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Original article

# Improving growth of infants with congenital heart disease using a consensus-based nutritional pathway

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SUMMARY

*Objective:* Infants with congenital heart disease (CHD) often experience growth failure prior to surgery, which is associated with increased paediatric-intensive-care unit length of stay (PICU-LOS) and post-operative complications. This study assessed the impact of a pre-operative, consensus-based nutritional pathway (including support from a multi-disciplinary team) on growth and clinical outcome.
*Design:* Single-centre prospective pilot study.
*Setting:* Tertiary paediatric cardiology surgical centre.
*Patients:* Infants with CHD.
*Intervention:* Infants with CHD were followed for up to 4-months-of-age before cardiac surgery and then to 12-months-of-age following the implementation of the consensus-based nutritional-pathway (Intervention group: November 2017–August 2018), with outcomes compared to a historic control group. The nutrition pathway involved a dietitian contacting parents of infants with the highest risk of growth failure weekly; reviewing weight gain and providing feeding support.
*Main outcome measure:* Growth (weight-for-age, WAZ, and height-for-age-z-score, HAZ) at 4 and 12 months-of-age.
*Results:* 44 infants in the intervention group were compared to 38 in the control group. Median (inter quartile range) change in WAZ from birth to 4 months-of-age (−0.9 (−1.5, 0.7)) and from birth to 12 months-of-age (−0.09 (−1.3, 1.1)) in the intervention group compared to the control group (−1.5 (−2.0, −0.4) ($p = 0.04$)) at 4 months-of age and at 12 months-of-age (−0.4 (1.9, 0.2) ($p = 0.03$)). HAZ at 4 months-of-age was −0.7 (−1.4, −0.1) vs. −1.0 (−1.9, −0.3) ($p = 0.6$) in the intervention and control groups respectively, and at 12 months-of-age HAZ was −0.7 (−1.9, −0.07) in the intervention group vs.-1.6 (−2.6, −0.4) in the control group ($p = 0.04$). Duration of PICU-LOS was 8.2 ± 11.6 days intervention vs. 18.3 ± 24.0 days control ($p = 0.006$).
*Conclusion:* Overall weight was well maintained and growth improved in infants who followed the pre-operative nutritional-pathway. The duration of PICU-LOS was significantly lower in the intervention group, which may be due to improved nutritional status, although this requires further investigation.


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**What we know:**

- Infants with congenital heart disease (CHD) often experience growth failure
- Poor growth in infants is associated with increased risk of post-operative complications and paediatric intensive care unit length of stay (PICU-LOS)
- Ensuring optimal growth before surgery has been identified as an important factor to improve short and longer term outcomes

**What this study adds:**

- Using a consensus-based nutritional pathway in daily clinical practise is possible for health care professionals and parents to use
- The use of a consensus-based nutritional pathway, including nutrient energy dense feed and regular monitoring by a dietitian, is associated with improved growth and shorter intensive care stay
- Further work is required to test the use of a consensus based nutritional pathway in a large multicentre study

## Introduction

Congenital heart disease (CHD) is the most common congenital anomaly, occurring in around 10% of live births worldwide [1–3], with a reported UK prevalence of univentricular physiology of 0.16 per 1000 live births [4] and ventricular septal defects (VSD) of 3.5 infants per 1000 births [5]. Advances in medical and surgical management have resulted in improved clinical outcomes [1,6]. However, nutritional impairment and poor growth amongst infants with CHD is common [7–9], and can have an adverse impact on clinical outcomes [10].

The majority of infants with CHD have a normal weight at birth [11]. However, during the first few months of life many experience growth failure, with a decline in weight-for-age z scores (WAZ) and height-for-age z scores (HAZ) of −0.8 and −0.5 respectively [8,9,12,13]. The prevalence of moderate malnutrition (defined as a WAZ of < -2) in infants with CHD is between 21 and 29% [7–9], and poor perioperative growth is associated with an increased risk of morbidity and mortality [10,14].

Children with CHD with persistent malnutrition have reduced post-operative resilience and longer length of paediatric intensive care unit length of stay (PICU-LOS) [15], which is likely to be due to diminished immune response and functional reserve, leading to impaired metabolic control [16,17]. As such, intervening early in life with the use of nutrient-energy dense infant feeds in addition to an infant's usual milk may reduce growth impairment, thereby improving growth and clinical outcomes. This concept has been demonstrated in other chronic diseases such as cystic fibrosis [18].

