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Original article

Improving the growth of infants with congenital heart disease using a consensus-based nutritional Pathway—A follow up study

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SUMMARY

Background & aims: Congenital Heart Disease (CHD) is the most common congenital abnormality, affecting 9 per 1000 live births. Advances in surgical techniques have significantly improved survival rates but growth failure is associated with increased risk of mortality post-cardiac surgery. Improving growth amongst infants with CHD whilst awaiting surgery is an important component to reducing morbidity as well as improving longer term metabolic outcomes. A consensus-based nutrition pathway was developed and implemented into a regional paediatric cardiology service in 2017. The aim of this study was to evaluate the impact of the pathway in a larger cohort of infants with CHD in two epochs: pre-nutrition pathway implementation (Jan 2013–Dec 2016) and post-nutrition pathway implementation (Jan 2017–June 2023).

Methods: Growth measures were extracted from electronic patient records and z-scores were calculated. SuperImposition by Translation And Rotation (SITAR) models were constructed to develop a single fitted curve of growth velocity for each of the two epochs.

Results: Infants with CHD in the post-implementation group achieved significantly better growth outcomes in the first 4-months of life. In addition, after adjustment for group differences, weight gain velocity was significantly higher in the post-implementation epoch ($p = 0.01$). There was no detectable change in the prevalence of overweight or obese children at older timepoints, suggesting that the intervention did not promote the development of obesity although further analysis will be required as the cohort gets older.

Conclusion: A nutrition pathway developed to support growth in infants with CHD before surgery was associated with better growth outcomes during the first year of life compared to an epoch when nutrition support was only given for malnourishment. Achieving normal growth patterns during the first year of life may help to reduce the risk of metabolic disease in later life, although further research will be required to elucidate this.

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1. Introduction

Congenital Heart Disease (CHD) is one of the most common congenital disorders occurring in about 9–10 per 1000 live births worldwide [1,2]. Advances in surgical techniques have improved survival and clinical outcomes [3,4]. Despite this, many infants with CHD experience growth failure prior to surgery which is associated with poorer neurodevelopmental outcomes [5,6], increased risk of mortality [7–12], and metabolic syndrome in adulthood [13]. Although most infants are born with a normal weight-for-age, growth failure often occurs within the first few weeks of life with a reported prevalence of malnutrition during the first 12 months (i.e., <-2 z-score) of 21–29 % for weight, height and weight for height [8,14]. Poor growth appears to occur irrespective of geographical location or disease severity [14]. Features correlated with increased risk of malnutrition are antenatal diagnosis, associated genetic syndrome, birth weight ≤3 kg, complexity of CHD (≥2 significant lesions, or double outlet right ventricle or single ventricle physiology), cardiac surgery after 30 days of life, or diuretic medication before surgery or 1 month following surgery [15]. Up to 35 % of infants with CHD experience nutrition and feeding difficulties as a result of i) restricted intake, ii) increased metabolic demand or iii) increased losses and often require the use of nutrient energy dense feeds or nasogastric tube feeding [15–17]. Nutrition awareness tools providing a standardised approach to identifying infants and children with CHD at risk may provide opportunities to for earlier nutrition support [18].

In other groups of vulnerable infants (e.g. preterm infants) at risk of poor growth, the implementation of nutritional care pathways has been associated with reduced incidence of growth faltering and subsequent malnutrition [19,20]. Similar efforts to prevent malnutrition in a CHD cohort during the first month of life, with to the use of nutrient energy dense feeds to support growth before surgery [21–23], have been shown to reduce weight loss following cardiac surgery [24–26] and promote post-operative catch-up weight gain and reduce the length of paediatric intensive care unit (PICU) and hospital stay [27]. In 2017, we developed a nutrition pathway to promote weight gain in infants with CHD before surgery using Delphi consensus methodology [22]. Following this, the pathway was implemented into a regional paediatric cardiology service. An initial study (n = 44) considering the use of a nutrition pathway to support growth in infants with CHD before surgery demonstrated significantly improved growth outcomes at 4 and 12 months of age [19]. We therefore aimed to evaluate the impact of this consensus-based nutrition pathway on growth in a larger cohort of infants with CHD following the implementation in a regional paediatric cardiology service over a five-year period.

2. Materials and methods

2.1. Demographics

Two epochs were defined from using a database of paediatric cardiac surgical cases supported by the nutrition multidisciplinary team (MDT). The two epochs comprised of i) a pre-nutrition pathway group which included infants born between January 2013 and December 2016, and ii) a post-nutrition pathway implementation group that included infants born from January 2017–June 2023. Before the nutrition pathway implementation, nutrition support was provided in the form of nutrient energy dense feeds in a more ad-hoc manner, usually commenced once an infant had experienced growth faltering and was malnourished [8]. The nutrition pathway promoted early use of nutrient energy dense feeds within the first few weeks of life, with the goal of supporting normal growth and preventing malnutrition, and has been described elsewhere, but in brief [22].

