prematurity	19 (2.0)	80.8 (18.9)	41.4 (11.3)	5 (26.3)	9 (47.4)	5 (26.3)

Cardiac arrest	10 (1.0)	87.0 (20.3)	34.4 (12.0)	3 (30.0)	4 (40.0)	3 (30.0)
Extracorporeal Life Support (ECLS)	3 (0.3)	79.3 (28.0)	20.0 (-)	1 (33.3)	1 (33.3)	1 (33.3)
Multiple risk factors						
Ethnicity^						
White	618 (66.0)	100.8 (21.1)	45.0 (12.4)	414 (67.0)	111 (18.0)	93 (15.0)
Black	113 (12.1)	100.2 (23.6)	48.7 (12.4)	74 (65.5)	19 (16.8)	20 (17.7)
Asian	133 (14.2)	101.1 (21.6)	44.5 (11.8)	91 (68.4)	26 (19.6)	16 (12.0)
Other	72 (7.7)	90.9 (28.0)	36.6 (14.1)	43 (59.7)	18 (25.0)	11 (15.3)
IMD^						
1st Quintile (most deprived)	195 (21.4)	99.9 (21.64)	46.4 (12.8)	128 (65.6)	37 (19.0)	30 (15.4)
2nd	274 (30.1)	99.8 (21.8))	45.8 (11.5)	185 (67.5)	46 (16.8)	43 (15.7)
3rd	162 (17.8)	98.9 (21.3)	43.6 (11.8)	100 (61.7)	40 (24.7)	22 (13.6)
4th	136 (14.9)	102.4 (21.8)	45.2 (12.7)	90 (66.2)	27 (19.8)	19 (14.0)
5th	144 (18.8)	103.1 (20.7)	46.6 (12.2)	104 (72.2)	22 (15.3)	18 (12.5)
Primary Language^	852 (91.4)	100.6 (21.5)	45.6 (12.4)	575 (67.5)	148 (17.4)	129 (15.1)
English	80 (8.6)	97.2 (20.1)	43.5 (11.9)	48 (60.0)	21 (26.2)	11 (13.8)
Other						
Maternal Education^	165 (20.4)	102.7 (20.1)	46.0 (11.9)	111 (67.3)	37 (22.4)	17 (10.3)
Postgraduate	283 (35.0)	103.1 (22.7)	45.7 (11.6)	202 (71.4)	44 (15.5)	37 (13.1)
Undergraduate	155 (19.2)	98.7 (19.3)	45.0 (13.6)	102 (65.8)	26 (16.8)	27 (17.4)
College/Training > 6th form (secondary school)	162 (20.0)	99.7 (21.1)	45.2 (12.1)	102 (63.0)	38 (23.4)	22 (13.6)
College/Training < 6th form (secondary school)	44 (5.4)	92.2 (23.6)	44.1 (12.1)	27 (61.4)	7 (15.9)	10 (22.7)
Other						

DD – developmental delay, IMD – Index of Multiple deprivation, MSEL - Mullen Scales of Early Learning.

^Missing data – ethnicity n=35 (3.6%), IMD n=60 (6.2%), primary language n=39 (4.0%), and maternal education n=162 (16.7%)

*The 'raw' scores on MSEL for four cognitive scales and separately for the gross motor are computed to form age standardized 'T scores' in each area. The mean 'T scores' for each scale within the general population are 50 with standard deviation 10. The cognitive 'T scores' applicable to the 4 cognitive scales combined may be further computed to generate a composite score which within the general population has a mean of 100 with standard deviation 15.

Table 2: Follow-up services by age band

	Age Band One 0 - 16 weeks n (%)	**Age Band Two** 17 - 34 weeks n (%)	**Age Band Three** 35 - 60 weeks n (%)	**Age Band Four** 15 months -2.9 years n (%)	**Age Band Five** 3.0 - 5.0 years n (%)	**All under fives** n (%)	**p-value***
Total patients	203	187	191	194	196	971	971
Child development, neurology or general paediatric teams (service type one)	32 (15.8)	45 (24.1)	37 (19.4)	41 (21.1)	44 (22.5)	199 (20.5)	0.33
Special senses teams (ophthalmology, audiology) (service type two)	24 (11.8)	28 (15.0)	25 (13.1)	40 (20.6)	46 (23.5)	163 (16.8)	< 0.001
Specialist medical or surgical teams excluding cardiology or cardiac surgery (service type three)	31 (15.3)	28 (15.0)	32 (16.8)	42 (21.7)	52 (26.5)	185 (19.1)	< 0.001
Follow-up by dietetics (service type four)	21 (10.3)	22 (11.8)	17 (8.9)	13 (6.70	15 (7.7)	88 (9.1)	0.16

*The p-value reflects the trend test over age bands.