Infants with the most severe forms of CHD, e.g. hypoplastic left heart syndrome are usually offered staged surgical palliation creating a univentricular circulation. Many of these infants are now included in home monitoring programs seeking to improve growth and reduce mortality between stages of surgical repair [19,20]. Conversely, those with (VSDs) are at risk of congestive heart failure and not usually included in home monitoring programs, despite growth being at significant risk [21,22]. In order to improve nutritional outcomes amongst infants with CHD before surgery, a consensus based pre-operative nutrition pathway has been developed [23], with the aim of i) reducing variation in nutrition management of infants with CHD, ii) promoting early use of energy-nutrient dense infant feeds (e.g. 100 kcal and 2.6 g protein per 100 ml) to reduce the risk of faltering growth and iii) reducing the prevalence of persistent malnutrition prior to surgery. The purpose of this study was to test the use and impact of the consensus based pre-operative nutrition pathway [23] within a tertiary paediatric cardiology service.

## Methods

### *Development of the pre-operative nutritional pathway*

The details of the development of the consensus-based pre-operative nutrition care pathway are published elsewhere [24], but briefly the following process was used: 1) initial development of pathway using available evidence, 2) initial stakeholder meeting to finalise draught guidelines and develop questions 3) a modified Delphi process based on 2 rounds of anonymous online survey, 4) regional cardiac conference and pathway revision, 5) final expert meeting and pathway finalization [24]. The pathway contains five sections: i) assess nutrition risk, ii) classify growth, iii) consider how and iv) what an infant is drinking and eating, iv) determine nutrition risk and appropriate care plan (A, B or C, see Fig. 1).

### *Participant study enrolment*

Infants (≤12 months) with CHD awaiting surgery were prospectively enrolled (November 2017–August 2018) at a single tertiary centre (University Hospital Southampton NHS Foundation Trust). Parents of eligible infants with CHD were approached during the first month of life by the study team. Parents who provided informed consent were regularly contacted by a dietitian from the Paediatric Cardiology Nutrition Multi-disciplinary team (PCNMDT). At each contact parents provided information on growth and nutritional intake. At enrolment, infants were assigned a nutrition care plan according to predefined nutritional risk factors, and followed-up until the time of surgery or 4 months-of-age. Following surgery, infants continued to receive nutrition support as part of standard nutrition practise from a paediatric dietitian until 12 months of age. Exclusion criteria included infants with other diseases which may impact on feeding e.g. neurological-disorders, oncological diagnoses, respiratory disease, primary gut disorders and renal disease.

*A priori* we included children with known growth perturbations such as trisomy 21 or Di-George syndrome (22q.11 micro-deletion), as we were interested in providing nutrition support to all infants considered to have increased nutrition risk. However, there are limitations to this approach as growth in infants with CHD and genetic conditions may have different predicted growth trajectories and so where available, syndrome-appropriate growth charts were used.

### *Paediatric cardiology nutritional multi-disciplinary team*

As part of this study, a PCNMDT 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 electronic patient record templates for Nutrition Care Plans A, B and C were created, which were given to parents and other health care professionals (HCPs) involved in the care of these infants, including their General Practitioners (Fig. 1). Dietitians involved in the study also visited nine district general hospitals within the Wessex Region to introduce