Epoch 1: Infants were reviewed by a dietitian and provided with nutrient energy of growth faltering. Support provided was ad-hoc and not standardised. **Epoch 2:** As part of this pathway development a paediatric cardiology nutrition group was formed, which included Paediatric Congenital Cardiac Nurses, Speech and Language Therapists and specialist paediatric dietitians. The team held weekly meeting to discuss patients. Standardised templates for Nutrition Care Plans A, B and C were available on the electronic health record. In brief ***Nutrition Care Plan A:*** infant is growing well, normal energy and protein requirements 90–100 kcal/kg, protein 1.5 g/kg (e.g. 2 g protein per 150 ml), continue with breastfeeding or standard infant formula on demand. ***Nutrition Care Plan B:*** Not growing well e.g. 1–2 centiles below birth centile and CHD lesion associated with higher nutrition risk, provide approximately 10 % extra energy 100–110 kcal/kg (protein contributing 9–12 % energy), as well as approximately 30–50 % extra protein (around 2.5 g/kg protein). Infants should be offered breastmilk or standard infant formula in addition to 30–80 % of nutrition requirements for nutrient dense infant formula per day. ***Nutrition Care Plan C:*** Not growing e.g. > 2 centiles below birth rate and CHD lesion associated with higher nutrition risk. Provided approximately 10–20 % extra energy 120–150 kcal/kg (protein contributing 10–15 % energy) and up to 50–100 % extra protein (up to 4 g/kg protein – check renal function). Infants should be offered breastmilk or standard infant formula in addition to 30–80 % of nutrition requirements for nutrient dense infant formula per day addition to a minimum of 50 % (and up to 100 %) of nutrition requirements as energy/nutrient dense infant formula or as overnight or nasogastric feeds. A multivitamin which included vitamin D was provided as per manufacturer recommendations to all infants (Supplementary File 1: Summary of nutrition pathway for improving growth in infants with CHD before surgery).

2.2. Data extraction

Age at first surgery, clinical diagnosis along with weight and length/height data were extracted from electronic patient records for infants from both epochs. Length/height data was matched to weight data for the closest match by date of measurement within the following time frames, to obtain a dataset for calculation of weight-for-height (WFH) z-scores:

- For patients under 12 months of age, weight data was matched with the length data for the closest measure within one month of the date of weight measure,
- For patients between 12 and 24 months of age, weight data was matched with the length data for the closest measure within two months of the date of weight measure,
- For patients over 24 months of age, weight data was matched with the length data for the closest measure within six months of the date of weight measure.

2.3. Statistical analysis

Categorical variables are presented as frequencies and continuous variables as mean and standard deviation (SD). All growth variables were converted into age- and gender-adjusted z-scores using relevant growth standards:

- For preterm infants, before term corrected age, re-analysed UK 1990 data (i.e., the RCPCH Newborn Infant Close Monitoring chart) was used for z-score calculation. This included infants

with trisomy 21 diagnosis, as recommended by the Down's Syndrome Medical Interest Group [28].
- For infants born at or after term (excluding those with a trisomy 21 diagnosis), the World Health Organisation (WHO) growth standard [29] were used for z-score calculation. A corrected age was used for all preterm infants throughout their inclusion period.
- For infants with trisomy 21 diagnosis at or after term corrected age, LMS values provided by Zemel et al. [30] were used for z-score calculations.

R-studio packages for calculation of z-scores were used where available. For z-score calculations using Zemel standard an R script was developed. WHO cut offs were used to define moderate malnutrition < −2 z-scores for wasting - weight for height z scores (WHZ), stunting - length for age z scores (HAZ) and underweight - weight for age z scores (WAZ). Overweight status was defined as WHZ > +2 and obese WHZ > +3 [31]. The main outcome measure was the calculated difference between z-score at each timepoint and the z-score at birth (z-score change). Ten different timepoints were defined for each cohort: birth, 1 month old, 2 months old, 3 months old, 4 months old, 12 months old, 2 years old, 3 years old and 5 years old. No inference was made when the birth measurement was missing. Unadjusted differences between groups were assessed by unpaired t-tests. Changes in SD score were adjusted for the prevalence of prematurity, Down's syndrome, cyanotic heart disease and single ventricle conditions in the two epochs. Super Imposition by Translation And Rotation (SITAR) models using R-studio (1.4.0, London, London, UK) were constructed to develop a single fitted curve of weight gain intensity and growth velocity for each epoch. A *p*-value of $p < 0.05$ was considered statistically significant.

2.4. Ethical considerations

The CHD nutrition pathway was applied to all infants who met the criteria for moderate to high risk for growth failure as part of a change in practice brought about through a quality improvement project. It was therefore the study of a clinical practice change using QI methodology and not an interventional study, with no ethical approval required. Growth data were collected as part of a registered audit of the new practice. Opinion regarding ethical review was sought from a local ethics committee regarding the use of growth data and felt to be unnecessary in the context of a service evaluation. The project was registered with the host institution as a service evaluation [number 7784].

3. Results

In total, there were 656 patients identified in the pre-pathway epoch and 528 patients identified in the post-pathway implementation epoch.

