Standardized Feeding Approach Mitigates Weight Loss in Infants with Congenital Heart Disease

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Objective To evaluate the effect of a standardized feeding approach using a clinical nutrition pathway on weight-for-age Z score (WAZ) over hospital length of stay (HLOS) for infants with congenital heart disease (CHD).

Study design A 10-year retrospective cohort study examined eligible infants who underwent neonatal cardiac surgery between July 2009 and December 2018 (n = 987). Eligibility criteria included infants born at least 37 weeks of gestation and a minimum birth weight of 2 kg who underwent cardiac surgery for CHD within the first 30 days of life. Using the best linear unbiased predictions from a linear mixed effects model, WAZ change over HLOS was estimated before and after January 2013, when the standardized feeding approach was initiated. The best linear unbiased predictions model included adjustment for patient characteristics including sex, race, HLOS, and class of cardiac defect.

Results The change in WAZ over HLOS was significantly higher from 2013 to 2018 than from 2009 to 2012 ($\beta = 0.16$; SE = 0.02; $P < .001$), after controlling for sex, race, HLOS, and CHD category, indicating that infants experienced a decreased WAZ loss over HLOS after the standardized feeding approach was initiated. Additionally, differences were found in WAZ loss over HLOS between infants with single ventricle CHD ($\beta = 0.26$; SE = 0.04; $P < .001$) and 2 ventricle CHD ($\beta = 0.04$; SE = 0.02; $P = .04$).

Conclusions These data suggest that an organized, focused approach for nutrition therapy using a standardized pathway improves weight change outcomes before hospital discharge for infants with single and 2 ventricle CHD who require neonatal cardiac surgery. *(J Pediatr 2021;231:124-30)*.

Growth is an important indicator of overall health in children. The prevalence of feeding difficulties and growth failure in neonates with congenital heart disease (CHD) is well-documented.[1-3] Growth failure in neonates with cardiac disease can have a detrimental effect on neurodevelopment, morbidity, and mortality.[4-6] Growth failure is multifactorial and may be influenced by a myriad of issues including disease severity and hemodynamics, duration of mechanical ventilation, disturbances in gastrointestinal function, alterations in metabolic demands, inadequate energy and protein intake, poor feeding skills, vocal cord dysfunction, chylothorax, neurologic dysfunction, and infection.[2,5,7-10] Although many of these factors are not modifiable, a standardized approach to nutrition, including the use of clinical nutrition pathways, has demonstrated improved outcomes in critically ill neonates undergoing surgery for CHD by minimizing variability for nutritional care between providers and ensuring modifiable factors are promptly identified and addressed.[11-15]

The Nutrition Quality Improvement Committee was formed in the Cardiac Center at Children's Hospital of Philadelphia to address the growth and nutrition deficiencies in infants with CHD requiring neonatal cardiac surgery. Rapid cycle improvement tests of change in Plan-Do-Study-Act steps were implemented in 2013 with the overall goal of enhancing nutritional therapy (**Table I**).[16] In 2014, the Nutrition Quality Improvement Committee began to organize these improvements into clinical pathways, and a comprehensive clinical pathway was implemented in November 2016. The goal of the clinical pathway is to support a standardized feeding approach in our cardiac intensive care unit (CICU) for both preoperative and postoperative neonates with both single and 2-ventricular physiology, with or without arch obstruction. The pathway is

CHD	Congenital heart disease
CICU	Cardiac intensive care unit
HLOS	Hospital length of stay
NEC	Necrotizing enterocolitis
PC4	Pediatric Cardiac Critical Care Consortium
WAZ	Weight-for-age Z score

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Table I. Timeline of quality improvement initiatives