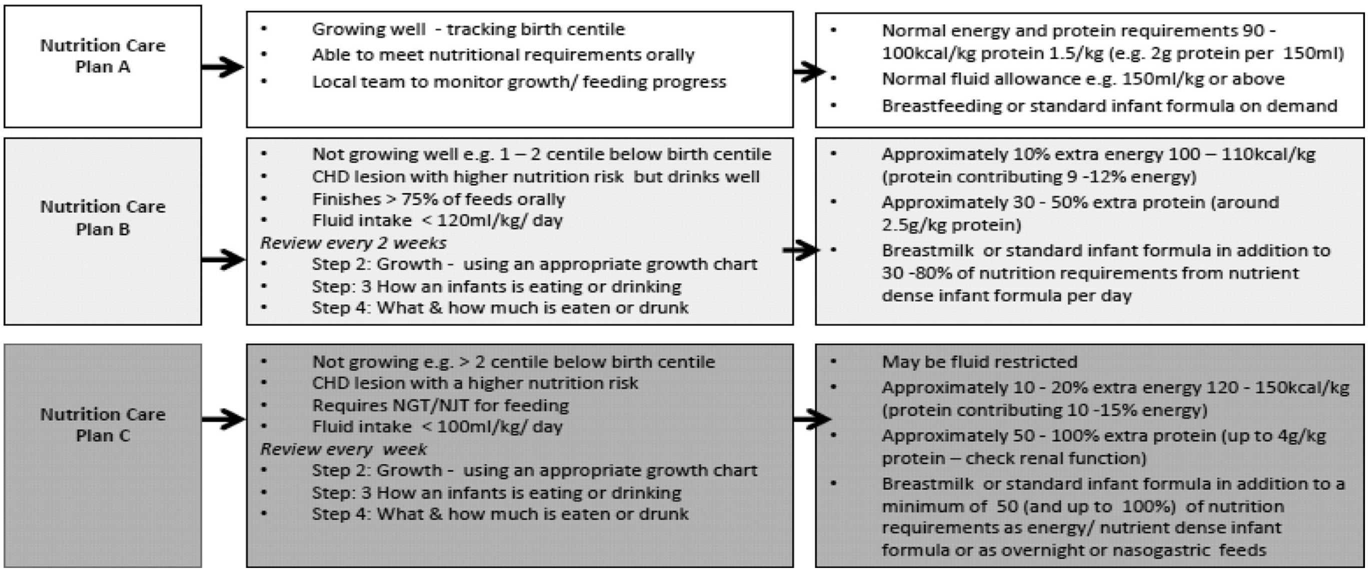


**Fig. 1.** Consensus based pre-operative nutritional pathway for infants with congential heart disease before surgery.

the consensus-based pre-operative nutrition pathway, explain the pathway referral criteria, and answer queries.

As part of the PCNMDT, information was recorded relating to the infants: diagnosis, feed type, most recent weight, weight gain. Infants' progress was discussed in terms of growth, actual versus recommended intake, method of feeding (i.e. oral, nasogastric or jejunal feeding tube and percutaneous endoscopic gastrostomy) and parental reported symptoms such as reflux or vomiting. A revised nutrition care plan was formulated together with individual patient goals, which was then communicated to parents/carers and associated HCPs.

### *Historic control and clinical outcomes*

Clinical outcomes including growth, duration of mechanical ventilation and PICU-LOS during the first year of life of the study group were compared to a historic control group from the same organisation. This was infants with CHD requiring surgery, cared for by the same regional cardiology service during 2012–2013, representing a time before structured routine nutrition input and follow up of infants was implemented. There are 11 Surgical Cardiac Centres in the United Kingdom. The Southampton–Oxford Network receives referrals from 23 district general hospitals as far north as Northamptonshire and as far south as Cornwall in addition to the Channel Islands. As such infants with CHD awaiting surgery are widely dispersed throughout a large regional Paediatric-Cardiac-Networks provision of nutrition support from a paediatric-dietitian varies considerably. Surgical strategy had not changed significantly during these two time periods.

### *Outcomes*

Clinical outcomes were; 1) growth; WAZ and HAZ at 4 months-of-age and 12 months-of-age, 2) duration of mechanical ventilation (MV) on PICU and 3) PICU-LOS.

### *Definitions of moderate malnutrition*

Z-scores were calculated using WHO Anthro software version 3.3.3 2011 [25]. Moderate malnutrition was defined as a WAZ $\leq$ -2 [26]. For ex-preterm infants weight z-scores were corrected using the Fenton growth charts for preterm infants [27] and for infants with Trisomy 21 [28].

### *Statistical analysis*

SPSS version 21 (Chicago, IL) was used for statistical analysis. Median and interquartile range (IQR) was used to summarise data where given that the sample size was small and therefore unable to be assessed formally for normality in a robust manner. Categorical variables are expressed as frequencies and percentages. Non-parametric tests (Mann Whitney) were used to examine differences between outcome variables; HAZ, WAZ, MV and PICU-LOS. A $p$ value of <0.05 was considered statistically significant.

This study was approved by a NHS research ethics committee (West of Scotland Research Ethics Service, reference 17/WS/0084).

## Results

Fifty-four patients parents were approached to participate in the study; of which 44 completed the study (hereafter termed the intervention group, Fig. 2). These were compared to a historical cohort of 38 infants (hereafter termed the control group). Patient characteristics of both the control and intervention groups are shown in Table 1.