3.1. Demographics

In the pre-pathway group, there were a total of 10 966 anthropometric measures i) 5592 WAZ, ii) 2718 HAZ, and 2656 WHZ and following the removal of duplicate measurements for the same patient within each timepoint there were unique measures for i) 2280 WAZ, ii) 1652 HAZ and 1605 WHZ. In the post-implementation group there were a total of 14 078 anthropometric measures i) 10170 WAZ, ii) 1933 HAZ, and 1975 WHZ and following the removal of duplicate measurements for the same patient within each timepoint there were unique measures for i) 2440 WAZ, ii) 1455 HAZ and 1364 WHZ. Demographic information was retrieved about clinical diagnosis, sex and co-morbidities which could affect growth such as trisomy 21 or premature birth, as well as cardiac lesion.

There was no statistically significant difference between the two epochs with regards to median age at first surgery (epoch 1: 67 days (Inter quartile range (IQR) 14–171) vs epoch 2: 60 days (IQR 12–156, Mann Whitney U test $p = 0.33$) (Table 1), or with regards to mortality including those infants with single ventricular physiology <12 months of age with 6 % (n = 3/50) and epoch 2: 7.8 % (n = 4/51) ($p = 0.40$). Mortality for matched time periods within the cohorts in epoch 1: 2.6 % (n = 17) and epoch 2: 3.7 % (n = 20) ($p = 0.2$). The total number of infants with necrotising enterocolitis in epoch 1: 5.9 % (n = 39) and epoch 2: 5.8 % (n = 31) ($p = 0.9$) and paediatric intensive unit care length of stay was epoch 1: 15.7 ± 0.6 days and

Table 1
Demographic information for both cohorts.

	Pre-nutrition pathway 55 % (n = 656)	Post-nutrition pathway implementation 45 % (n = 528)	*P* value
Female gender (%, n)	46.8 % (n = 307)	42.6 % (n = 225)	0.15
Infants born preterm (%, n)	16.6 % (n = 109)	15.73 % (n = 83)	0.68
Trisomy 21 (%, n)	7.5 % (n = 49)	12.7 % (n = 67)	**0.003**
Deceased (%, n)	4.4 % (n = 29)	5.5 % (n = 29)	0.40
Paediatric intensive care unit (PICU) length of stay (days±SD)	15.7 ± 70.6	15.0 ± 96.0	0.9
Necrotising enterocolitis total	5.9 % (n = 39)	5.8 % (n = 31)	0.9
Mortality	2.6 % (n = 17)	3.7 % (n = 20)	0.2
Diagnosis			
Single ventricular physiology	7.8 % (n = 51)	9.5 % (n = 50)	0.39
Acyanotic	59.0 % (n = 387)	50.2 % (n = 265)	**<0.001**
Shunt lesions	38.9 % (n = 255)	30.9 % (n = 163)	**<0.001**
Anomalies of extra pericardial arterial trunks	13.6 % (n = 89)	13.3 % (n = 70)	0.76
Anomalies of ventricular outflow tracts	3.8 % (n = 25)	4.4 % (n = 23)	0.53
Anomalies of AV junction and AV valves	0.5 % (n = 3)	0.4 % (n = 2)	0.81
Arrhythmias	1.2 % (n = 8)	0.2 % (n = 1)	0.06
Cardiomyopathies	1.1 % (n = 7)	1.1 % (n = 6)	0.96
Cyanotic	27.3 % (n = 179)	37.9 % (n = 200)	**<0.001**
Complex anomalies of ventricular outflow tracts and Pas	23.0 % (n = 151)	33.5 % (n = 177)	**<0.001**
Anomalies of venous return	2.7 % (n = 18)	2.7 % (n = 14)	0.97
Miscellaneous	1.5 % (n = 10)	1.7 % (n = 9)	0.87
Missing diagnosis data	6.9 % (n = 45)	3.6 % (n = 19)	**0.01**
Age at first surgery days, median (inter quartile range)	60 (14–171)	67 (12–156)	0.33

epoch 2: 15.0 ± 96.0 (p = 0.9), all of which were in line with national average.

Standardised nutrition care plans were implemented into the electronic patient records (2017). In epoch 2 infants <12 months with recorded nutrition care plans; nutrition care plan A 1 % (no follow up) (n = 5/456), B (bi-monthly review) 10 % (n = 45/456), and C (weekly review) 89 % (n = 406/456) 406 (89 %). Infants moved up from one category to another more than once; i) episodes of moving from A to B: 3. Infants who moved from A to B at least once: 3, ii) episodes of moving from B to C: 42. Infants moved from B to C at least once: 34 and iii) episodes of moving from A to C: 7. Infants moved from A to C at least once: 4.