Dates	Intervention
May 2013	Staff education within the CICU on anthropometrics, including daily weights and weekly lengths and head circumference. PDSA: trial mandatory nasogastric tube placement for all postoperative neonates ≤30 days of age within 24 hours of initiation of oral/enteral feeds.
July 2013	Goal achieved for >90% compliance on daily weight measurements. PDSA: Provided guidance for ad lib by mouth feeding. Instituted a smart phrase in the electronic health record that standardized ad lib oral feeding to include minimum volumes, frequency of feeding, and feeding based on infant feeding cues.
October 2013	PDSA: Instituted a practice change for intravenous fluid carriers standardized and safe minimized volumes identified for maintaining line patency but preventing excessive fluid administration. *Caring for Your Baby with an NG Tube* Brochure created and published. Added to documents reviewed during prenatal consult as well as new CICU admission packets for parents.
April 2014	Development of a standardized pathway began for preoperative and postoperative neonates with both single and 2 ventricle CHD to improve WAZ change over HLOS. Literature review of 35 articles specific to needs of neonates with CHD. Pathway content was created based on existing evidence and expert recommendation by committee members.
September 2014	Infant driven feeding education provided to nursing staff. New documentation rows added to electronic health record nursing flowsheet.
November 2014	Preoperative Pathway implemented.
January 2016	Postoperative Pathway implemented.
November 2016	Comprehensive Nutrition Pathway implemented. Key practice recommendations supported by the pathway: ○ Pre and postoperative parenteral nutrition ○ Enteral feeding readiness assessment ○ Mandatory early use of NG tubes (must be taking full caloric goals for 2 consecutive days before removal) ○ No ad lib feeding orders postoperatively ○ Promotion of human milk, special considerations for breast feeding, and fortification guidelines ○ Infant driven feeding practices and oral aversion prevention ○ Feeding tolerance evaluation and recommendations

PDSA, Plan-Do-Study-Act.

accessible to the public and can be found at www.chop.edu/clinical-pathway/nutrition-neonates-undergoing-surgery-chd-clinical-pathway.

The aims of this study were to evaluate the effect of a standardized feeding approach including a clinical nutrition pathway on (1) weight-for-age Z score (WAZ) change over hospital length of stay (HLOS) for infants with CHD, (2) WAZ change over HLOS for infants with single ventricle CHD and with 2 ventricle CHD, and (3) mortality, HLOS, and tube feeding status at hospital discharge for infants with single ventricle CHD and with 2 ventricle CHD.

Methods

This retrospective cohort study included eligible infants admitted to the CICU who underwent neonatal cardiac surgery between July 2009 through December 2018, as far back as our data warehouse could provide complete data on infants before our standardized feeding approach. Infants were included who had a gestational age 37 weeks or greater, birth weight of 2 kg or greater, and underwent cardiac surgery for CHD at no more than 30 days of age. Infants who did not require surgery in the neonatal period were excluded. Data were queried from our institution's local Pediatric Cardiac Critical Care Consortium (PC4) and Society of Thoracic Surgeons databases. The PC4 database was used for hospitalization and CICU encounter-level data, and the Society of Thoracic Surgeons database was used for surgical data. Demographics data were extracted from both databases. The cohort of infants was defined by the infants' age at surgery, date of surgery, operation type, gestational age, and birth weight.

Demographic data abstracted for all eligible infants included sex, race/ethnicity, diagnosis, gestational age at birth, and birth weight. CHD diagnoses were categorized into four previously described categories that have been shown to predict perioperative mortality: class I, 2 ventricles with no aortic arch obstruction; class II, 2 ventricles with aortic arch obstruction; class III, a single ventricle without arch obstruction; and class IV, a single ventricle with arch obstruction.[17,18] For example, patients with d-transposition of the great arteries are usually categorized as class I, and patients with hypoplastic left heart syndrome are categorized class IV. Date and weight at hospital admission and hospital discharge were captured to calculate the HLOS and WAZ change during hospitalization. The WAZ for each infant was calculated using the World Health Organization standards.[19] In addition, the use of an enteral feeding tube at hospital discharge (present vs not present) and mortality (alive at discharge) were also collected. Owing to the retrospective nature of its design, this study met the criteria for exempt status by the institutional review board at our hospital.

