Balancing Nutrients and Ensuring Growth in Preterm Infants

Ariel A. Salas, MD, MSPH

UAB MEDICINE
NEONATOLOGY

Children's
of Alabama

Disclosure

Dr. Ariel A. Salas has disclosed the following financial relationships. Any real or apparent conflicts of interest related to the content of this presentation have been resolved.

Affiliation / Financial Interest	**Organization**
Research Funding	NICHD, Reckitt, Neonatal Network
Scientific advisor	Mead Johnson Nutrition, Resbiotic
Invited speaker	WebMD, Mead Johnson Nutrition
Patent co-owner	University of Alabama

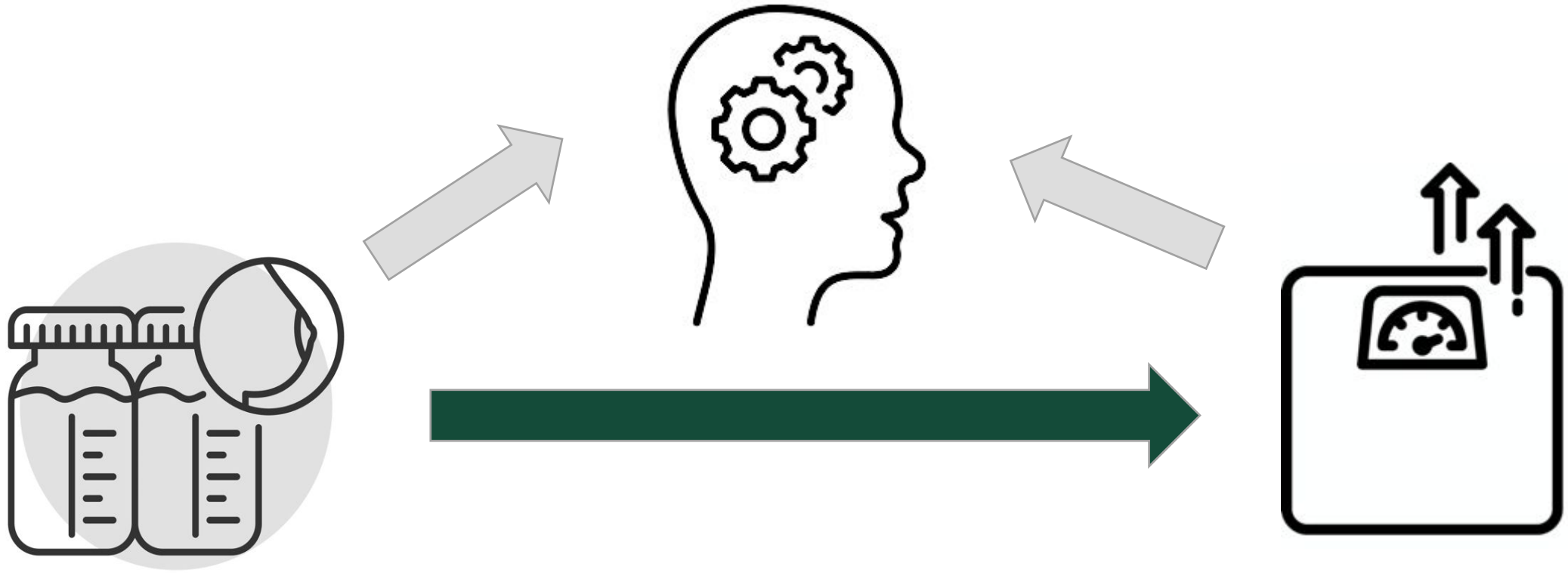
Learning objectives

Identify	Interpret	Recognize	Compare
key macronutrients essential for optimal growth and development in preterm infants.	growth charts and Z-scores to assess postnatal growth and nutritional adequacy.	common barriers to achieving optimal growth in the NICU	strategies for providing balanced nutrition

Learning objectives

Identify	Interpret	Recognize	Compare
key macronutrients essential for optimal growth and development in preterm infants.	growth charts and Z-scores to assess postnatal growth and nutritional adequacy.	common barriers to achieving optimal growth in the NICU	strategies for providing balanced nutrition

Providing optimal nutrition boosts growth and strengthens neurodevelopment in both term and preterm infants.



Feeding strategies for high-risk infants are guided by their postnatal age

1 Acute (0 – 14 days)

Most of the cumulative nutritional deficits occur during this phase (PN > EN)

2 Convalescent (14 - 90 days)

HMFs are added to maternal or donor milk

Feeding volumes are increased to 170 – 200 ml/kg/day

Preterm formula is offered if maternal milk is insufficient at 34 weeks PMA

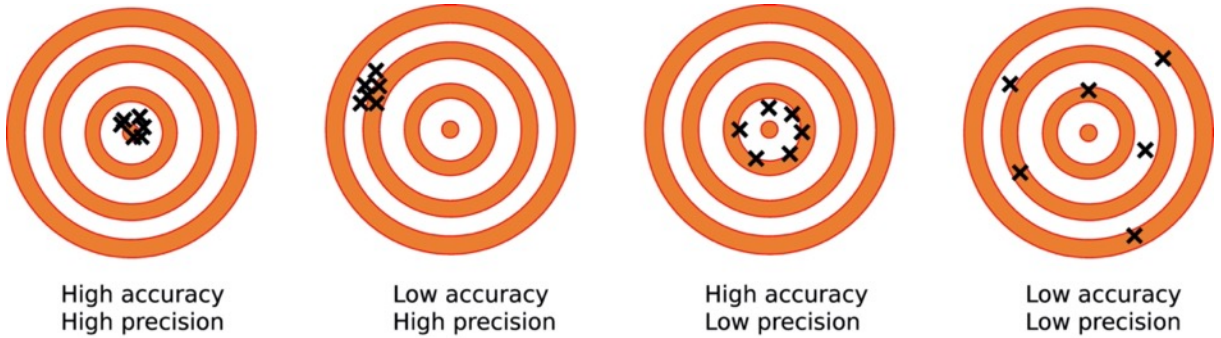
3 Discharge

Learning objectives

Identify	Interpret	Recognize	Compare
key macronutrients essential for optimal growth and development in preterm infants.	growth charts and Z-scores to assess postnatal growth and nutritional adequacy.	common barriers to achieving optimal growth in the NICU	strategies for providing balanced nutrition

One of the primary goals of preterm nutrition is to support growth rates and body composition that closely mirrors *in utero* development

AAP, Pediatric Nutrition, 8th Ed, 2019



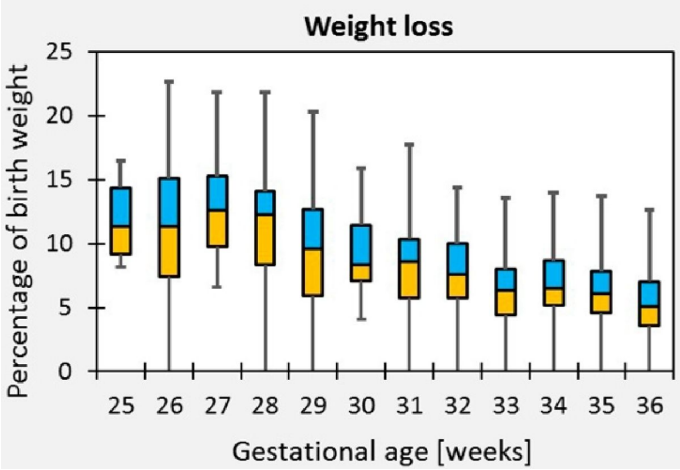
However, many growth metrics used in preterm infants are based on outdated or inaccurate sources

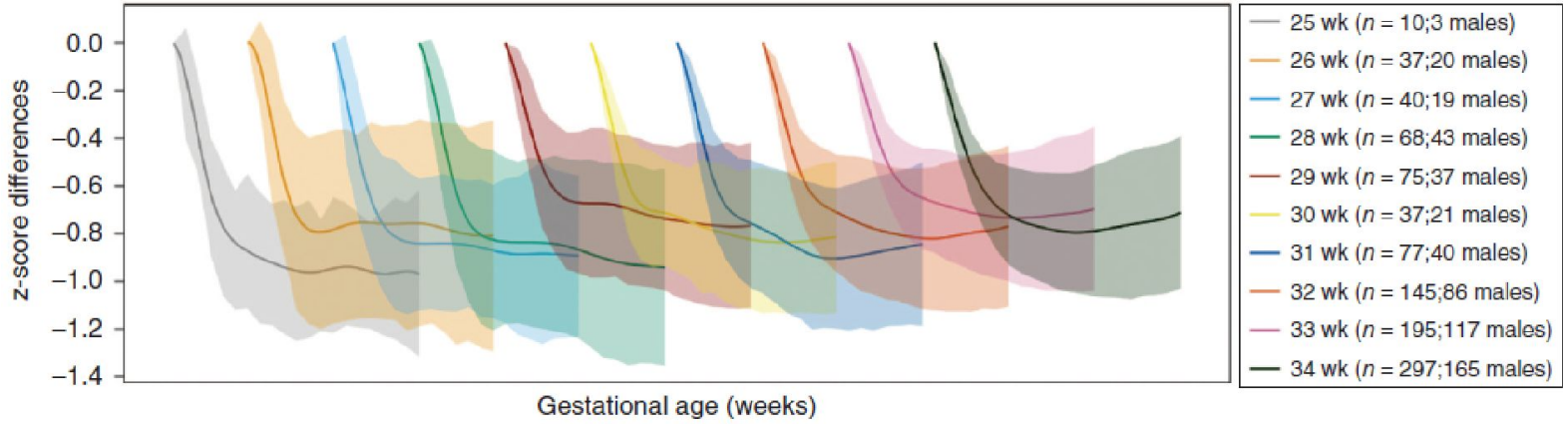
Prenatal measurements

Birth measurements

Postnatal measurements

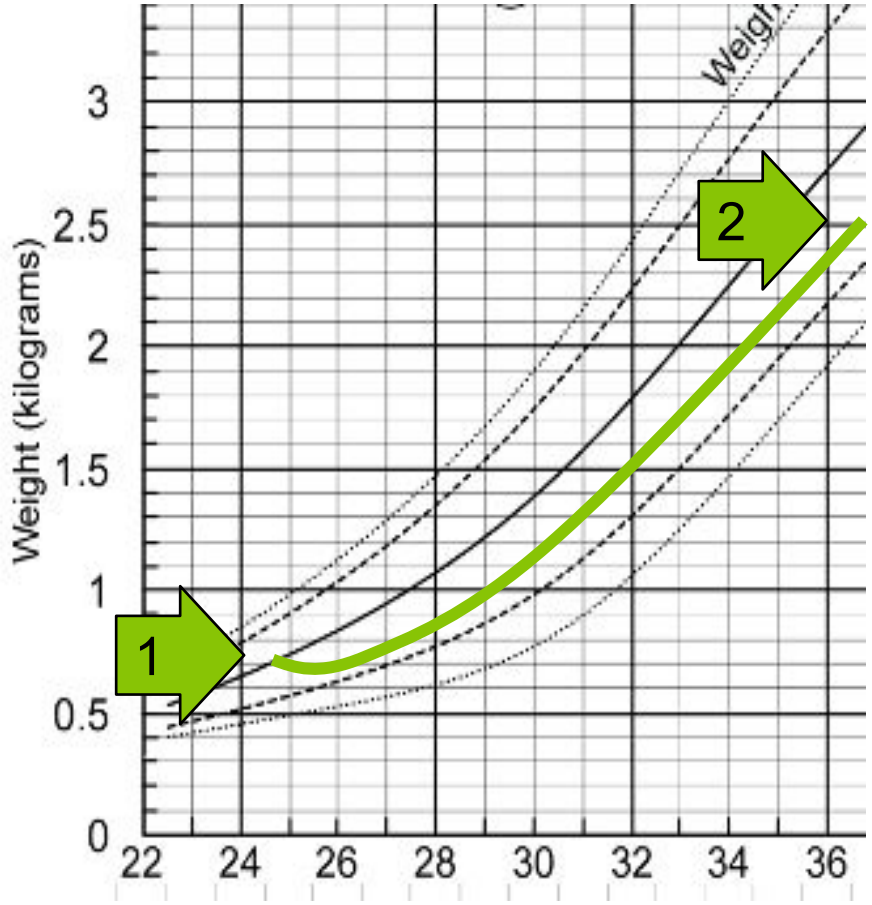
Growth charts relying on cross-sectional birthweight data often fail to account for physiological weight loss

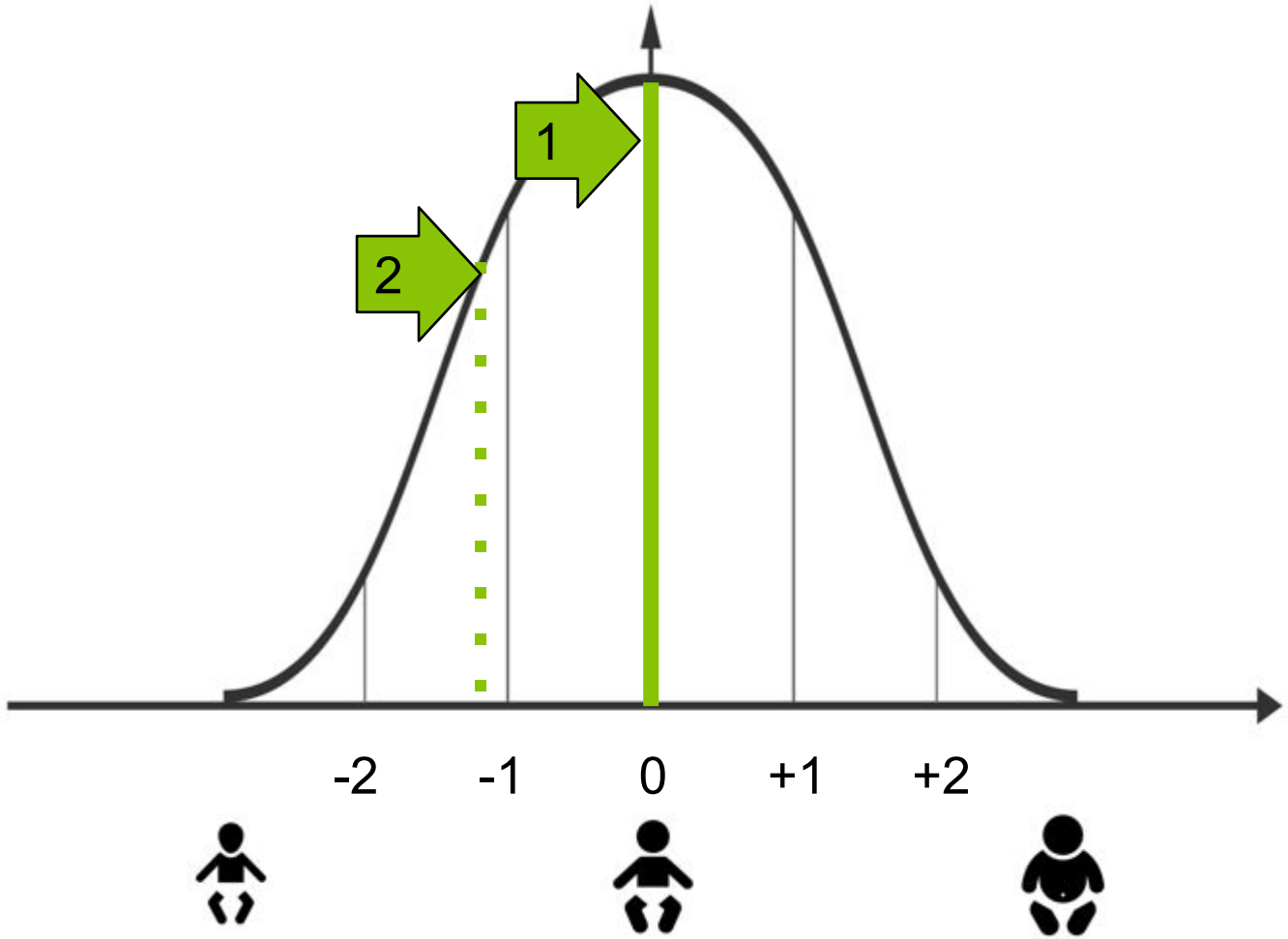




Rochow N, et al. Pediatr Res 2016

We assess growth outcomes in preterm infants by calculating centiles and z-scores based on the 2013 Fenton growth curves

