USE OF MATERNAL VS DONOR MILK IN VLBW INFANTS

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FACULTY DISCLOSURES

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Speakers Bureau	Mead Johnson Nutrition
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THE UNIQUE NUTRITIONAL NEEDS OF PRETERM INFANTS

Despite clear advantages of human milk for preterm infants, several challenges remain:[1],[2]

- Rapid growth rate of preterm infants (twice the rate of term infants) and high metabolic demands
- Suboptimal gestational nutrient accretion and deficient nutrient stores
- Weight-appropriate human milk feeding volumes insufficient to meet nutritional needs due to fluid restrictions
- Variability of human milk composition

[1]. Hay WW, Jr. *Pediatr Gastroenterol Hepatol Nutr*. 2018;21(4):234-247. [2]. Kleinman RE, Greer FR, eds. *Pediatric Nutrition, 8th ed.* American Academy of Pediatrics; 2020.

ENTERAL NUTRITION RECOMMENDATIONS FOR PRETERM INFANTS

Nutrient	2022 ESPGHAN Guidelines[1],[a] per kg/d
Fluid, mL	150–180 (135–200)
Energy, kcal	115–140 (–160)
Protein, g	3.5–4.0 (–4.5)
Carbohydrate, g	11–15 (–17)
Fat, g	4.8–8.1
Sodium, mg	69–115 (–184)
Potassium, mg	90–180
Chloride, mg	106–177 (–284)
Calcium, mg	120–200
Phosphorus, mg	68–115
Iron, mg	2–3 (–6)
Zinc, mg	2–3

Parentheses indicate ranges or upper intakes that may be needed for certain neonates.

- Data are limited regarding optimal intake for many macro- and micronutrients
- Recommendations are based on expert consensus
- Fluid and nutrient requirements vary with gestational age and birth weight
- Prior to increasing energy or protein beyond recommended intake for growth, optimize other nutrients and rule out alternate causes for suboptimal growth

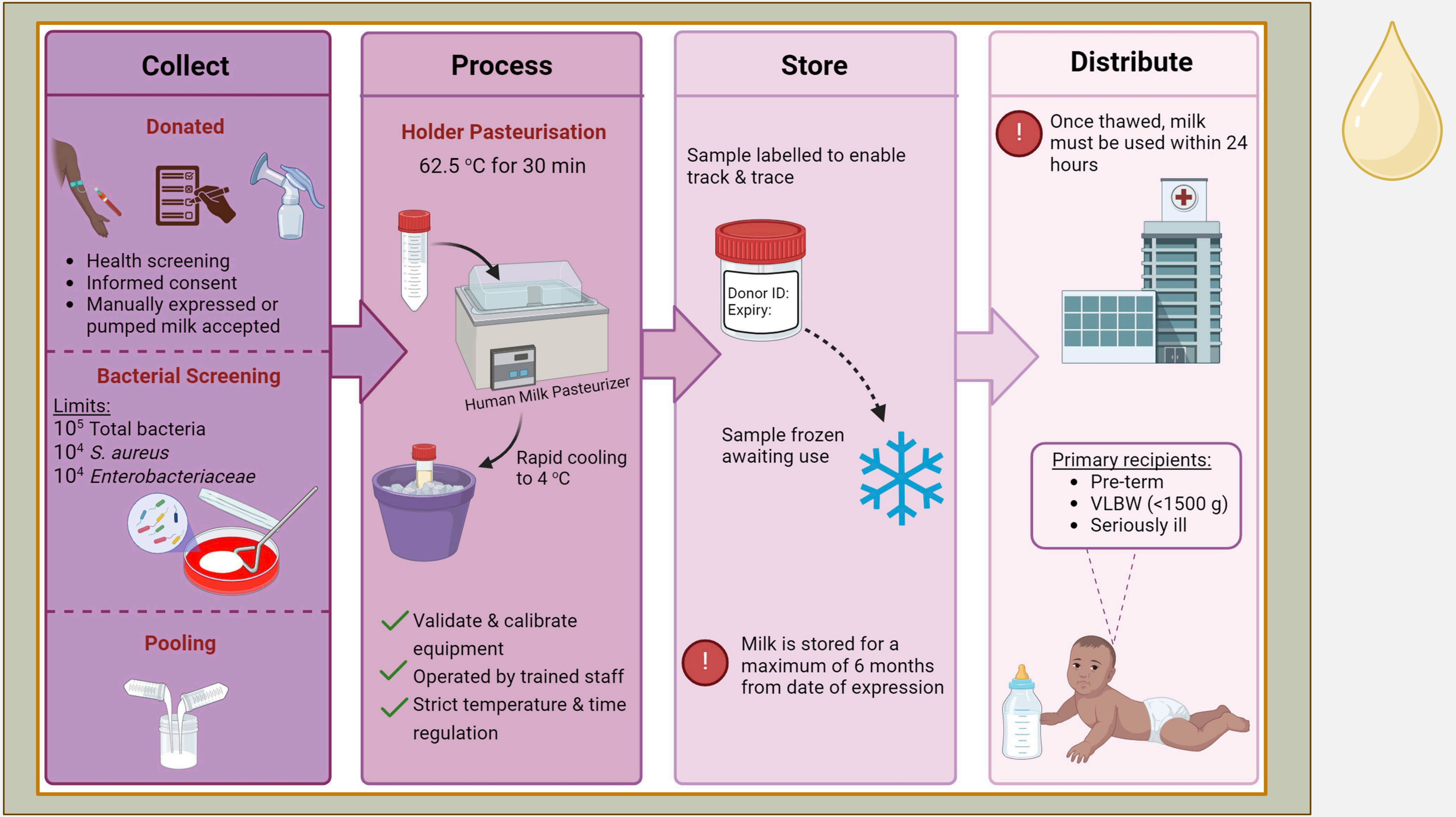
[1]. Embleton ND et al. *J Pediatr Gastroenterol Nutr*. 2023;76(2):248-268.

MOM

Preterm
Colostrum
Early Lactation
Tailored
Fresh

DHM

Term
“Excess” Milk
Later Lactation
Pooled
Pasteurized



Conboy-Stephenson et al. *Front. Nutr.* 2024;Nov.

HUMAN MILK PASTEURIZATION

Changes in bioactive components[1]–[4]

- Complete loss of certain **enzymes** (e.g. lipase), **lactoferrin**, and maternal **cell populations** (e.g. neutrophils, stem cells)
- Reduced activity level or concentration of other **enzymes**, **cytokines**, **growth factors**, **immunoglobulins**, and **hormones**

Changes in macronutrient composition[5]

- Reduced levels of **lipids** and **long-chain polyunsaturated fatty acids**

Changes in vitamin & micronutrient composition[1]

- Reduced **ascorbic acid** and **vitamin B6**

[1]. Peila C et al. *Nutrients*. 2016;8(8):477. [2]. Hård AL et al. *Acta Paediatr*. 2019;108(6):998-1007. [3]. Kleinman RE, Greer FR, eds. *Pediatric Nutrition, 8th ed*. American Academy of Pediatrics; 2020. [4]. Davis A et al. *Cur Dev Nutri*; 2025;Jun 21;9(8). [5]. Koletzko B et al, eds. In: Koletzko B et al, eds. *Nutritional Care of Preterm Infants. Scientific Basis and Practical Guidelines, 2nd ed*. Karger; 2021.

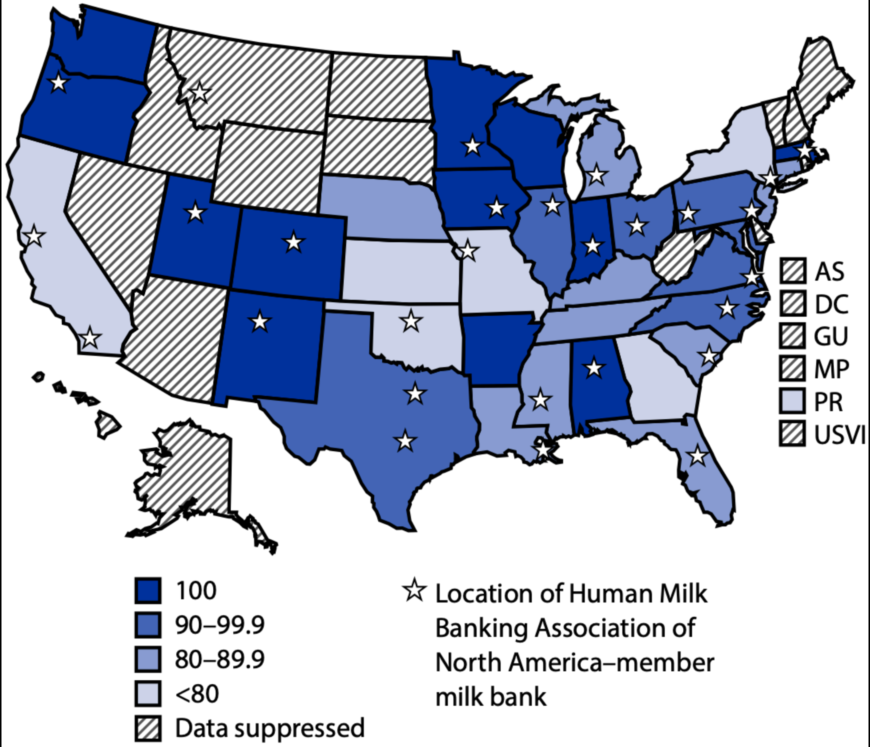
Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 71 / No. 33 August 19, 2022