Finally, we examined the overall adherence to our comprehensive clinical pathway for one year in the postimplementation period from July 1, 2017, to June 30, 2018. We categorized adherence as meeting the following 3 criteria: (1) appropriate use of preoperative parenteral nutrition according to pathway recommendations; (2) appropriate use of postoperative parenteral nutrition according to pathway recommendations; and (3) appropriate use of a nasogastric

or orogastric feeding tube according to pathway recommendations. We also examined the data on necrotizing enterocolitis (NEC) in our PC4 dataset, which were available starting in 2013. In PC4, NEC is defined as an acute decrease in the supply of oxygenated blood to the small intestine or large intestine, typically resulting in acidosis, abdominal distention, pneumatosis, and/or intestinal perforation, that prompts initiation of antibiotics or exploratory laparotomy. Therefore, infants were coded as positive for NEC when there was documented abdominal distention, pneumatosis (on radiographs or ultrasound examination), and placed on antibiotics for any length of time.

Our analysis plan took into consideration the variation in practices over time. Outcomes in the same year could be correlated owing to the possibility that infants may receive similar care in the CICU during a particular period of time, creating a batch effect. Therefore, we used a linear mixed effects model with random intercept for year to study the change of WAZ and HLOS. Specifically, we estimated the year-specific outcomes after adjusting for infant and hospital characteristics, using the best linear unbiased predictor, and used the standard error (SE) of best linear unbiased predictions to account for the uncertainty in the estimates and batch effect.[20] To evaluate the impact of the standardized feeding approach on outcomes, we tested the difference in each outcome before and after January 2013, using weighted linear regression models (weighted by the 1/variance of the estimated year-specific outcomes to decrease the study bias caused by small sample size in some of the years). For the binary outcomes of mortality and tube feeding status at hospital discharge, we used multilevel logistic regression models to test the difference in outcomes before and after January 2013 and considering random effects across years. We then separated our sample into infants with 2 ventricle CHD (classes I and II) and infants with single ventricle CHD (classes III and IV) and repeated the same analyses for these groups.

We also performed an exploratory analysis of the primary outcome on a subgroup of the highest risk infants in our cohort with an HLOS of more than 30 days. Using the same methods as the primary analysis, we estimated the year-specific outcomes of WAZ over HLOS after adjusting for infant and hospital characteristics, using the best linear unbiased predictions and the SE of the best linear unbiased predictions to account for the uncertainty in the estimates and batch effect. We tested the difference in WAZ over HLOS before and after January 2013 using weighted linear regression models.

Finally, we separately analyzed our pathway adherence data over one year by calculating the percent of infants that met all 3 criteria of adherence, as defined previously. We also separately calculated the yearly rate of NEC diagnosed in our cohort from 2013 to 2018, per the PC4 criteria.

Results

A total of 1059 patients was identified as eligible between July 1, 2009, and December 31, 2018, with 987 of these having complete WAZ data for analysis (Figure 1). Over the 10-year period, the majority of infants were male (59%), White, and non-Hispanic (60%), with a range of classified diagnoses in CHD categories from classes I to IV (Table II). Mean infant birth weight was 3.27 ± 0.50 kg. Infants lost an average of 1 WAZ over HLOS, ranging from −3.58 to 4.37.

The change in WAZ over HLOS differed significantly across years after controlling for sex, race, HLOS, and CHD category (β = 0.02; SE = 0.01; P = .02). Infants' change in WAZ over HLOS was significantly higher during 2013-2018 than during 2009-2012 (β = 0.16; SE = 0.02; P < .001), after controlling for sex, race, HLOS, and CHD category (Figure 2). The total sample across the 10-year period was divided into 2 groups: infants with 2 ventricle CHD (class I and II) (n = 637) and infants with single ventricle CHD (class III and IV) (n = 350). The change in WAZ over HLOS was also found to be significantly higher during 2013 to 2018 when compared with 2009 to 2012 in infants with single ventricle CHD (β = 0.26; SE = 0.04; P < .001) and those with 2 ventricle CHD (β = 0.04; SE = 0.02; P = .04) (Figure 3; available at www.jpeds.com).