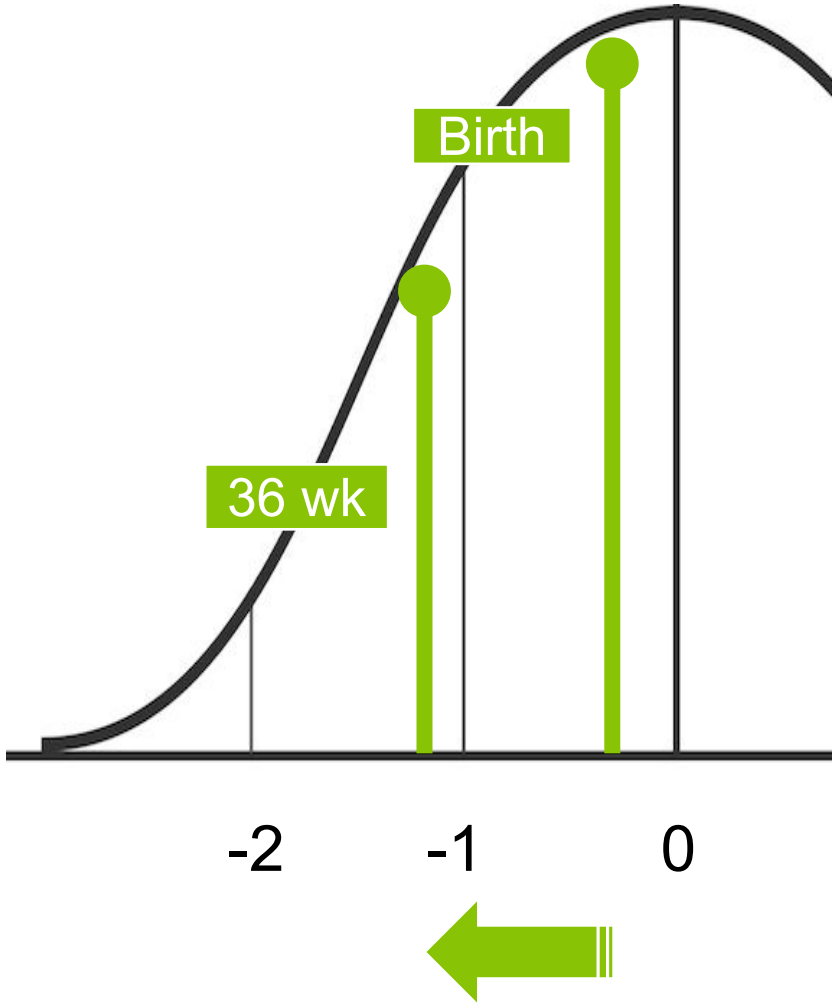




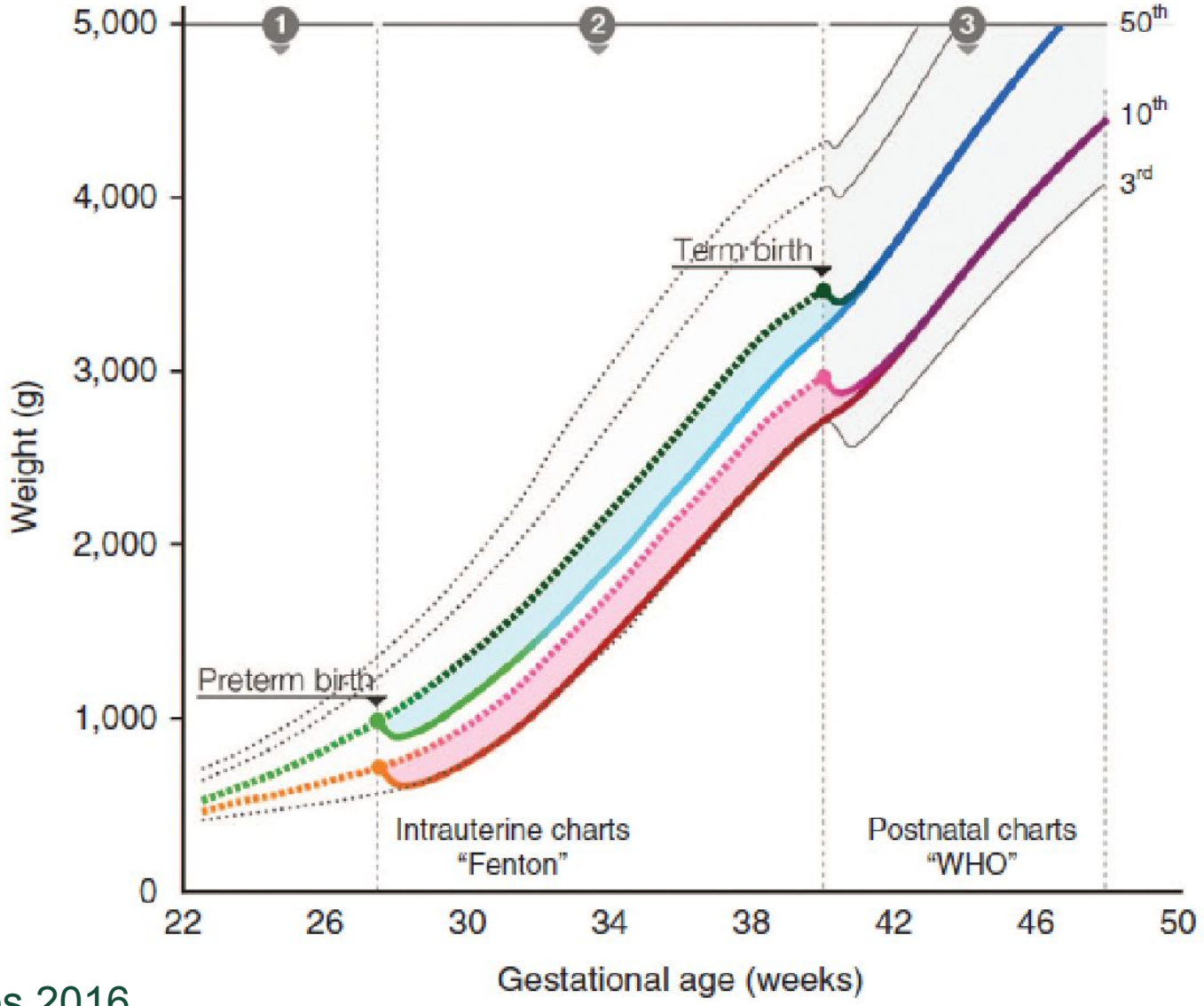
A drop of 0.8 units in weight z-scores during the first two weeks after birth aligns with physiologic weight loss

Moderate to severe malnutrition is defined as a drop in weight z score of 1.2 units from birth to 36 weeks PMA

After NICU discharge, no further declines in weight z scores are expected



Once this weight adjustment is factored in, comparisons between postnatal and intrauterine growth rates become more reliable

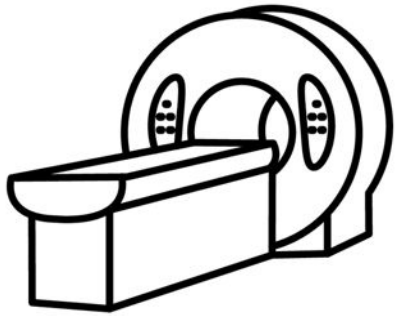


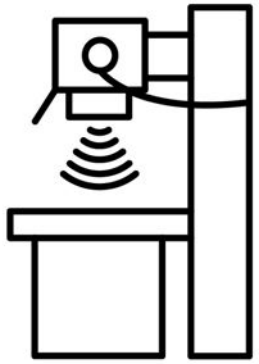
Rochow N, et al. Pediatr Res 2016

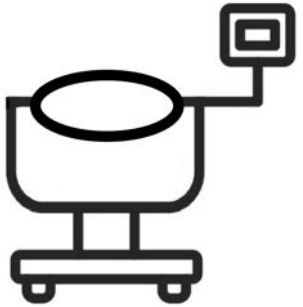
Body composition is generally recognized as a superior indicator of fatness compared to BMI in preterm infants

Susceptibility to early metabolic programming demands careful assessment of both quantitative and qualitative outcomes of growth

In stable preterm infants, body composition can be measured with MRI, DEXA, and ADP







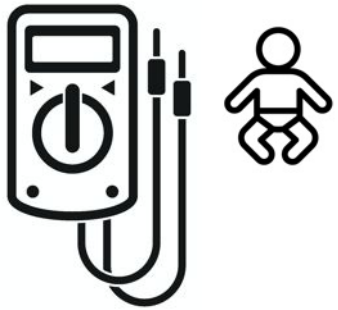
MRI: 10 – 30 min.

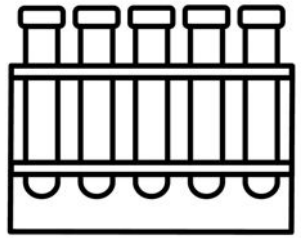
DEXA: 5 – 6 min.

ADP: 2 – 3 min.

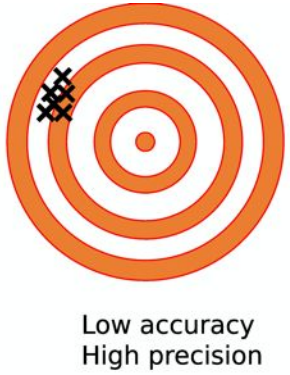
Bell KA, et al. J Perinatol 2022

In critically ill preterm infants, body composition can be measured with BIA, US, and D3-creatine





BIA	US	D-creatine method

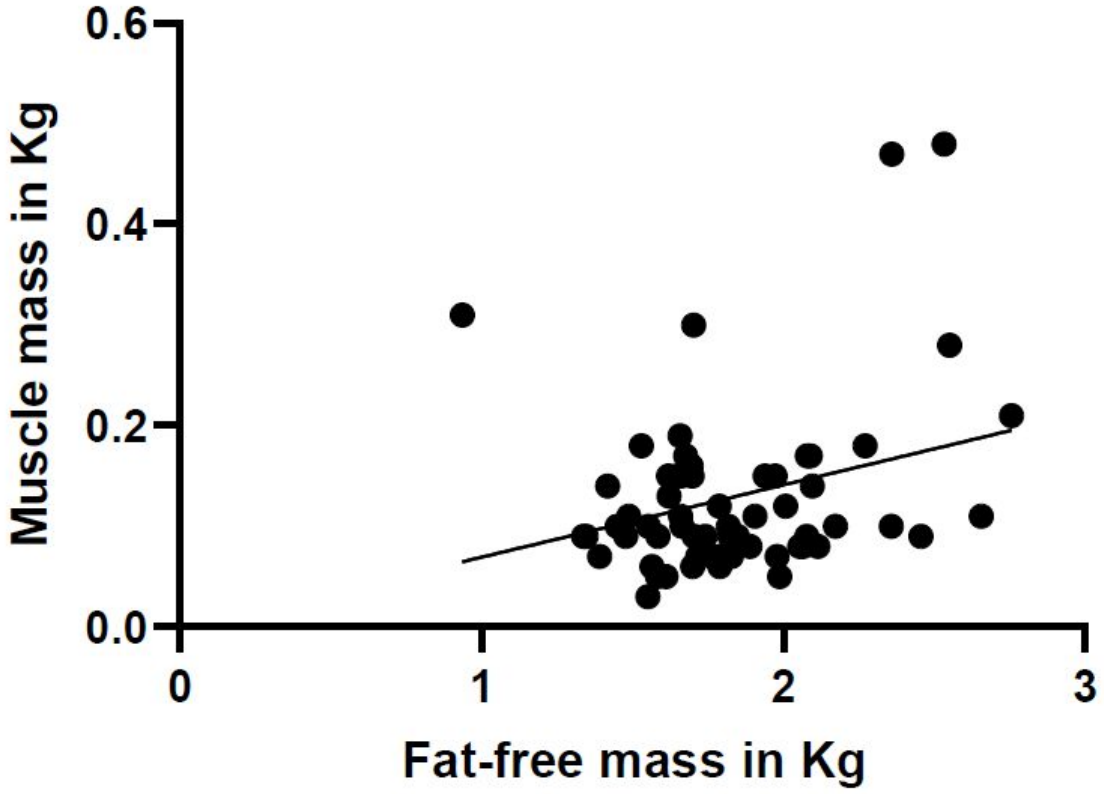


Bell KA, et al. J Perinatol 2022

The correlation between ADP-measured FFM and muscle mass measured by the D3-creatine method is moderate (r=0.4)

Cyrus K, et al. J Pediatr 2024

FFM and SMM are related but distinct concepts in body composition



SMM requires sustained nutrition (adequate protein intake), physical activity input, and more time to develop compared to other components of FFM