Donor Human Milk Use in Advanced Neonatal Care Units — United States, 2020

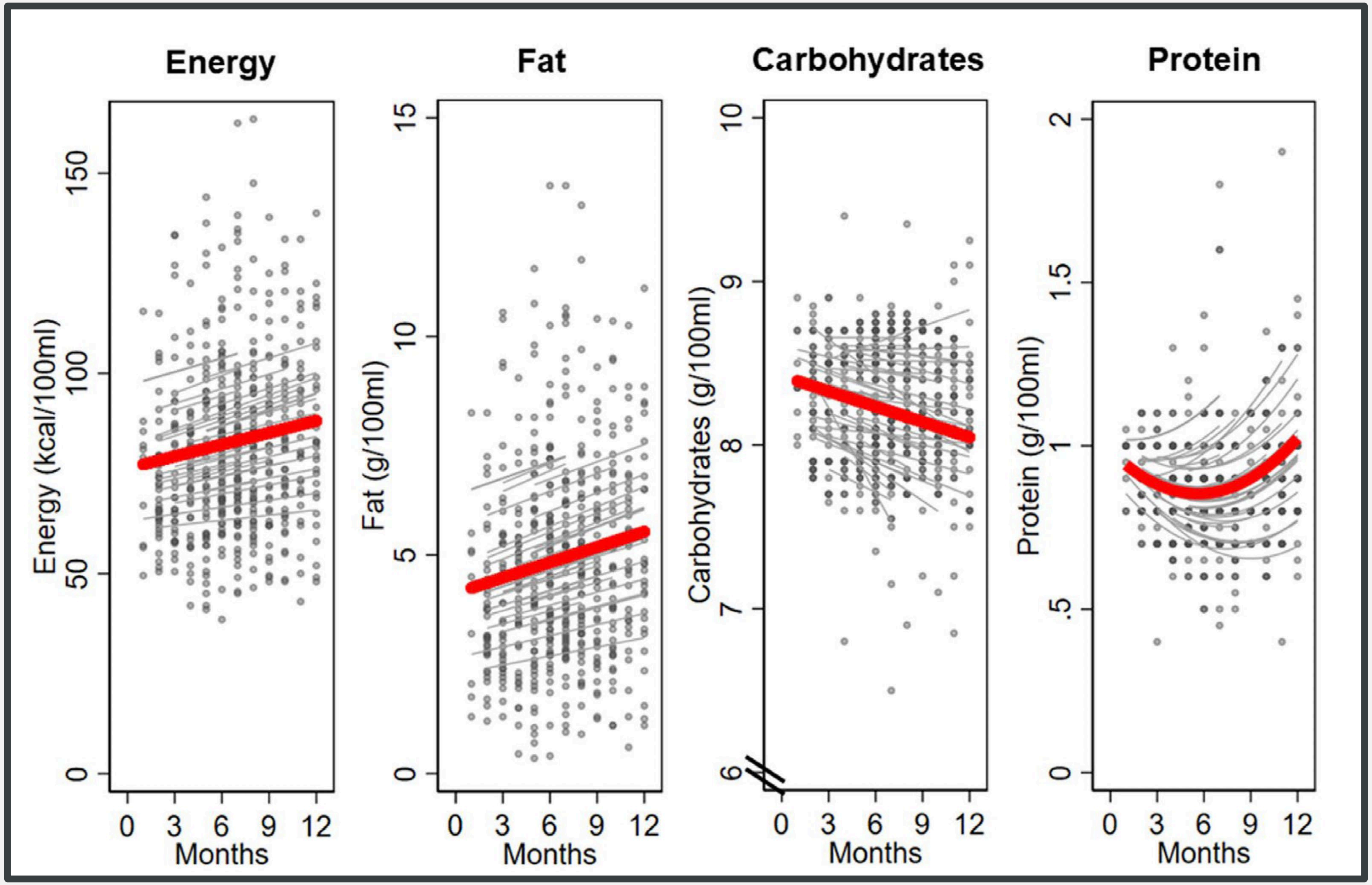
Ellen O. Boundy, ScD[1]; Erica H. Anstey, PhD[1]; Jennifer M. Nelson, MD[1]

TABLE 1. Donor milk use among infants in hospitals with advanced neonatal care units, by infant weight and unit level — Maternity Practices in Infant Nutrition and Care, United States, 2020*,†

Infant weight/ Neonatal care unit level	No. of hospitals	% of hospitals§,¶				
		Donor milk not available	% of infants receiving donor milk			
			0–19	20–49	50–79	≥80
<1,500 g						
Total	**616**	**13.0**	**5.0**	**10.1**	**17.2**	**54.7**
Level III	526	14.8	4.4	9.9	17.1	53.8
Level IV	90	2.2	8.9	11.1	17.8	60.0
≥1,500 g						
Total	**1,256**	**40.1**	**14.7**	**14.7**	**14.6**	**15.9**
Level II	640	65.3	7.0	7.3	8.0	12.3
Level III	526	15.8	23.4	21.7	20.2	19.0
Level IV	90	3.3	17.8	26.7	28.9	23.3



DONOR HUMAN MILK COMPOSITION



Holte K et al. *Acta Pediatr.* 2025;Oct;114(10):2675-2682.

DONOR HUMAN MILK COMPOSITION

Energy (kcal/dL)	Carbs (g/dL)	Protein (g/dL)	Fat (g/dL)

Perrin MT et al. *Adv Nutr.* 2020;July:960-970.

Nutrient composition of preterm mother's milk and factors that influence nutrient content

Amy Gates,[1] Terri Marin,[2] Gianluca De Leo,[1] Jennifer L Waller,[3] and Brian K Stansfield[4]

- Women who delivered ≤33 weeks' gestation (N = 38)
- Pooled 24-hour milk samples from days 7, 14, 21, and 28
- Assessed macro- and micronutrient composition

	Mean ± SD or N (%)	Range
Maternal age, y	27 ± 5.1	18–37
EGA, wk	28.2 ± 2.8	22.9–33.0
EGA <28 wk	16 (42)	
Infant birth weight, g	1098 ± 347.3	545–2130
Male infant sex	20 (53)	
Race		
Black	25 (66)	
White	13 (34)	

EGA, estimated gestational age; SD, standard deviation.

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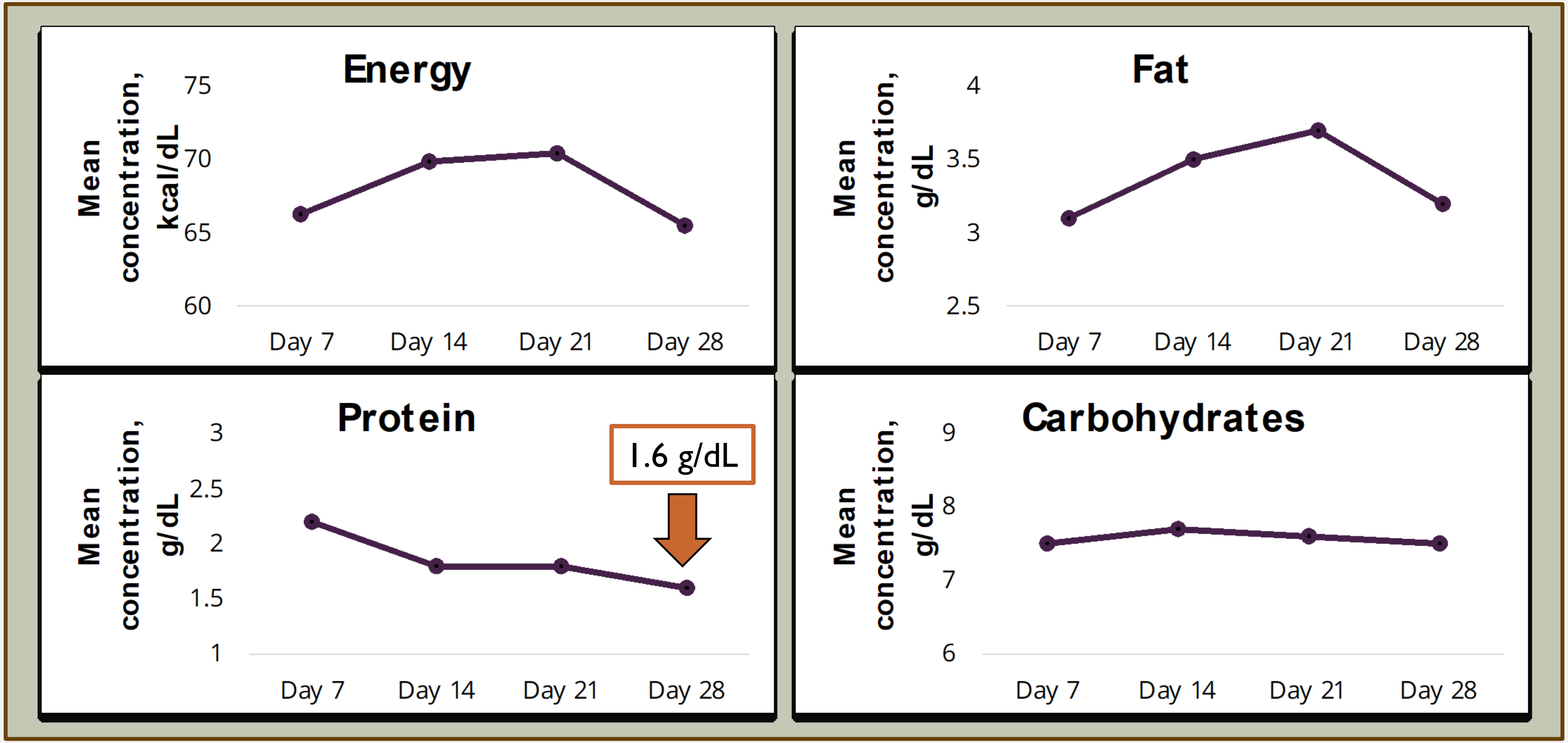