After adjusting for sex, race, HLOS, and CHD category, there were no differences in mortality between groups in either the 2009-2012 or the 2013-2018 cohorts for infants with both single (β = 0; SE = 0; P = 1.00) and 2 ventricle (β = −0.01; SE = 0.02; P = .56) CHD. After adjusting for sex, race, HLOS, and CHD, there were also no differences in tube feeding status at hospital discharge for infants with both single (β = 0.01; SE = 0.01; P = .09) and 2 ventricle (β = 0.05; SE = 0.03; P = .10) CHD. Finally, no significant differences in HLOS were found for infants with both single (β = 3.81; SE = 3.47; P = .30) and 2 ventricle ($\beta = 5.35^{-21}$; SE = 1.76^{-20}; P = .76) CHD, after adjusting for sex, race, and CHD category.

For the exploratory analysis of the subgroup of highest-risk infants in our cohort, we identified 225 infants over the 10-year study period whose HLOS was greater than 30 days. In this subgroup, mean HLOS was 74.6 ± 58.7 days (range, 31-381 days). After adjusting for sex, race, CHD category, and HLOS, the change in WAZ over HLOS differed significantly across years. Infants with an HLOS of greater than 30 days demonstrated higher change in WAZ over HLOS during 2013-2018 than during 2009-2012 (β = 0.27; SE = 0.05; P < .001).

Our 1-year adherence data included 99 total infants who were eligible for the nutrition pathway, with 84 infants meeting the 3 criteria of adherence with the pathway. This resulted in adherence of 85%. The most common reason for pathway deviation was lack of adequate intravenous access for the provision of parenteral nutrition. The frequency of NEC in our cohort from 2013 to 2018, using the PC4 database definition, was 4.73%, with sequential yearly rates starting in 2013 as follows: 6.78%, 6.56%, 4.31%, 1.75%, 5.30%, and 3.45%.

Discussion

The findings of this study demonstrate benefits derived from initiation of a standardized approach to nutrition therapy in critically ill neonates undergoing surgery for CHD in our institution. The results indicate a decreased WAZ loss over HLOS after 2013, suggesting that the implementation of a

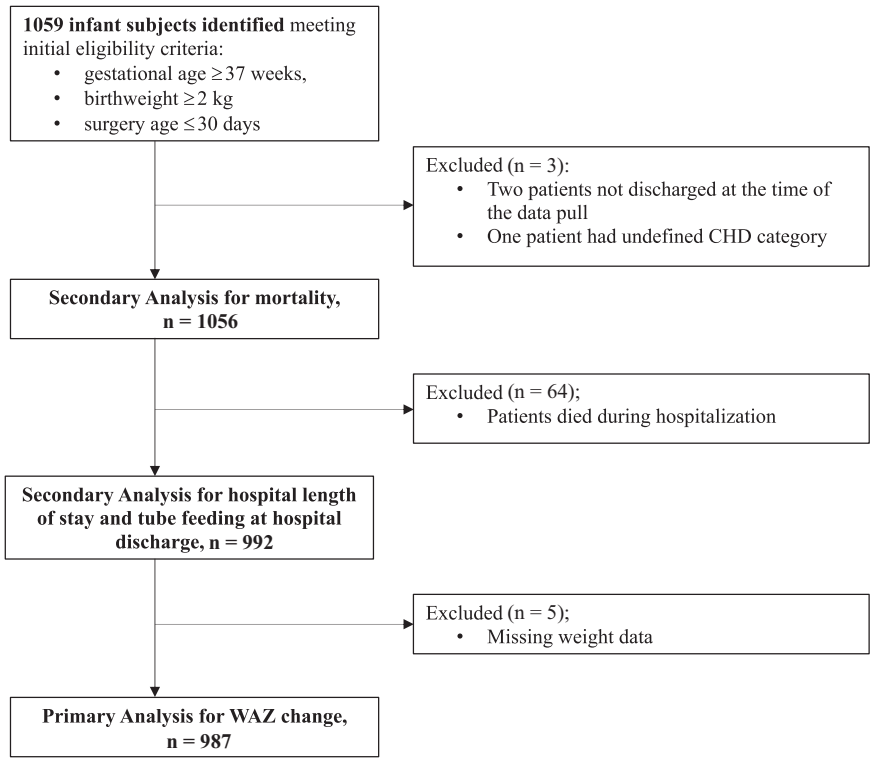

Figure 1. Study screening and enrollment.

standardized nutrition pathway had a positive impact on growth outcomes in infants with CHD with both single and 2 ventricle physiology. We did not find a negative impact on the overall mortality or HLOS related to our approach to nutrition therapy in this cohort. Overall, the use of a standard feeding approach in our population mitigated weight loss without negatively impacting HLOS or mortality.