### *Nutrition care plans in the intervention group*

During the intervention period the majority of infants were on Nutrition Care plan C (64%) with the remainder on Nutrition Care Plan B. The majority (54.6%) of infants were managed using nutrient-energy dense feed (including extensively hydrolysed) alone, with the remainder given a combination of nutrient energy dense feed and breastmilk (27%), or standard infant formula (15.6%). A minority (1.8%) of infants during the intervention period received an amino acid infant formula. 39.2% of infants in the intervention period were reported to have symptoms of reflux and 30% required a enteral feeding tube.

### *Growth during the first year of life*

Growth outcomes are summarised in Table 2 and Fig. 3. There was a significant reduction in the median (IQR) change in WAZ

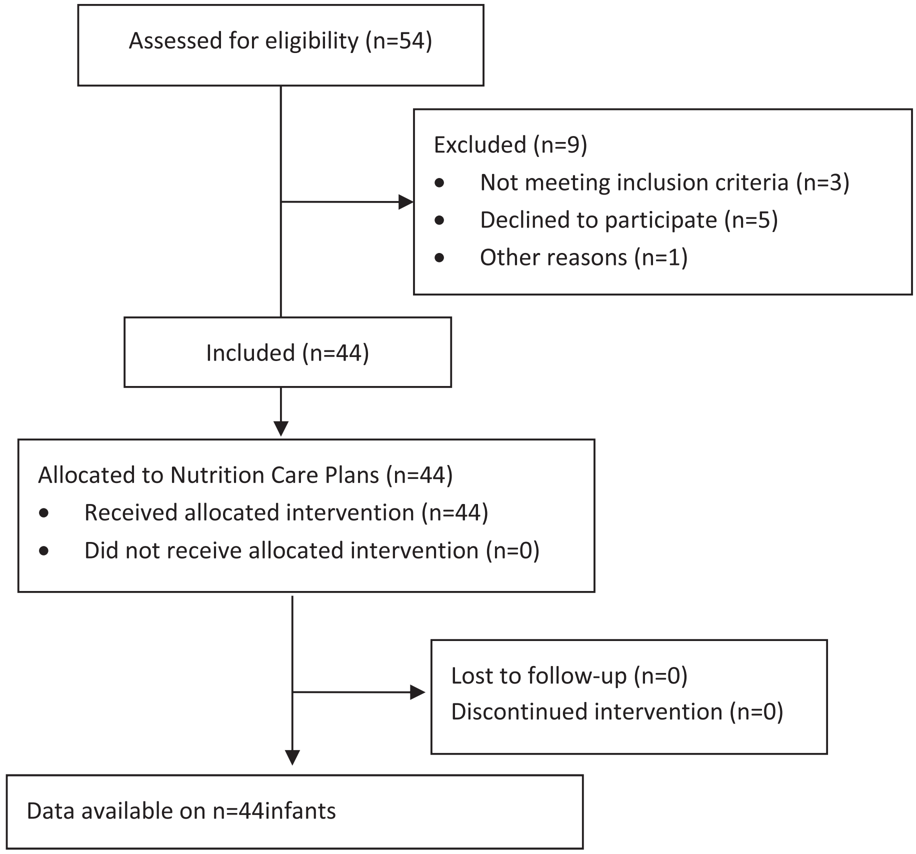


**Fig. 2.** Flow diagram of study participants.

from birth to 4 months-of-age (−0.9 (−1.5, 0.7)) and from birth to 12 months-of-age (−0.09 (−1.3, 1.1)) in the intervention group compared to the control group (−1.5 (−2.0, −0.4) ($p = 0.04$)) at 4 months-of age and at 12 months-of-age (−0.4 (−1.9, 0.2) ($p = 0.03$)), see Fig. 3a). There were no significant differences between the intervention and control groups for WAZ at baseline, 4 months and 12 months (Fig. 3b), nor were there for weight for length z scores at 4 months and 12 months (Fig. 3c). Median (IQR)