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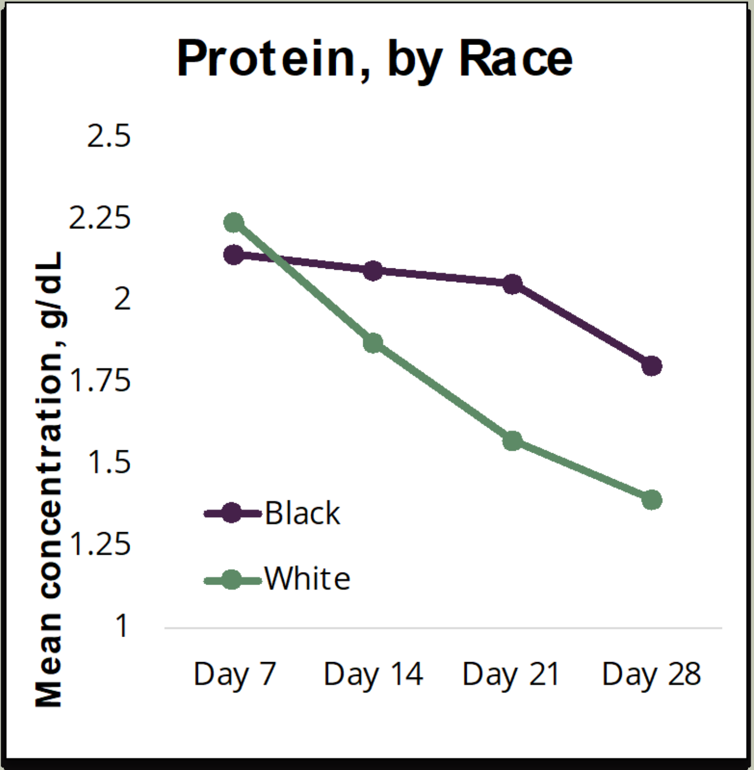

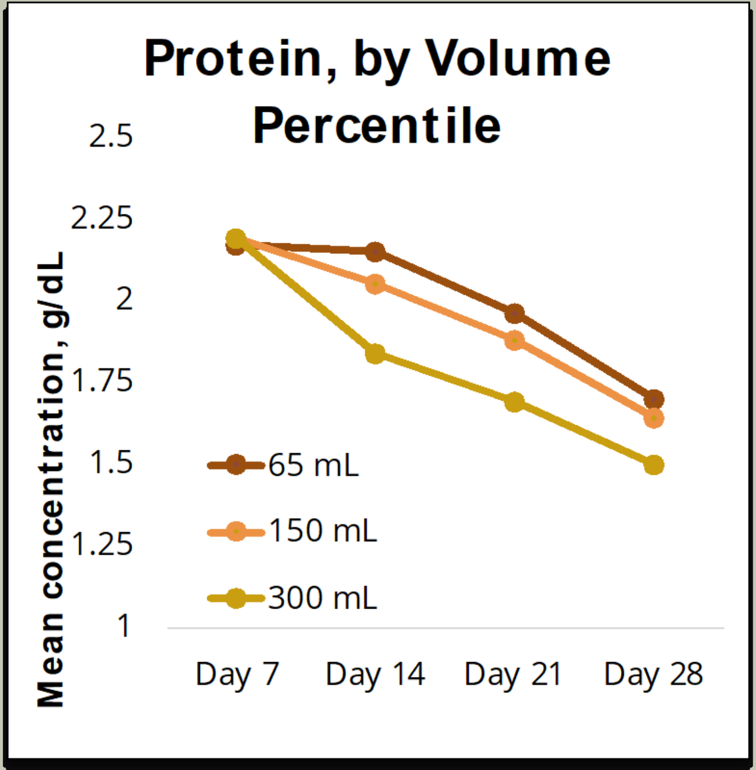

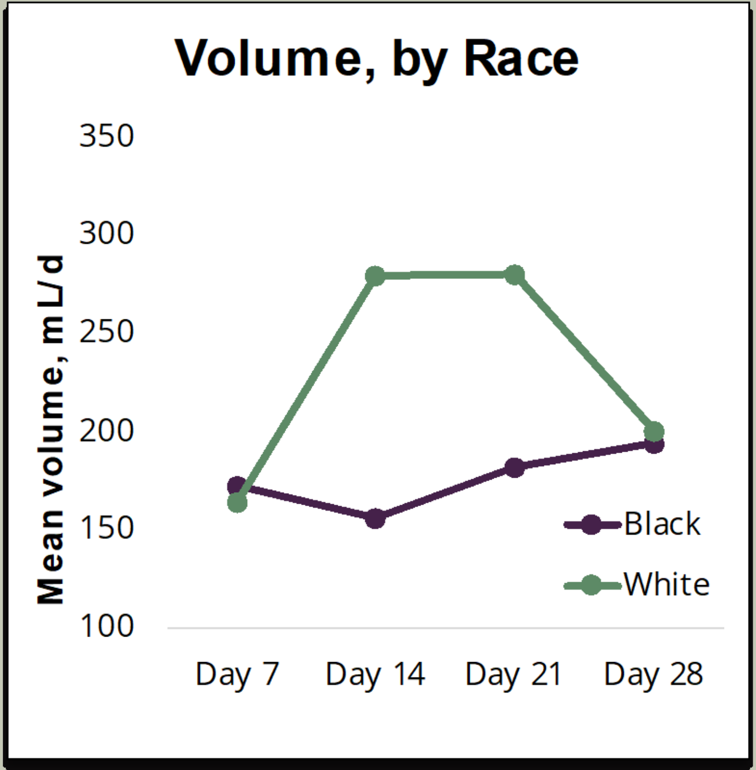

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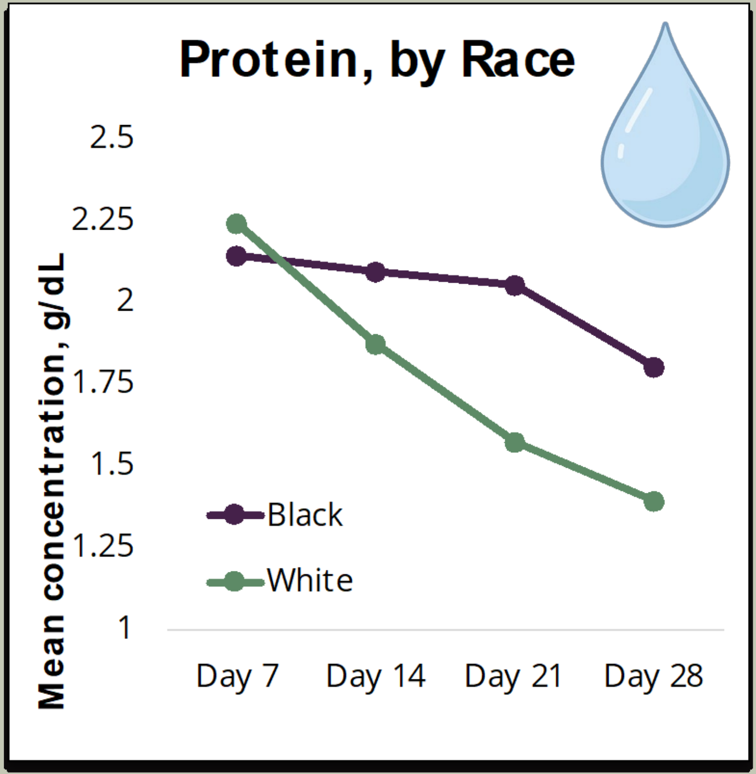


