Nutrition and Weight Gain in the Infant with CHD

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Cardiology 2018

- Consultant in the past for Danone Medical.
- No conflict of interest.

- How does nutrition and “weight gain” in the infant influence outcomes?
- How does nutrition and “growth" in the infant influence outcomes?

- Growth pattern and prevalence of growth failure.
- Impact of growth on outcomes.
- Interventions.

Introduction

- Neonates with complex CHD are usually born full term and within normal weight ranges.
- Growth issues often emerge shortly after surgery and persist throughout the first years of life.
- Most at risk are infants with Single Ventricle heart defects.

Enalapril in Infants With Single Ventricle
Results of a Multicenter Randomized Trial

Daphne T. Hsu, MD; Victor Zak, PhD; Lynn Mahony, MD; Lynn A. Sleeper, ScD; Andrew M. Atz, MD; Jami C. Levine, MD; Piers C. Barker, MD; Chitra Ravishankar, MD; Brian W. McCrindle, MD; Richard V. Williams, MD; Karen Altmann, MD; Nancy S. Ghanayem, MD; Renee Margossian, MD; Wendy K. Chung, MD; William L. Border, MBChB, MPH; Gail D. Pearson, MD, ScD; Mario P. Stylianou, PhD; Seema Mital, MD; for the Pediatric Heart Network Investigators

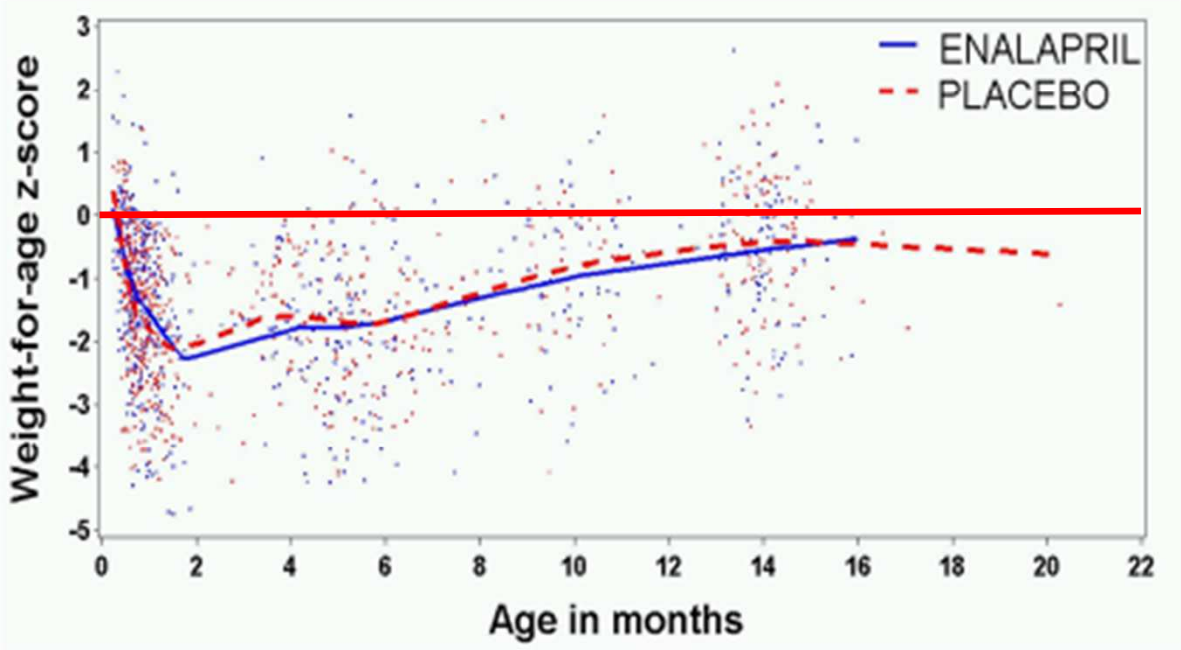
Circulation 2010 ;122:333-40

PHN Infant Single Ventricle Trial

- Placebo controlled, double blind, randomized trial of ACE inhibitor (enalapril) therapy in infants with SV.
- 10 centers in the US and Canada.
- Exclusion: GA<35 wks, SGA, genetic syndromes.
- 230 infants <45 days enrolled from Aug 2003 to May 2007.
- HLHS in 59%
- Primary endpoint: weight for age z-score at 14 months.

*Hsu DH et al. *Circulation* 2010;122:333-340.