**Table 1**
Baseline characteristics values.

| Variables | Control (n = 38) | | Intervention (n = 44) | P= |
|---|---|---|---|---|
| Gender | | | | |
| Female | 23 | | 17 | 0.06 |
| Male | 13 | | 27 | 0.02 |
| Age | Median (IQR) | | Median (IQR) | |
| Age (months) – entry | 0.4<br>(0.2, 1.0) | | 0.1<br>0.1 (0, 0.7) | 0.01 |
| Age (months) – 4 months | 3.8<br>(3.2, 4.1) | | 4<br>(3.9, 4.3) | 0.2 |
| Age (months) – 12 months | 11.6<br>(9, 12.6) | | 11<br>(10, 12.1) | 0.8 |
| Trisomy 21 | 0 | | 7 | 0.01 |
| Ex premature infants | 1 | | 2 | 0.2 |
| Other (genetic) | 0 | | 1 | 0.7 |
| Cardiac diagnosis | Arterioventricular septal defect | 7 | Arterioventricular septal defect | 9 |
| | Cardiac Fibroma | 0 | Cardiac Fibroma | 1 |
| | Critical aortic stenosis | 2 | Critical aortic stenosis | 1 |
| | Double inlet left ventricle | 0 | Double inlet left ventricle | 2 |
| | Double outlet right ventricle | 3 | Double outlet right ventricle | 4 |
| | Ebstein anomaly | 0 | Ebstein anomaly | 1 |
| | Hypoplastic left heart syndrome | 4 | Hypoplastic left heart syndrome | 2 |
| | Mitral valve atresia | 0 | Mitral valve atresia | 1 |
| | Pulmonary atresia | 1 | Pulmonary atresia | 1 |
| | Pulmonary stenosis | 1 | Pulmonary stenosis | 1 |
| | Tetraology of Fallot | 6 | Tetraology of Fallot | 6 |
| | Tricuspid valve atresia | 1 | Tricuspid valve atresia | 1 |
| | Ventricular septal defects | 13 | Ventricular septal defects | 14 |

**Table 2**
Growth characteristics.

| | Control | Intervention | |
|---|---|---|---|
| **Weight** | **Median (IQR)** | **Median (IQR)** | |
| Weight (kg) – birth | 3.18 (2.9,3.6) | 3.16 (2.5,3.4) | 0.2 |
| Weight (kg) – entry | 3.4 (2.9, 3.9) | 3.3 (2.8, 3.5) | 0.08 |
| Weight (kg) – 4 months | 5.4 (4.1, 6.0) | 5.4 (4.8, 6.5) | 0.2 |
| Weight (kg) – 12 months | 8.0 (7.4, 9.0) | 8.3 (7.9, 9.1) | 0.3 |
| **Infants with Weight for age <−2 scores** | **%** | **%** | |
| WAZ – entry | 25% | 29% | 0.6 |
| WAZ – 4 months | 28% | 20% | 0.3 |
| WAZ – 12 months | 28% | 14% | 0.5 |
| **Weight for age z score** | **Median (IQR)** | **Median (IQR)** | |
| WAZ – birth | −0.13 (−0.7, 0.6) | −0.24 (−1.2, 0.2) | 0.2 |
| WAZ – entry | −0.6 (−2.0, 0.1) | −0.6 (−1.8, 0.01) | 0.8 |
| WAZ – 4 months | −1.5 (−2.3, −0.3) | −1.0 (−1.5,−0.1) | 0.1 |
| WAZ – 12 months | −1.1 (−2.1, −0.2) | −0.8 (−1.3, −0.2) | 0.1 |
| **Change in Weight for age z score** | | | |
| Birth to 4 months | −1.5 (−2.0, −0.4) | −0.9 (−1.5, 0.7) | 0.04 |
| Birth to 12 months | −0.4 (−1.9, 0.2) | −0.09 (−1.3, 1.1) | 0.03 |
| **Weight for length for age z score** | **Median (IQR)** | **Median (IQR)** | |
| WHZ– 4 months | −0.3 (−0.7, 0.6) | −1.0 (−1.7, 0.3) | 0.2 |
| WHZ – 12 months | −0.4 (−1.0, 0.6) | −0.8 (−1.4, 0.1) | 0.4 |
| **Height for age z score** | **Median (IQR)** | **Median (IQR)** | |
| HAZ – 4 months | −1.1 (−2.3, −0.1) | −0.7 (−1.4, −0.4) | 0.6 |
| HAZ – 12 months | −1.3 (−2.6, −0.3) | −0.7 (−1.2, −0.06) | 0.04 |
| Died | 3 | 1 | 0.2 |

WAZ = weight for age z scores; WHZ = weight for length z scores; HAZ = height for age z scores; IQR = inter-quartile range; n = number.