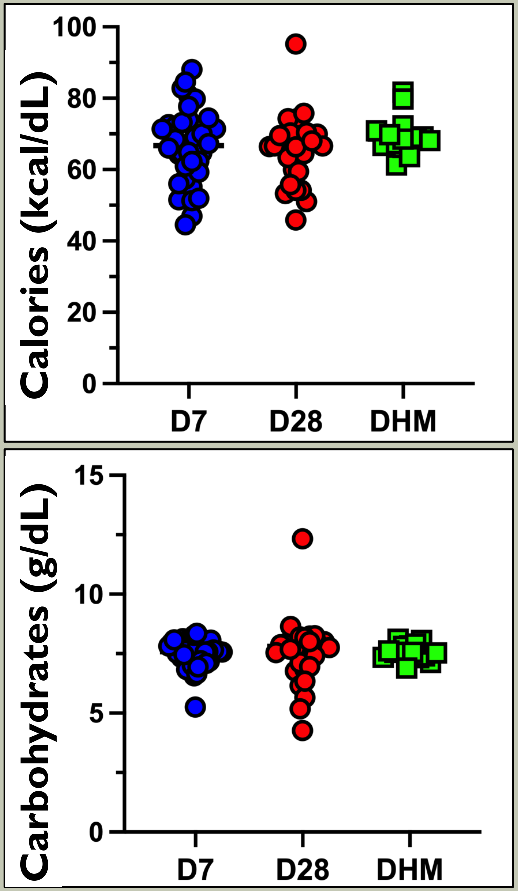
Donors

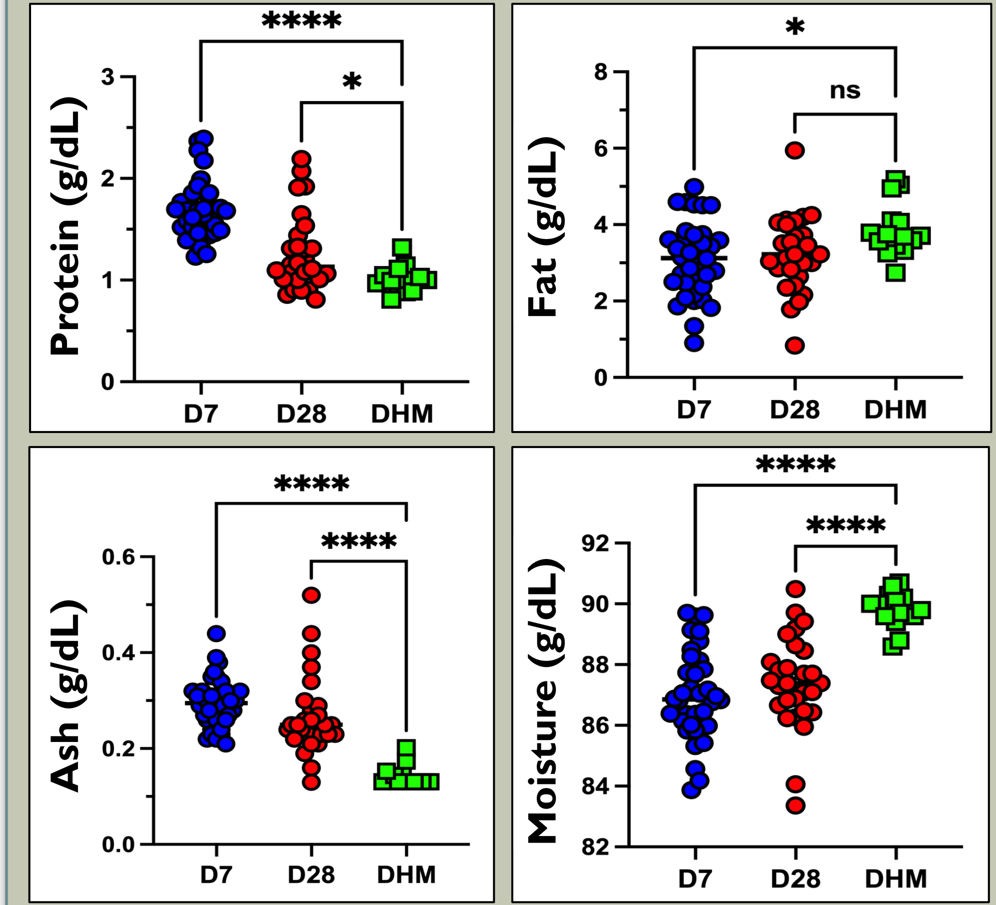
VLBW

Holte K et al. *Acta Pediatr.* 2025;Oct;114(10):2675-2682; Heinonin E et al. *JAMA Open* 2025; Jan2;8(1); Hooperton K et al. *AJCN.* 2024; Dec;120(6):1419-1431; CDC Births 2022

DONOR VS PRETERM MOM

No significant difference in **calorie** or **carbohydrate** content between preterm and donor milk





Higher protein and **ash** content with preterm milk

Lower moisture content with preterm milk

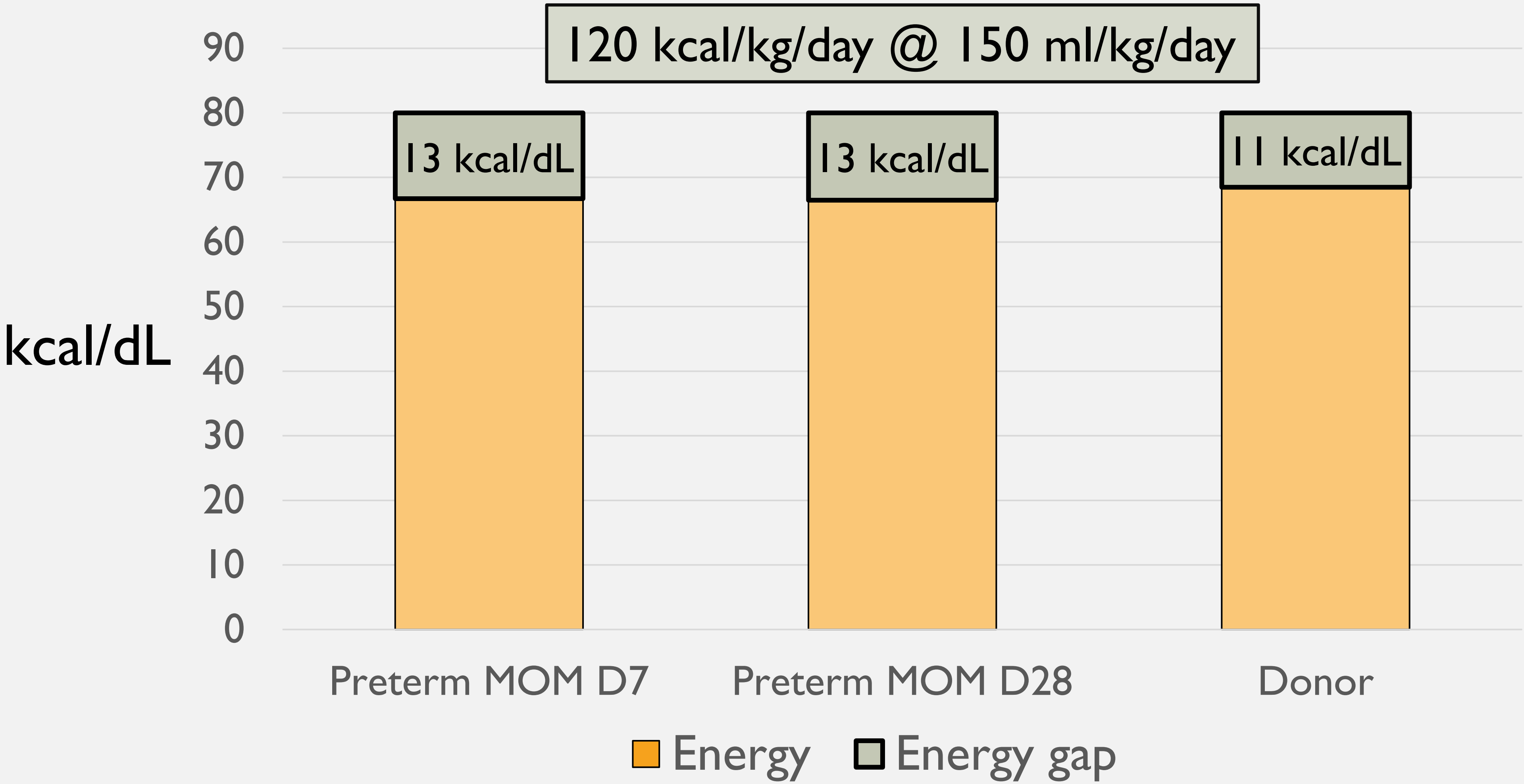
Lower fat content with day-7 preterm milk

**P* < .05, ***P* < .01, ****P* < .001, *****P* < .0001

D7, day 7 of preterm milk; D28, day 28 of preterm milk; DHM, donor human milk.

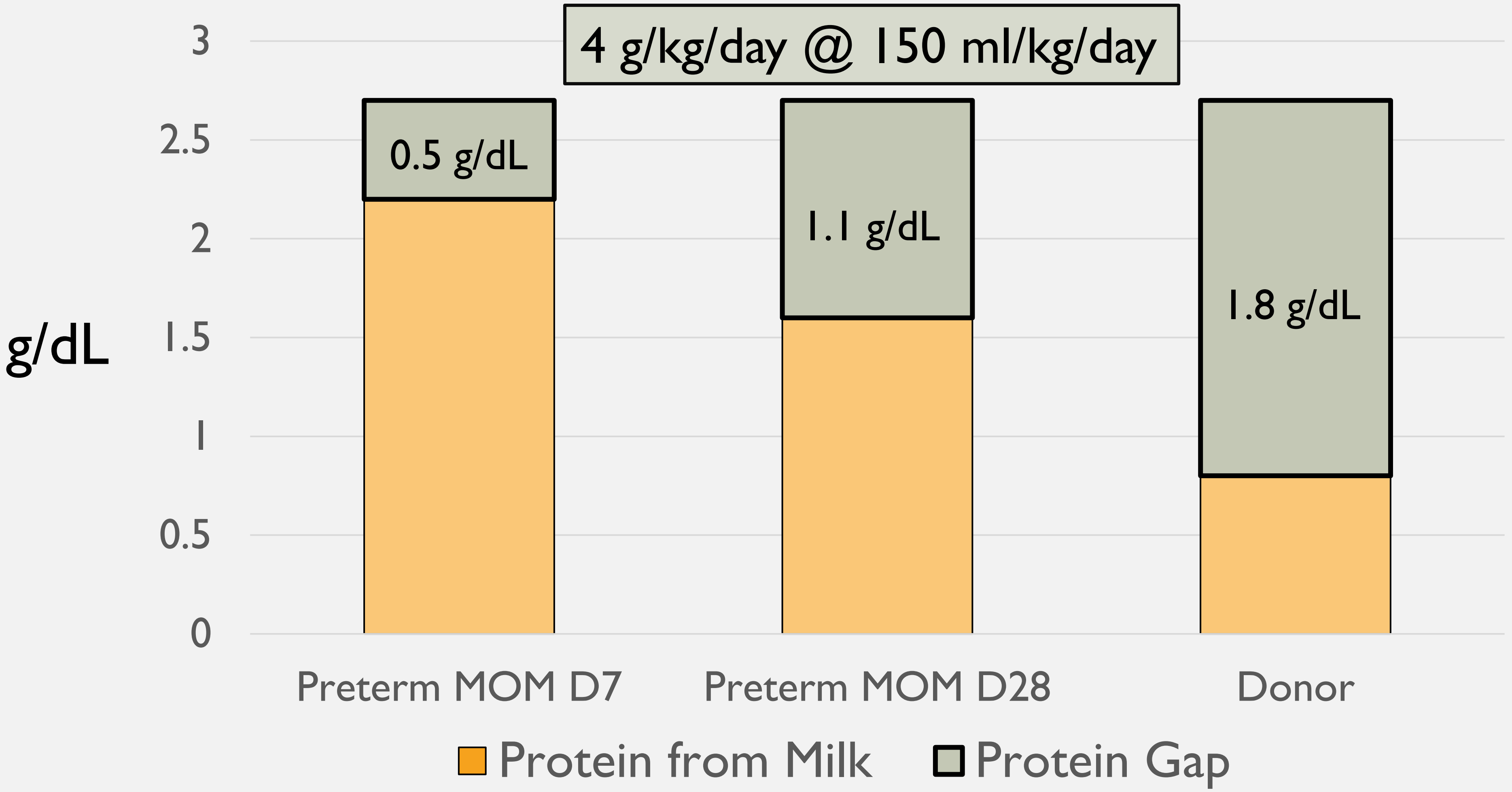
Gates A et al. *J Nutrition*. 2023

GAPS IN NUTRITION: ENERGY



Malley. *Arch Dis Child.* 2019; Gates. *Nutr Clin Pract.* 2020; Gates. *AJCN.* 2021