3.2. Prevalence of underweight, overweight and other growth derangements

The prevalence of underweight children (WAZ < −2), stunted children (HAZ < −2) and children with wasting (weight-for-length z-score < −2) was recorded at each timepoint (Table 2). There was a significantly higher proportion of infants with Trisomy 21 in epoch 2 12.5 % vs. 7.5 % in epoch 1 (p=<0.03), which may have impacted on low weight for age and weight for height at 3 years of age. There were also significantly more children with shunt dependent lesions in epoch 2 with 37.9 % compared to 27.2 % from epoch 1 which may also have impacted weight for height. The prevalence of overweight and obesity was low in this cohort and did not increase at any time point (Table 3). Infants born premature (corrected for gestational age) and those with trisomy 21, who may experience different growth patterns to those of other children, were included.

3.3. Change in anthropometry from birth across various timepoints

In unadjusted analysis, there was a significant difference in WAZ change from birth to various time points within the first 4 months of life, with the pre-pathway cohort experiencing a larger reduction in WAZ (Table 4). Although infants in the post-implementation group also experienced a drop in WAZ from birth, this was significantly lower (Table 4 and Fig. 1). After adjustment for the differing prevalence of prematurity, Down's syndrome, cyanotic heart disease and single ventricle defects, an effect persisted at 4 months of life but not at other time points. There were no significant differences in height and weight-for-height growth between the two epochs (except a slight reduction in height growth at the 4-year timepoint).

For SITAR analysis of early weight gain, infants were selected if they were weighed at least three times in their first 150 days of life, including at least one weight in the first seven days of life and one between 120 and 150 days of life (71 infants in the pre-pathway epoch and 258 in the post-pathway epoch). The SITAR model assessed for associations between epoch and the size, timing and velocity of weight gain. There was no difference in the size metric (p = 0.73, reflecting similar size at birth) but the timing of peak weight gain velocity was earlier (p < 0.01) and the overall velocity was faster (p < 0.01). These effects are illustrated by the weight gain and velocity curves generated by the SITAR model (Fig. 2A-B). The effects persisted when the patient population was limited to infants with a two ventricle physiology (size p = 0.74, timing p < 0.01, velocity p = 0.02) (Fig. 2C). Differences appeared similar in the population with single ventricle physiology but did not reach statistical significance in this smaller cohort (size p = 0.73, timing p = 0.20, velocity p = 0.20) (Fig. 2D).

Table 2
Prevalence of malnutrition defined as < -2SD at various timepoints.

Weight-for-age z-score < -2SD	Pre-nutrition pathway	Post-nutrition pathway	*p*-Value
Birth (%, n)	5 % (8/146)	8 % (29/364)	0.43
1 month (%, n)	35 % (61/175)	31 % (106/340)	0.46
2 months (%, n)	44 % (77/174)	39 % (124/321)	0.26
3 months (%, n)	47 % (71/151)	42 % (142/336)	0.38
4 months (%, n)	44 % (69/156)	42 % (128/308)	0.65
12 months (%, n)	17 % (36/209)	18 % (38/209)	0.90
2 years (%, n)	7 % (15/203)	13 % (17/135)	0.16
3 years (%, n)	10 % (31/311)	10 % (16/156)	1.00
4 years (%, n)	6 % (16/276)	14 % (14/99)	**0.02**
5 years (%, n)	8 % (14/181)	12 % (6/50)	0.51
Height-for-age z-score < -2SD	**Pre-nutrition pathway**	**Post-nutrition pathway**	***p*-Value**
Birth (%, n)	17 % (7/41)	12 % (13/109)	0.58
1 month (%, n)	24 % (20/83)	30 % (43/142)	0.40
2 months (%, n)	24 % (21/86)	27 % (33/124)	0.84
3 months (%, n)	35 % (27/77)	31 % (41/134)	0.61
4 months (%, n)	33 % (32/96)	28 % (32/116)	0.45
12 months (%, n)	19 % (32/170)	19 % (30/155)	1.00
2 years (%, n)	20 % (34/171)	22 % (23/106)	0.83
3 years (%, n)	15 % (40/274)	21 % (30/143)	0.13
4 years (%, n)	16 % (38/245)	21 % (19/92)	0.34
5 years (%, n)	13 % (21/163)	18 % (8/45)	0.55
Weight-for-height z-score < -2SD	**Pre-nutrition pathway**	**Post-nutrition pathway**	***p*-Value**
Birth (%, n)	8 % (3/38)	11 % (10/92)	0.85
1 month (%, n)	9 % (7/76)	22 % (27/125)	0.04
2 months (%, n)	17 % (14/83)	19 % (23/119)	0.79
3 months (%, n)	18 % (14/76)	19 % (26/136)	1.00
4 months (%, n)	20 % (19/97)	19 % (23/119)	1.00
12 months (%, n)	12 % (20/170)	11 % (17/158)	0.91
2 years (%, n)	4 % (6/171)	8 % (9/108)	0.14
3 years (%, n)	3 % (7/271)	7 % (10/140)	0.05
4 years (%, n)	1 % (3/232)	7 % (6/83)	0.02
5 years (%, n)	2 % (3/146)	5 % (2/40)	0.64

Table 3
Prevalence of overweight and obese children at each time point.

