SUPPLEMENTING MICRONUTRIENTS AND TRACE ELEMENTS IN VLBW INFANTS

Brian Stansfield, MD

Professor and Vice Chair for Research

Medical College of Georgia

Augusta University

Wellstar Children's Hospital of Georgia

FACULTY DISCLOSURES

Brian Stansfield, MD

Speakers Bureau	Mead Johnson Nutrition
Funding Sources	National Institutes of Health Department of Defense Children's Tumor Foundation Knight's Templar Eye Foundation Mead Johnson Nutrition

LEARNING OBJECTIVES

By participating in this education, you will better:

- Identify mineral and trace element deficiencies in preterm and donor human milk
- Design supplementation strategies to replete micronutrients for preterm infants

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.

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

MOM **DHM**

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MOM	DHM
220 mL	440 mL

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

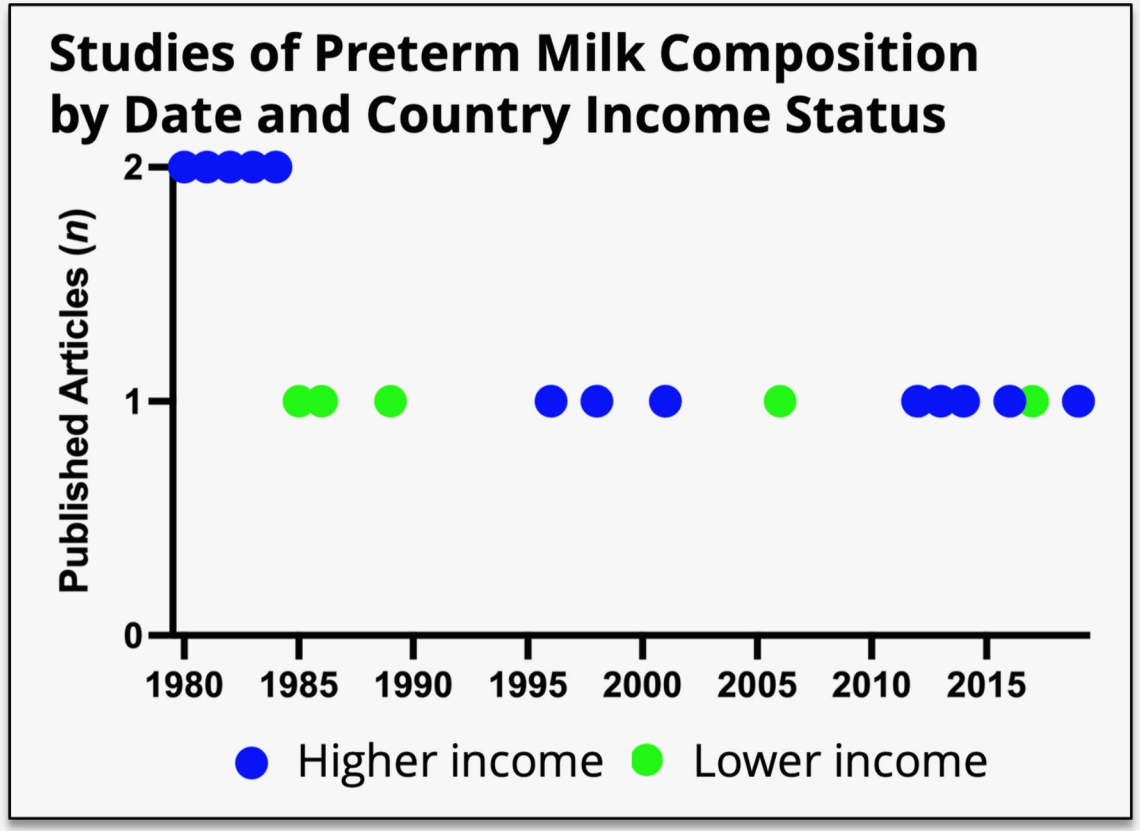
MOM	DHM
220 mL	440 mL
240 mL	630 mL
570 mL	600 mL
540 mL	580 mL
>2000 mL	>6000 mL
670 mL	2000 mL

Review of Preterm Human-Milk Nutrient Composition

Amy Gates, PhD, RDN, CSP, LD[1]; Terri Marin, PhD, MS, NNP[2]; Gianluca De Leo, PhD, MBA[1]; and Brian K. Stansfield, MD[3]

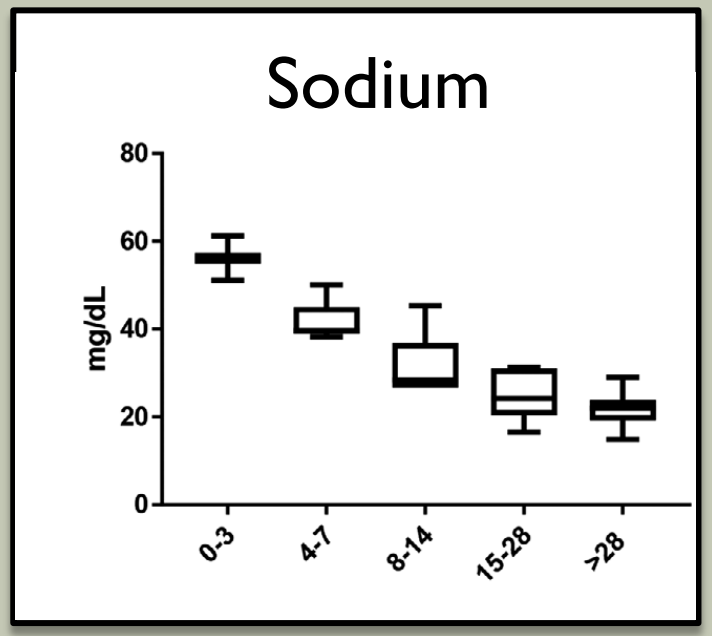
In a review of 27 articles with original data on composition of preterm milk, several literature deficits were identified:

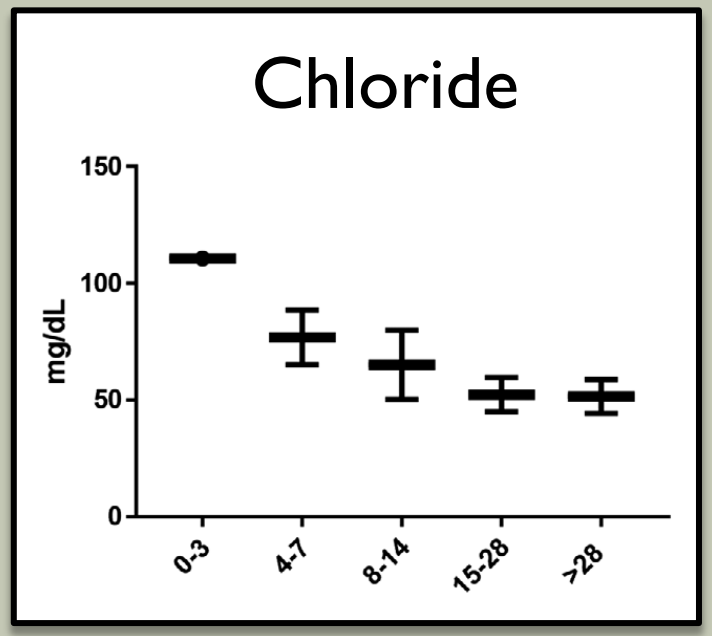
- Underrepresentation of Black women
- Underrepresentation of deliveries <28 weeks' gestation

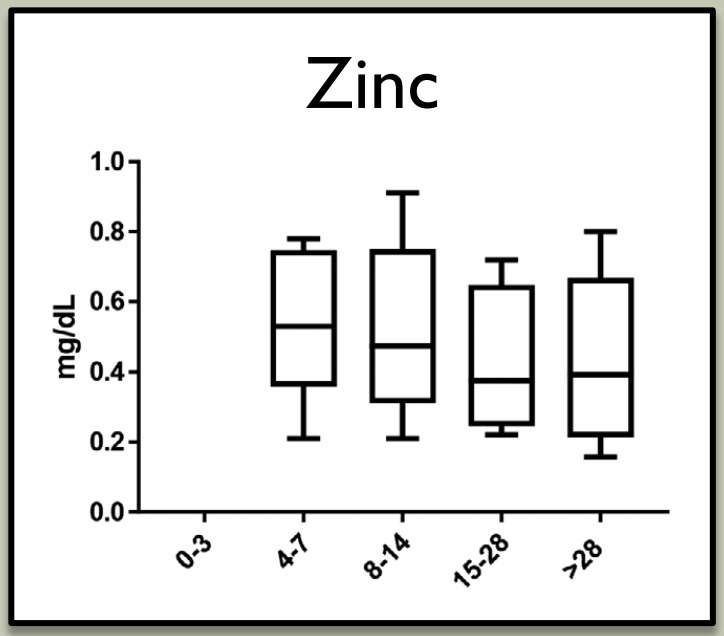


Gates A et al. *Nutr Clin Pract.* 2021;36(6):1163-1172. Figure not in print article.

PRETERM HUMAN MILK COMPOSITION







Postnatal Day

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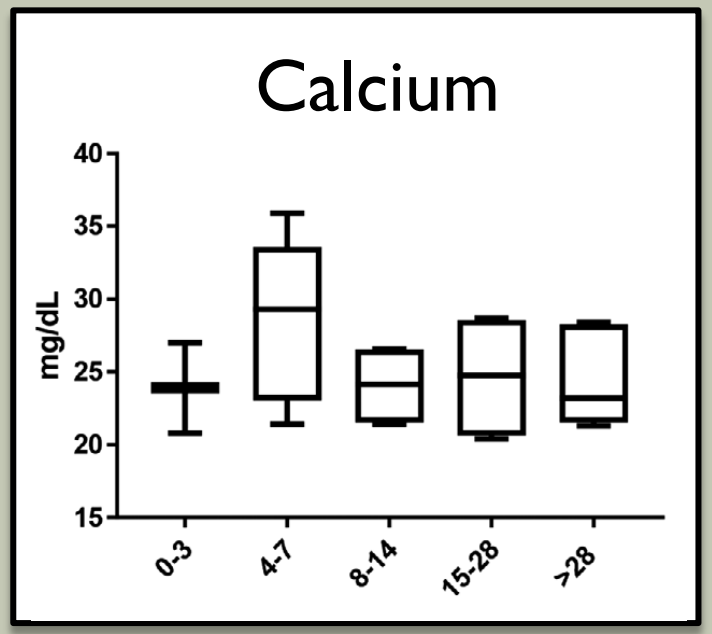