GAPS IN NUTRITION: PROTEIN



Malley. *Arch Dis Child*. 2019; Gates. *Nutr Clin Pract*. 2020; Gates. *AJCN*. 2021

HUMAN MILK COMPOSITION

Human milk (MOM & DHM) <u>cannot</u> meet the nutritional needs of preterm infants

Little insight into composition of donor human milk

Fortification must be multi-nutrient and holistic

- Particular attention to protein, sodium, and zinc for growth

MULTI-NUTRIENT FORTIFICATION

GOALS FOR FORTIFICATION

Augment (not replace) human milk

- MOM displacement
- Support milk supply
- Limit formula exposure

Provide optimal Protein, Ca^{2+}, P, Mg^{2+}, vitamins, and trace elements in a limited volume

HUMAN MILK ALONE IS NOT ENOUGH

Nutrient	Preterm milk (per 100 mL)	Donor milk (per 100 mL)	Recommended intake (per kg/day)
Energy, kcal	66-70	65-70	110-130
Protein, g	1.6-2.2	0.8-1.2	3.5-4.5
Carbohydrate, g	7.5-7.7	6.7-7.8	11-13
Fat, g	3.1-3.7	3.2-3.6	4.5-8.0
Sodium, mg	29-36	11-15	69-115
Potassium, mg	50-64	40-55	78-195
Chloride, mg	58-70	40-50	107-178
Calcium, mg	21-24	20-25	120-220
Phosphorus, mg	13-15	12-16	70-120
Iron, mg	0.09[2]	0.03-0.09	2-3
Zinc, mg	0.3-05	0.1-0.3	2-3

Recommended preterm feeding volume:
135-200 mL/kg/day

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MOM	DHM
220 mL	440 mL

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Recommended preterm feeding volume:
135-200 mL/kg/day

MOM	DHM
220 mL	440 mL
240 mL	630 mL
570 mL	600 mL
540 mL	580 mL
>2000 mL	>6000 mL
670 mL	2000 mL

IMPORTANCE OF HUMAN MILK FORTIFICATION FOR PRETERM INFANTS

Term infant formula and unfortified human milk do not meet the nutritional requirements of preterm infants[1]

In a meta-analysis of 18 trials (N = 1456), human milk fortification was associated with several growth benefits during hospitalization:[2]

- Increased **weight gain** (mean difference vs unfortified milk, 1.76 g/kg/d; 95% CI, 1.30–2.22 g/kg/d)
- Increased **body length** (0.11 cm/week; 0.0–0.15 cm/week)
- Increased **head circumference** (0.06 cm/week; 0.0–0.08 cm/week)

[1]. Kleinman RE, Greer FR, eds. *Pediatric Nutrition, 8th ed*. American Academy of Pediatrics; 2020. [2]. Brown JV et al. *Cochrane Database Syst Rev*. 2016;(5):CD000343.

METHODS OF HUMAN MILK FORTIFICATION

Standard
most common & easiest

- Fixed amount of fortifier added to fixed human milk volume
- Based on manufacturer's instructions, which typically assumes starting protein and energy content of 1.5 g/dL and 20 kcal/oz, respectively

Adjustable
more cost efficient & less labor intensive than individualized

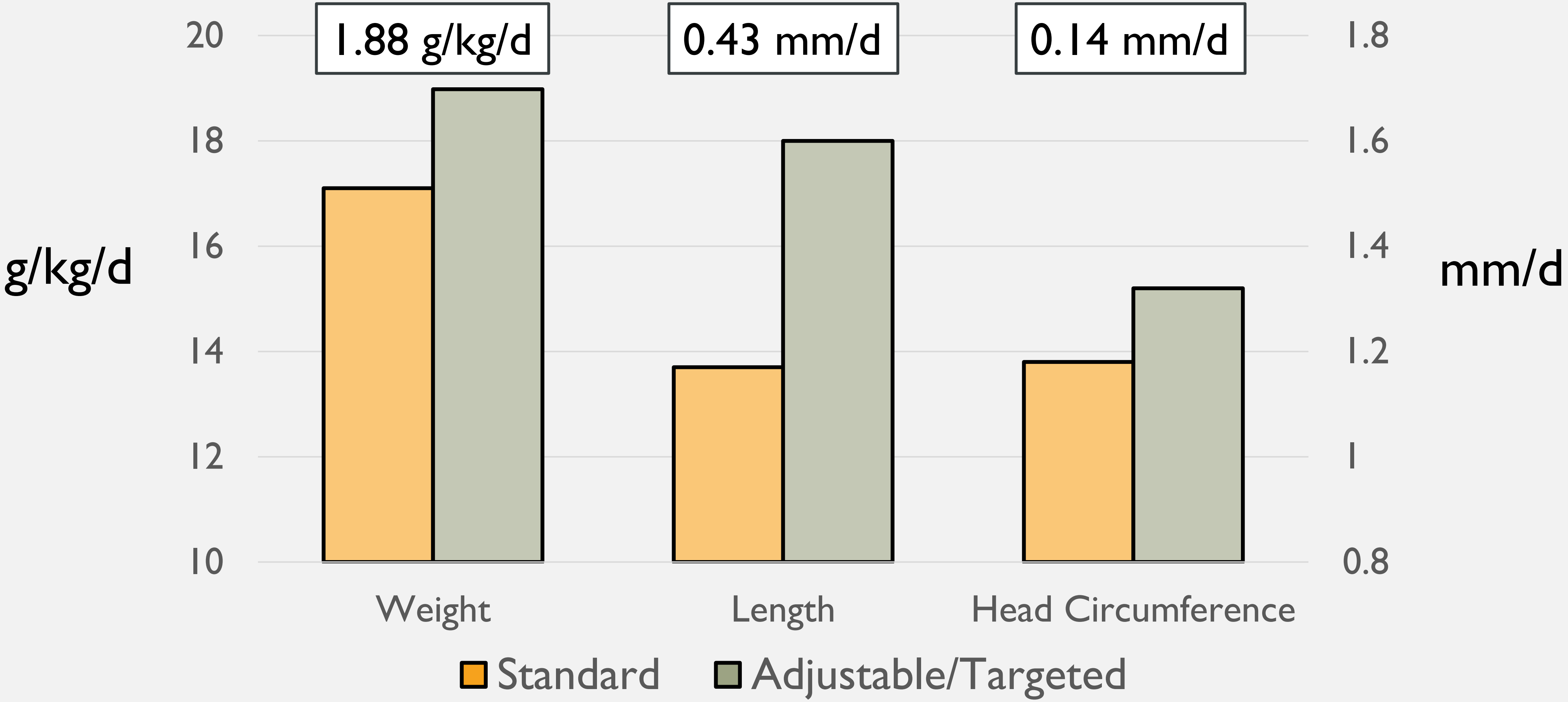
- Protein concentration is adjusted based on serial BUN measurements
- Additional protein supplementation added to standard fortification if BUN is <10 mg/dL

Targeted
most accurate & most costly

- Macronutrient concentrations in human milk are analyzed with a bedside human milk analyzer
- Fortification procedures are based on analysis