Weight-for-length/BMI z-score > +2SD (Overweight)	Pre-nutrition pathway	Post-nutrition pathway	*p*-Value
Birth (%, n)	2 % (3/146)	2 % (7/364)	1.00
1 month (%, n)	0 % (0/175)	0 % (1/340)	1.00
2 months (%, n)	0 % (0/174)	1 % (2/321)	0.76
3 months (%, n)	0 % (0/151)	1 % (2/336)	0.85
4 months (%, n)	1 % (1/156)	1 % (2/308)	1.00
12 months (%, n)	2 % (5/209)	1 % (3/209)	0.72
2 years (%, n)	2 % (4/203)	2 % (3/135)	1.00
3 years (%, n)	2 % (7/311)	4 % (6/156)	0.49
4 years (%, n)	3 % (9/276)	4 % (4/99)	0.97
5 years (%, n)	4 % (8/181)	2 % (1/50)	0.71
Weight-for-length z-score > +3SD (Obese)	**Pre-nutrition pathway**	**Post-nutrition pathway**	***p*-Value**
Birth (%, n)	0 % (0/146)	1 % (3/364)	0.65
1 month (%, n)	0 % (0/175)	0 % (0/340)	–
2 months (%, n)	0 % (0/174)	0 % (0/321)	–
3 months (%, n)	0 % (0/151)	0 % (0/336)	–
4 months (%, n)	0 % (0/156)	0 % (0/308)	–
12 months (%, n)	0 % (1/209)	0 % (0/209)	1.00
2 years (%, n)	0 % (1/203)	1 % (1/135)	1.00
3 years (%, n)	0 % (0/311)	1 % (2/156)	0.21
4 years (%, n)	1 % (3/276)	1 % (1/99)	1.00
5 years (%, n)	1 % (1/181)	0 % (0/50)	1.00

Table 4
Change in z-score birth for weight, length and weight-for-length/BMI for both cohorts across various timepoints. *unpaired t-test; ** linear regression model assessing influence of epoch on change in z-score after adjustment for prevalence of prematurity, Down's syndrome, cyanotic heart disease and single ventricle defects.

	Pre-nutrition pathway	Post-nutrition pathway	Unadjusted *P* value*	Adjusted P value**
Change in WAZ since birth	**Mean ± SD**	**Mean ± SD**		
1 month	−1.37 ± 0.84	−1.2 ± 0.76	0.16	0.26
2 months	−1.65 ± 0.97	−1.34 ± 1	**0.02**	0.09
3 months	−1.73 ± 1.18	−1.35 ± 1.12	**0.03**	0.06
4 months	−1.84 ± 1.15	−1.27 ± 1.2	**0.01**	**0.02**
12 months	−0.63 ± 1.32	−0.38 ± 1.32	0.24	0.35
2 years	−0.29 ± 1.4	−0.27 ± 1.16	0.92	0.96
3 years	−0.08 ± 1.22	−0.05 ± 1.17	0.85	1.00
4 years	0.08 ± 1.3	−0.21 ± 1.21	0.18	0.10
5 years	−0.08 ± 1.37	−0.11 ± 1.07	0.91	0.67
Change in HAZ since birth				
1 month	0.07 ± 1.19	−0.46 ± 1.12	0.25	0.13
2 months	−0.69 ± 0.89	−0.66 ± 1.56	0.94	0.87
3 months	−0.76 ± 0.86	−0.79 ± 1.82	0.94	0.54
4 months	−0.54 ± 1.48	−0.56 ± 1.69	0.98	0.59
12 months	0.01 ± 1.28	−0.13 ± 1.52	0.77	0.99
2 years	−0.29 ± 1.47	−0.42 ± 1.24	0.79	0.64
3 years	0.17 ± 1.33	−0.26 ± 1.35	0.30	0.14
4 years	−0.03 ± 0.97	−0.42 ± 1.09	0.31	0.03
5 years	−0.25 ± 1.16	−0.13 ± 1.3	0.84	0.29
Change in WFHZ since birth				
1 month	−2.47 ± 1.79	−0.95 ± 1.75	0.06	0.03
2 months	−1.32 ± 1.37	−0.49 ± 1.6	0.13	0.21
3 months	−0.97 ± 1.51	−0.56 ± 1.83	0.56	0.27
4 months	−1.71 ± 1.8	−0.29 ± 1.52	0.10	0.08
12 months	−0.04 ± 1.42	−0.42 ± 1.27	0.46	0.44
2 years	−0.5 ± 1.02	0.16 ± 1.77	0.20	0.22
3 years	0.03 ± 1.57	0.19 ± 1.7	0.76	0.90
4 years	0.27 ± 2	1 ± 1.91	0.31	0.30
5 years	0.02 ± 2.16	0.05 ± 1.67	0.98	0.77

SITAR models were also built for the same infants during the first two years of life and the first five years of life (Fig. 3A and B respectively). In these models, early differences are smoothed out. In the case of the model for the first five years of life, there is a divergence at age five, with children in the post-implementation cohort being lighter at this age and causing the overall velocity to be slower ($p = 0.03$).