UAB MEDICINE
NEONATOLOGY

Cyrus K, et al. J Pediatr 2024

Children's of Alabama

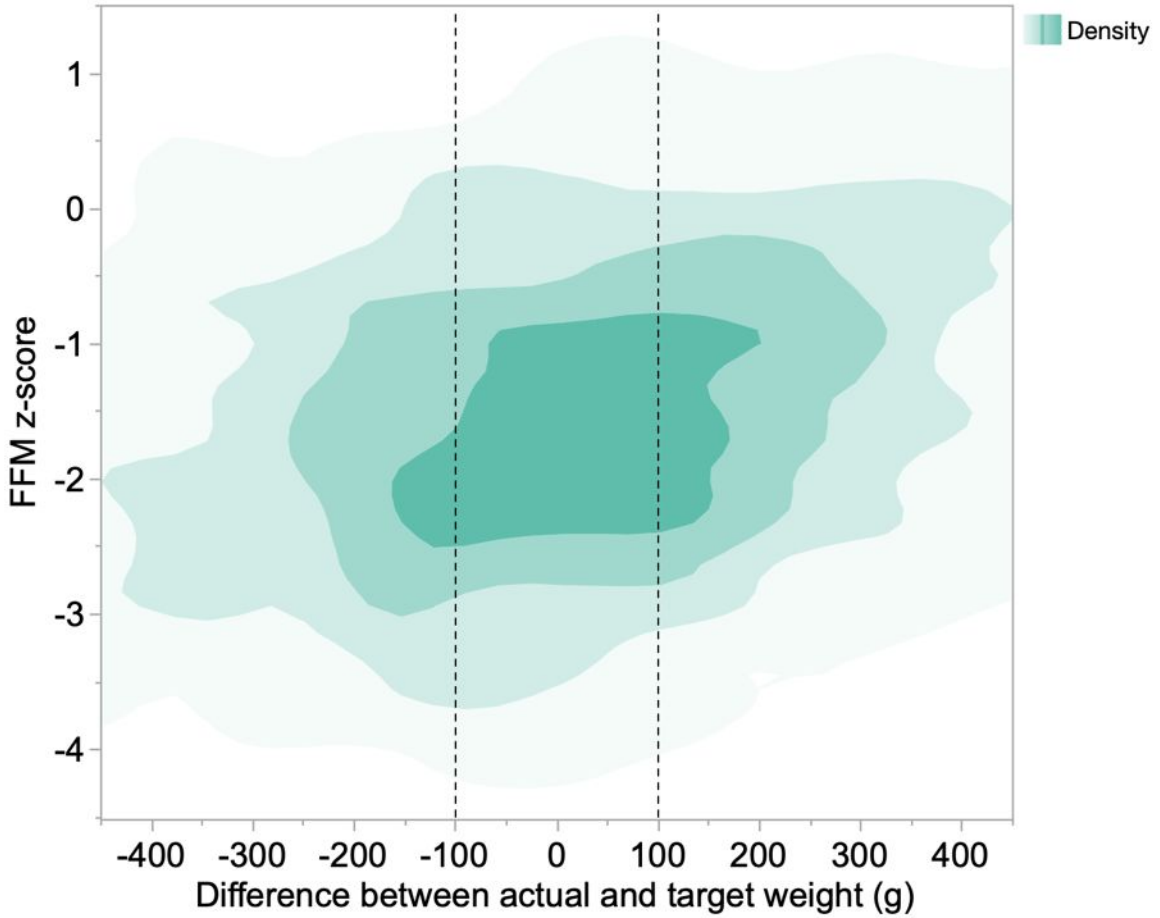
Key growth indicators such as weight gain (g/kg/day), length gain (cm/week), and MUAC at TEA can accurately predict body fat percentage

Razzaghy J, et al. JPEN 2023

UAB MEDICINE
NEONATOLOGY

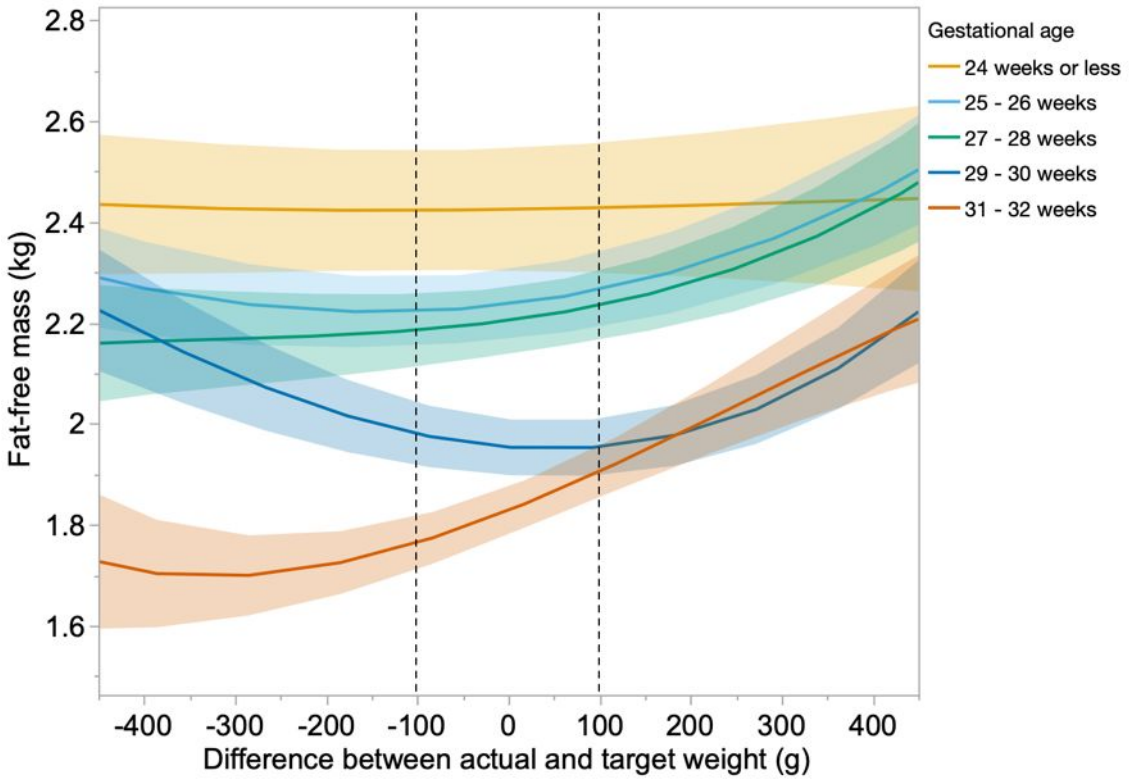
By leveraging data from preterm infants born across multiple countries, we could re-define optimal body composition at TEA

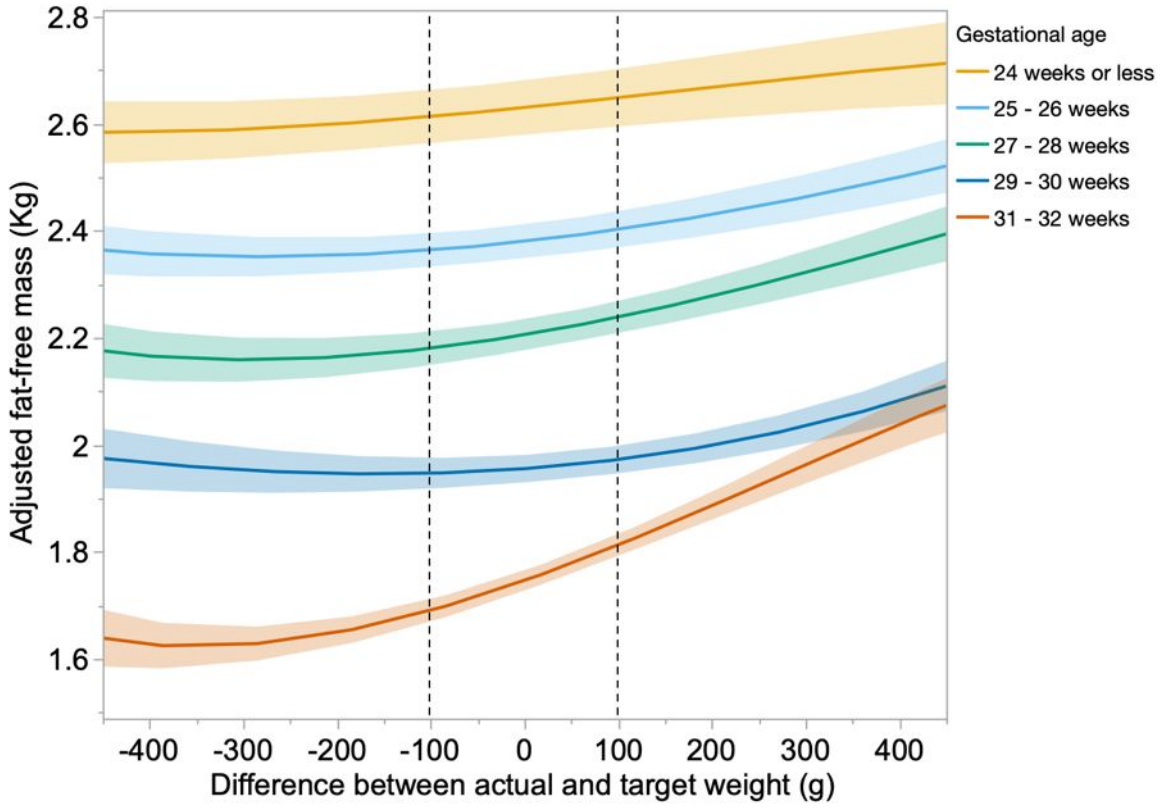
Achieving growth within target does not necessarily correlate with the highest FFM accretion (n=1052)



Salas AA & Rochow N. PAS 2023

Monitoring absolute FFM gains, rather than z scores, may offer a better approach to tracking body composition across different gestational age groups





Salas AA & Rochow N. PAS 2023

UAB MEDICINE NEONATOLOGY

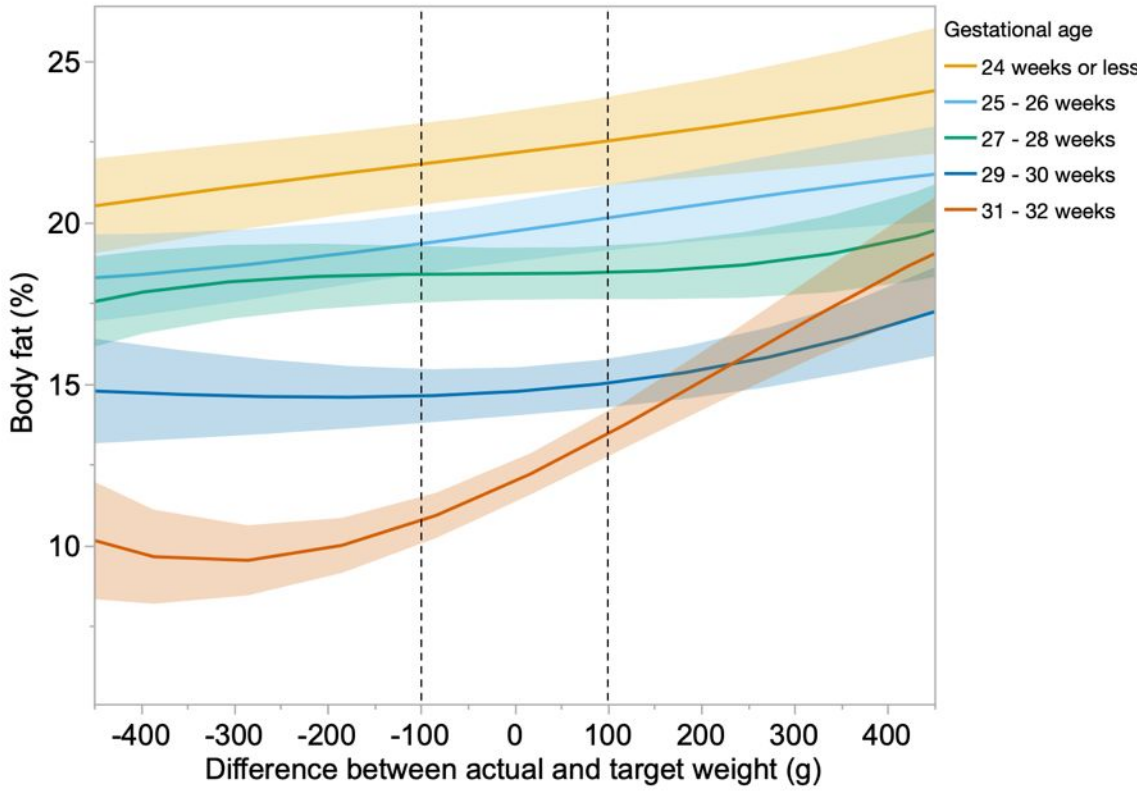
McMaster University

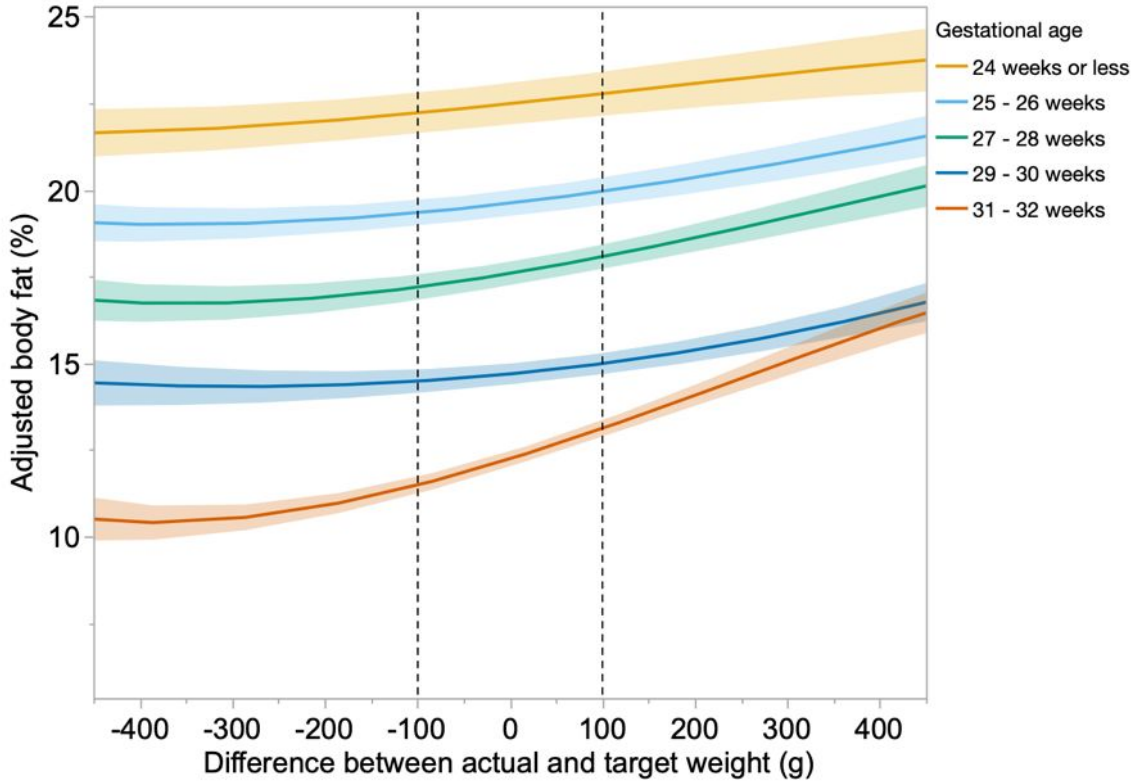
KLINIKUM NÜRNBERG

MEDICAL UNIVERSITY OF VIENNA

Universitätsklinikum Tübingen

Preterm infants with growth trajectories within target exhibit distinctive body fat percentages at TEA according to GA