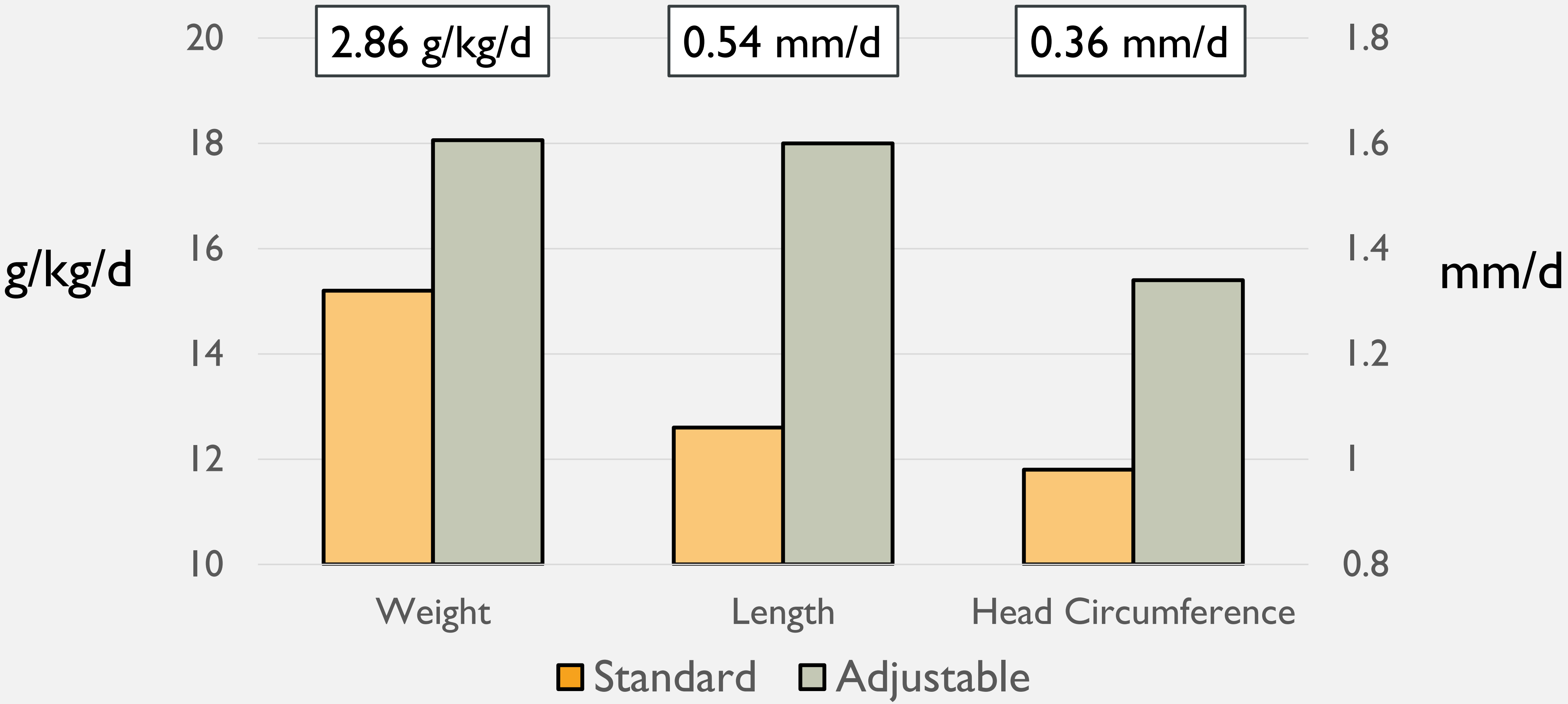
Bergner EM et al. *Clin Perinatol.* 2022;49(2):447-460.

STANDARD VS ADJUSTABLE OR TARGETED FORTIFICATION



[1]. Bulut O et al. *Nutr Clin Pract.* 2020;35(2):335-343. [2]. Embleton ND et al. *J Pediatr Gastroenterol Nutr*. 2023;76(2):248-268; Rochow N et al. *Clin Nutr.* 2021;40(1):54-63.; Fabrizio et al. *Cochrane*. 2020

STANDARD VS ADJUSTABLE FORTIFICATION



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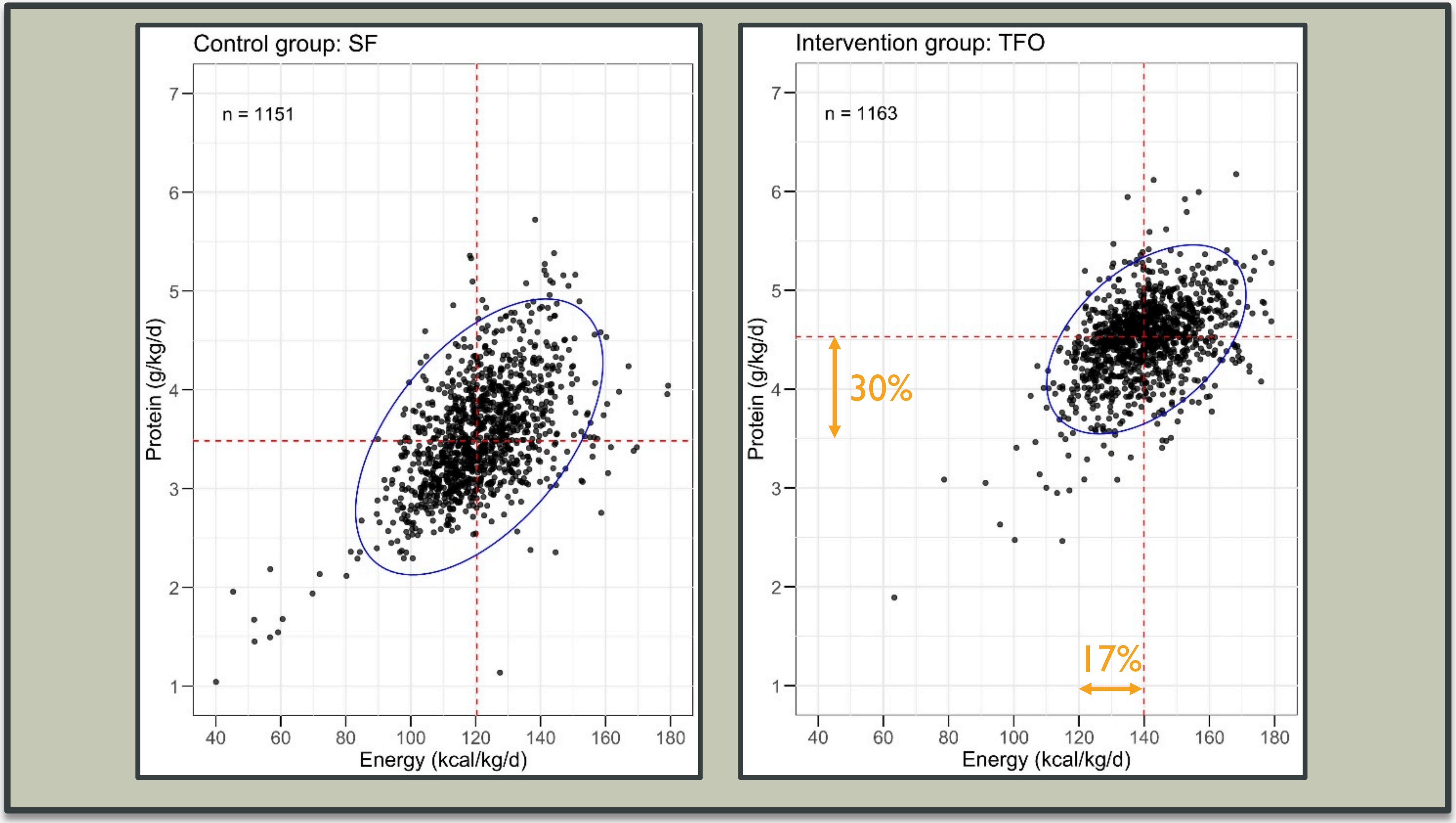
STANDARD VS TARGETED FORTIFICATION: EFFECTS ON GROWTH



Rochow N et al. *Clin Nutr.* 2021;40(1):54-63, Rochow N et al. *Nutrients*. 2025.

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Bergner EM et al. *Clin Perinatol.* 2022;49(2):447-460.

GAPS IN NUTRITION: NON-PROTEIN NITROGEN

Perrin 2025

Donor Milk Label

Total Nitrogen

Stansfield. *Nutr Clin Pract.* 2024; Perrin. *AJCN*. 2025; Gates. *J Nutr*. 2023

DILEMMAS IN HUMAN MILK FORTIFICATION: DECISION POINTS

Decision 1

Base milk?

- Mother's own milk vs donor milk
- Protein content differences
- Effects of processing on bioactive components
- Heterogeneity by gestational age and lactational stage

Decision 2

Fortifier type?

- Bovine human milk fortifier vs donor human milk–derived fortifier
- Liquid vs powder (bovine)
- Extent of research support
- Cost differences

Decision 3

Timing?

- Early (<100 mL/kg/d) vs late (≥100 mL/kg/d) fortification
- Challenges meeting nutritional requirements

Decision 4

Duration of fortification?

- Discharge vs term postmenstrual age vs beyond
- Patient characteristics and clinical needs

Hair AB et al. *J Perinatol.* 2023;43(1):103-107

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DILEMMAS IN HUMAN MILK FORTIFICATION: DECISION POINTS

Decision 1	**Decision 2**	Decision 3	Decision 4
Base milk?	**Fortifier type?**	Timing?	Duration of fortification?
• Mother's own milk vs donor milk • Protein content differences • Effects of processing on bioactive components • Heterogeneity by gestational age and lactational stage	• Bovine human milk fortifier vs donor human milk–derived fortifier • Liquid vs powder (bovine) • Extent of research support • Cost differences	• Early (<100 mL/kg/d) vs late (≥100 mL/kg/d) fortification • Challenges meeting nutritional requirements	• Discharge vs term postmenstrual age vs beyond • Patient characteristics and clinical needs

Hair AB et al. *J Perinatol.* 2023;43(1):103-107

HUMAN VS BOVINE HMF

N-Forte Randomized Clinical Trial

22 – 27^6 weeks PMA
n = 228

Avg GA: 26 weeks
Avg BW: 790 g
Female: 46%
SGA: 10 – 15%

Articles

Effect of human milk-based fortification in extremely preterm infants fed exclusively with breast milk: a randomised controlled trial

Georg Bach Jensen [a], Magnus Domellöf [b], Fredrik Ahlsson [c], Anders Elfvin [d e], Lars Navér [f g], Thomas Abrahamsson [a]