To date, 11 clinical pathways have been published addressing preoperative and/or postoperative nutrition therapy for infants with CHD, with all except two indicating positive outcomes related to pathway implementation.[8,21-30] A total of 7 pathways were described exclusively for single ventricle physiology and/or hypoplastic left heart syndrome, and one of these was expanded for use with both single and 2 ventricle CHD neonates.[8,21,23-27,31] In addition, 1 pathway provided guidance on perioperative feeding for infants with 2 ventricle CHD, but was later evaluated for both single and 2 ventricle patients.[22,32] Our pathway contributes additional support to the current published recommendations on similarly feeding both single and 2 ventricle infants with CHD, with or without arch obstruction.[28-30] In this way, our pathway provides a comprehensive approach for feeding, minimizing confusion for staff and variability in practice. Interestingly, our comprehensive feeding approach seemed to have a greater effect in the infants with single ventricle CHD vs infants with 2 ventricle CHD. Pathways have mostly targeted infants with single ventricle CHD owing to their enhanced risk for feeding difficulties and growth failure and may have a greater response to standardized feeding pathways that ensure the provision of adequate nutrition. However, our results demonstrate that infants with 2 ventricle CHD benefitted from standardized feeding methods with improved growth outcomes and should be included in future efforts and research targeting growth and nutrition in CHD.

Although the benefits of feeding protocols have been demonstrated, the components of a successful pathway for the CHD population have not been as clearly delineated. In 2013, at the initiation of our standardized feeding approach, there was less available supporting literature providing evidence-based strategies for feeding infants before and after cardiac surgery. When supportive evidence is lacking, clinical decision-making is often based on provider experience, comfort level, and expert opinion to reach a consensus in unique patient populations, such as the infant cardiac surgical population. We used a quality improvement methodology, as described by other investigators, in developing pathway content.[32] During development of our clinical nutrition pathway, the National Pediatric Cardiology Quality Improvement Collaborative published recommendations for calorie goals, initiation of preoperative oral feeding, and use of parenteral and enteral nutrition.[8] Our pathway content expanded on similar themes within the National Pediatric Cardiology Quality Improvement Collaborative guidelines and included amended components from other published pathways.

The successful provision of optimal nutrition to infants with CHD must leverage the specialized expertise of registered dieticians, feeding specialists such as speech language pathologists, and clinical nurses.[8,21-23,26,28-30] Our clinical pathway is the first to highlight the value of using a lactation consultant in addition

Table II. Infant characteristics

Infant characteristics	No.	%
Categorical variables		
Sex		
Male	588	59.6
Female	399	40.4
Race/ethnicity		
White, NH	593	60.1
Black, NH	108	10.9
Hispanic	133	13.5
NH other	153	15.5
Year of hospital admission		
2009	36	3.6
2010	83	8.4
2011	93	9.4
2012	102	10.3
2013	110	11.1
2014	114	11.6
2015	107	10.8
2016	109	11.0
2017	124	12.6
2018	109	11.0
CHD category*		
I	389	39.4
II	248	25.1
III	142	14.4
IV	208	21.1
Continuous variables	**Mean**	**SD**
Birth weight (kg)	3.27	0.50
Gestational age (weeks)	38.66	0.97
HLOS (days)	28.95	37.78
Hospital admission weight (kg)	3.29	0.52
Hospital discharge weight (kg)	3.60	0.88
WHO 2006 WAZ for hospital admission weight	−0.16	1.10
WHO 2006 WAZ for hospital discharge weight	−1.17	1.14
WAZ change over HLOS	−1.00	0.73