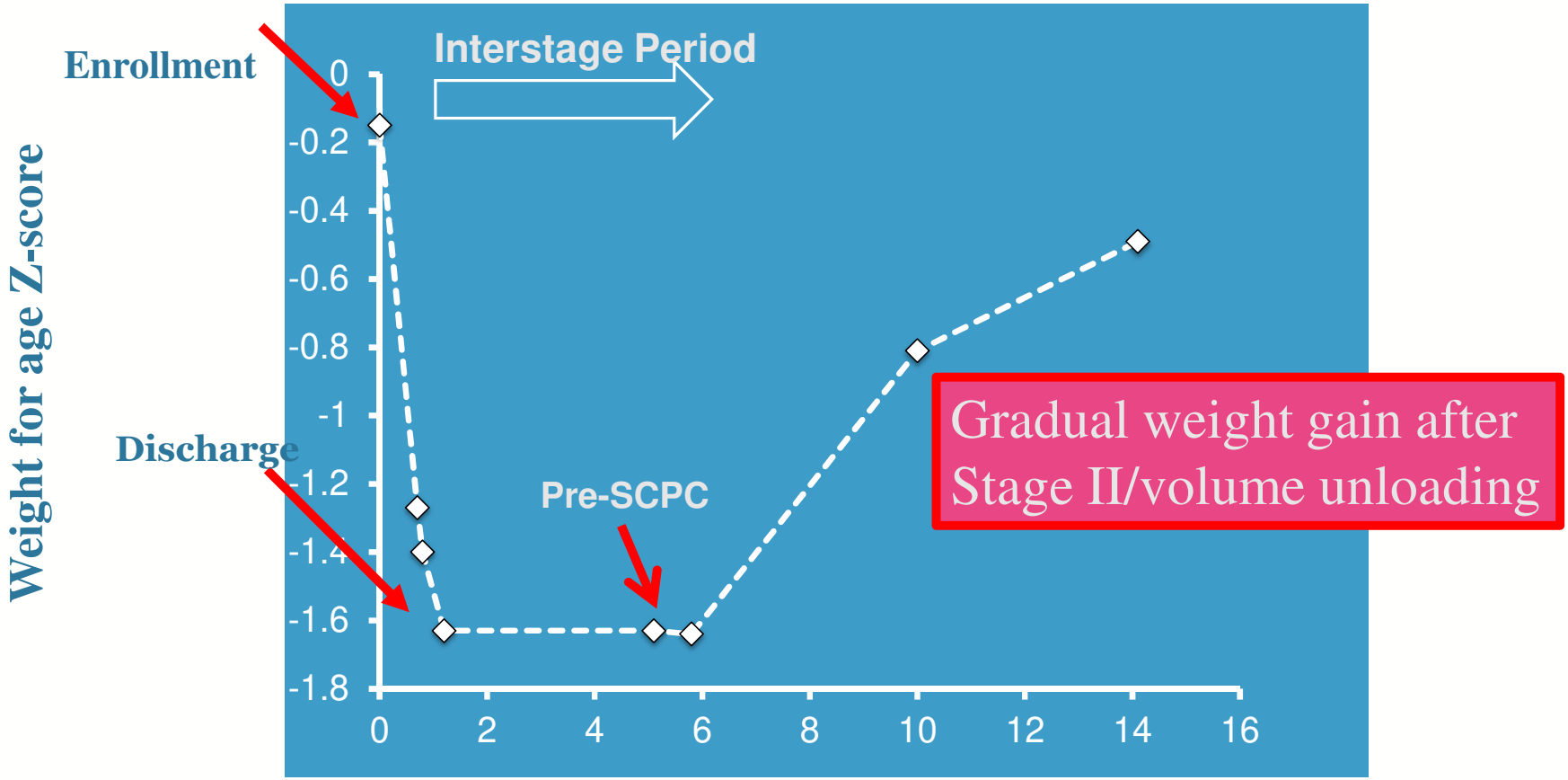
ISV Trial Results



Hsu DH et al. Circulation 2010

CR1

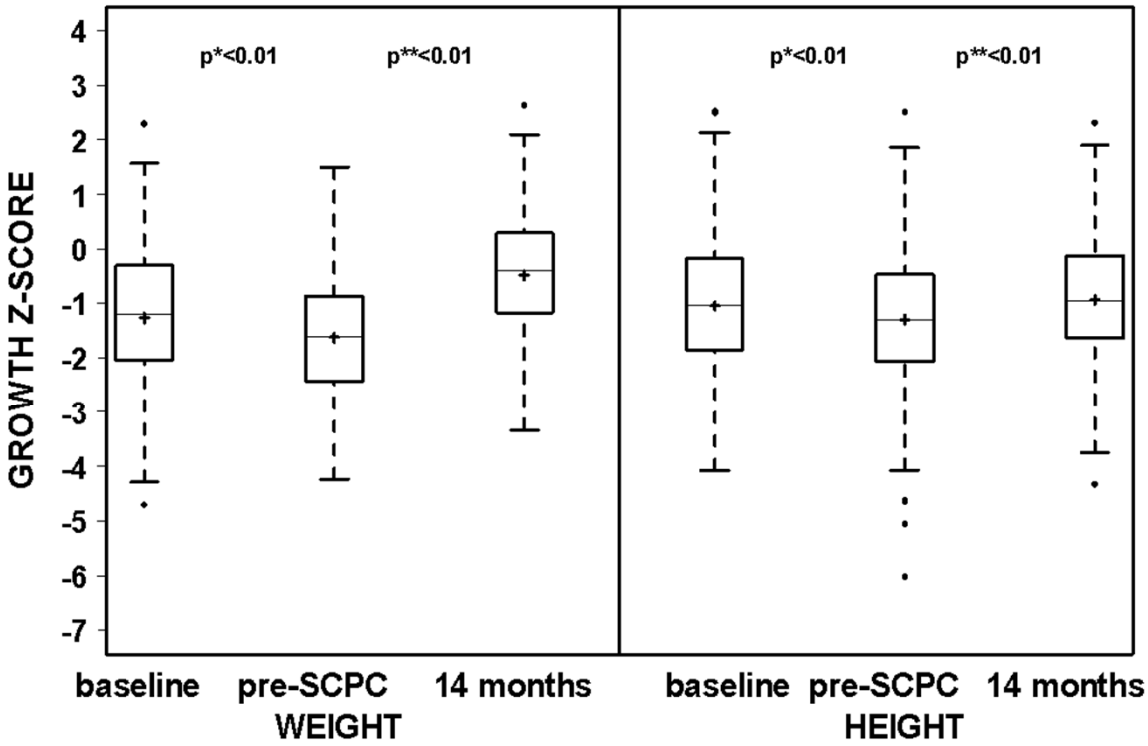
Mean Weight for Age Z-score vs. Age



Slide 9

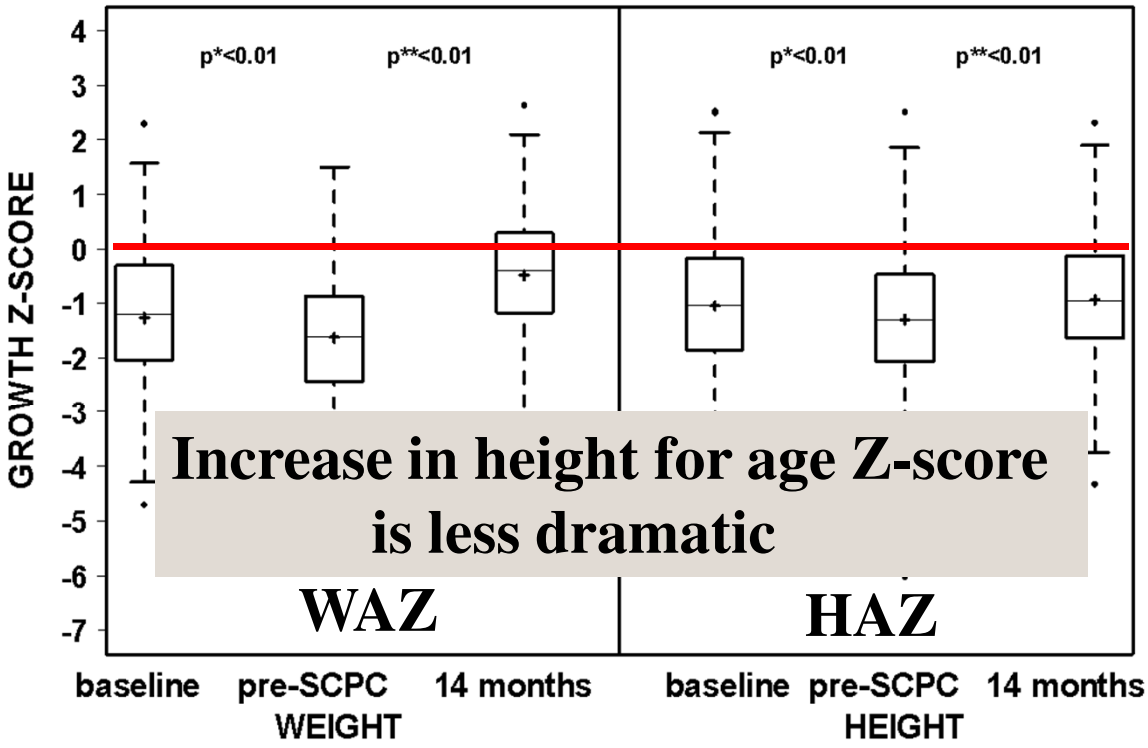
CR1 CHITRA RAVISHANKAR, 2/11/2018

Growth Z-Score vs. Age



*Hsu DH et al. *Circulation* 2010;122:333-340.

Growth Z-Score vs. Age



Failure to thrive in SV infants

Weight for age Z-score (WAZ) <-2

- 26% at study enrollment.
- 36% before stage II.
- 11% at 14 months.

*Hsu DH et al. *Circulation* 2010;122:333-340.

Prospective Study on Feeding Behaviors and Energy Costs in Infants with CHD

- Assess growth pattern in neonates from surgical intervention to discharge and identify predictors of growth.
- ND at 6 months and 12 months.
- Study period: March 2003 to May 2007.
- 61 neonates with SV physiology.
- 76 neonates with BV physiology.

Medoff-Cooper B. et al
Cardiol Young 2011;21:136-141

Anderson JB et al.
Cardiol Young 2011;21:421-429.