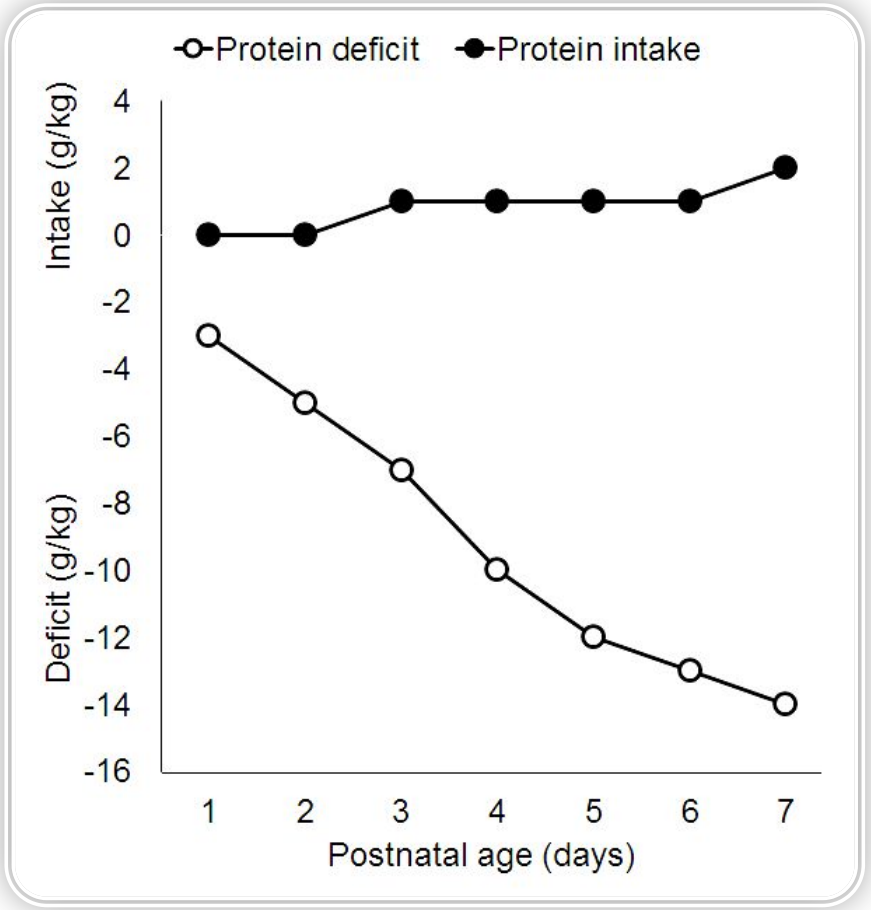
Salas AA & Rochow N. PAS 2023

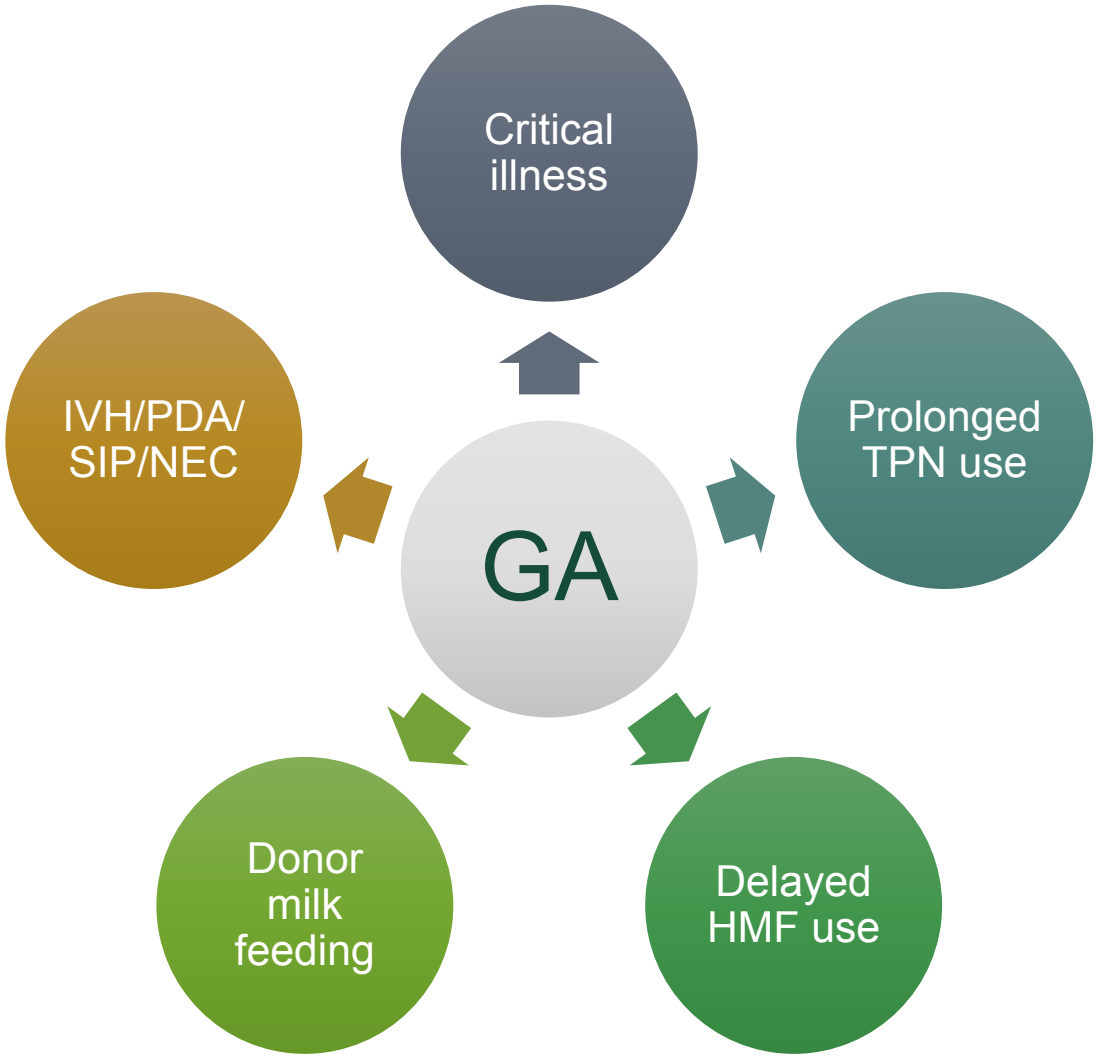
UAB MEDICINE NEONATOLOGY · McMaster University · KLINIKUM NÜRNBERG · MEDICAL UNIVERSITY OF VIENNA · Universitätsklinikum Tübingen

Learning objectives

Identify	Interpret	Recognize	Compare
key macronutrients essential for optimal growth and development in preterm infants.	growth charts and Z-scores to assess postnatal growth and nutritional adequacy.	common barriers to achieving optimal growth in the NICU	strategies for providing balanced nutrition

Protein deficit is a risk factor for suboptimal growth

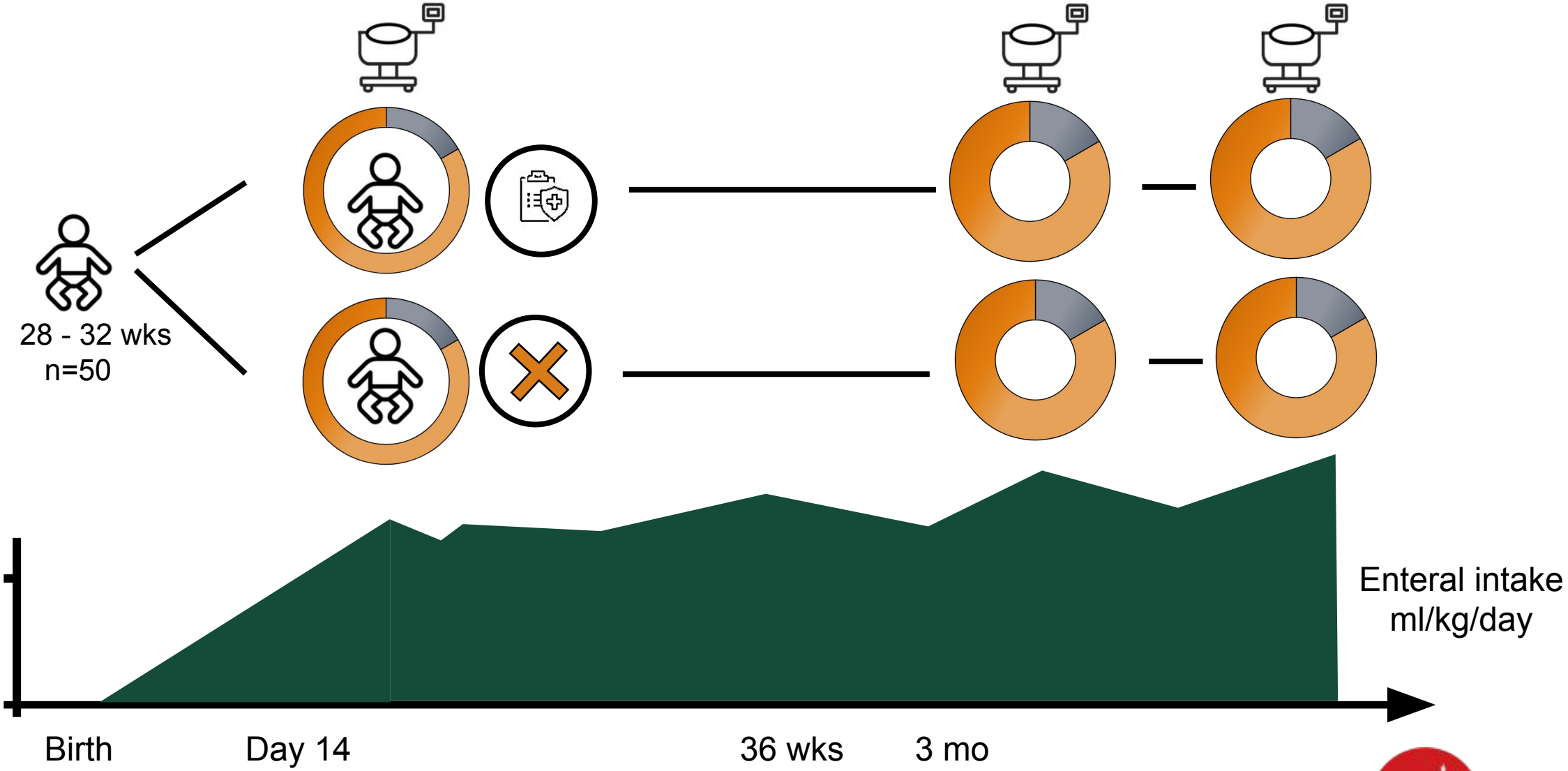




Learning objectives

Identify	Interpret	Recognize	Compare
key macronutrients essential for optimal growth and development in preterm infants.	growth charts and Z-scores to assess postnatal growth and nutritional adequacy.	common barriers to achieving optimal growth in the NICU	strategies for providing balanced nutrition

BFA: HCPs received body composition data of preterm infants fed human milk or formula around postnatal day 14

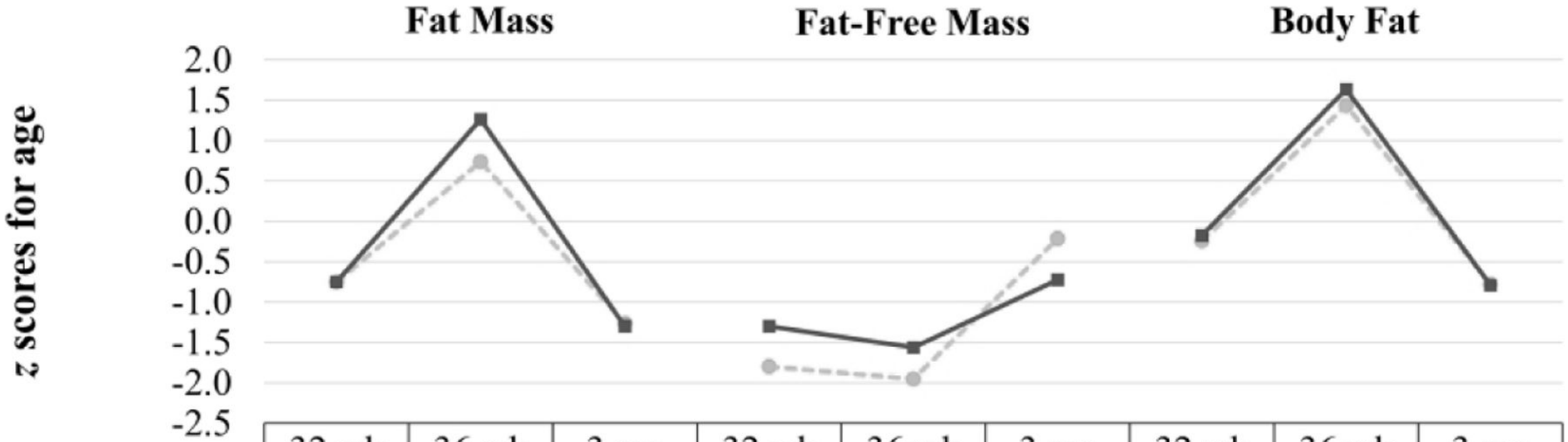


Salas AA, et al. Pediatr Res 2020

UAB MEDICINE NEONATOLOGY

Children's of Alabama

Providing infant body composition data to HCPs did not influence nutritional practices or growth