NH, non-Hispanic; *WHO*, World Health Organization.
*CHD category: I = 2 ventricles, no arch obstruction; II = 2 ventricles, with arch obstruction; III = single ventricle, no arch obstruction; IV = single ventricle, with arch obstruction).

to prioritizing the use of human milk through maternal or donor milk.[8,24,26] Additional major strategies within our pathway supported in other published pathways include preoperative enteral feeding, including those infants with ductal-dependent lesions on prostaglandin infusions, use of preoperative and postoperative parenteral nutrition, and early initiation of enteral feeding in the postoperative period via the use of a nasogastric or orogastric feeding tube.[8,21-30] Furthermore, our pathway includes clear definitions of hemodynamic stability for feeding and explicitly describes feeding intolerance.[8,21-26,28,29] Although variation exists across pathways for each of these definitions, it seems that the integration of clear definitions for these components of feeding is an important aspect for pathway content. Furthermore, our pathway included guidelines on holding and advancing feeds, oral feeding readiness assessment, and frequent monitoring of anthropometrics.[8,21-30] With a clear delineation of key components of nutrition therapy for preoperative and postoperative infants with CHD and the improvement we demonstrated in WAZ, our pathway has filled gaps that have previously not been addressed for feeding critically ill infants with CHD.

Our pathway is both readily available to the public and is also linked to the electronic health record when ordered for a patient at our institution. It is accessible as a teaching tool for nurses and front-line providers. Inherent in the pathway design is an abundance of resources for parents and clinicians, giving basis and rationale for how nutrition therapy in these infants is initiated and advanced.

A retrospective study design has inherent limitations and biases and should be interpreted with caution. Our heterogenous population created challenges; therefore, we categorized CHD diagnoses into classes to account for severity of disease. Although we saw an overall improvement in WAZ, it is possible that other unmeasured changes in care could have affected the primary outcomes in this study. Owing to the retrospective nature of this study, we could only examine data that were available in the electronic health records over the 10-year period. We were unable to obtain other growth measures, including accurate lengths and head circumferences at the time of discharge, to examine these as outcomes. Additionally, it was beyond the scope of this study to analyze the caloric and protein intake of each patient on study, and we were unable to measure NEC or other infection rates across the 10-year study period. Our NEC prevalence from 2013 to 2018 should be interpreted with caution, especially because our therapeutic approach and use of diagnostics (radiographs vs ultrasound examination) changed across these years. We also do not have data on pathway adherence over the entire study time frame. However, our 1-year adherence data suggest that the core practice changes that were initiated with our standardized feeding approach were applied to a majority of infants. Adherence was encouraged in real time during daily rounds as often as possible and by a consistent roster of members on the Nutrition Quality Improvement Committee. Although we have seen success in WAZ over the course of hospitalization, more research is needed to determine which aspects of standardized nutrition therapy have the most impact in this patient population. Future work should include defining and monitoring pathway adherence to better understand influences on patient outcomes. ■

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Data Statement

Data sharing statement available at www.jpeds.com.