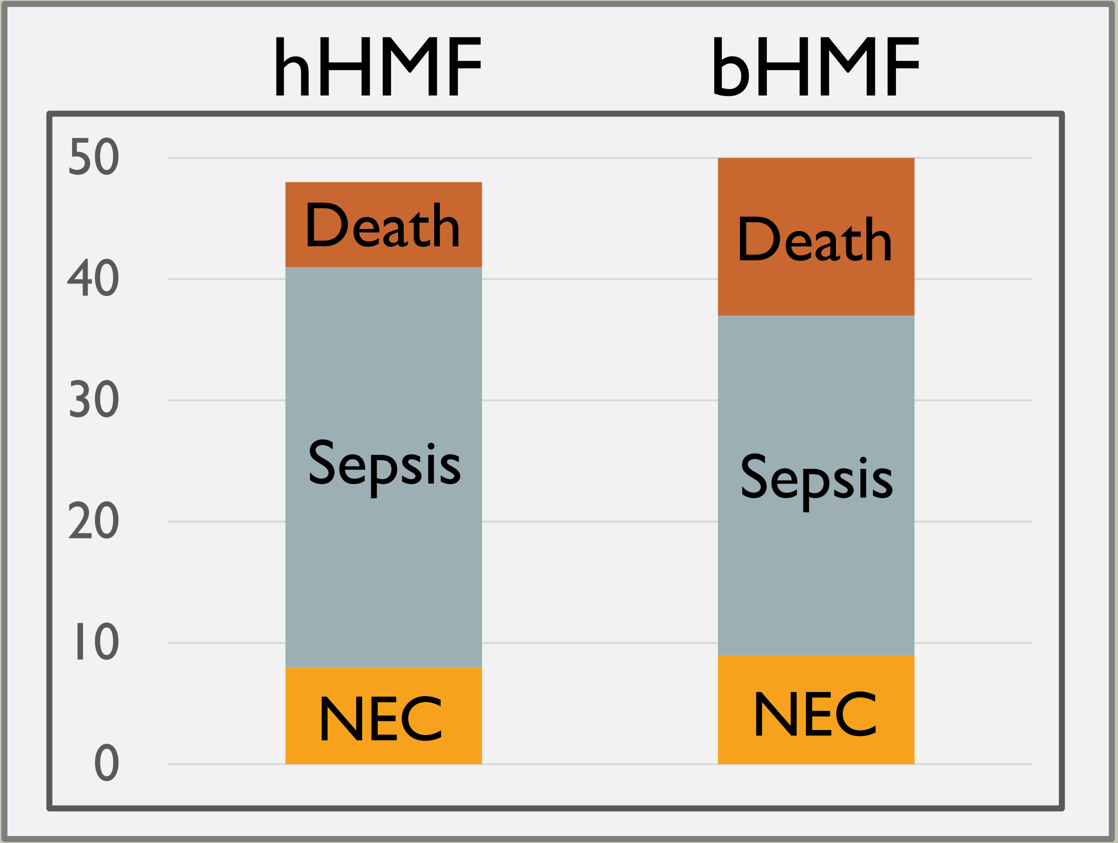
Jensen et al. *Lancet.* 2024

HUMAN VS BOVINE HMF

N-Forte Randomized Clinical Trial

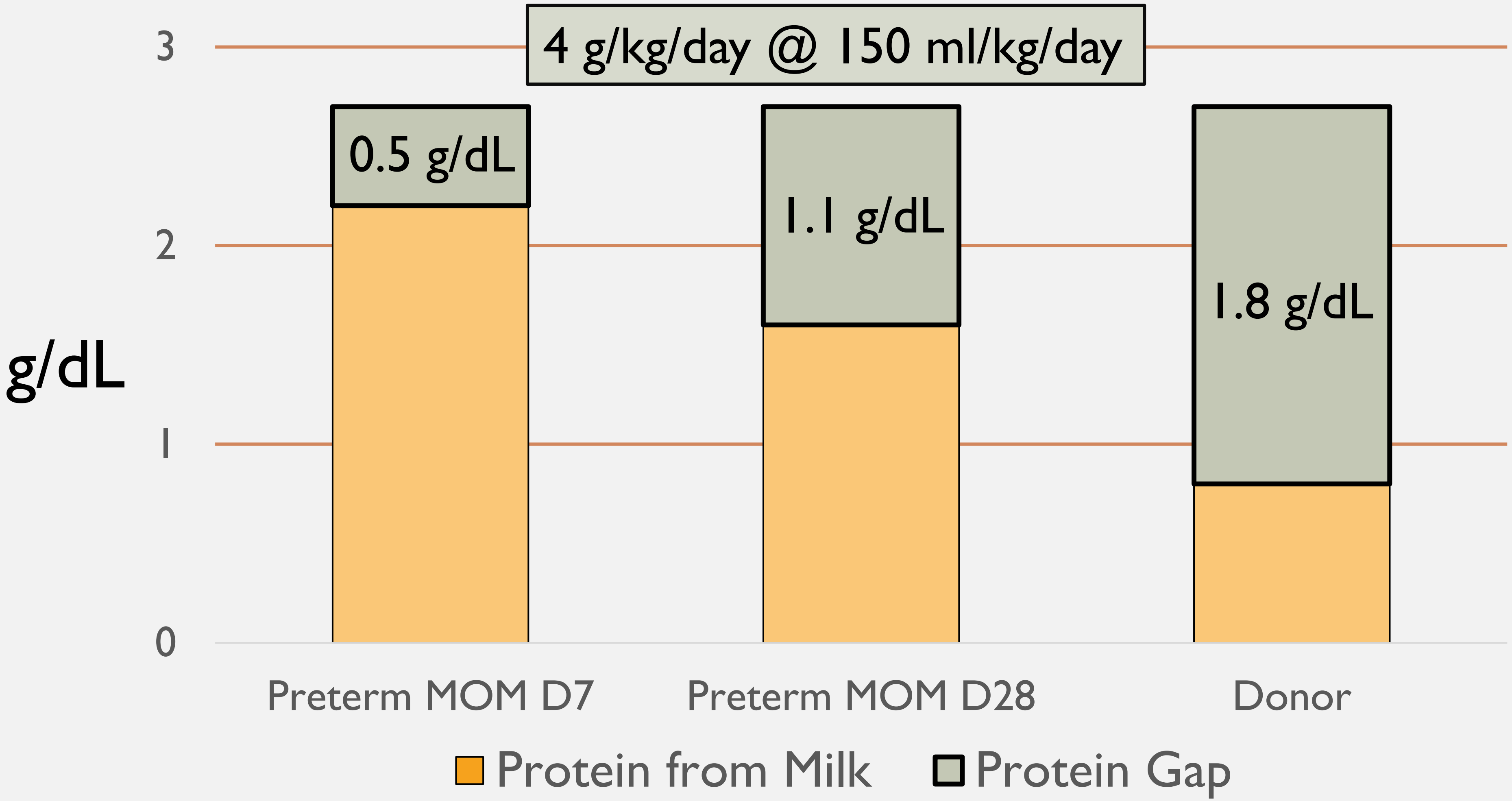
Composite Outcome:
Death, Sepsis, or NEC

35.7% in Human HMF
34.7% in Bovine HMF



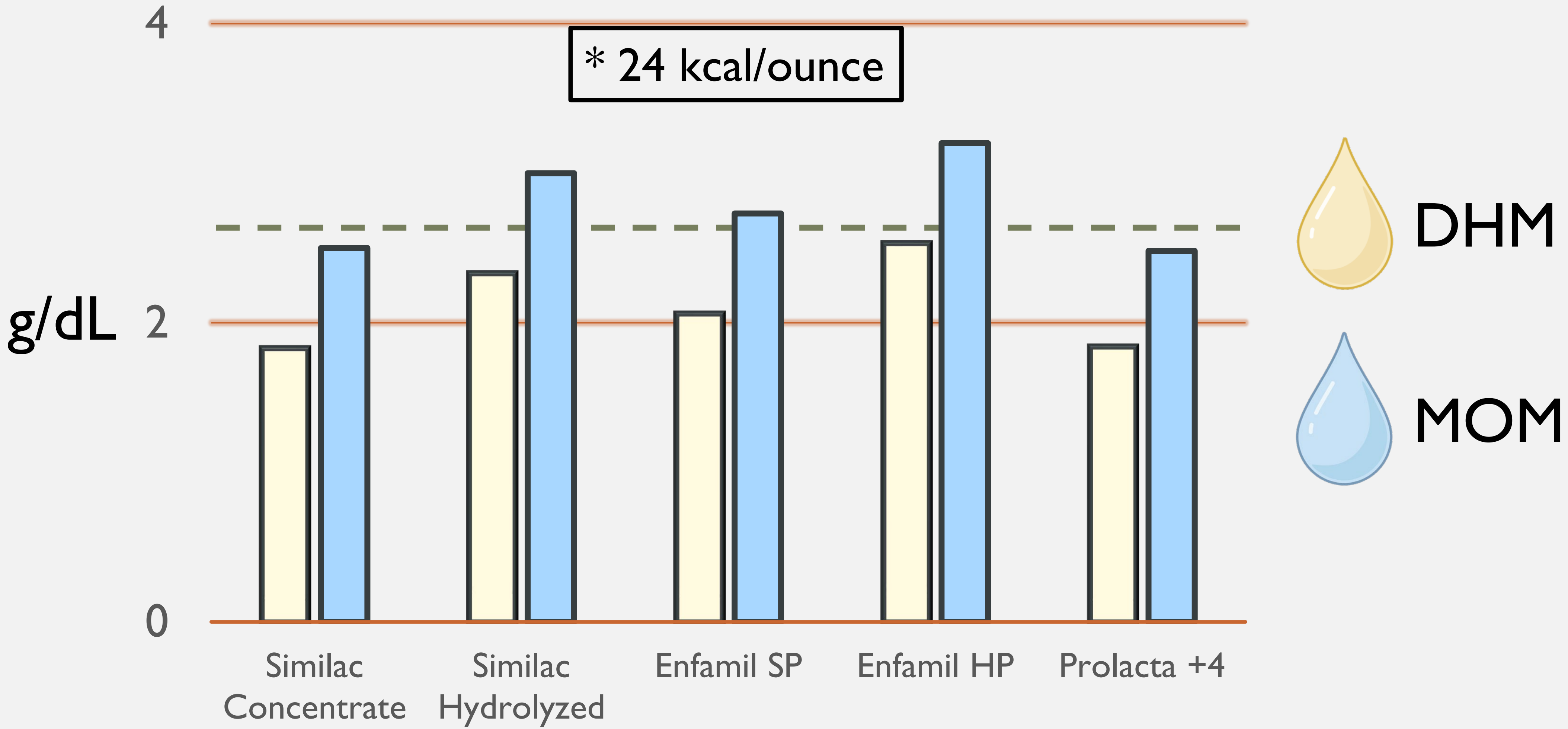
Jensen et al. *Lancet.* 2024

GAPS IN NUTRITION: PROTEIN



Malley. *Arch Dis Child.* 2019; Gates. *Nutr Clin Pract.* 2020; Gates. *AJCN.* 2021

PROTEIN IN FORTIFIED DHM*



Malley. *Arch Dis Child.* 2019; Gates. *Nutr Clin Pract.* 2020; Gates. *AJCN.* 2021

CONSIDERATIONS: DISPLACEMENT

DILEMMAS IN HUMAN MILK FORTIFICATION: DECISION POINTS

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Hair AB et al. *J Perinatol.* 2023;43(1):103-107

WHEN CAN I SAFELY ADD HMF?