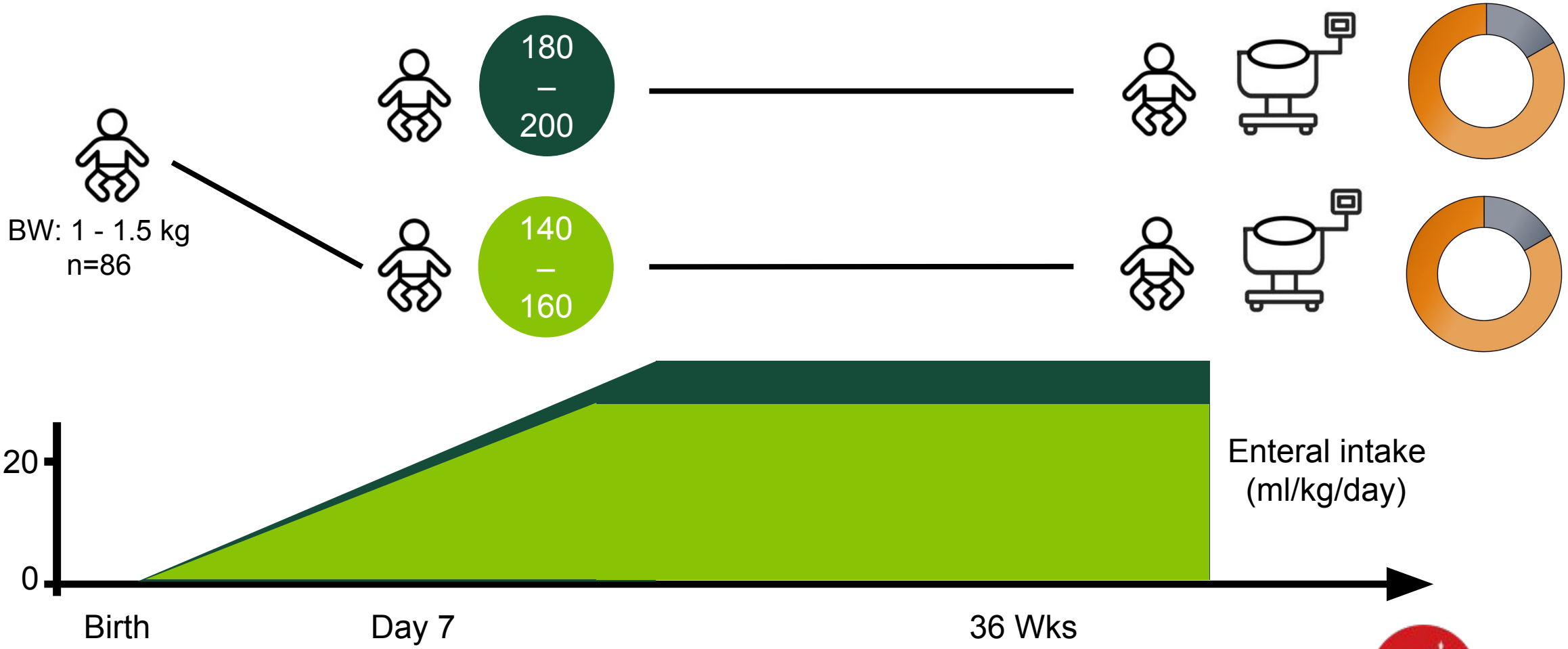
	Fat Mass			Fat-Free Mass			Body Fat		
	32 wk	36 wk	3 mo	32 wk	36 wk	3 mo	32 wk	36 wk	3 mo
Control	-0.8	0.7	-1.3	-1.8	-2.0	-0.2	-0.2	1.4	-0.8
Intervention	-0.8	1.3	-1.3	-1.3	-1.6	-0.7	-0.2	1.6	-0.8

UAB MEDICINE NEONATOLOGY

Salas AA, et al. Pediatr Res 2020

Children's of Alabama

HVF: Preterm infants fed human milk or formula were randomized to receive feeding volumes of up to 200 ml/kg/day

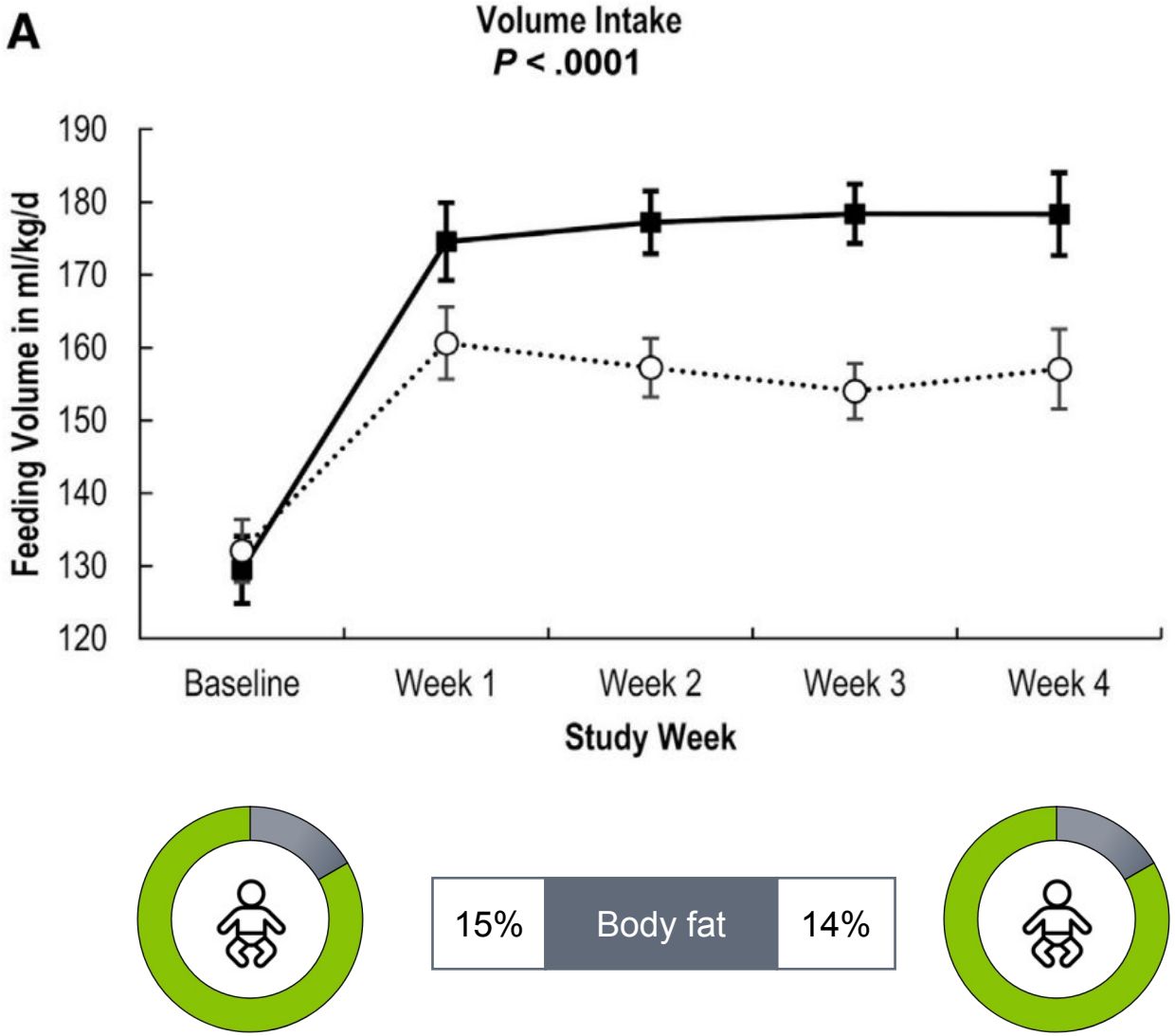


Salas AA, et al. J Pediatr 2021

UAB MEDICINE NEONATOLOGY

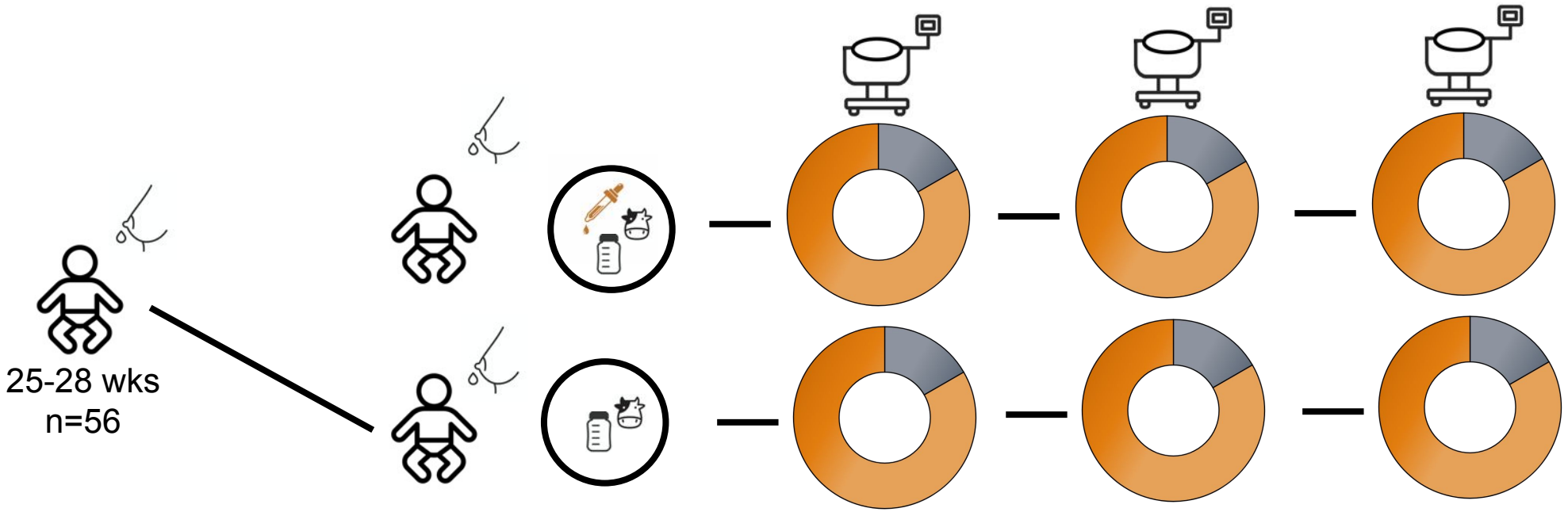
Children's of Alabama

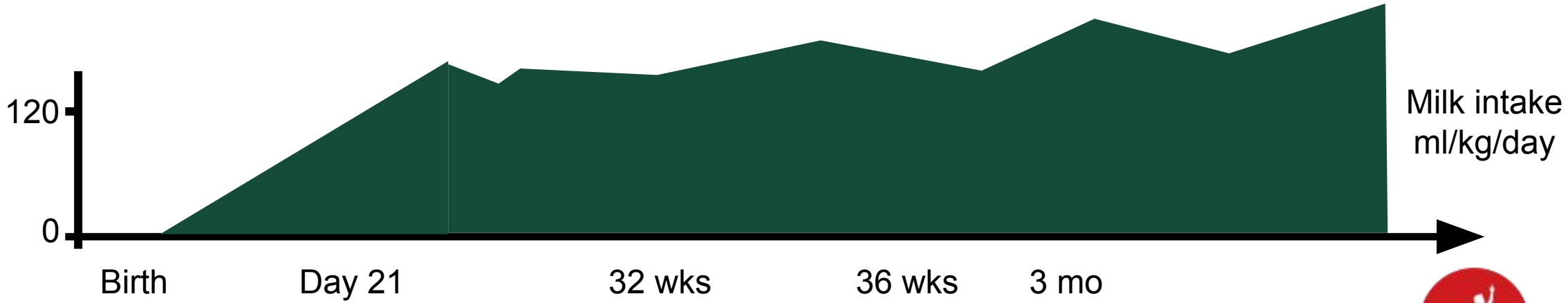
High-volume feeding increased body fat percentage by ≤2% at 36 weeks PMA (within a predefined range of equivalence)



Salas AA, et al. J Pediatr 2021

HPS: EPT infants were randomized to receive fortified milk plus hydrolyzed protein around postnatal day 21



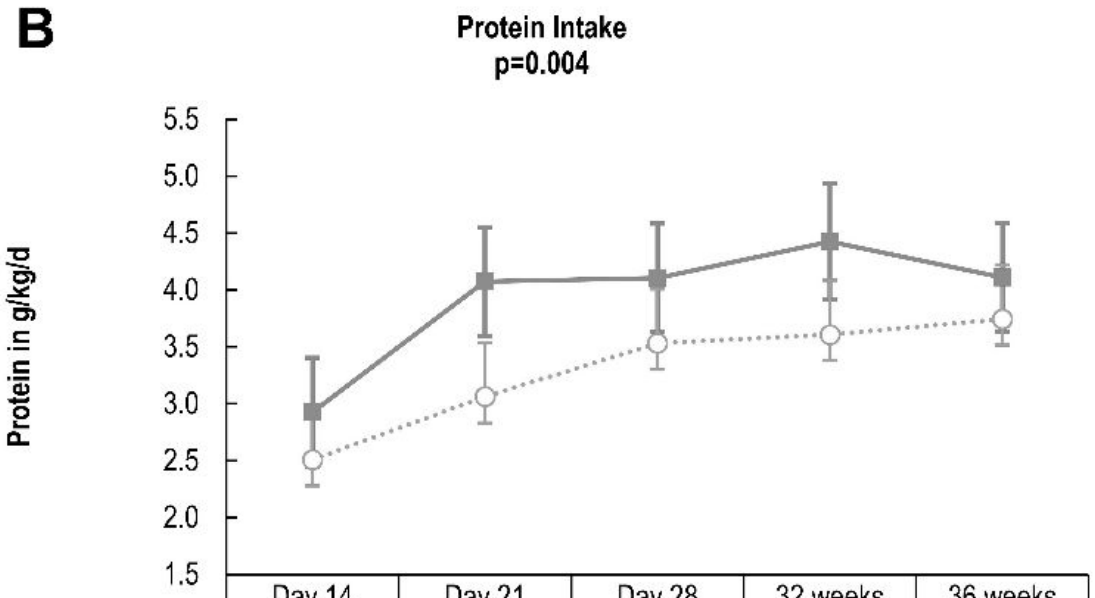


Salas AA, et al. Pediatr Res 2022

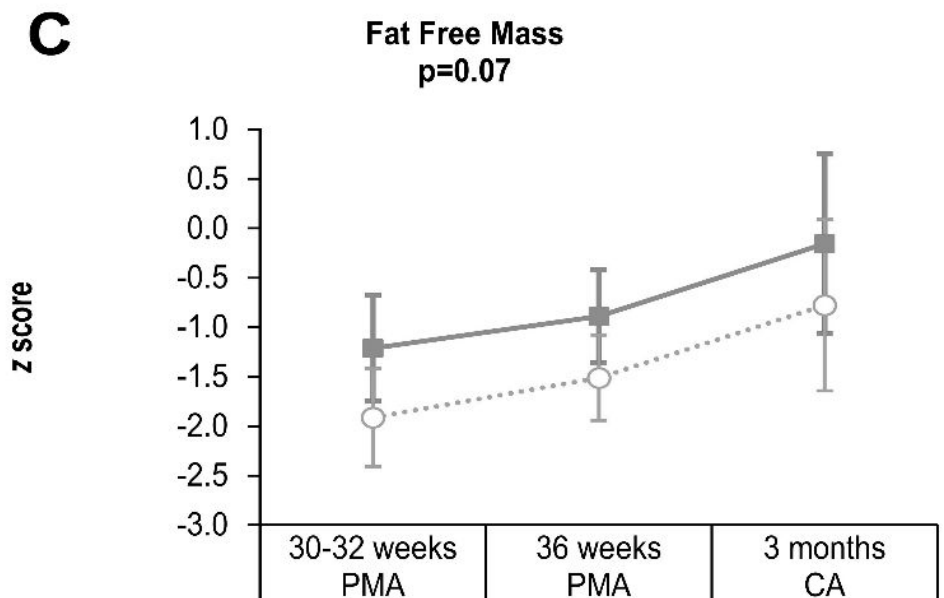
UAB MEDICINE NEONATOLOGY

Children's of Alabama

Increased enteral intake of protein improved FFM accretion in infants receiving protein-enriched, fortified human milk.