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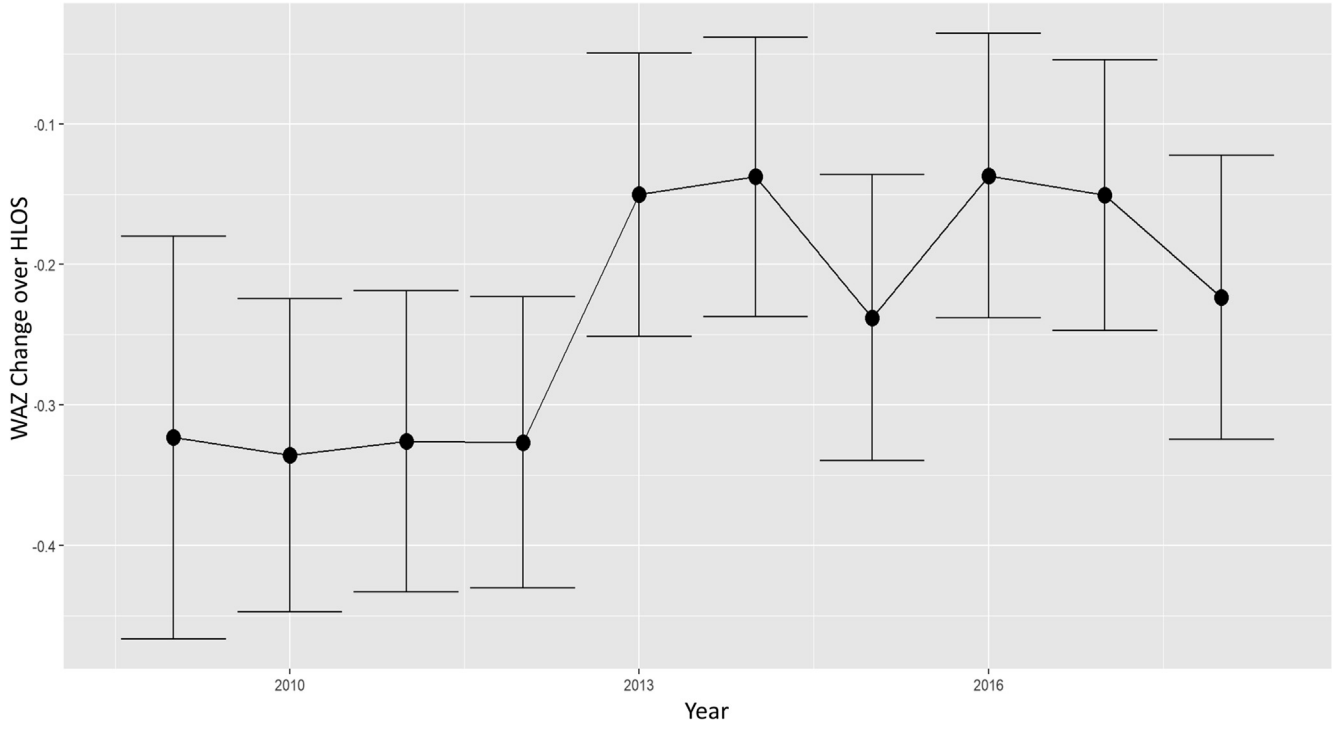

Figure 2. Best linear unbiased predictions for weight-for-age Z-score change over hospital length of stay.

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The Oxygen Dilemma

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Oxygen toxicity was long recognized and feared among neonatologists owing to its association with retrolental fibroplasia. When Northway et al described bronchopulmonary dysplasia in 1967, oxygen toxicity was immediately suggested as a contributing factor.[1] At the end of the 1960s, it was therefore realized that oxygen may be toxic to organs other than the retina. These considerations are reflected in Peter Auld's commentary in *The Journal* 50 years ago. At that time, monitoring oxygenation was difficult. One common method was to titrate oxygen concentration in the incubator until cyanosis disappeared. Intermittent puncture of the temporal artery was conducted to check oxygenation levels. Transcutaneous pO_2 electrodes were introduced a few years later to allow continuous monitoring of oxygenation. In the following decade, pulse oximeters became available, representing another revolution. Today, we also have access to near infrared spectroscopy to assess oxygenation.

The mechanism of oxygen toxicity was not understood in 1970, and it took another decade until the concept of oxidative stress and oxygen radicals was applied to premature infants, allowing us to understand that hyperoxia is not the only factor leading to oxidative stress.[2]

Auld ended his commentary by pointing to the challenge of finding the right balance between providing adequate oxygenation while at the same time minimizing the possible harmful effects of oxygen toxicity. The Neoprom study testing high vs low oxygen saturation targets for immature newborn infants emphasizes that we are facing this same dilemma, 50 years after.[3]

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2. Saugstad OD. Is oxygen more toxic than currently believed? Pediatrics 2001;108:1203-5.
3. Askie LM, Darlow BA, Davis PG, Finer N, Stenson B, Vento M, et al. Effects of targeting lower versus higher arterial oxygen saturations on death or disability in preterm infants. Cochrane Database Syst Rev 2017;4:CD011190.