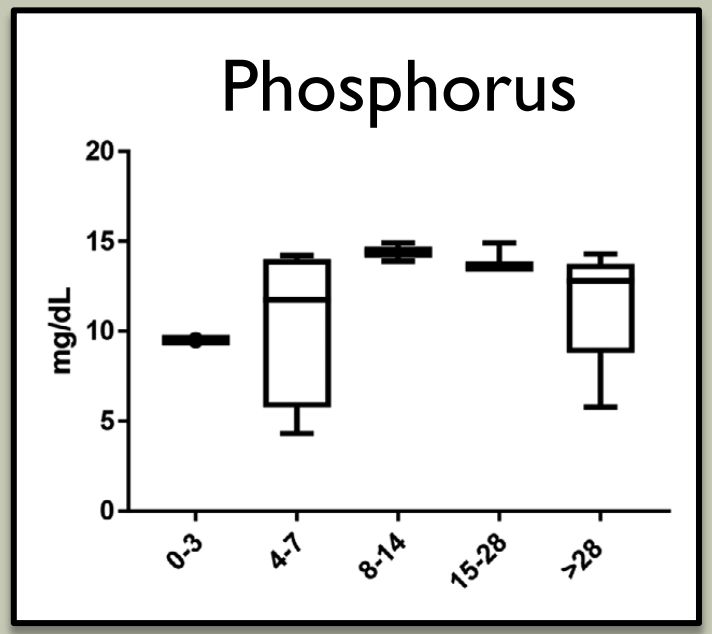

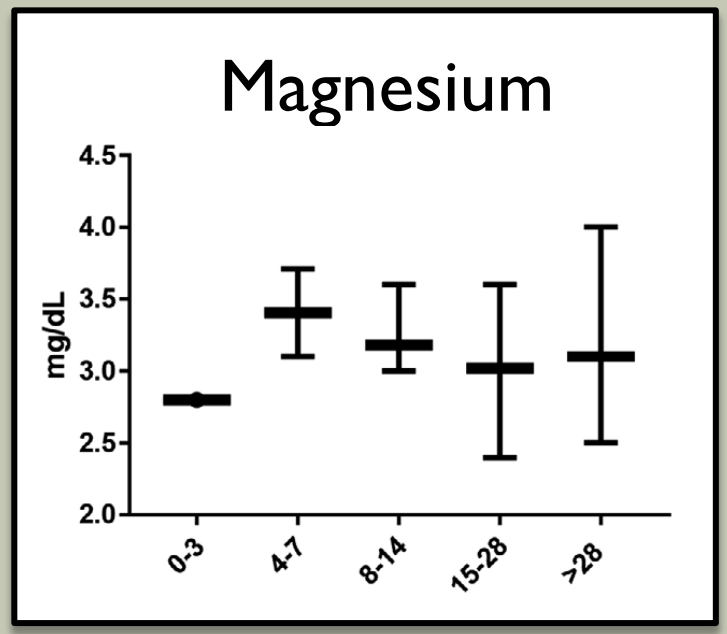

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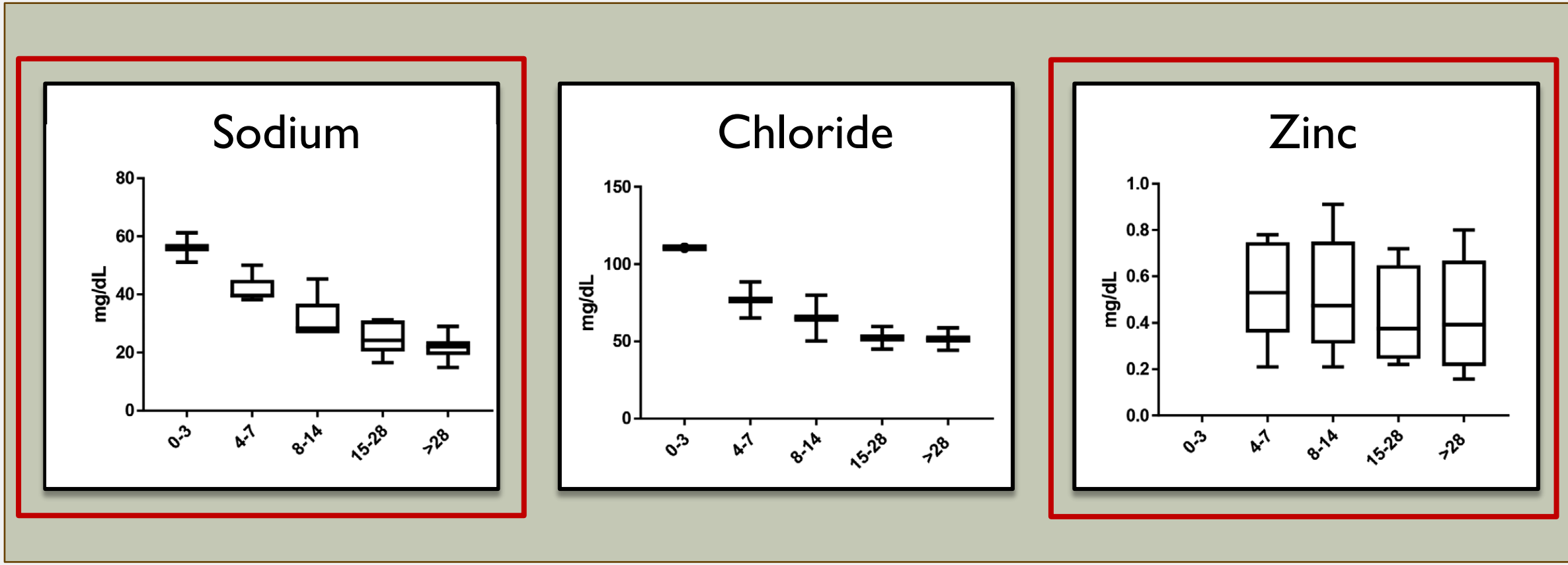

Postnatal Day

Gates A et al. *Nutr Clin Pract.* 2021;36(6):1163-1172.