WAZ<-2 in infancy at discharge

Month	Overall	SV N=61	BV N-76	p-values[a]
Discharge	30%	28%	31%	0.99
Month 3				
Month 6				
Month 9				
Month 12				

Medoff-Cooper B. et al
Cardiol Young 2011;21:136-141

Anderson JB et al.
Cardiol Young 2011;21:421-429

WAZ<-2 in infancy

Month	Overall	SV N=61	BV N-76	p-values[a]
Discharge	30%	28%	31%	0.99
Month 3	27%	33%	22%	0.40
Month 6	16%	28%	9%	0.11
Month 9	9%	11%	7%	0.99
Month 12	3%	6%	0%	0.22

Medoff-Cooper B. et al
Cardiol Young 2011;21:136-141

Anderson JB et al.
Cardiol Young 2011;21:421-429

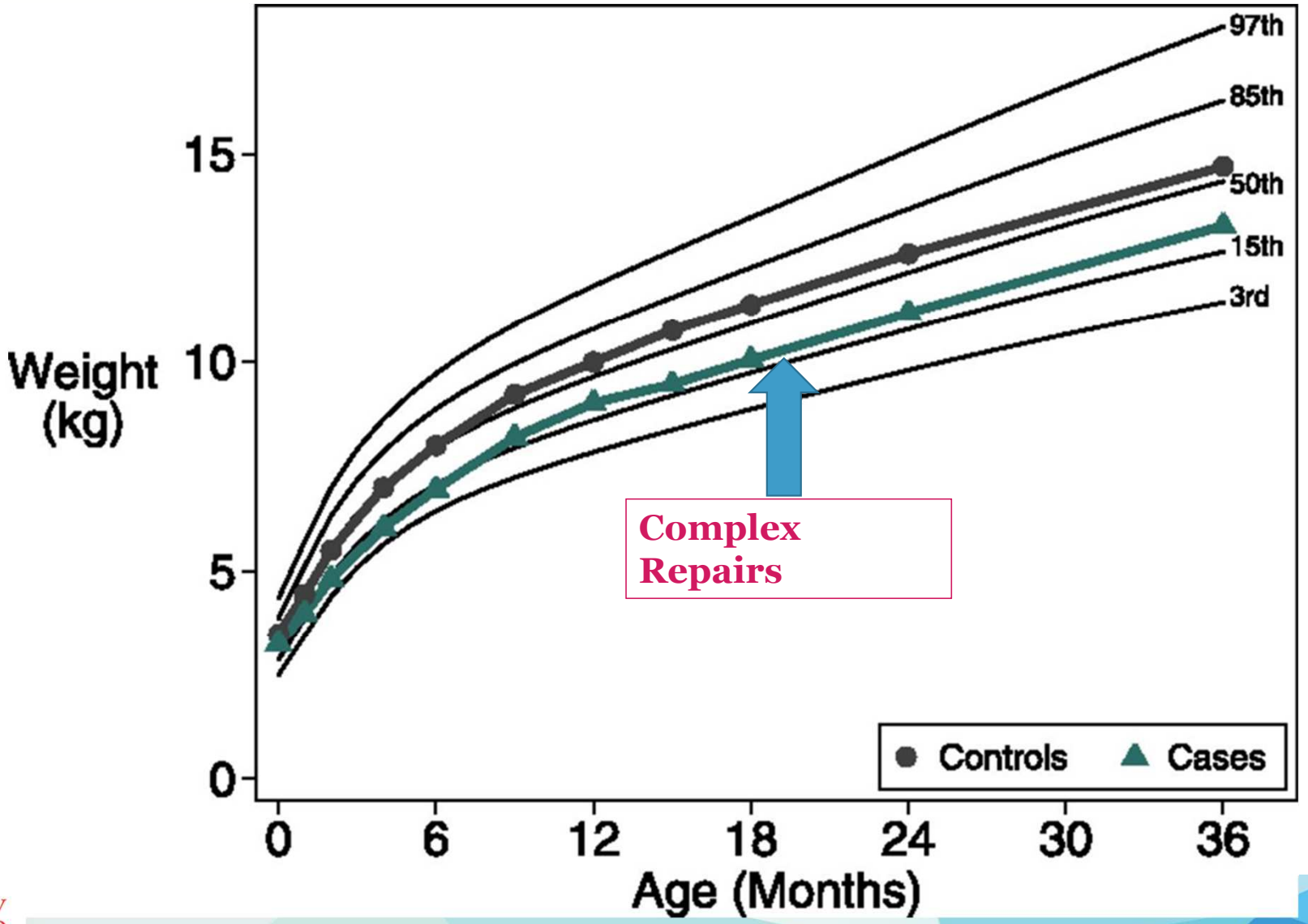
Growth in children with CHD

- A retrospective cohort matched study identified children with CHD in a large primary care network in Pennsylvania, New Jersey and Delaware and matched them 10:1 with control subjects.
- Primary outcome
- Difference in weight for age, length for age and HC for age z-scores at traditional ages for preventive visits.

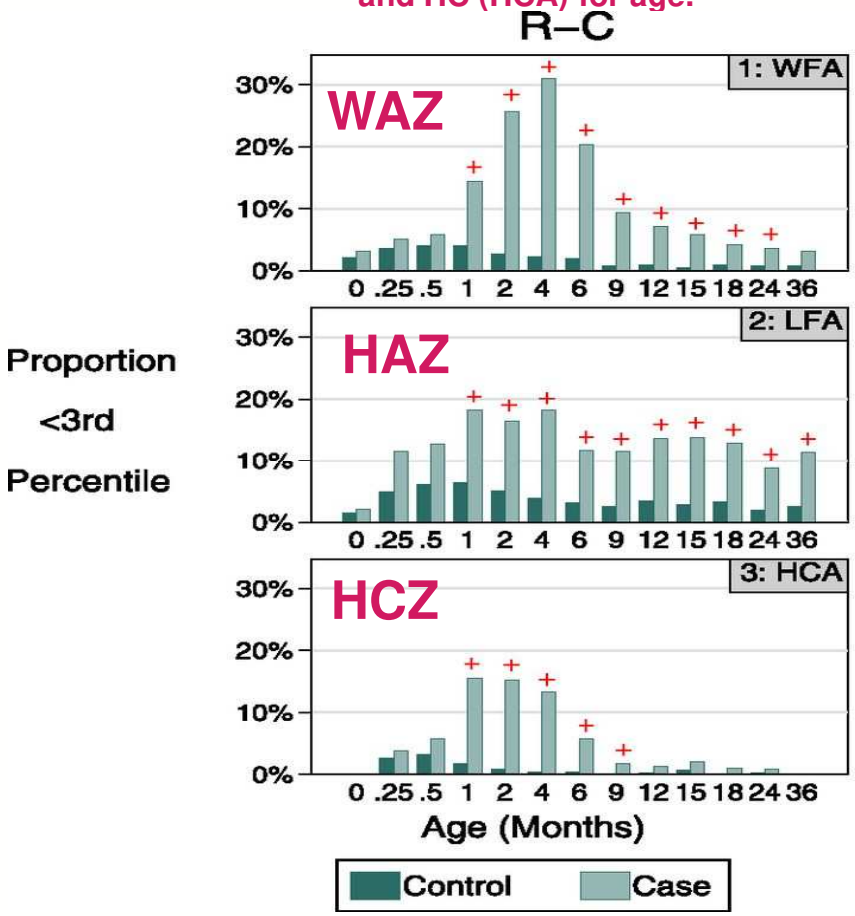
Modified from: Carrie Daymont et al. Pediatrics 2013;131:e236-e242.