	Day 14	Day 21	Day 28	32 weeks	36 weeks
High	2.9	4.1	4.1	4.4	4.1
Standard	2.5	3.1	3.5	3.6	3.7



	30-32 weeks PMA	36 weeks PMA	3 months CA
High	-1.2	-0.9	-0.2
Standard	-1.9	-1.5	-0.8

UAB MEDICINE NEONATOLOGY

Salas AA, et al. Pediatr Res 2022

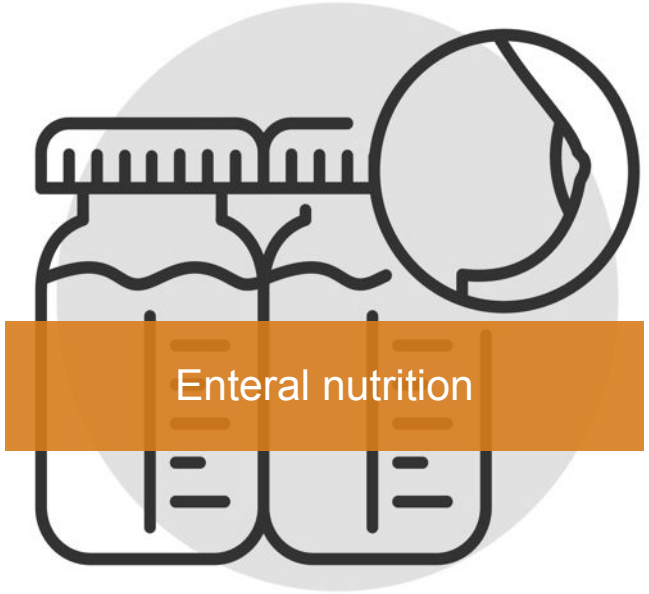
Children's of Alabama

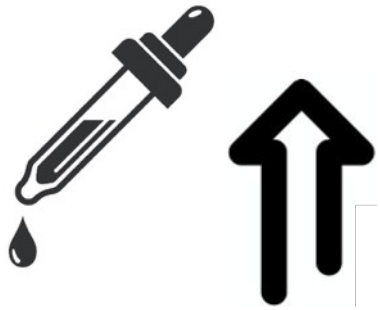
Protein-enriched, fortified human milk does not appear to affect growth or neurodevelopment at 2 years of age, LTFU: 40%

Characteristics	Intervention group	Control group
Moderate to severe NDI (%)	44	40
Bayley Cognitive Composite (median, IQR)	80 (70 - 85)	85 (80 - 85)
Bayley Language Composite (median, IQR)	79 (70 - 86)	77 (72 - 92)
Bayley Motor Composite (median, IQR)	86 (82 - 94)	85 (79 - 94)
Weight in kg at 18 - 26 months (median, IQR)	9.9 (8.9 - 11.4)	10.6 (9.9 - 11.8)
Length in cm at 18 - 26 months (median, IQR)	81 (75 - 84)	82 (80 - 85)
BMI (median, IQR)	14.9 (14.5 - 16.2)	15.9 (15.3 - 16.9)

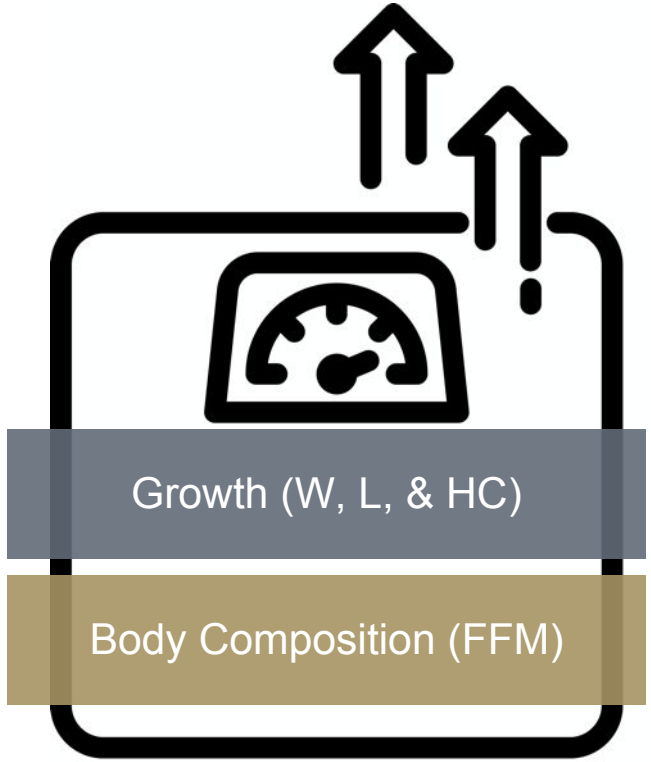
Jeffcoat S & Salas AA. unpublished data

Providing fortified human milk shortly after birth may support better growth and increase FFM accretion in EPT infants



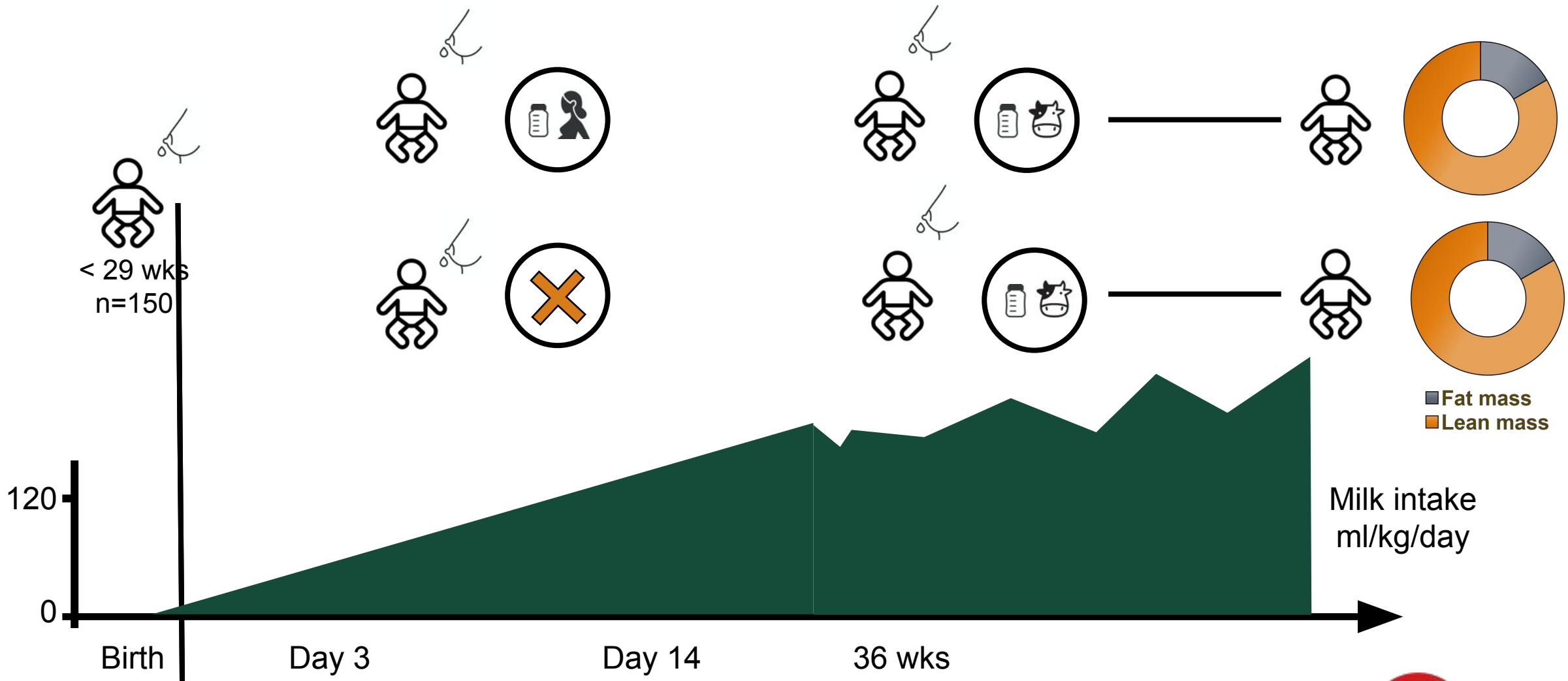


P/E ratio



Salas AA, et al. Pediatrics 2023

IMPACT: Human milk-fed infants received a human-derived HMF around day 3 and a bovine-derived HMF around day 14

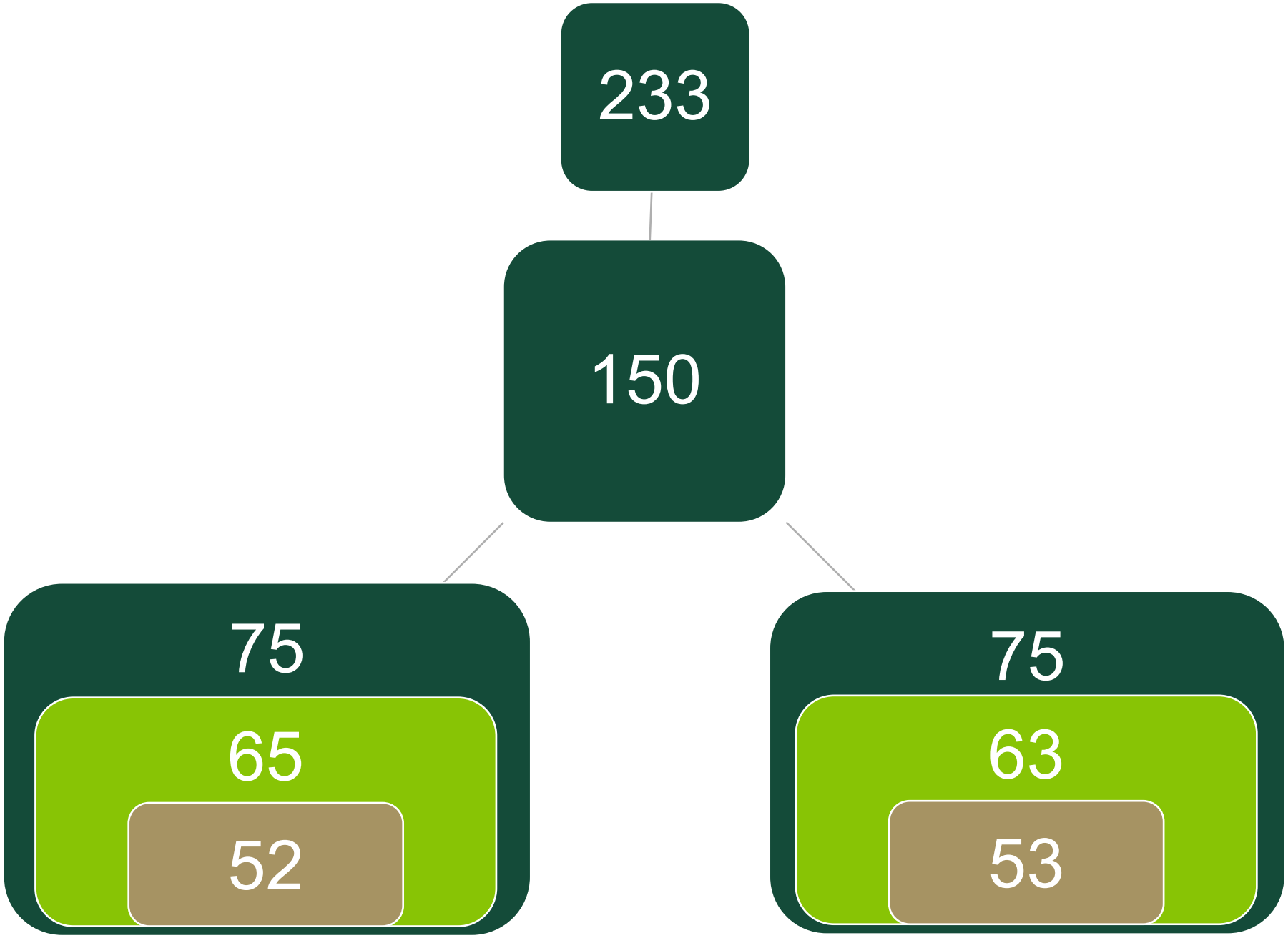


Salas AA, et al. Pediatrics 2023

UAB MEDICINE NEONATOLOGY

Children's of Alabama

CONSORT Diagram



UAB MEDICINE
NEONATOLOGY

IMPACT: By chance, there was a slight overrepresentation of SGA and female infants in the intervention group

Characteristics	Intervention group (n=75)	Control group (n=75)
Birthweight in grams	770 ± 254	820 ± 245
Gestational age in weeks	26 (24-27)	26 (24-27)
SGA at birth, n (%)	**15 (20)**	**8 (11)**
Female sex, n (%)	**43 (57)**	**29 (39)**
Black race, n (%)	45 (60)	38 (51)
Apgar score at 5 minutes	8 (7-9)	8 (7-9)
Exposure to antenatal steroids, n (%)	66 (88)	66 (88)

Salas AA, et al. Pediatrics 2023

IMPACT: Feeding practices during the first 2 weeks after birth did not differ between groups

Characteristics	Intervention group (n=75)	Control group (n=75)
Postnatal age at initiation of enteral feeding in days	2 (2-3)	2 (2-3)
Postnatal age at full enteral feeding (120 ml/kg/d) in days	8 (7-12)	8 (7-11)
Postnatal age at initiation of bovine-based fortifier in days	15 (14-20)	15 (12-18)
Maternal milk intake on postnatal day 7 in ml/kg/day	91 ± 55	96 ± 54
Maternal milk intake on postnatal day 14 in ml/kg/day	127 ± 58	135 ± 60

Salas AA, et al. Pediatrics 2023

IMPACT: There were no significant differences in safety outcomes between groups

Characteristics	Early group (n=75)	Late group (n=75)
NEC stage 2 or greater, n (%)	1 (1)	3 (4)
SIP, n (%)	5 (7)	4 (5)
Death, n (%)	6 (8)	5 (7)
NEC, SIP or death, n (%)	9 (12)	10 (13)

Salas AA, et al. Pediatrics 2023

IMPACT: Early HMF increases length gain velocity and prevents declines in HC z scores in critically ill EPT infants

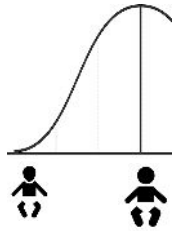
	Characteristics	Early group	Late group
FFM	**Z score at 36 weeks PMA**	-1.7	-1.6
Weight	**Z score decline from birth to postnatal day 14**	**-0.8 ± 0.6**	**-1.1 ± 0.6**
	Z score decline from birth to 36 weeks	-1.0 ± 0.7	-1.2 ± 0.8
	Weight gain velocity in g/kg/day	14.7 ± 2.5	13.9 ± 2.5
Length	**Gain velocity in cm/week from birth to 36 weeks**	**0.9 ± 0.2**	**0.8 ± 0.3**
	Z score decline from birth to 36 weeks	-1.5 ± 1.0	-1.9 ± 1.3
Head circumference	Gain velocity in cm/week from birth to 36 weeks	0.7 ± 0.1	0.7 ± 0.2
	Z score decline from birth to 36 weeks	**-0.9 ± 0.8**	**-1.3 ± 1.1**