Author	Study Group	Study Size	Intervention	Control	Weight	Length	NEC
Wynter, Z 2024	<1,500 g	52	Feeding Day 1 (bHMF)	Feeding Day 9 (bHMF)	↑	↑	—
Salas, A 2023	<28 wk	150	Feeding Day 1 (hHMF)	Feeding Day 14 (bHMF)	↑	↑	—
Sullivan, S 2010	<1,250 g	207	40 ml/kg (hHMF)	100 ml/kg (hHMF)	—	—	—
Shah, S 2016	<1,500 g	100	20 ml/kg (bHMF)	100 ml/kg (bHMF)	↑	—	—
Alizadeh Taheri, P 2016	<34 wk	72	~20 ml/kg (bHMF)	~75 ml/kg (bHMF)	—	—	—

Wynter Z et al. *J Perinatol.* 2024; Salas A et al. *Pediatrics*. 2023; Sullivan S et al. *J Pediatrics*. 2010; Shah S et al. *J Pediatrics*. 2016; Alzadeh Taheri P et al. *J Peri Med*. 2016

DILEMMAS IN HUMAN MILK FORTIFICATION: DECISION POINTS

Decision 1

Base milk?

- Mother's own milk vs donor milk
- Protein content differences
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- Heterogeneity by gestational age and lactational stage

Decision 2

Feeding volume?

- Bovine human milk fortifier vs donor human milk–derived fortifier
- Liquid vs powder (bovine)
- Extent of research support
- Cost differences

Decision 3

Timing?

- Early (< 100 ml/kg/d) vs late (> 100 ml/kg/d) fortification
- Challenges meeting nutritional requirements

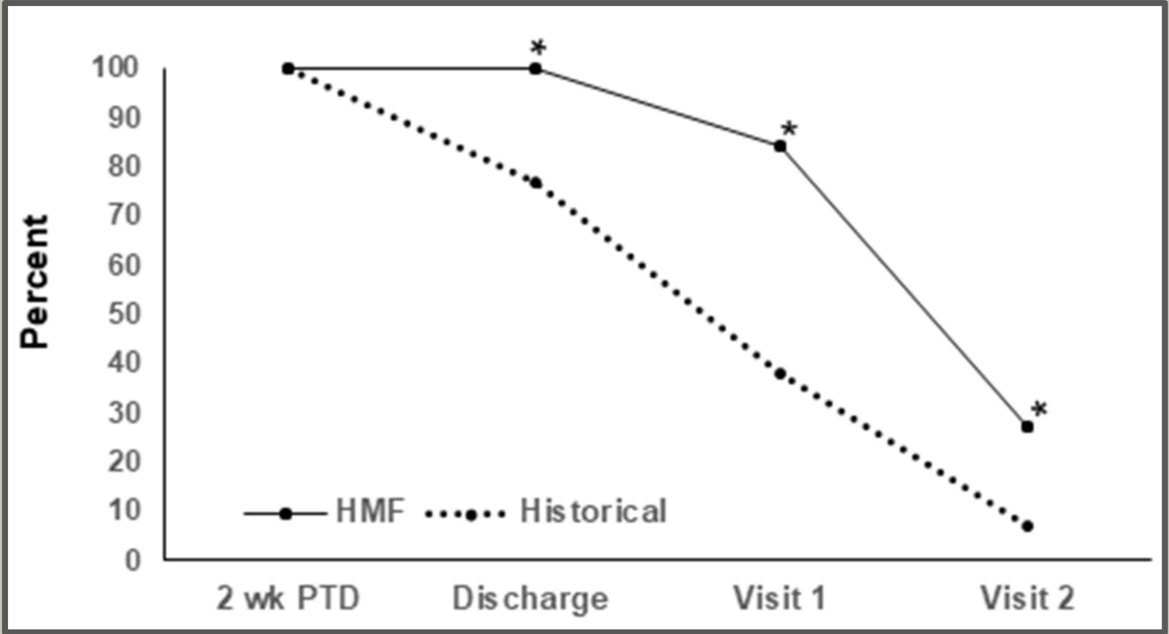
Decision 4

Duration of fortification?

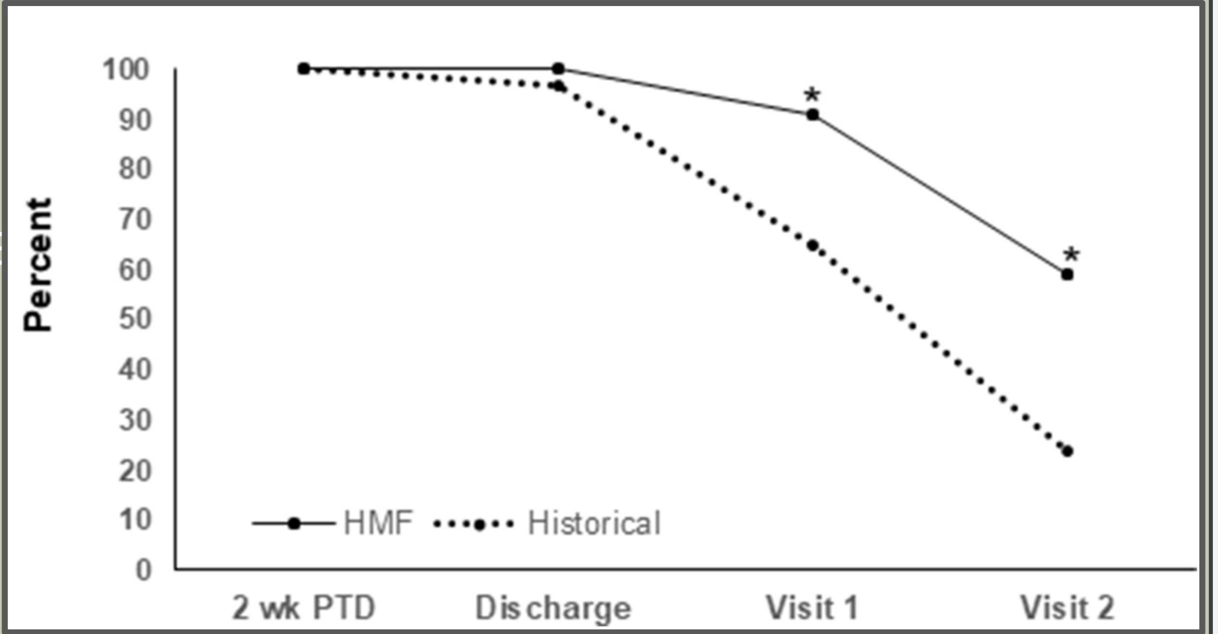
- Discharge vs term postmenstrual age vs beyond
- Patient characteristics and clinical needs

HMF AFTER DISCHARGE

Exclusive Human Milk



Any Human Milk



Lamport L et al. *J Nutr.* 2024;154: 610-616

KEY TAKEAWAYS

OPTIMIZING HUMAN MILK

Preterm MOM ≠ DHM

Preterm MOM is dynamic

- Protein-rich through first week → SEQUENTIAL FEEDING
- Higher protein than DHM, but similar carbohydrate, energy, & fat
- Recognize that GA and race may influence MOM composition

DHM is pooled and pasteurized

- Reflects later lactation stage from mothers of term infants
- Largely unknown composition beyond macronutrients

OPTIMIZING HUMAN MILK

Pooling MOM (24 hrs) provides more even distribution of nutrients

Fortification (designed for day 28 preterm MOM)

- Early fortification appears safe
- Consider displacement if MOM is primary
- Consider increasing protein delivery if BUN < 10 mg/dL in setting of slow growth (Adjustable Fortification)
- Powder formula meets caloric needs, but not Calcium, Sodium, Protein, Zinc

THANK YOU

LEARNING ASSESSMENT QUESTIONS

- All of the following statements regarding human milk fortifiers are true except?

  a) Bovine milk-derived HMFs provide less protein than human milk-derived HMFs at equivalent caloric densities.
  b) HMFs improve preterm infant weight, length, and head circumference growth
  c) No difference in death, NEC, or sepsis was identified in a recent RCT comparing bovine and human milk-derived HMFs.
  d) Addition of HMF with first feeds is safe and may improve growth

LEARNING ASSESSMENT QUESTIONS

- In comparison to Caucasian mothers of preterm infants, mother's own milk from mothers who are African American is enriched for which of the following?

  a) Fat
  b) Carbohydrates
  c) Vitamin D
  d) Protein