Growth in children with CHD

- 856 Cases
- 37 with Single Ventricle (SV) repair.
- 52 with complex biventricular repair or CR (RACHS ≥3).
- 159 with simple biventricular repair or SR(RACHS 1 or 2).
- 608 no repair.


97th
85th
50th
15th
3rd
15
10
5
0
Weight (kg)
0
6
12
18
24
30
36
Age (Months)
Controls
Cases
Complex Repairs

Proportion of controls versus cases below the third percentile for weight (WFA), length (LFA), and HC (HCA) for age.



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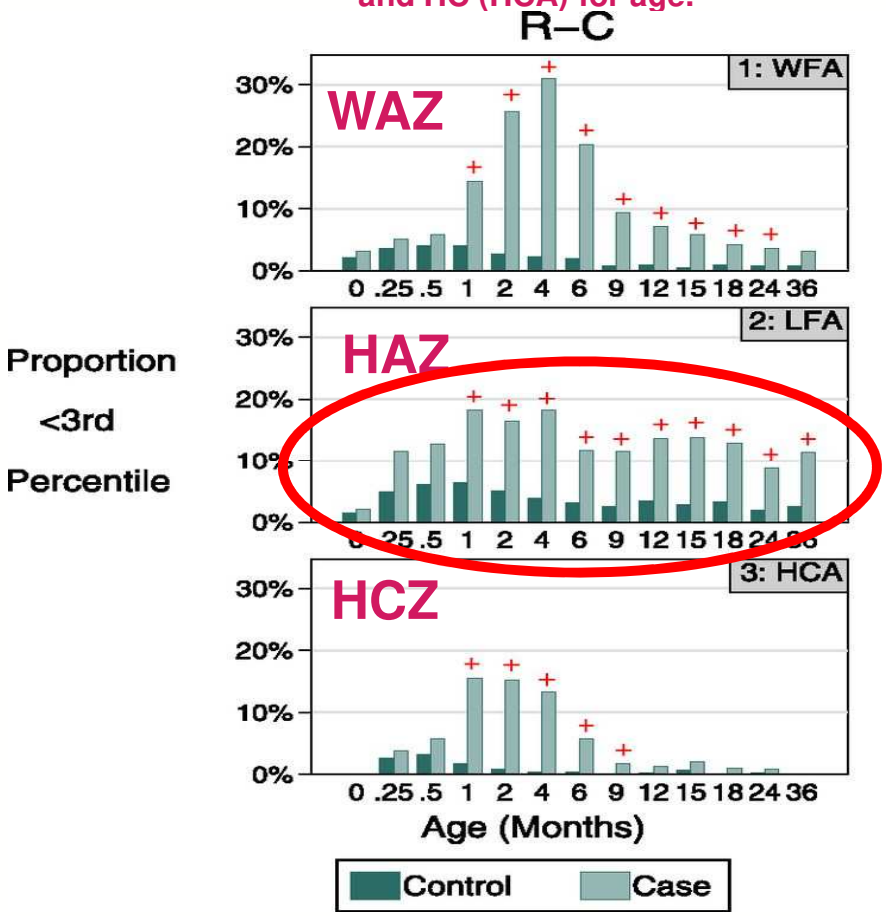


Carrie Daymont et al. Pediatrics 2013;131:e236-e242

Impact of poor growth

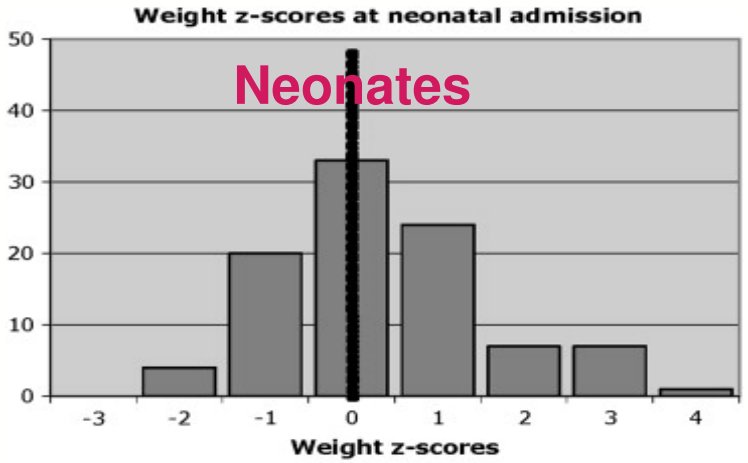
Postoperative morbidity

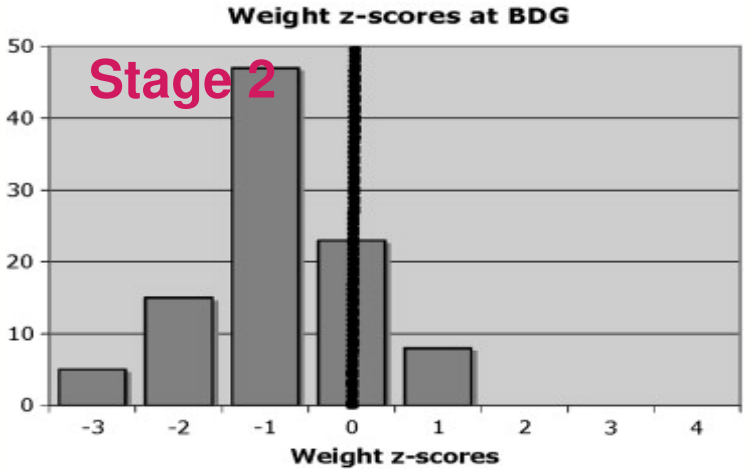
- In adults, poor nutrition and growth has been associated with longer hospital LOS and higher risk of infection.
- Do we have similar data in children with CHD?

Weight at stage 2 and LOS

- 100 pts undergoing stage 2 between 2001 and 2007.
- At neonatal admission
- Median weight 3.1 kg (2.2–4.4) with a median **WAZ of -0.4** (-2.6 to 3.2).
- Age at stage 2: 5.1 months(2.4–10).
- Median weight: 5.7 kg (3.6–8.4 kg).
- Median WAZ: **-1.3 (-3.9 to 0.6).**

Anderson JB et al. J Thorac Cardiovasc Surg 2009;138:397-404.





Anderson JB et al. J Thorac Cardiovasc Surg 2009;138:397-404.

WAZ and LOS

- Lower WAZ was independently associated with longer LOS (p=0.02).
- Younger age independent of WAZ was associated with longer LOS.

Anderson JB et al. J Thorac Cardiovasc Surg 2009;138:397-404.

Growth and Infection

- 55 patients undergoing Fontan at a single center.
- Median WAZ at Fontan was -1.0 (-3.8 to 2.0).
- WAZ <-2.0 was independently associated with a risk of postoperative infection (p=0.006).

Anderson JB et al. Ann Thorac Surg 2011;91:1460-6

Growth and postoperative outcome

- Multicenter study using the STS database.
- 2747 patients from 68 centers had Fontan operation from 2000 to 2009.
- Weight at the time of Fontan did not affect mortality, Fontan failure or LOS.

Wallace MC, et al, Ann Thorac Surg 2011; 91:1445-52.