UAB MEDICINE NEONATOLOGY

Salas AA, et al. Pediatrics 2023

Children's of Alabama

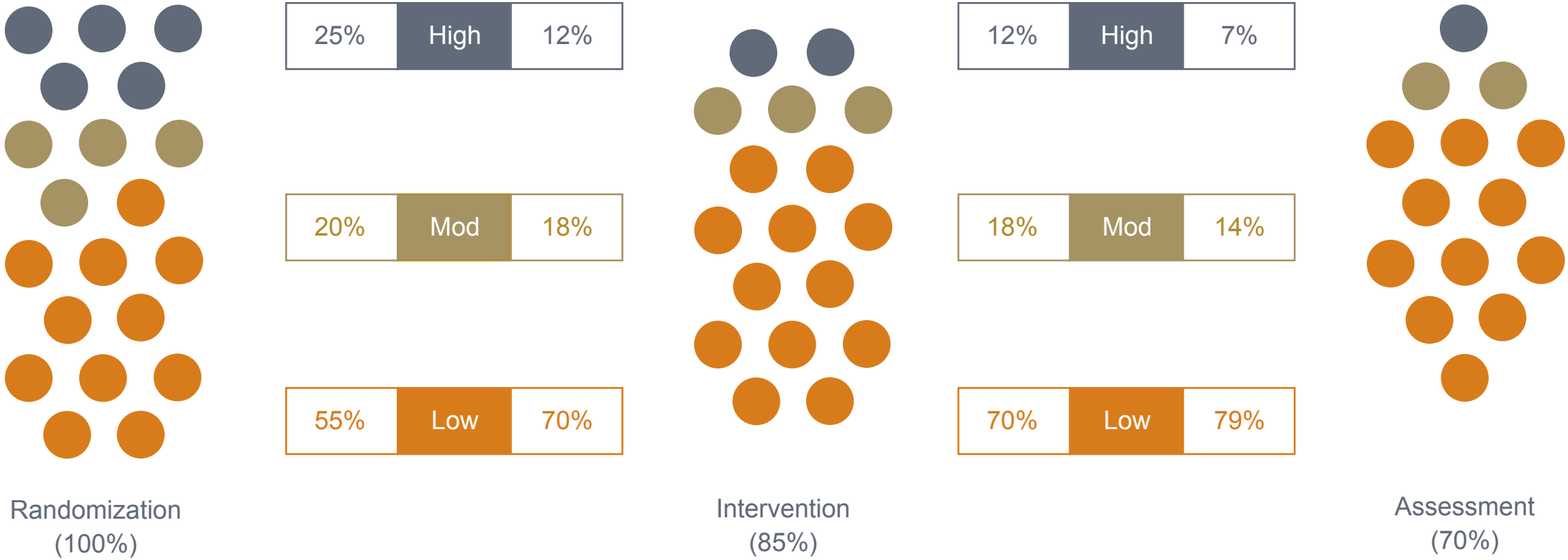
After excluding SGA infants from the analysis, several differences between groups were statistically significant



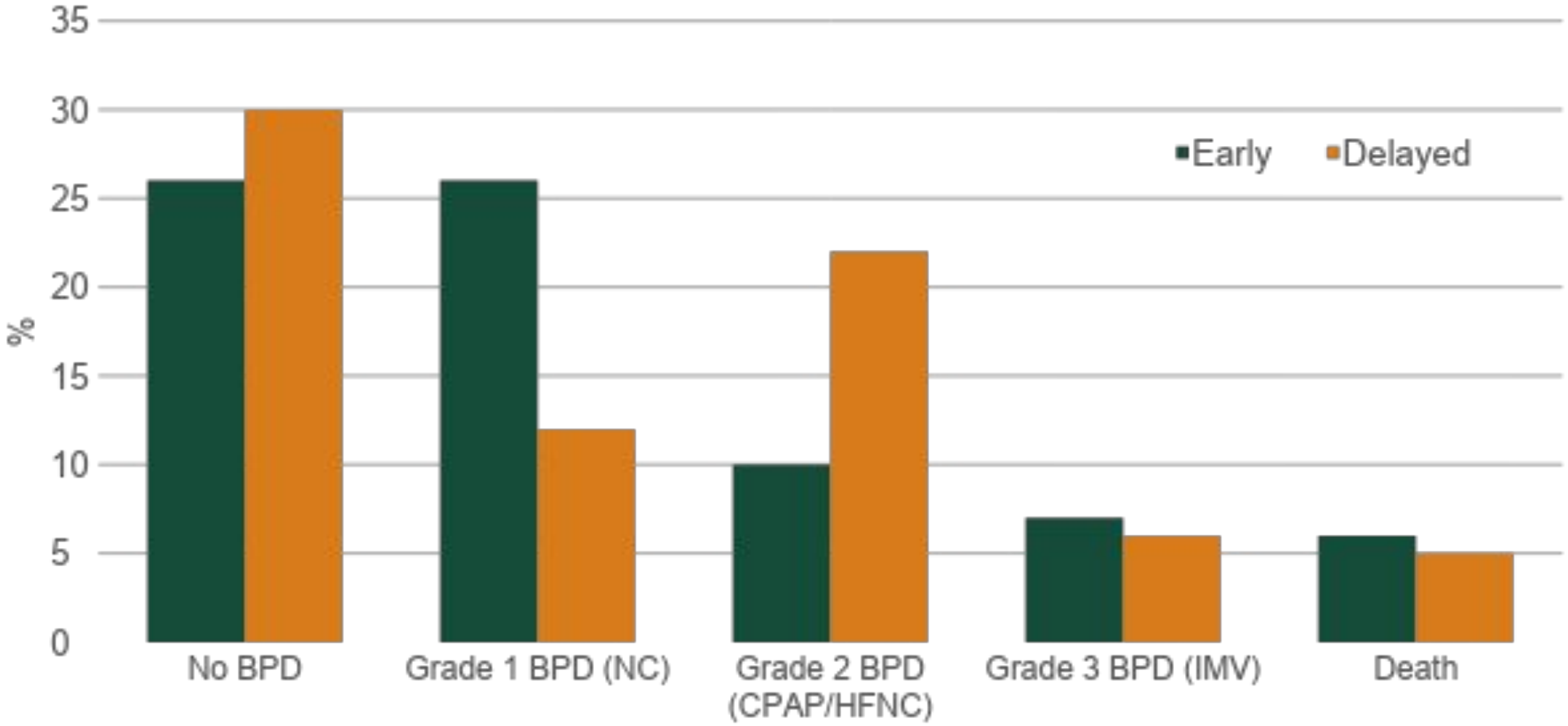
Outcome	Intervention (n=52)	Control (n=60)	p
FFM-for age z score at 36 weeks PMA	-1.2 ± 1.4	-1.4 ± 1.4	0.68
Declines in weight-for-age z score from birth to 36 weeks PMA	**-1.0 ± 0.7**	**-1.3 ± 0.8**	**0.05**
Declines in weight-for-age z score from birth to 36 weeks PMA > 1.2 (%)	19 (37)	31 (52)	0.11
Weight gain velocity in g/kg/day from birth to 36 weeks PMA, mean ± SD	14.4 ± 2.1	13.6 ± 2.3	0.06
Length gain velocity in cm/week from birth to 36 weeks PMA	**0.9 ± 0.2**	**0.8 ± 0.3**	**0.01**
Declines in length-for-age z score from birth to 36 weeks PMA	**-1.5 ± 1.0**	**-2.0 ± 1.3**	**0.04**
Head circumference gain velocity in cm/week from birth to 36 weeks PMA	**0.74 ± 0.1**	**0.68 ± 0.2**	**0.05**
Declines in head circumference-for-age z score from birth to 36 weeks PMA	**-0.9 ± 0.8**	**-1.4 ± 1.1**	**<0.01**

Critical illness affects our ability to assess body composition in preterm infants

Risk distribution at different stages of a clinical trial

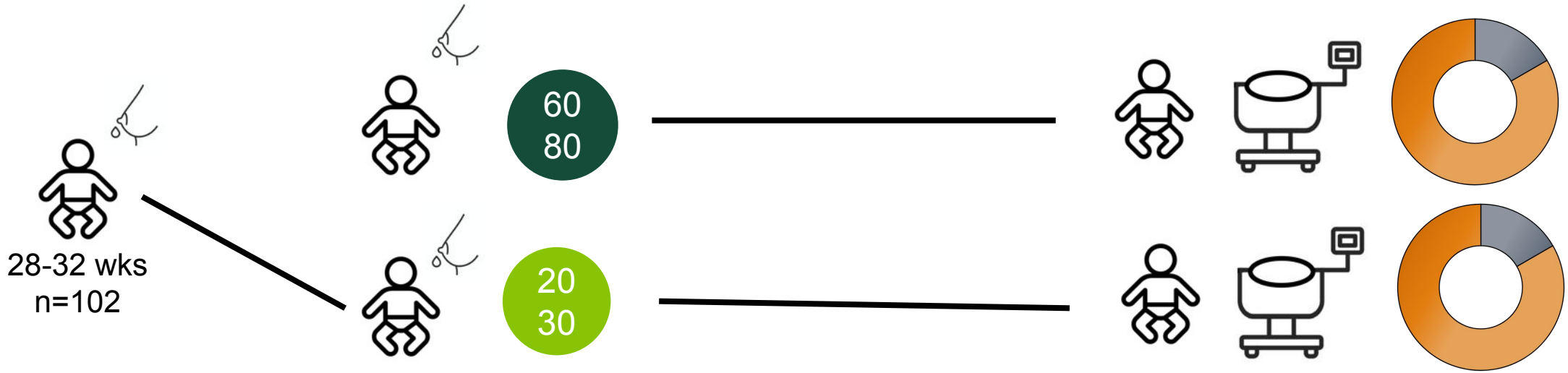


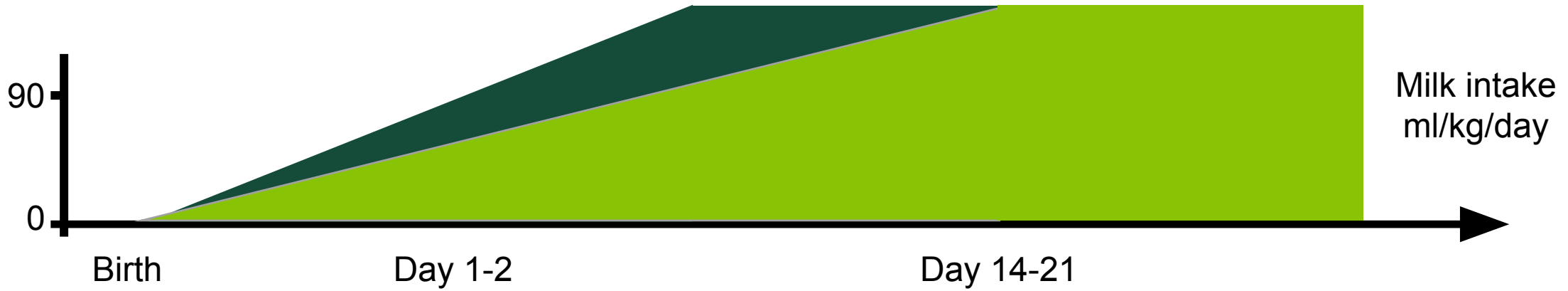
Early HMF may also reduce the severity of BPD in EPT infants



Tucker M & Salas AA. unpublished data

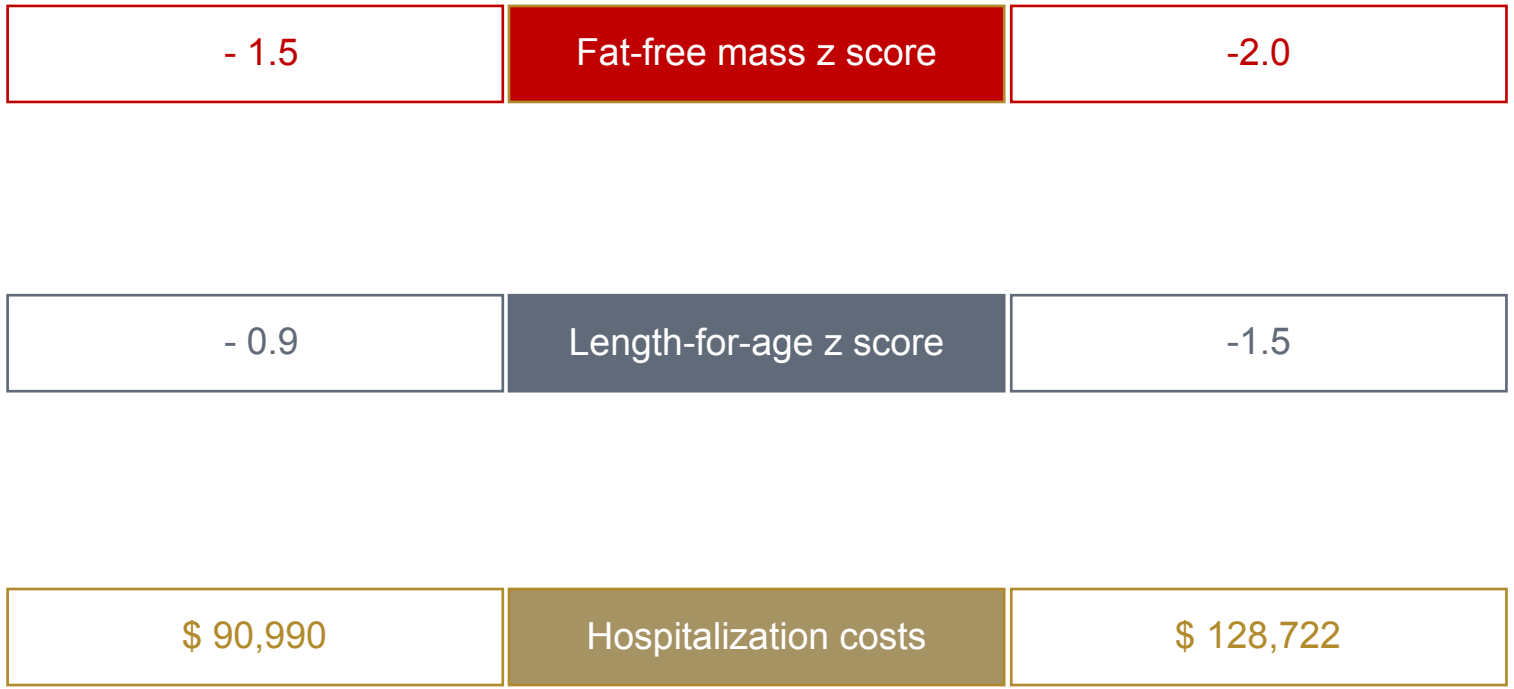
E^{3}NACT: Preterm infants were randomized to receive 60-80 ml/kg/day of MOM or DM within the first 36 hours after birth