MOTHER'S OWN MILK COMPOSITION FOR PRETERM VS TERM INFANTS

Nutrient	2022 ESPGHAN Guidelines[1],[a] per kg/d	Preterm milk (per 100 mL)
Energy, kcal	115 – 140 (-160)	66–70
Protein, g	3.5 – 4.0 (-4.5)	1.6–2.2
Carbohydrate, g	11 – 15 (-17)	7.5–7.7
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[1]. Gates A et al. *Am J Clin Nutr.* 2021;114(5):1719-1728. [2]. Kim SY, Yi DY. *Clin Exp Pediatr.* 2020;63(8):301-309.

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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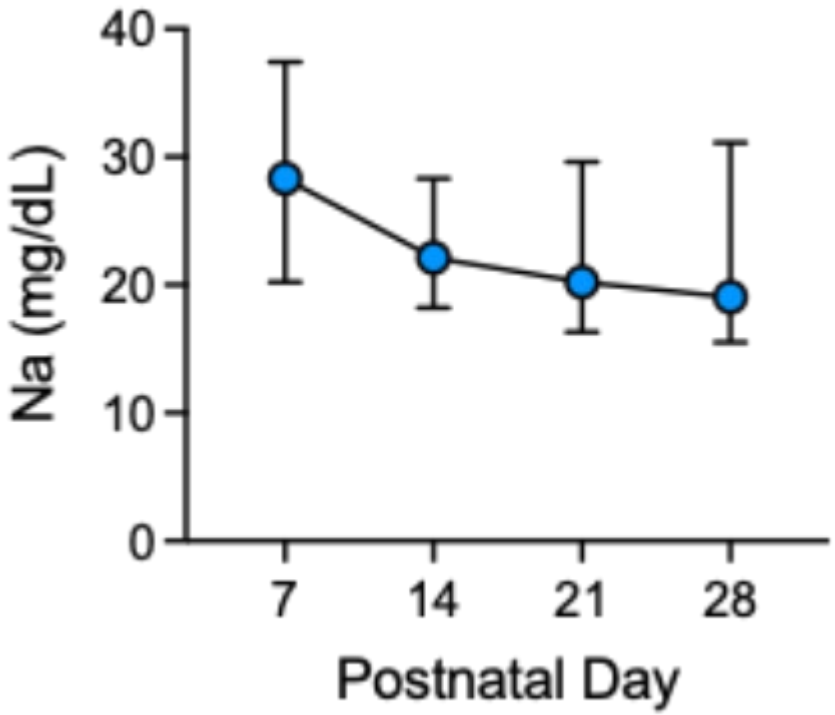