HAZ at 4 months in the intervention was similar at −0.7 (−1.4, −0.1) compared to the control groups −1.0 (−1.9, −0.3) ($p = 0.6$) respectively. However, at 12 months median (IQR) HAZ was significantly greater in the intervention group at −0.7 (−1.9, −0.07) - compared to −1.6 (−2.6, −0.4) in the control group ($p = 0.04$), Fig. 3d).

The prevalence of moderate malnutrition (WAZ < -2) at 4 months-of-age was 20% in the intervention group and 28% in the control group ($p = 0.7$). At 12 months-of-age, the prevalence of moderate malnutrition was 14% in the intervention group and 28% in the control group ($p = 0.1$).

*Duration of mechanical ventilation and PICU-LOS*

Cumulative duration of mechanical ventilation during the first year of life was significantly shorter in the intervention group compared to the control group (5.1 ± 8.2 vs 11.7 ± 15.8 days, $p = 0.009$). PICU-LOS in the intervention group was significantly shorter compared to the control group (8.2 ± 11.6 days vs 18.3 ± 24.0 days, $p = 0.006$) (Fig. 4). Age of palliative/corrective surgery was 7.3 ± 4.9 months in the intervention and 4.0 ± 3.2 in the control ($p = 0.001$).

## Discussion

This single centre prospective cohort study has shown the use of consensus based standardized pre-operative nutrition pathway has the potential to improve both growth and important clinical outcomes in infants with CHD, and may warrant testing in a larger cohort of infants in a multicentre study. With a median (IQR) change in WAZ from birth to 12 months of nearly zero, the use of the pathway enabled these infants to achieve growth along birth centile lines, avoiding the faltering growth often seen.

Based on recommendations from Golden et al. [16], our pathway aimed to prevent the early growth faltering commonly seen in infants with CHD by increasing both the quality and quantity of dietary nutrients prior to surgery by a focus on the use of a nutrient-energy dense feed in addition to, or alongside, an infant's usual milk. Short term use of nutrient-energy dense infant feeds amongst these infants is associated with improved weight gain and achievement of nutritional targets [29,30]. Overall, the use of nutrient dense infant formula was well tolerated, although 30% of the cohort did have symptoms of reflux or required an enteral feeding tube. The following strategies are employed to improve tolerance feed tolerance 1) inserting a naso-gastric feeding tube to provide bolus or continuous feeds via an enteral feeding pump 2) changing to an extensively hydrolysed version of the nutrient energy dense feed and 3) if those strategies did not provide symptom resolution the enteral feeding tube was advanced to a naso-jejunal tube.

Although, the fall in WAZ between birth and both 4 and 12 months-of-age were significantly reduced in the intervention group compared to the control group, it is important to note that weight gain alone or improved weight for height does not indicate nutritional rehabilitation in the presence of stunting or low height for age, as it suggests there is insufficient nutrients to support linear growth, resulting in overweight stunted children [31], which is increasingly reported in older children with CHD [32]. As such improving linear growth during the first year of life is a priority and may reduce cardiovascular risk in later life [33]. In this study linear growth at 12 months-of-age was significantly improved in infants with CHD who followed the pre-operative nutrition pathway, when compared to a historic control.

A proportion of the cohort continued to have moderate malnutrition, with a low WAZ at 4 months-of-age (20%) despite seemingly adequate amounts of nutrition and dietetic support, which is similar to those described by other groups [34–36]. El-Koofy et al. [37] describes the use of Nutrition Care plans based on a traffic light system as part of a programme of nutritional rehabilitation in 50 infants with left to right cardiac shunts. Plans were graded from green, through amber to red, where the red plan represented more aggressive nutritional management for the highest risk infants or those with the poorest growth This resulted in a significant improvement in the prevalence of moderate malnutrition from 28% prior to implementation, to 23% afterwards, representing similar figures to those described in the present study. Gongwer et al. [34] reported significant improvements in changes to WAZ from baseline to 6 months following the implementation of a structured approach to the nutritional care of inpatient infants with CHD, which included daily nutrition review and a weekly nutrition team assessment. However, at exit from the programme the median WAZ was still low at −3.5, suggesting that although there was improved weight gain, overall the cohort was significantly malnourished.