4. Discussion

The goal of early nutrition support in infants with CHD is to support normal growth by providing additional energy, protein and nutrients required for i) increased metabolic demand, ii) reduced appetite or intake due to early satiety or iii) increased losses due to emesis. In this quality improvement project, infants supported by

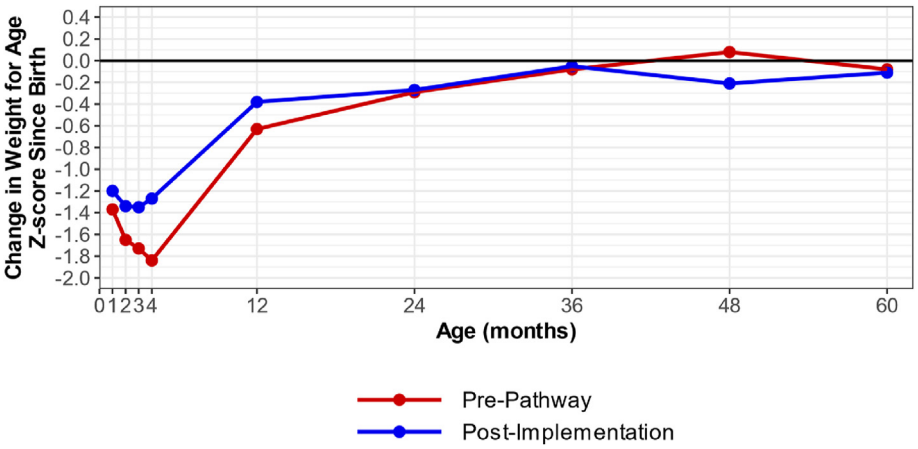

Fig. 1. Mean change in weight for age z-score since birth.

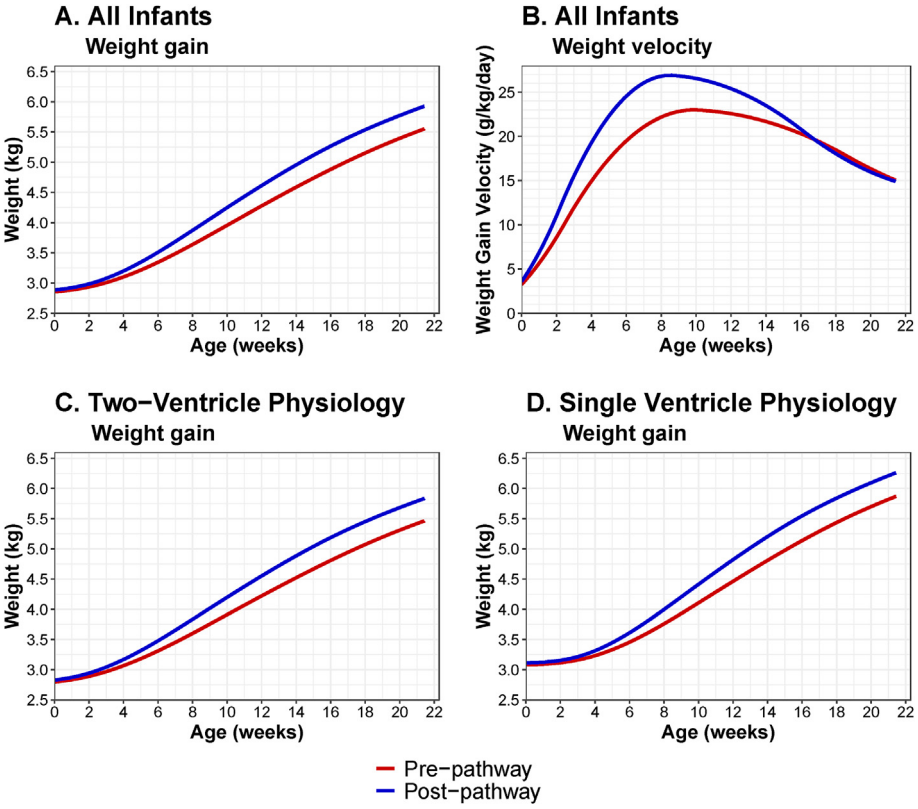

Fig. 2. SITAR curves showing the effect of pathway introduction on A. the early weight gain pattern; B. early weight gain velocity for infants born with congenital heart disease; C. the early weight gain pattern of infants with two ventricle physiology; and D. the early weight gain pattern of infants with single ventricle physiology.

in the post-nutrition pathway implementation group had better growth outcomes and clinical outcomes [19,22], compared to the pre-pathway epoch. However, despite improvements in growth velocity and similar age at the time of the first surgery, many infants continue to experience growth faltering in the face of seemingly adequate amounts of nutrition support, with high levels of malnutrition in both epochs.