Table 3: Percentage of children under follow-up services linked to child development in different patient categories of interest

	Age Band One 0-16 weeks N=203	**Age Band Two** 17-34 weeks N=187	**Age Band Three** 35-60 weeks N=191	**Age Band Four** 15 months - 2.9 years N=194	**Age Band Five** 3.0-5 years N=196	**All under fives** N=971
Number and Percentage of children under services – groups one and two						
Known group (n=236)	21/39 53.9%	32/49 65.3%	26/44 59.1%	34/47 72.3%	46/57 80.7%	159 /236 67.4%
No known group (n=735)	26/164 15.9%	18/138 13.0%	20/147 13.6%	25/147 17.0%	19/139 13.7%	108/735 14.7%
Previous history of clinical event linked to DD (n=130)	16/36 44.4%	16/26 61.5%	5/15 33.3%	15/28 53.6%	13/25 52.0%	65/130 50.0%
No previous history of clinical event linked to DD (n=841)	31/167 18.6%	34/161 21.1%	41/176 23.3%	44/166 26.5%	52/171 30.4%	202/841 24.0%
DD based on MSEL (n=147)	3/3 100.0%	14/24 58.3%	22/41 53.7%	28/41 68.3%	31/38 81.6%	98/147 66.7%
No DD based on MSEL (n=824)	44/200 22.0%	36/163 22.1%	24/150 16.0%	31/153 20.3%	34/158 21.5%	169/824 20.5%

DD – Developmental delay, MSEL – Mullen Scales of Early Learning
Comparisons for all children under 5 years, between having a factor and being under services 1 and 2, using Chi square test: known group, previous factor and DD - $P < 0.001$ for all.

Table 4: Multivariable model for pre-specified risk factors for developmental delay based on Mullen Scales of Early Learning scores

	Odds Ratio 95% CI	**p-value**
Male		
Female	0.91 (0.57, 1.46)	0.71
Age group		
0 - 34 weeks	-	
35 - 60 weeks	9.66 (4.61, 20.23)	< 0.001
15 months - 2.9 years	6.70 (3.25, 13.81)	< 0.001
3 years - 4.9 years	4.45 (2.19, 9.04)	< 0.001
Diagnosis		
Functionally univentricular heart	1.04 (0.46, 2.38)	0.92
Procedures		
Surgery - No		
1 or more	1.43 (0.86, 2.37)	0.17
Catheter interventions - No		
1 or more	1.27 (0.72, 2.22)	0.41
Known group - None		
Any known condition	13.28 (8.06, 21.88)	< 0.001
Previous history of clinical event linked to DD - None		
Any previous history	1.13 (0.57, 2.21)	0.73
Ethnicity - Caucasian	-	-
Black	1.34 (0.64, 2.79)	0.44
Asian	0.66 (0.30, 1.47)	0.31
Other	0.68 (0.28, 1.65)	0.40
IMD		
1st Quintile (most deprived)	-	-
2nd	0.86 (0.43, 1.71)	0.66
3rd	0.55 (0.24, 1.27)	0.16
4th	0.78 (0.33, 1.87)	0.58
5th	0.68 (0.28, 1.65)	0.37
Primary Language - English		
Other	0.50 (0.18, 1.38)	0.18
Maternal Education - Graduate		
School /College	1.12 (0.69, 1.82)	0.64

CI – confidence interval, DD – developmental delay, IMD – Index of multiple deprivation, MSEL – Mullen Scales of Early Learning.

Low scores on MSEL refer to MSEL score of more than 2 SD below the normative mean in *either* the cognitive domain (MSEL-cognitive) *or* the gross motor (MSEL-motor) domain in children <33 months and MSEL-cognitive more than 2 SD below the normative mean for children of 33-59 months.