Many factors affect growth in infants with CHD [38–40]. Heart failure is common, which increases metabolic demands, and may result in acute and chronic mesenteric hypoperfusion [41], compromising intestinal absorption of nutrients [42,43], and

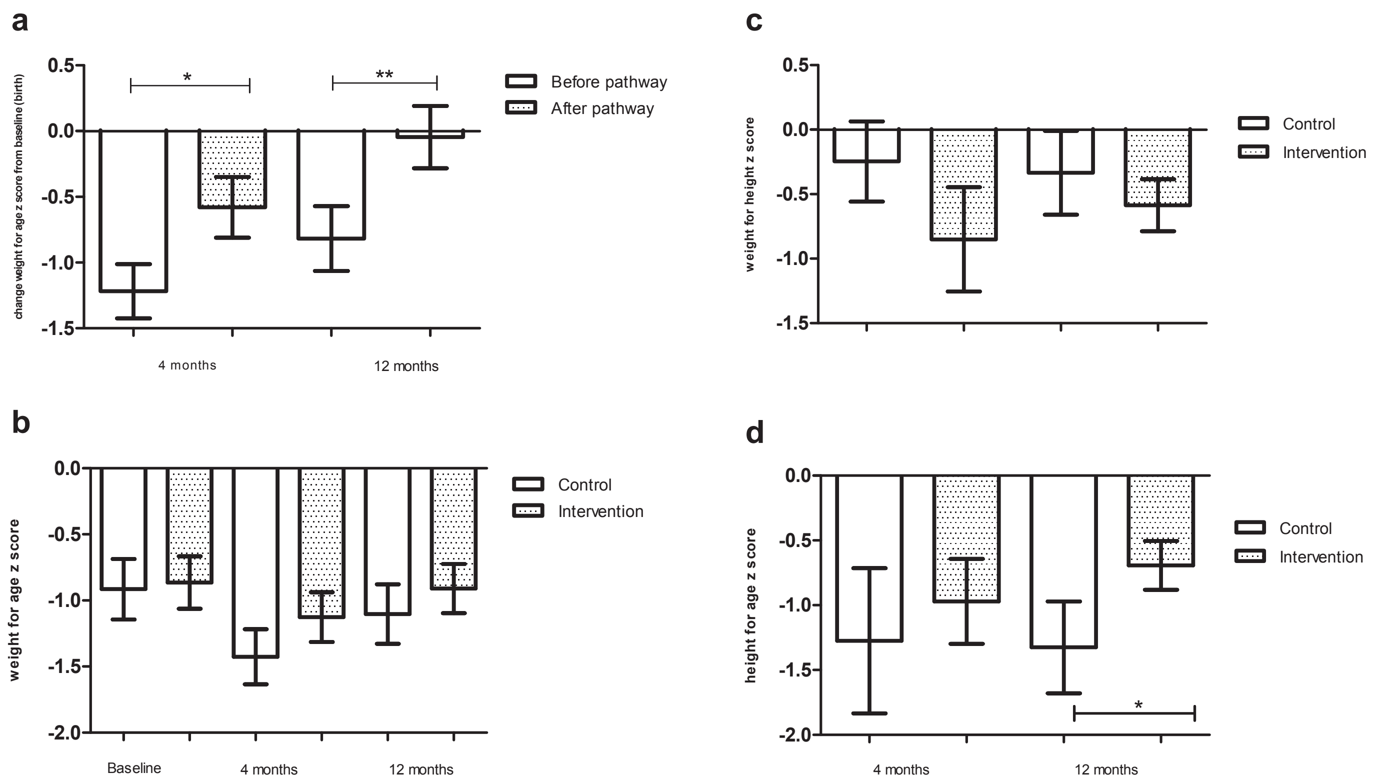


**Fig. 3.** a) Change in weight for age z scores from birth before implementation of the control (n = 38) and intervention (n = 44) at 4 months ($p = 0.04$) and 12 months ($p = 0.03$). (b) Weight for age z scores before implementation of the control (n = 38) and intervention (n = 44) at baseline ($p = 0.8$), 4 months ($p = 0.1$) and 12 months ($p = 0.1$). (c) Weight for length z scores before implementation of the control (n = 38) and intervention (n = 44) at 4 months ($p = 0.2$) and 12 months ($p = 0.4$). (d) Length for age z score before implementation of the control (n = 38) and intervention (n = 44) at 4 months ($p = 0.6$) and 12 months ($p = 0.04$).