Nutritional requirements for infants with CHD are suggested to be around 130–150 kcal/kg/day and 3–3.9 g/kg of protein with a protein:energy ratio of 10 % [24,32–35], and recommended were delivered within the post-implementation nutrition pathway [19,22]. For infants with CHD, growth faltering depends on the type of cardiac lesion with the most abnormal being observed in those with tetralogy of Fallot, hypoplastic left heart syndrome or other single ventricle physiology [9]. Faltering growth can be defined as a fall in weight for age z (WAZ) score of $\geq$1 occurring over a 1-month period (excluding the first two weeks of life) [36,37]. Catch up growth is where there is increased growth velocity after illness or starvation, with a physiological increase in WAZ following a period of growth faltering usually to the original (birth) WAZ [36]. For infants, normal growth is defined as having occurred when a child has “caught up” to the growth centile line on which the child was growing before the fall in centiles occurred. This needs to be distinguished from when there is accelerated or rapid growth,

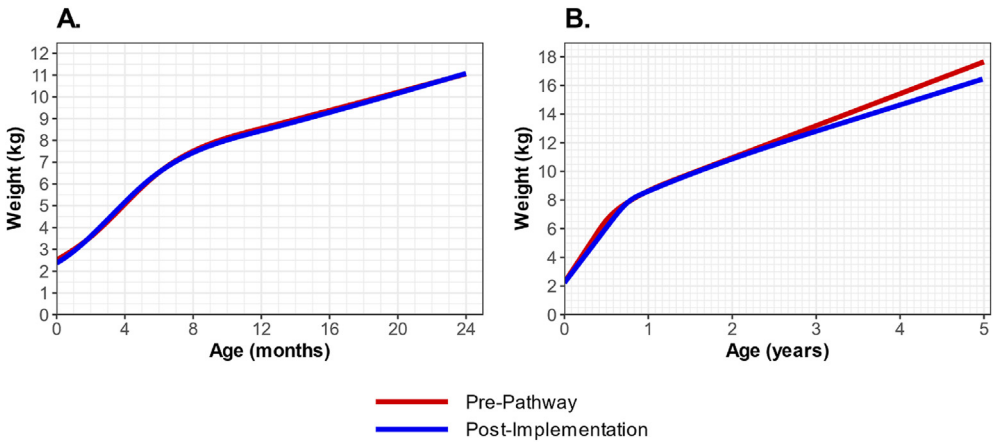

Fig. 3. SITAR curves showing later weight gain patterns for infants with congenital heart disease. A. For the first 2 years of life. B. For the first 5 years of life.

defined as upward crossing of centiles in weight ≥1.0 [36,37], which is not preceded by a period of growth faltering and so is different. This can occur in infants for a variety of reasons (e.g. infants born small for gestational age) or as a result of overfeeding with intake of macronutrients in excess of metabolic requirements [36]. In infants with CHD there is often rapid catch-up weight gain following surgical correction which can lead to unhealthy growth patterns. This is most commonly seen in infants with complex lesions, resulting in weight gain exceeding ≥1.0 rise in z-score, increasing the risk of excess weight, shorter stature during adolescence and adulthood [9,38,39], insulin resistance, higher central adiposity, adverse lipid profiles [40], increasing the risk of developing cardiovascular disease in adulthood [39,41].

In the present study, the use of a nutrition pathway significantly improved weight gain velocity in infants during early life often preceding surgery. Enhanced growth during this period is associated with improved clinical outcomes including reduced length of paediatric intensive care unit stay [19]. However, despite early intervention with regular support using nutrient energy dense feeds, many infants continued to experience malnutrition with 18 % of infants with a WAZ < -2 at 12 months of age. This finding has been described by others including Shi et al., who used a machine learning approach to consider factors associated with postoperative malnutrition in infants with CHD 1 year after complete surgical repair. Results from the work showed that the three most important predictive features for underweight, wasting and stunting status were i) underweight: 1 month postoperative weight for age z-score (WAZ), discharge WAZ and preoperative WAZ, ii) wasting: hospital length of stay, formula intake, and discharge weight for height z-score (WHZ) and iii) stunting: 1 month postoperative height for age z-score (HAZ), discharge HAZ, and aortic clamping time [42]. Similar findings have been described by Brief et al. [15], where despite palliative or corrective surgery 16 % continue to have growth failure at 6 and 12 months post-surgery despite presurgical support with nutrient energy dense feeds. Lisanti et al. have previously identified a range of growth trajectory classes which correlate with clinical indicators and suggest that there are high risk groups within the cohort who may merit closer monitoring and more intensive intervention [43]. Shime et al. reported infants referred to a dietitian had shorter time to receiving nutrition support of any form, enteral feeds and achieving energy requirements. However, despite this group receiving ongoing nutritional support from a dietitian, at stage 3 (Fontan) surgery, 15 % of infants were classified as stunted (height for age z score < -2) [44]. Ours and the work of others suggests more research is required to better understand putative factors preventing normal growth velocity such as increased metabolic demand [32,45], microbiome dysbiosis [46–48], and delayed metabolic maturation [49].