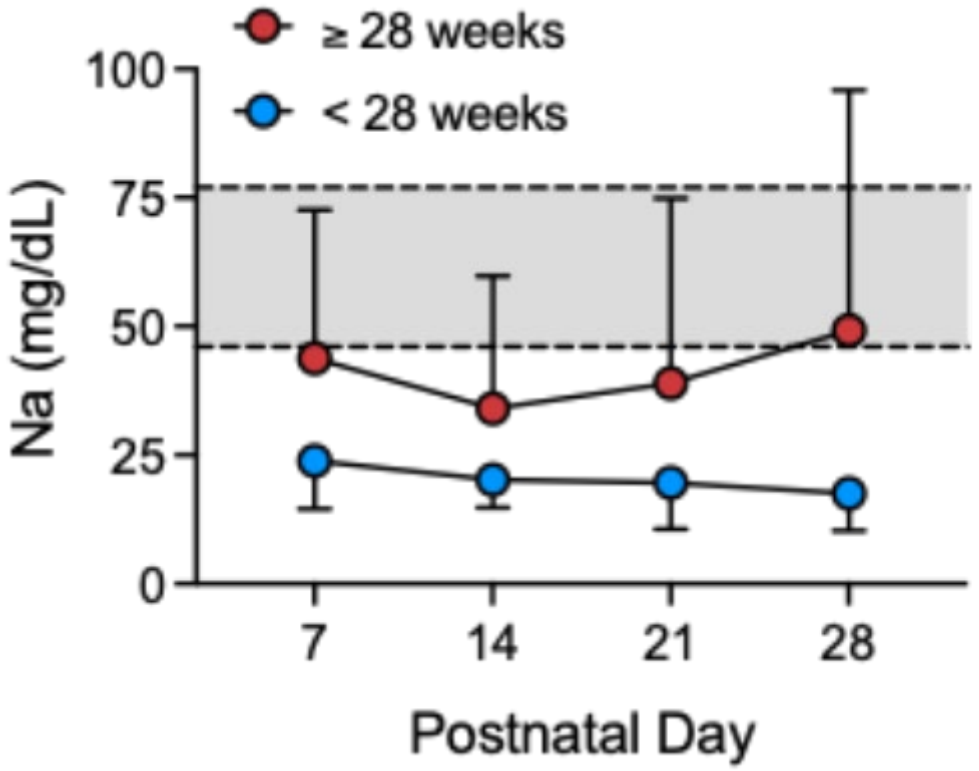

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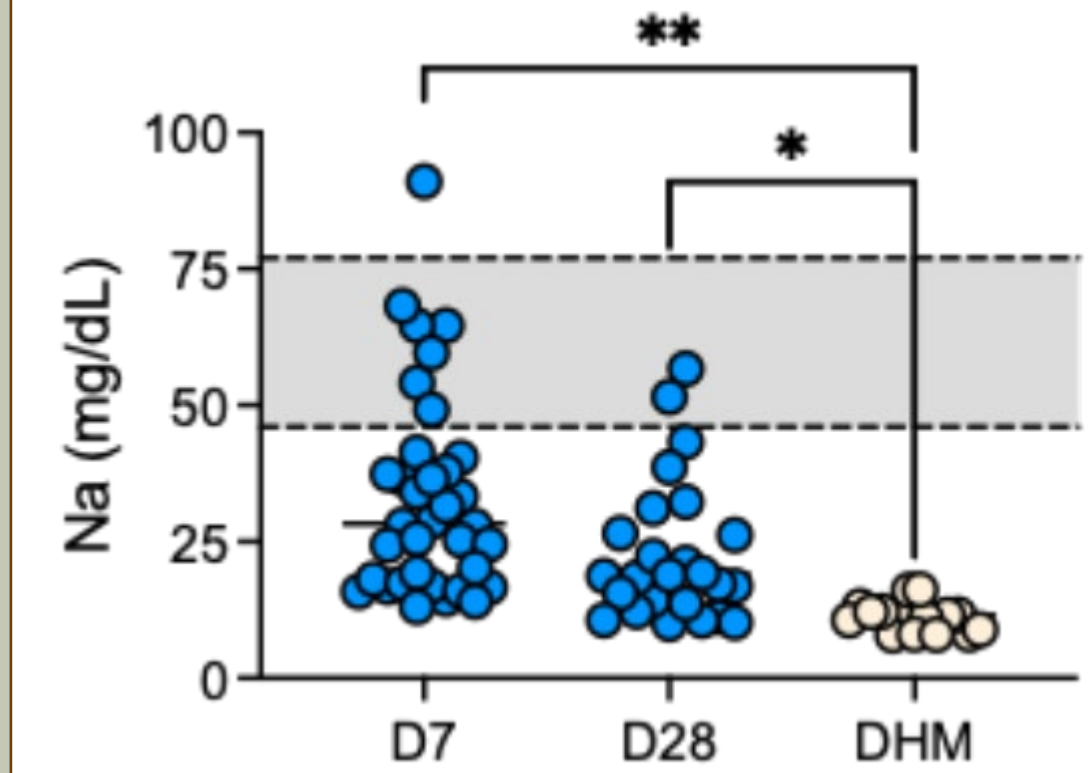
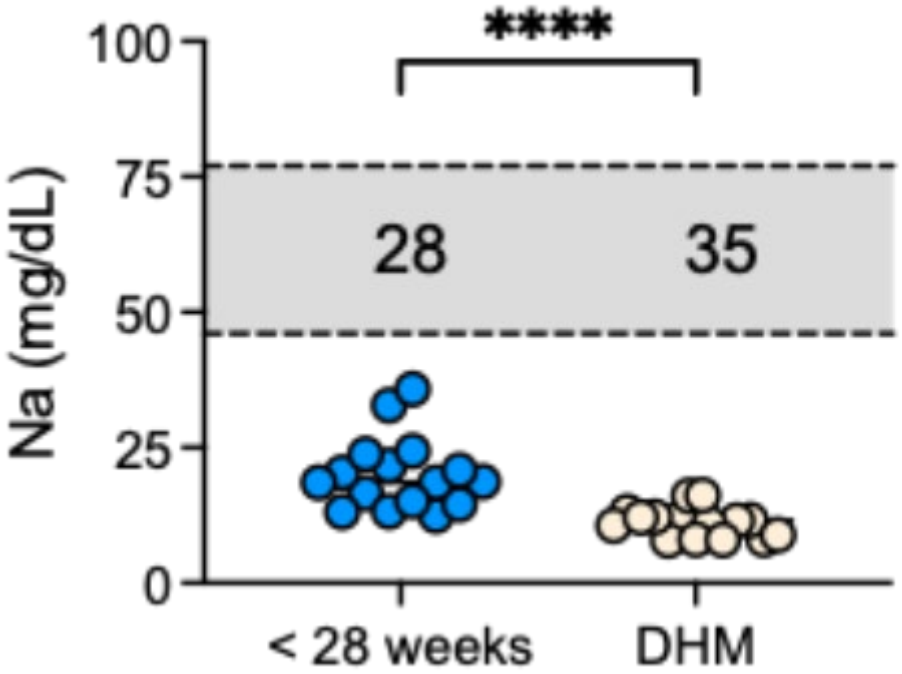
DONOR VS PRETERM MOM: SODIUM