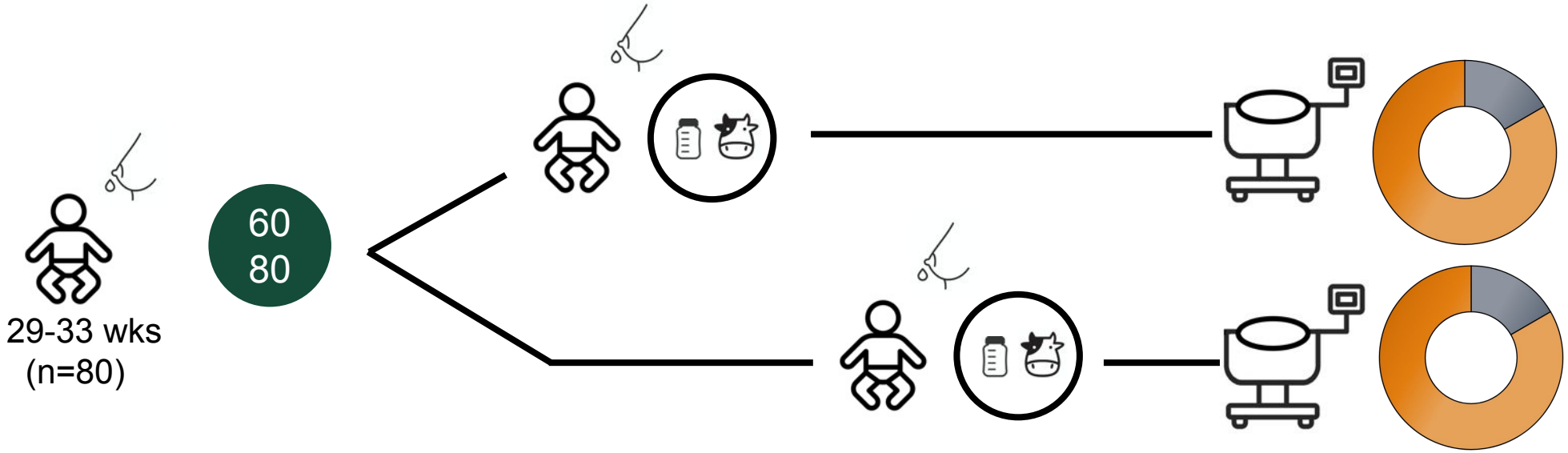
Razzaghy J. Arch Dis Child Fetal Neonatal Ed. 2024

Early and exclusive enteral nutrition may improve fat-free mass accretion, increase length, and reduce hospitalization costs



Razzaghy J. Arch Dis Child Fetal Neonatal Ed. 2024

E^{3}NACT+: VPT infants who reached full enteral feeding volumes shortly after birth began receiving HMF around postnatal day 6



Salas AA, et al. AJCN 2025

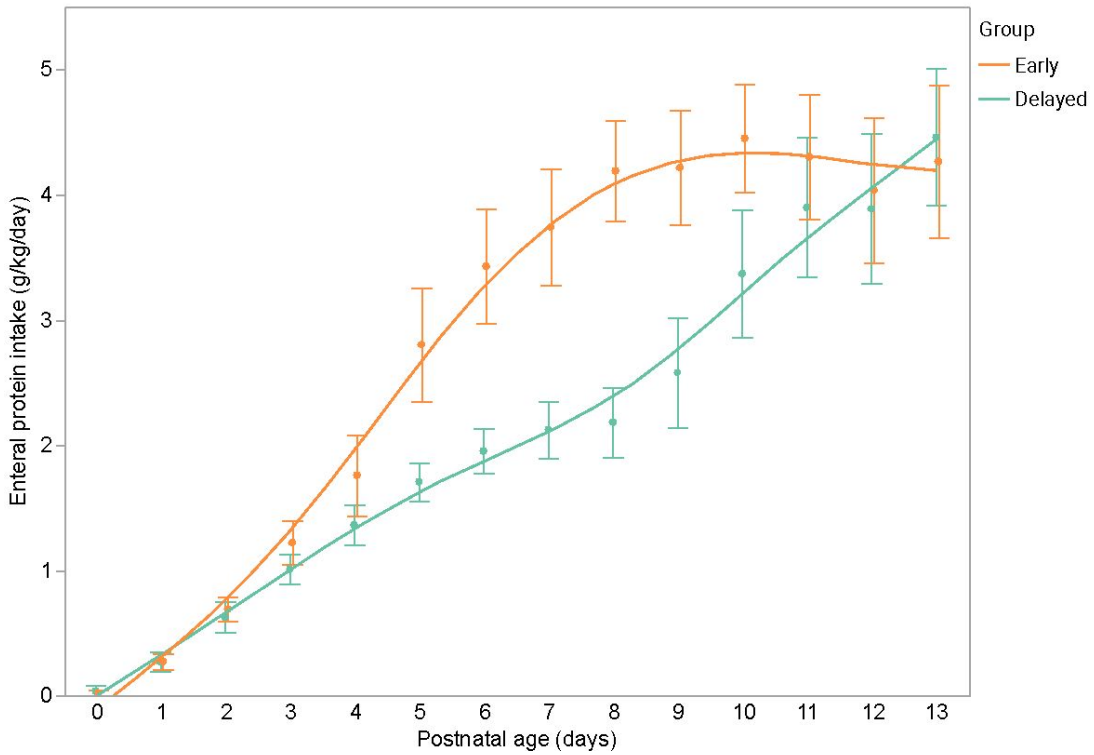
UAB MEDICINE NEONATOLOGY

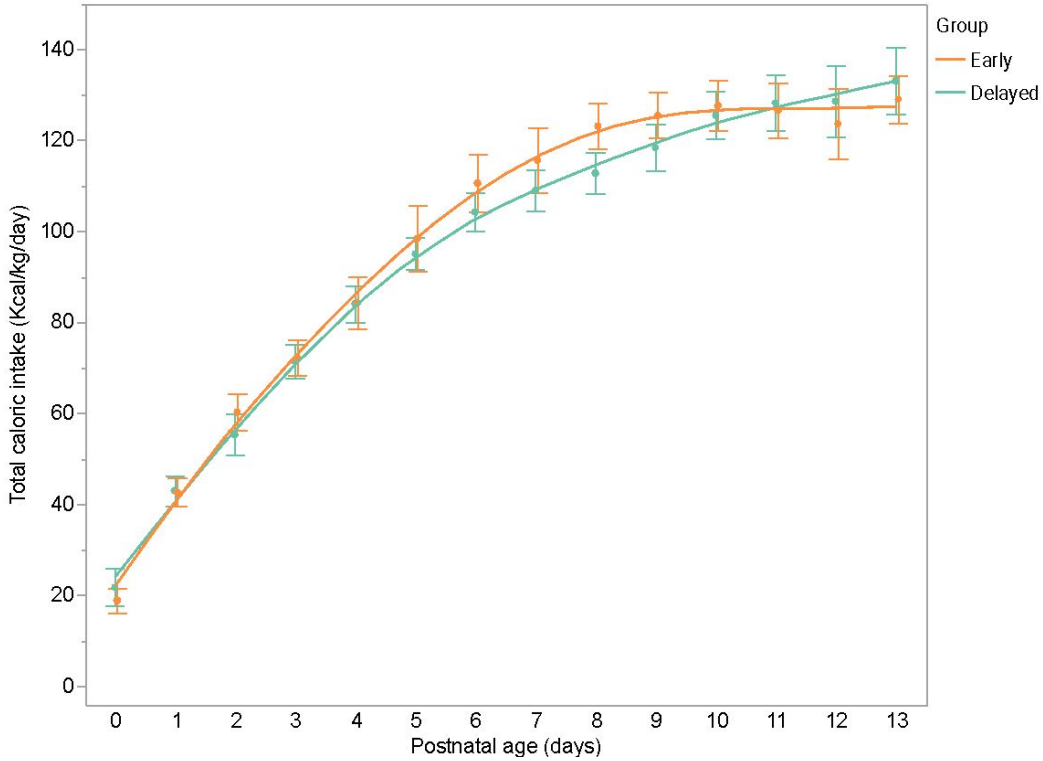
Children's of Alabama

ENACT+: Baseline characteristics did not differ between groups

BASELINE CHARACTERISTICS	Early Fortification Group (n=40)	Delayed Fortification Group (n=40)
Birth weight in grams, mean ± SD	1524 ± 210	1452 ± 251
Gestational age in weeks, median (IQR)	31 (30-32)	31 (30-32)
Male, n(%)	20 (50)	16 (40)
Black race, n(%)	14 (35)	14 (35)
Exposure to antenatal steroids, n(%)	35 (88)	38 (95)

ENACT+: Although the early fortification group had a higher enteral protein intake, energy intake remained similar between the groups.



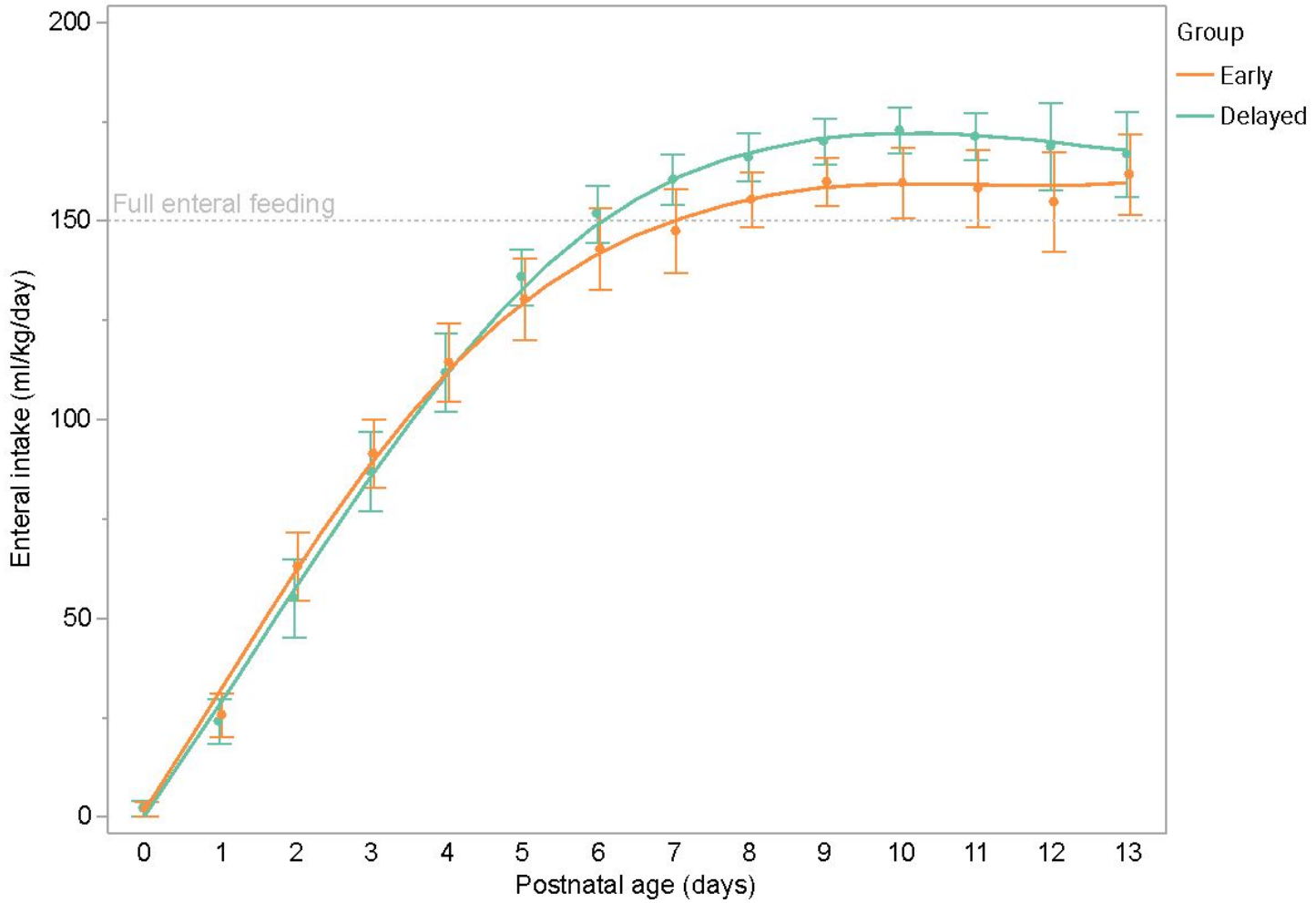


Salas AA, et al. AJCN 2025

UAB MEDICINE
NEONATOLOGY

Children's of Alabama

ENACT+: Enteral intake by postnatal age was transiently higher in the delayed fortification group



Salas AA, et al. AJCN 2025

E^{3}NACT+: Except for timing of fortification, feeding practices during the first 2 weeks did not differ between groups

Characteristics	Intervention group	Control group
Postnatal age at start of enteral feeding in hours, mean ± SD	24 ± 12	24 ± 13
Postnatal age at enrollment in hours, median (IQR)	25 (19-32)	25 (18-37)
Enteral feeding started before enrollment, n (%)	18 (45)	16 (40)
Postnatal age at exclusive enteral feeding in days, median (IQR)	5 (4-6)	5 (4-7)
Postnatal age at enteral feeding ≥150 ml/kg/day in days, median (IQR)	8 (7-10)	8 (7-9)
Percent maternal milk intake in the first 14 days, median (IQR)	54 (29-81)	48 (14-77)
Postnatal age at the time of human milk fortification in days, median (IQR)	7 (6-8)	12 (11-14)

Salas AA, et al. AJCN 2025

E^{3}NACT+: There were no differences in fat-free mass (FFM) z-scores between the groups around postnatal day 21

Outcome	Intervention group	Control group
FFM-for-age z score at postnatal day 21	-1.7 ± 0.9	-1.8 ± 0.9
FFM at postnatal day 21, g	**1707 (1581-1848)**	**1581 (1499-1714)**
Weight at postnatal day 21, g	**1905 (1730-2080)**	**1750 (1632-1948)**
Length at postnatal day 21, cm	**42 ± 2**	**41 ± 2**
Weight z-score at 36 weeks PMA/discharge	-1.07 ± 0.72	-1.22 ± 0.55
Length at 36 weeks PMA/discharge, cm	**44 ± 2**	**43 ± 2**
Length z-score at 36 weeks PMA/discharge	-1.0 ± 0.8	-1.3 ± 0.8

Salas AA, et al. AJCN 2025

Measuring infant body composition will improve our understanding of how nutrition affects growth and neurodevelopment

Nutritional strategies can optimize body composition.

A healthy body composition could prevent adverse metabolic and cognitive outcomes.

Questions?

www.neonatalnutritionresearch.com

@ArielSalasMD