Improved growth outcomes for infants with CHD during the first year of life may help to reduce the risk of poorer longitudinal growth [50] by supporting normal growth patterns in early life [36]. This is important, as malnutrition has long term negative outcomes including reduced longitudinal growth. Moore and coworkers state that *'Growth reflects a complex interaction between nutritional, genetic, hormonal, and environmental factors. It is "programmed" to occur within a "critical time frame" or "epoch" which if missed may not be recoverable'* [51]. Even short-term growth deficit during infancy has been associated with long-term impact on the growth of organs and their function [36,51]. Abnormal growth during infancy, as seen in preterm infants and those born small for gestational age, is associated with increased risk of obesity [52]. Obesity is a is a public health epidemic, with more than 4 million global deaths in 2015, of which 70 % were attributed to cardiovascular disease [39]. Excess weight is a modifiable risk factor for children with CHD [53], with an interplay of factors increasing the risk of obesity, including accelerated catch-up growth following corrective surgery, poor dietary behaviour [54] and reduced physical activity [55]. The prevalence of excess weight in children with CHD is reported to be equal to that of their non-CHD peers [56,57]. Obesity is known to impact on cardiac function for children with certain congenital defects, so supporting normal growth to prevent later obesity is vital [58]. We did not observe an increase in obesity. As this cohort gets older, further analysis will be required to assess whether there is a reduction in the prevalence of obesity. This will be an important area of research, as Aguila et al. have described the negative impact of poor early growth and the impact on abnormal growth patterns of children with CHD from 2 years onwards [9].

Growth faltering resulting in malnutrition causes significant amounts of parental distress [59,60], and whilst the use of this pathway [19,22] has led to slightly less abnormal growth before surgery with regards to length and weight gain. Linear growth is important to support organ maturation [61] and improve cognitive and developmental outcomes [5]. Despite this there was still significant malnutrition even though there was regular support from a dietitian. As such, more work is required to determine the factors influencing growth in this vulnerable cohort, as well as ensuring there is adequate adherence by healthcare professional to the nutrition pathway, i.e. infants considered to be hight risk should have early nutrition support initiated. Our results also suggest

infants continue to experience malnutrition post-surgical repair into the early years of childhood and may require ongoing nutrition support in the months and years following initial palliative surgery particularly in those with complex CHD lesions.

5. Limitations

There are several limitations to this work including issues relating to missing data points especially for length in both epochs, making the interpretation of growth patterns challenging. Birthweight was commonly not recorded in the pre-intervention cohort. It was also not possible to identify difference in co-morbidities associated with genetic conditions such as Trisomy 21, which may introduce bias. We were not able to extract the information relating to tube feeding, specific cardiac information associated with risks of heart failure including aortic valve regurgitation, aortic arch gradient, medication and the relationship these may have with growth outcomes. We were also not able to ascertain parental compliance with dietary recommendations of the use of nutrient-energy dense feeds. We have been unable to ascertain the impact of COVID-19 on growth, as during the pandemic weight and length measures were recorded by parents remotely at home, limiting the quality assurance and quality control of these measures. As the nutrition pathway was only implemented in 2017, it is still too early to tell whether by achieving more normal patterns of growth during the first year of life positively impacts on body habitus or metabolic outcomes during adolescence and adulthood. Longer and larger cohort studies considering the benefits of improved nutrition support, along with advances in medical management, in this vulnerable infant group are required, as well as gaining a better understanding of whether CHD retards metabolic maturation and subsequent growth.

6. Conclusions

A nutrition pathway developed to support growth in infants with CHD before surgery was associated with better growth outcomes during the first year of life compared to an epoch when nutrition support was more *ad-hoc*. Achieving normal growth patterns during the first year of life may help to reduce the risk of metabolic disease in later life, although further research will be required to elucidate this.

Informed consent statement

As this project was considered a service evaluation relating to a current clinical service offered using pseduoanonymised data patient consent was waived.

Author contributions

Conceptualization, LVM; methodology, LVM, MJJ, AY.; formal analysis, CF, AY, LVM.; investigation, LVM, CF; data extraction and curation CD, CF, AR; writing—original draft preparation, LVM, CF; writing—review and editing, RMB, MJJ, LVM, TB, EA, AY; supervision, LVM.; project administration, CF. All authors have read and agreed to the published version of the manuscript.

Institutional review board statement

The use of CHD nutrition-pathway was applied to all infants who met the criteria for moderate to high risk for growth failure as part of a change in practice brought about through a quality improvement project. It was therefore the study of a clinical practice change using QI methodology and not an interventional study, with no ethical approval required. Growth data were collected as part of a registered audit of the new practice. Opinion regarding ethical review was sought from a local ethics committee regarding the use of growth data and felt to be unnecessary in the context of service evaluation. The project was registered on University Hospital Southampton NHS Foundation Trust clinical governance system Ulysess as a service evaluation [Number 7784].

Data availability statement

The data presented in the study are available on request from the corresponding author as part of a data sharing agreement. The data are not publicly available due to University Hospital Southampton Foundation Trust data sharing policy.

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Conflict of interest

Luise Marino has received honorarium to give lectures for Abbott Laboratories, Danone and Nestle, who had no role in role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results. The initial study was supported by a NIHR Integrated Clinical Academic (ICA) Clinical Lectureship ICA-CL-2016. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results. None of the other authors declare no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clnu.2025.03.012.

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