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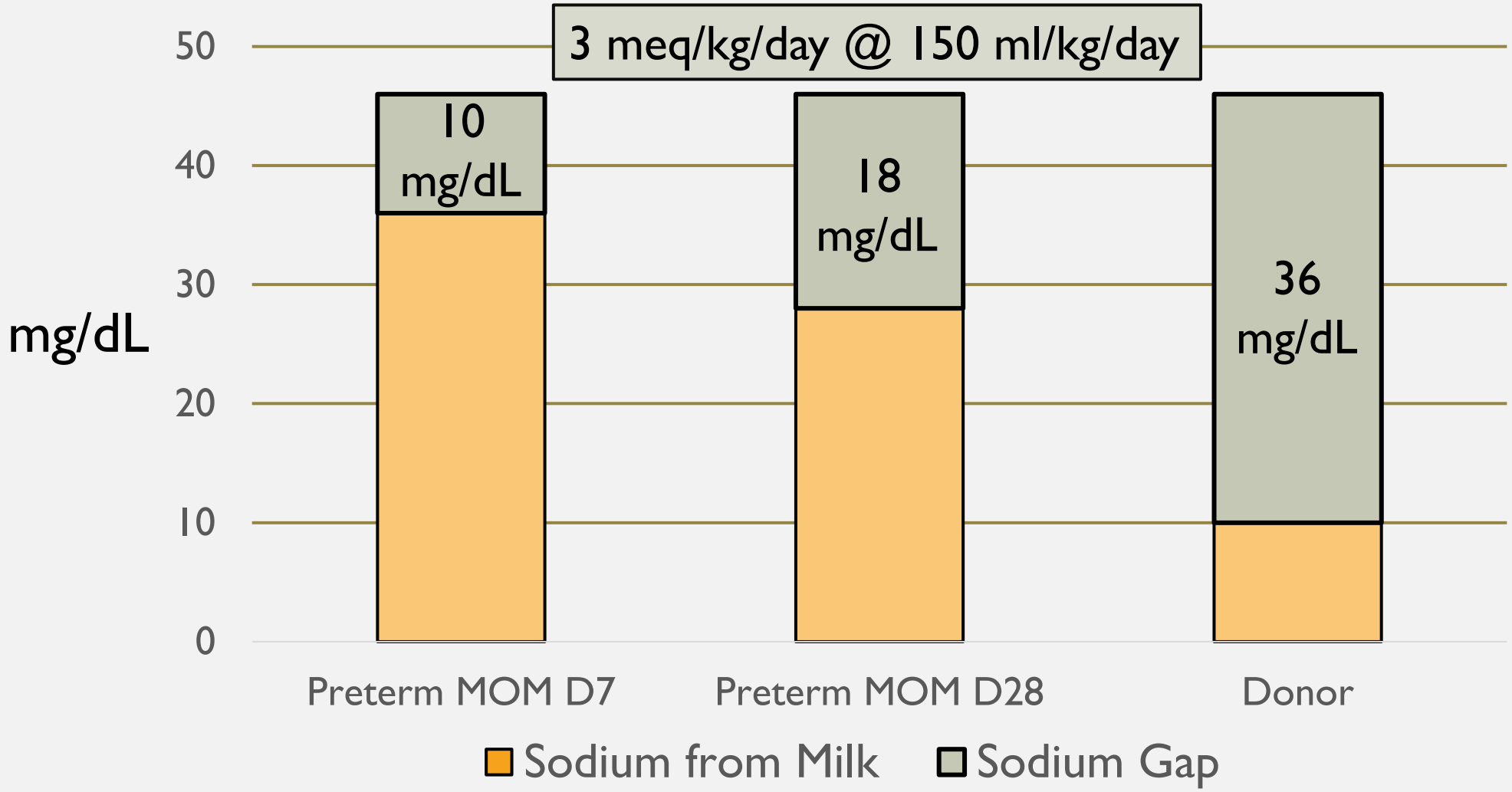
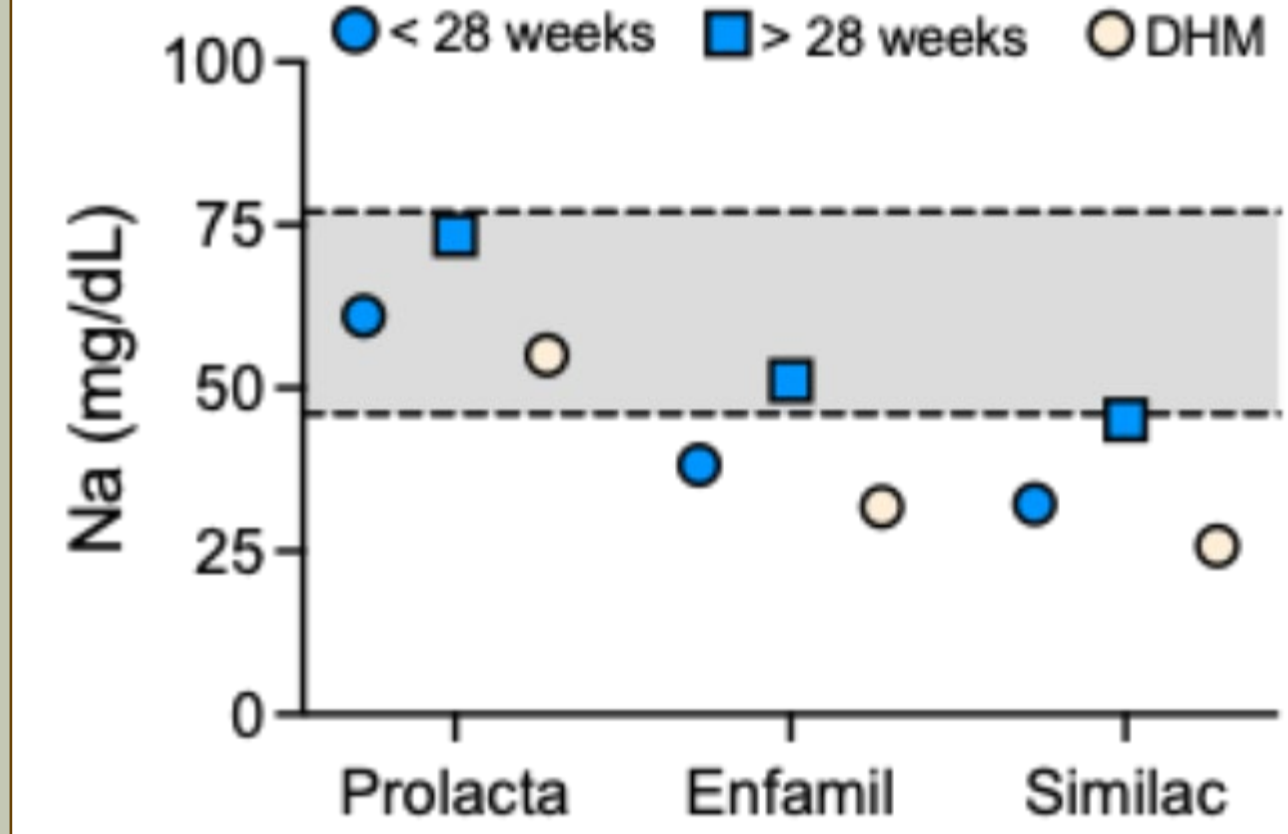
GAPS IN NUTRITION: SODIUM