Poor growth and postoperative outcome

WAZ <-2 was associated with the following independent of patient and center characteristics:

- Increase in postoperative mortality (2.73, 95% CI:1.09, 6.86).
- Fontan failure (OR: 2.59, 95% CI:1.24, 5.40).
- Longer LOS (+1.2 days, 95% CI :0.1-2.4).

Impact on neurodevelopment

- Growth failure in infancy in children **without** CHD has been associated with worse neurodevelopmental outcome in older children.

Association of Impaired Linear Growth and Worse Neurodevelopmental Outcome in Infants with Single Ventricle Physiology: A Report from the Pediatric Heart Network Infant Single Ventricle Trial

Chitra Ravishankar, MD, Victor Zak, PhD, Ismee A. Williams, MD, MS, David C. Bellinger, PhD, MSc, J. William Gaynor, MD, Nancy S. Ghanayem, MD, Catherine D. Krawczeski, MD, Daniel J. Licht, MD, Lynn Mahony, MD, Jane W. Newburger, MD, MPH, Victoria L. Pemberton, RNC, MS, Richard V. Williams, MD, Renee Sananes, PhD, Amanda L. Cook, MD, Teresa Atz, MSN, Svetlana Khaikin, BSc, MPH, and Daphne T. Hsu, MD for the Pediatric Heart Network Investigators

J Pediatr. 2013; 162: 250-256

Neurodevelopmental Testing in ISV Trial

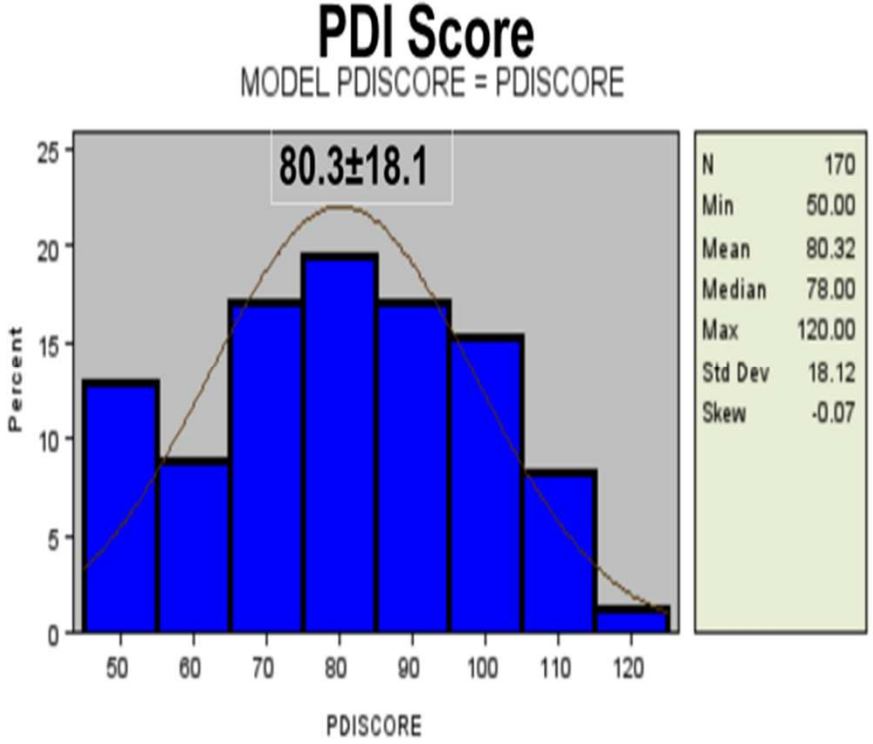
- ND testing with the BSID-II (Bayley Scales) was performed at the PHN sites by a designated PHN site psychologist at 12 months in 170 infants with SV physiology.

Two Scores:

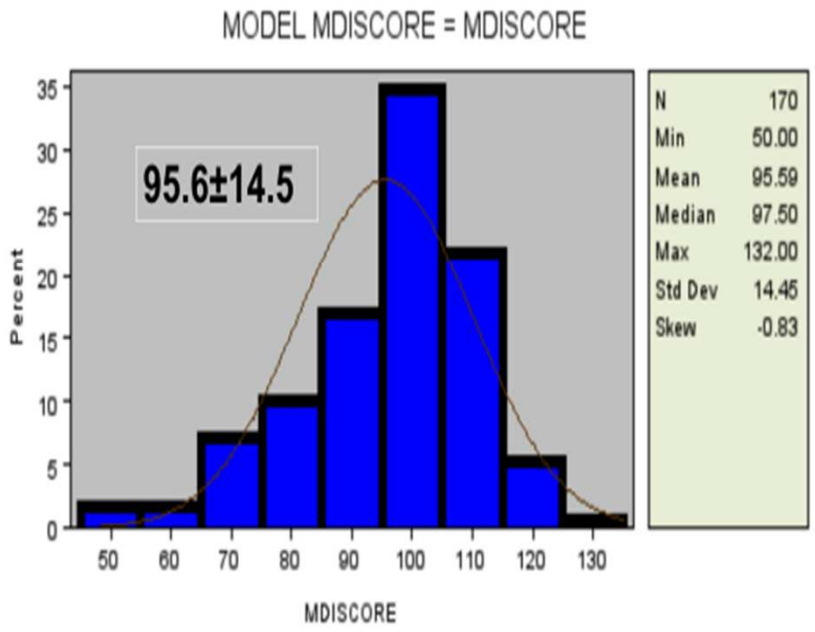
- Psychomotor Developmental Index (PDI).
- Mental Developmental Index (MDI).
- Normal: 100±15.

Ravishankar C et al. J Pediatr. 2013; 162: 250-256.