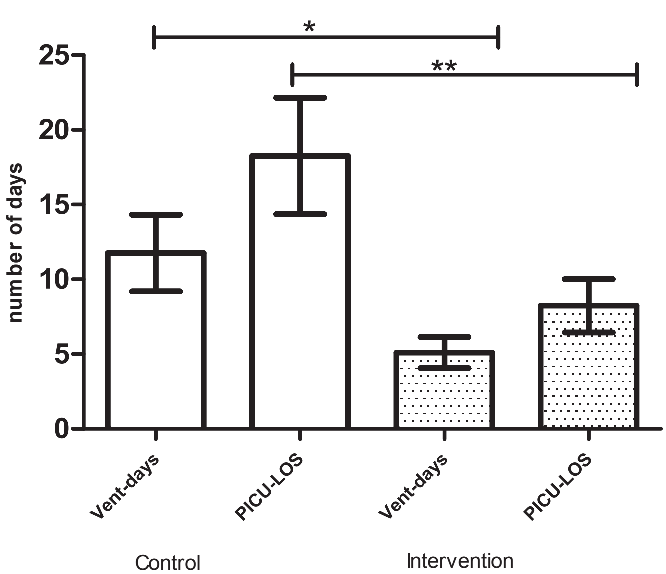


**Fig. 4.** Number of days of mechanical ventilation* ($p = 0.009$) and paediatric intensive care length of stay** ($p = 0.006$) during the first 12 months – in the control (n = 38) and intervention (n = 44).

subsequently limiting growth. Gastroesophageal reflux disease (GORD) [44,45] may also contribute towards poor intake and subsequent poor growth [46]. In the present study cohort almost 40% of infants were reported to have GORD, which may have contributed towards reduced oral intake.

Clinical outcomes were improved in infants who followed the pre-operative nutritional pathway, with significant reductions in the duration of MV and PICU-LOS compared to a historic control. We have previously described poorer post-operative resilience amongst children with CHD who had persistent malnutrition (e.g. stunting with a HAZ of < -2) at the time of surgery, which was associated with a significantly increased risk of PICU-LOS [15]. Others have described a relationship between persistent malnutrition and poorer clinical outcomes [47,48]. While the reduced duration of MV and PICU-LOS in this cohort may be as a result of improved nutritional status, it may also be as a result of other factors such as changes in surgical or post-operative medical management. However, the mean age for palliative/corrective surgical procedures in the intervention group was later, and one explanation for this may be that continued good growth meant that the need for imminent surgical intervention was not as pressing, and so surgery could be deferred as medical management appeared adequate. This requires further investigation amongst a larger cohort of infants within a prospective randomised national study that is sufficiently powered to confidently detect differences in clinical outcomes.

There are a number of limitations to this study, which include the use of historic control group rather than a prospectively enrolled cohort. We were also not able to accurately determine daily intake of infant milk and the exact proportion of nutrient-energy dense feeds when mixed with breastmilk or standard infant formula. The sample size of both cohorts was also small, which although allowed us to draw some conclusions about efficacy, is not sufficiently powered to be assured the effects seen are reproducible, particularly with respect to the duration of MV and PICU-LOS.

## Conclusions

This single centre study has shown that the use of consensus based standardized nutritional pathway in infants with CHD before surgery is feasible, and has the potential to improve growth and clinical outcomes.

Overall growth significantly improved in infants who followed the pre-operative nutritional-pathway, with a reduced fall in WAZ from birth and better linear growth at 12 months-of-age, which may be as a result of the early use of nutrient-energy dense infant formula to prevent growth faltering. The duration of MV and PICU-LOS was significantly lower in the intervention group, but other factors associated with medical/surgical management may have contributed to these improvements, which warrant further investigation in a larger cohort of infants in a national, multi-centre study.

## Conflict of Interest

None.


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## Contributors statement

Authors made the following contribution to the manuscript: (1) Luise Marino formulated the original idaea and wrote the initial nutritional pathway, collated the parent information, completed statistical analysis and draughted the manuscript. (2) Luise Marino, Natalie Davies, Catherine Kidd, Clare Riches, Julie Fienberg were involved in consenting parents to participate in the study. (3) Ann-Sophie Darlington, Mark Beattie, Mark Johnson, Trevor Richens and Tara Bharucha, contributed to revising the manuscript for important intellectual content, (4) and all authors provided final approval of the version to be submitted.


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