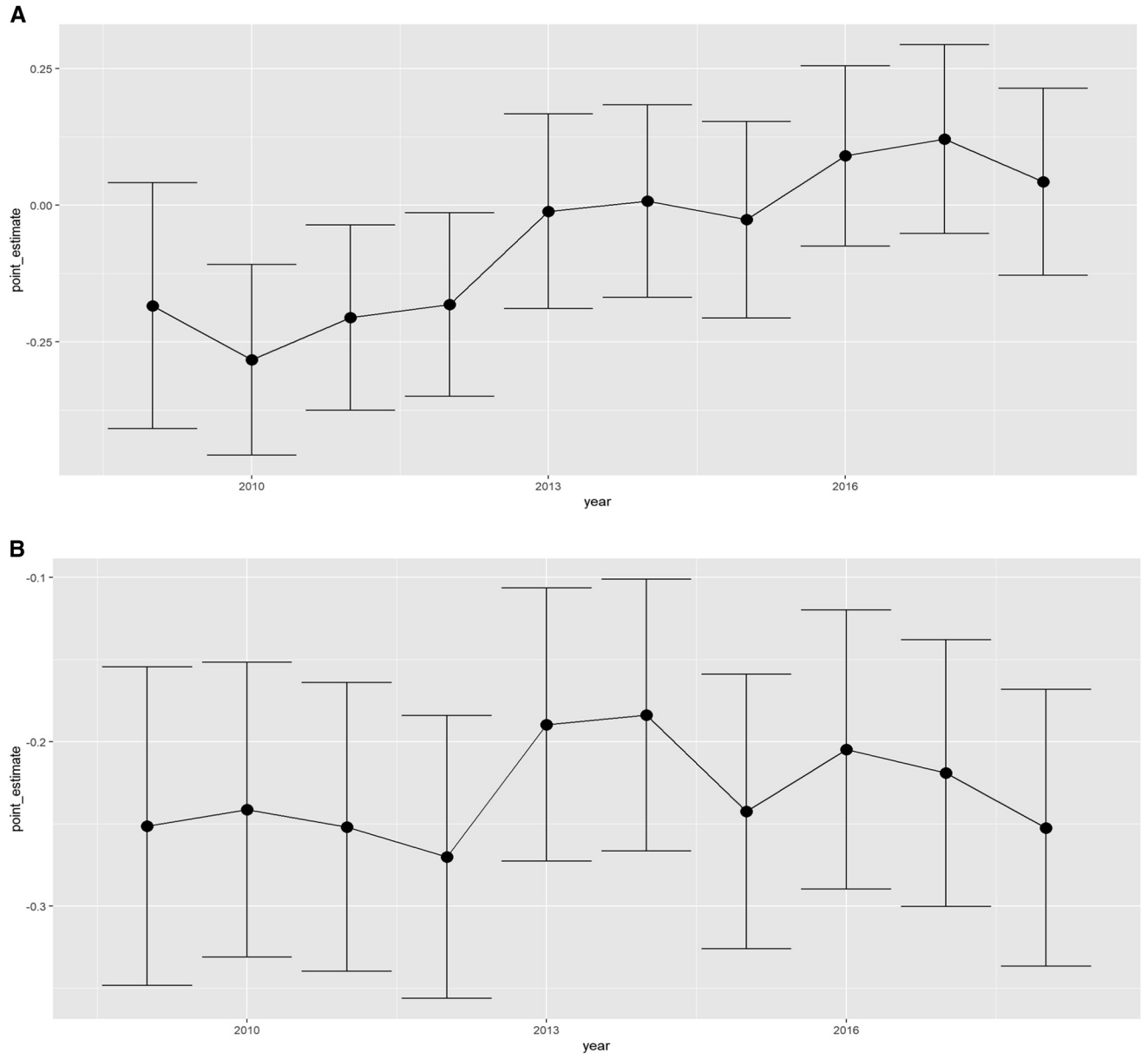

Figure 3. **A,** Weighted linear regression model with random effects model result for single ventricle group across years after adjusting for sex, race, HLOS, and CHD category. **B,** Weighted linear regression model with random effects model result for 2 ventricle group across years after adjusting for sex, race, HLOS, and CHD category.