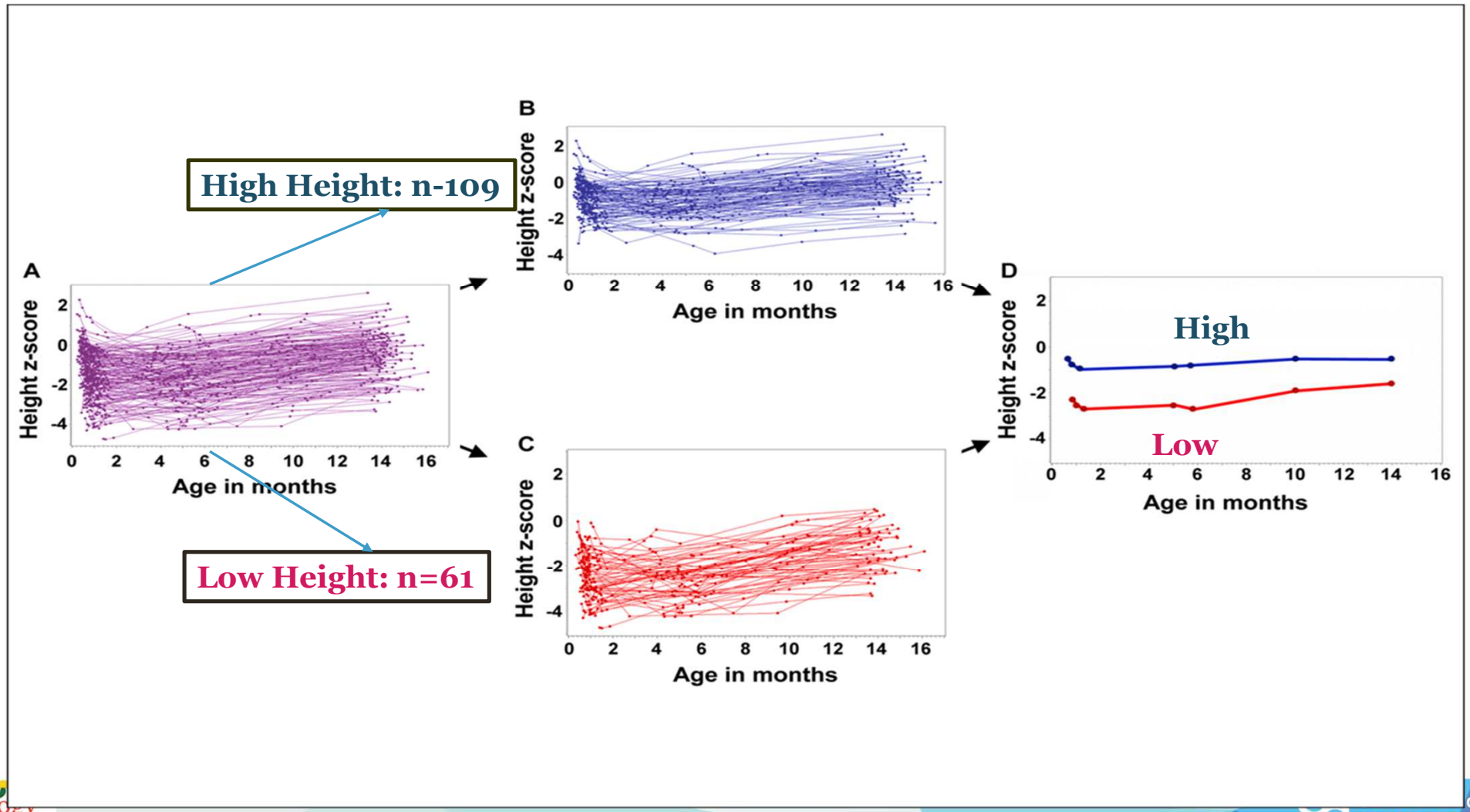
PDI Score



MDI Score



Height Trajectories



Multivariable Model for PDI at 14 months

Co-variate	PE (PDI)	Bootstrapping	p
Height trajectory (high)	14.9	100	<0.001
No of SAEs <2	10.6	56.2	0.016
2-4	3.8		
>4	ref		
Site		85.5	0.020

SAE: Serious Adverse Event, PE: Parameter Estimate

Multivariable model for MDI at 14 months

Co-variate	PE (MDI)	Bootstrapping	P
Height trajectory (high)	12.3	97	<0.001
Site		94.7	<0.001
ECMO	-13.3	48.2	0.01
Supplemental oxygen	-11.2	56.6	0.01

Co-variate	PE (MDI)	Bootstrapping	P
Height trajectory (high)	12.3	97	<0.001
Site		94.7	<0.001
ECMO	-13.3	48.2	0.01
Supplemental oxygen	-11.2	56.6	0.01
Height/BNP tr Interaction			<0.01
High-High	4.5		
High-Low	4.6		
Low-High	-12.8		
Low-Low	Ref		
Hispanic	-5.6	57.7	0.05

Short children with evidence of heart failure had the lowest predicted MDI

Comparison of ND Outcomes by Feeding Mode

	MDI at 6 mo Mean (SD)	MDI at 12 mo Mean (SD)
Physiology		
Single ventricle	90.53 (8.78)	91.18 (10.33)
Bi-ventricle	92.81 (10.56)	97.05 (12.60)
Sub-sample P value	0.435	0.035
Feeding mode at discharge		
Orally fed	94.62 (10.25)	96.16 (12.68)
Tube assisted	89.04 (8.79)	92.18 (10.70)
Sub-sample P value	0.045	0.157
Feeding mode at 3 months		
Orally fed	93.18 (9.14)	94.98 (12.15)
Tube assisted	80.8 (10.33)	89.9 (9.35)
Sub-sample P value	0.007	0.211

Medoff-Cooper B. et al. J. Pediatr. 2016;169: 154-159.

Comparison of ND Outcomes By Feeding Mode

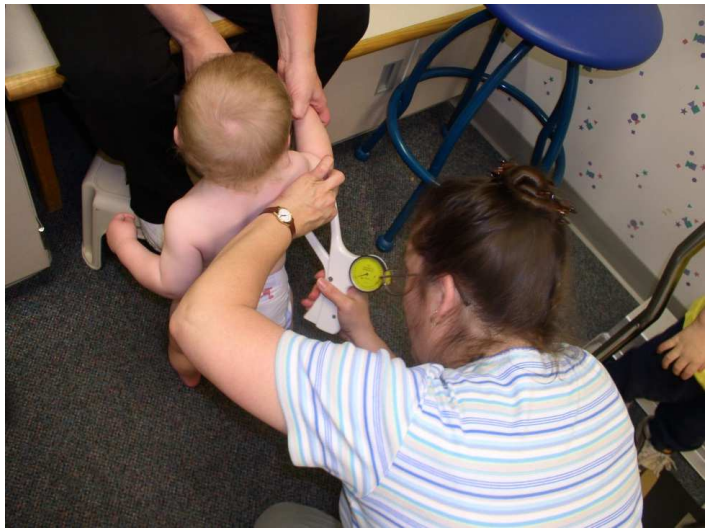
	PDI at 6 mo Mean (SD)	PDI at 12 mo Mean (SD)
Physiology		
Single ventricle	76.58 (14.77)	73.94 (15.78)
Bi-ventricle	83.97 (13.47)	84.58 (15.33)
Sub-sample P value	0.074	0.005
Feeding mode at discharge		
Orally fed	85.70 (11.58)	80.47 (15.36)
Tube assisted	76.17 (15.54)	78.53 (17.54)
Sub-sample P value	0.016	0.618
Feeding mode at 3 months		
Orally fed	83.43 (12.85)	81.84 (15.36)
Tube assisted	60.8 (10.71)	65.4 (15.75)
Sub-sample P value	<0.001	0.003

Medoff-Cooper B. et al. J. Pediatr. 2016;169: 154-159.

Nutrition and Development

- Lower z-scores for weight, length and HC at 3 months were the most significant predictors of lower BSID assessments at 6 and 12 months of age.

- Growth/Nutrition matters!



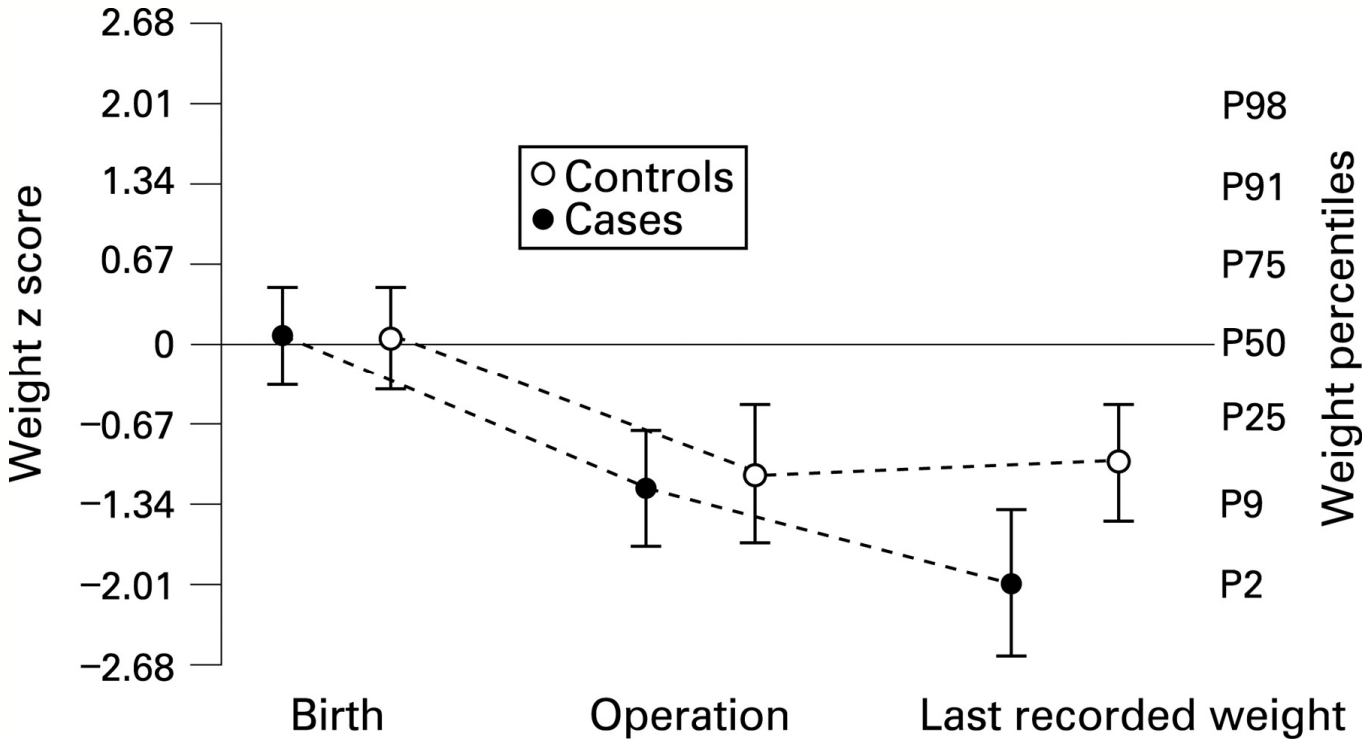
Medoff-Cooper B. et al. J. Pediatr. 2016;169: 154-159.

Growth and late mortality

- Case control study from Norway: late mortality (>30 days) after surgery for CHD.
- 2247 surgeries for CHD from 1990 to 2002.
- 204 deaths including 80 late deaths.
- 74/80 had sufficient data on weight and were compared with matched controls.

Eskedal LT et al. Arch Dis Child 2008;93:495-501..

Mean weight z scores with 95% confidence intervals at birth, at last operation and at last recorded weight in 31 cases and 31 controls without extra-cardiac anomalies.



Modified from: L T Eskedal et al. Arch Dis Child 2008;93:495-501

Growth and late mortality

- Median follow up after last recorded operation was 4.8 months, 70 died before 2 years of age.
- **If WAZ decreased by ≥0.67 after last recorded operation, odds ratio for mortality was 13.5 (95% CI 3.6 to 51).**
- Conclusion: Inadequate weight gain on follow up can be an ominous sign and should alert clinicians to look for hemodynamic causes of poor weight gain.

Interventions?

General Guidelines

Preoperative period

- Use of enteral feeding (po or NG) in prostaglandin dependent neonates who are hemodynamically stable.
- Early use of parenteral nutrition.

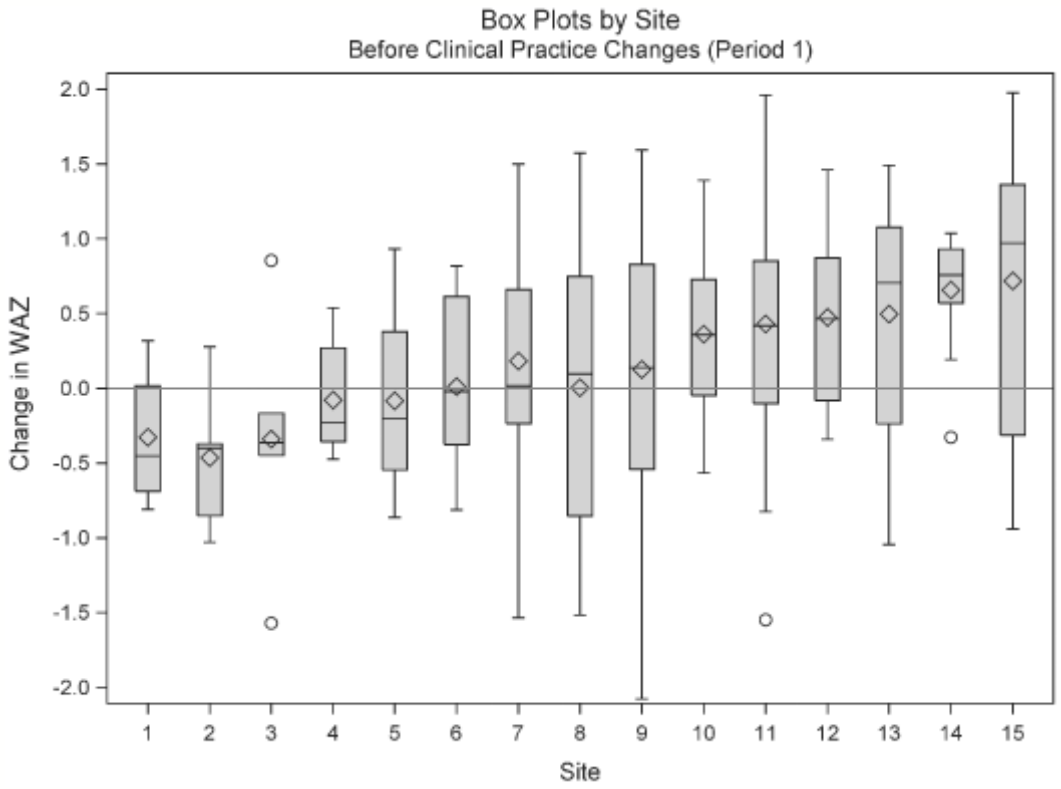
Postoperative Period

- Active involvement of a registered dietician.
- Initiate enteral feeds (po or NG) as soon as hemodynamic stability is achieved.
- Advance feeds based on a standardized protocol.
- Nutritional pathway is live at CHOP (Amy Lisante and Melanie Savoca).

After discharge

- Ongoing nutritional surveillance and intervention is critically important.

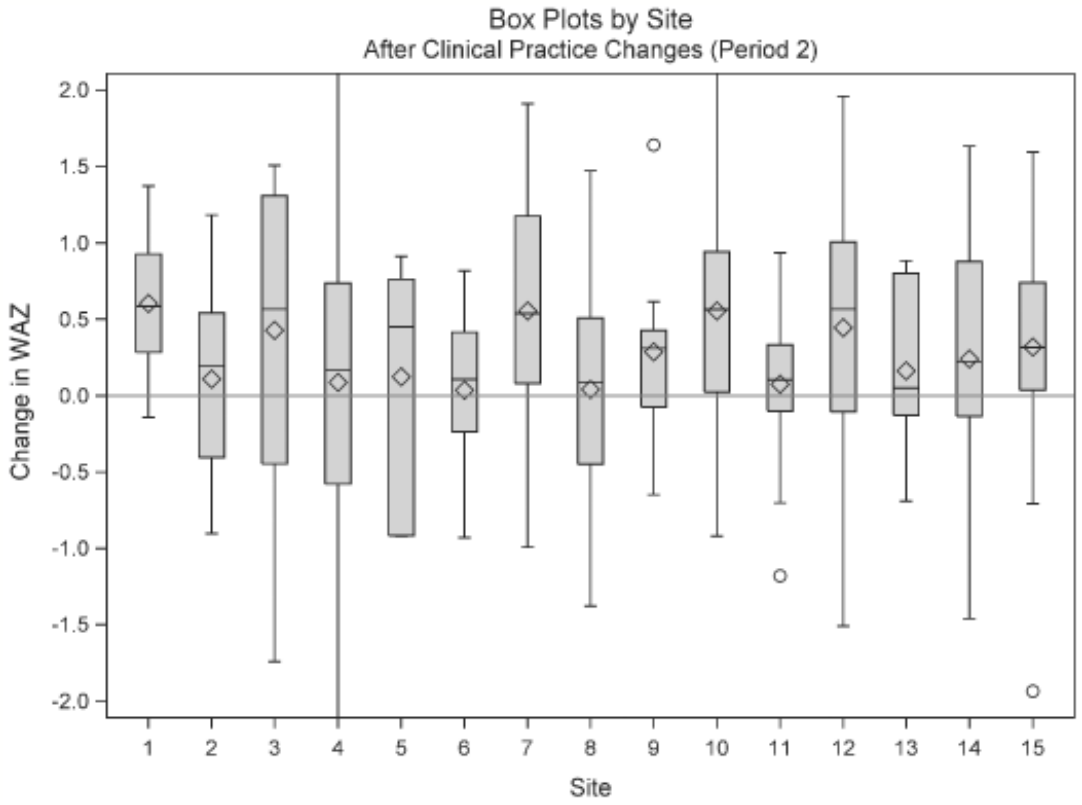
Use of a Learning Network to Improve Variation in Interstage Weight Gain after the Norwood Operation



Modified from Anderson JB et al. Congenit Heart Dis. 2014;9:512-520.

Use of a Learning Network to Improve Variation in Interstage Weight Gain after the Norwood Operation

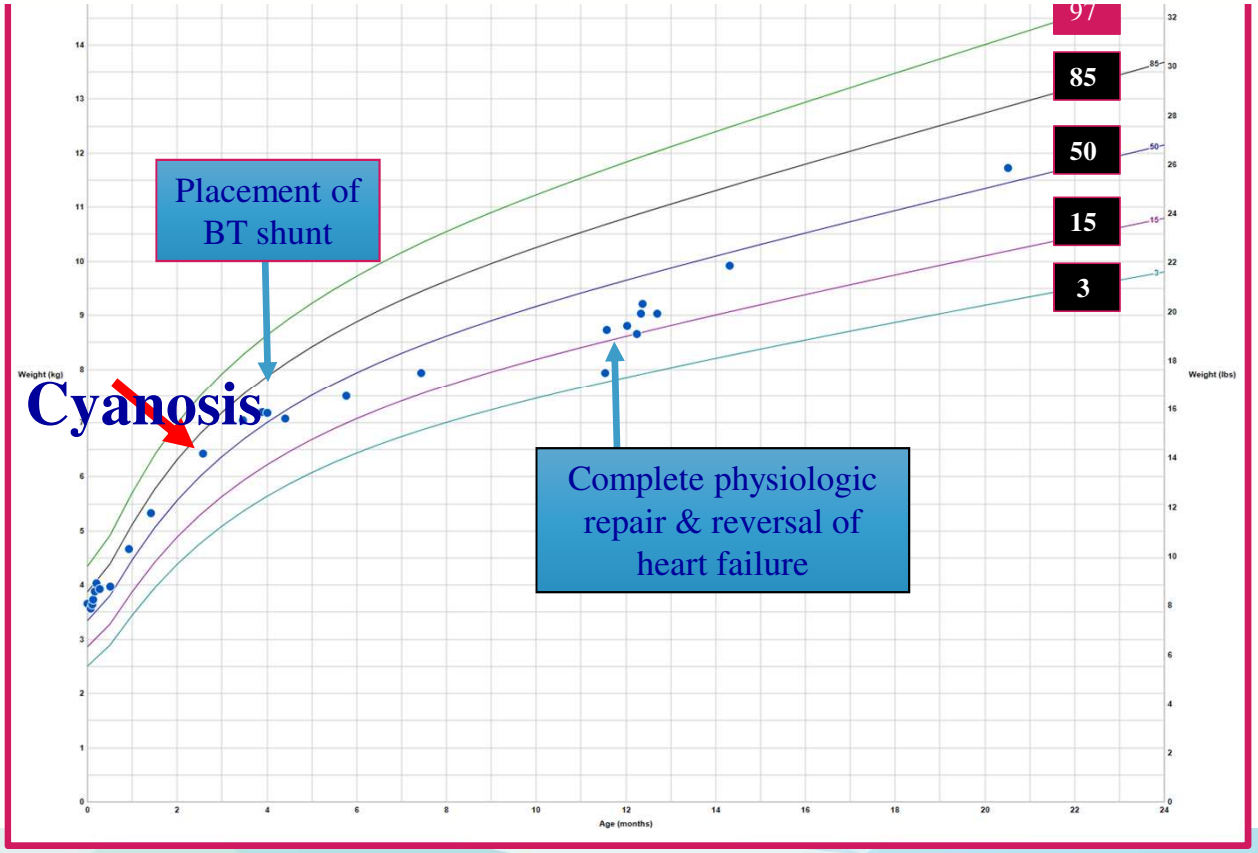
Implementation of a growth bundle



Modified from Anderson JB et al. Congenit Heart Dis. 2014;9:512-520.

D-TGA / VSD / PS

Nutrition matters but physiology may matter more...



Conclusions

- Feeding difficulties and impaired growth are life long issues for children with CHD, particularly those with SV physiology.
- Neonates undergoing biventricular repair are not spared.
- In SV patients, “volume unloading” resulting from Stage II has a positive impact on growth.
- Growth failure in infancy can affect postoperative mortality and morbidity.

Conclusions

- “Stunting” or short stature is a significant problem in children with complex CHD.
- “Stunting” in infancy has been associated with worse early neurodevelopmental outcome.
- Clinicians should be attentive to poor linear growth in infancy as a marker for potential neurodevelopmental issues.
- More to growth than nutrition alone.

Future Trends

- Better understanding of mechanism of growth failure.
- Collaboration with other sub-specialties and share lessons learned.

- Dr. Vicki Vetter
- Dr. Daphne Hsu
- Dr. Barbara Medoff-Cooper

Thank You!

Preoperative anthropometry

- Assess the relationship between preoperative triceps skin fold thickness z-score (TSFZ) and postoperative outcomes.
- 71 patients with CHD were enrolled in a prospective, two-center cohort (UCSF and UNICAR,Gautemala).
- RACHS ≤3, Median age 10.2 months
- An increase in TSFZ (total body fat mass) was associated with:
- decreased ICU LOS,
- decreased duration of mechanical ventilation,
- decreased duration of inotropes

Radman M. et al. J Thorac Cardiovasc Surg. 2014 January ; 147: 442-4550.

HLHS, severe PI, TR, RV dysfunction