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

SODIUM & HUMAN MILK FORTIFICATION



1-2 meq/kg/day

SODIUM SUPPLEMENTATION

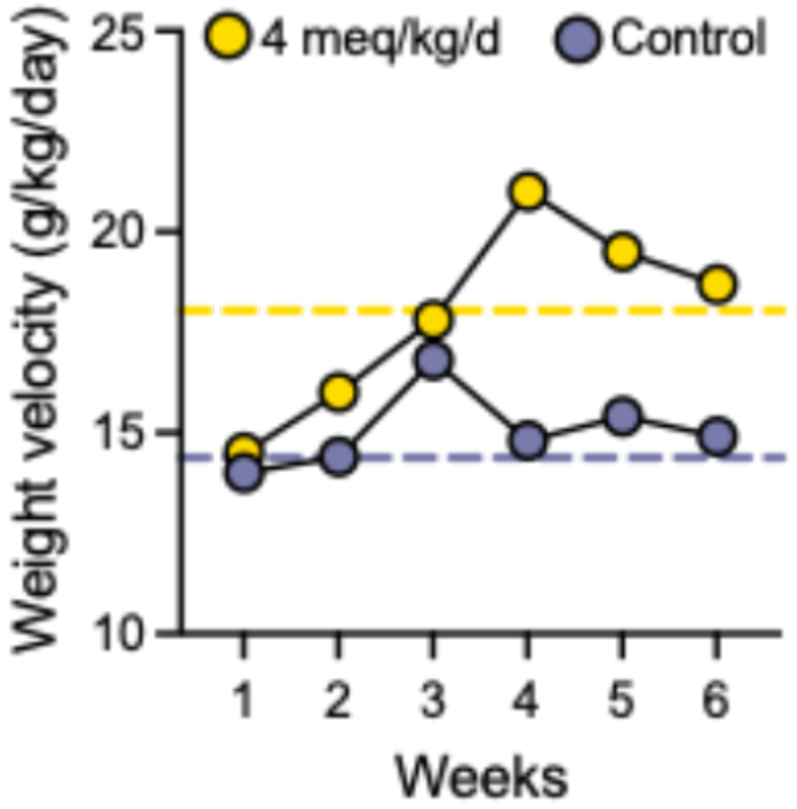
Double Masked RCT in India

Eligibility:

- 25 – 30^{6} weeks
- Enteral feedings of 100 ml/kg/day
- Serum Na < 145 meq/L

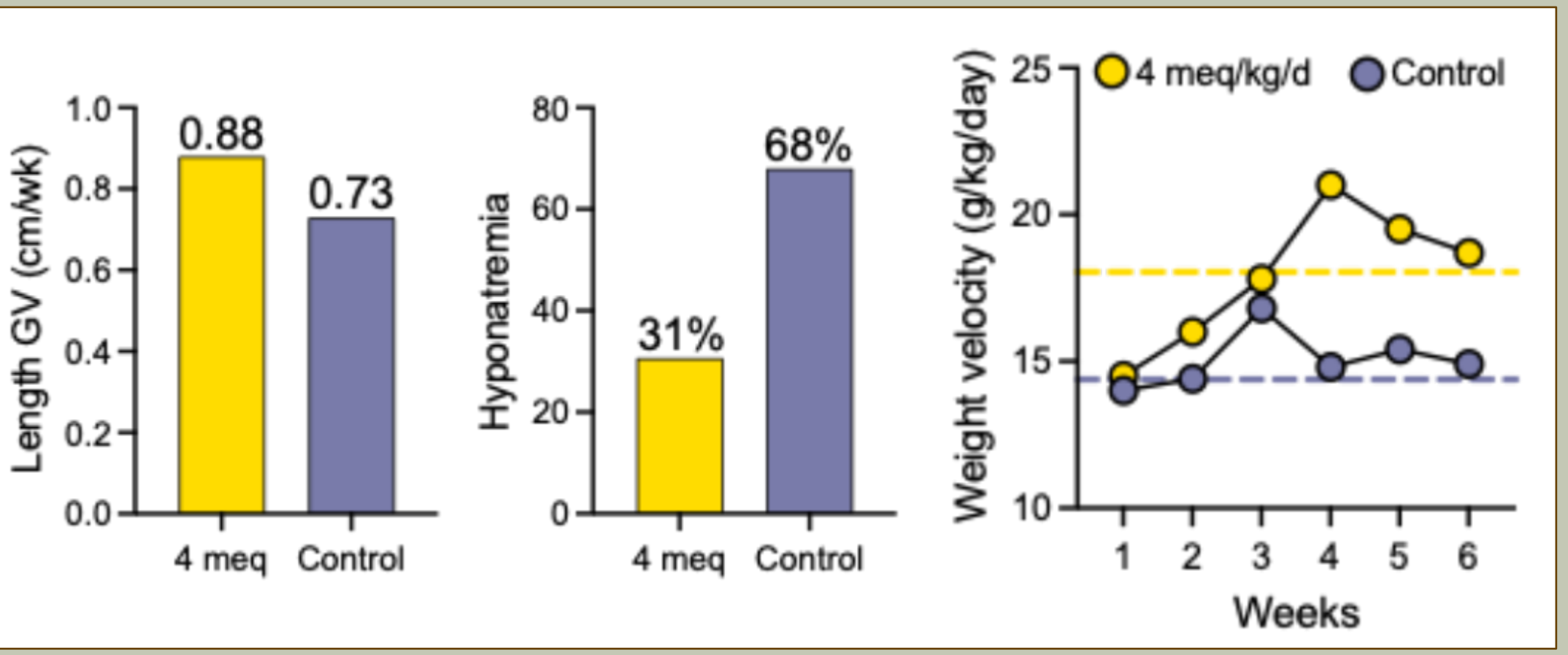
Intervention:

- 4 meq/kg/day vs 0.1 meq/kg/day
- Correction for Na < 135 with 3% NaCl



Amiti. *BMJ Pediatr* 2025

SODIUM SUPPLEMENTATION



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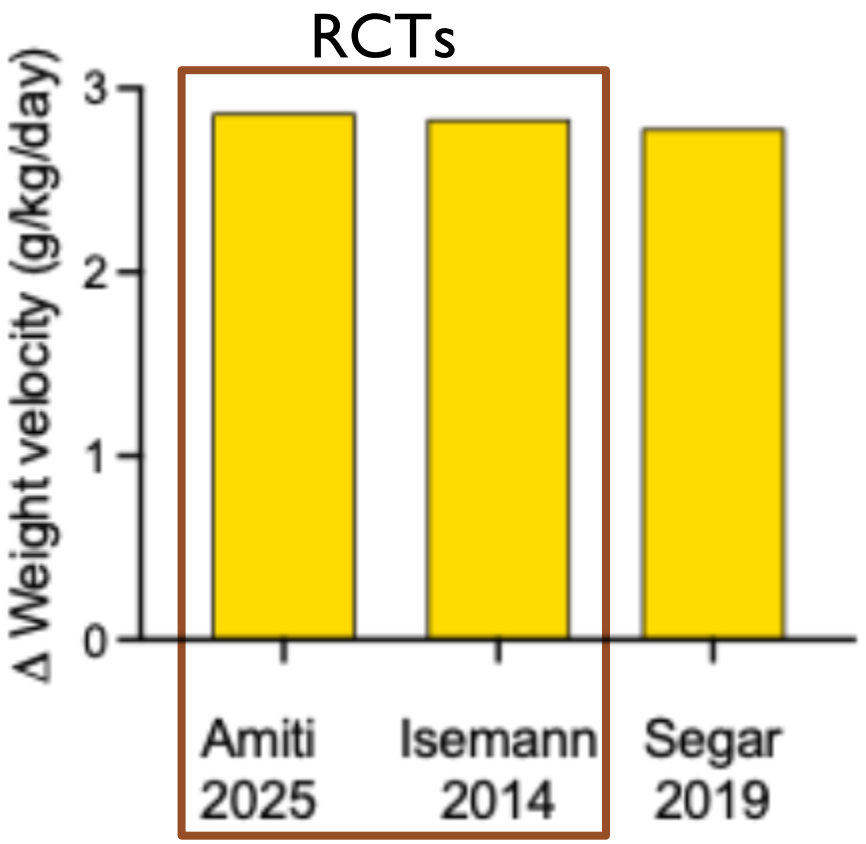

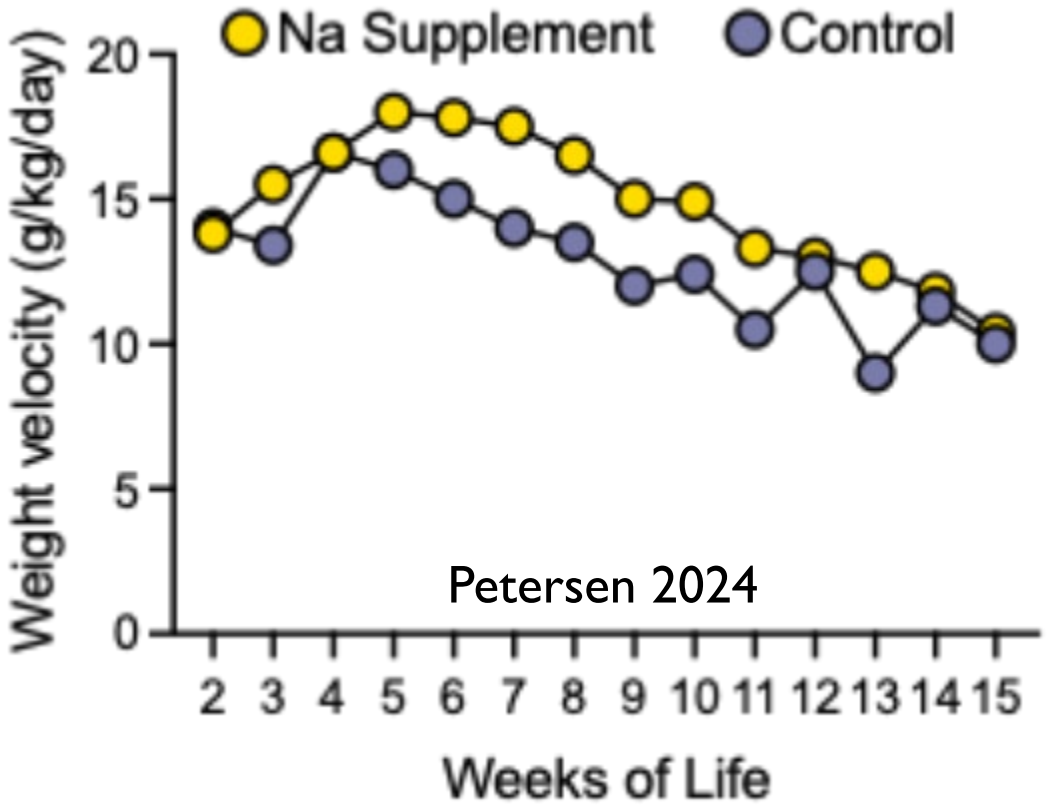

Stalter. *J Perinatol.* 2024; Petersen. *J Perinatol.* 2024; Segar. *Am J Perinatol.* 2019; Isemann. *JPEN.* 2014; Amiti. *BMJ Pediatr* 2025

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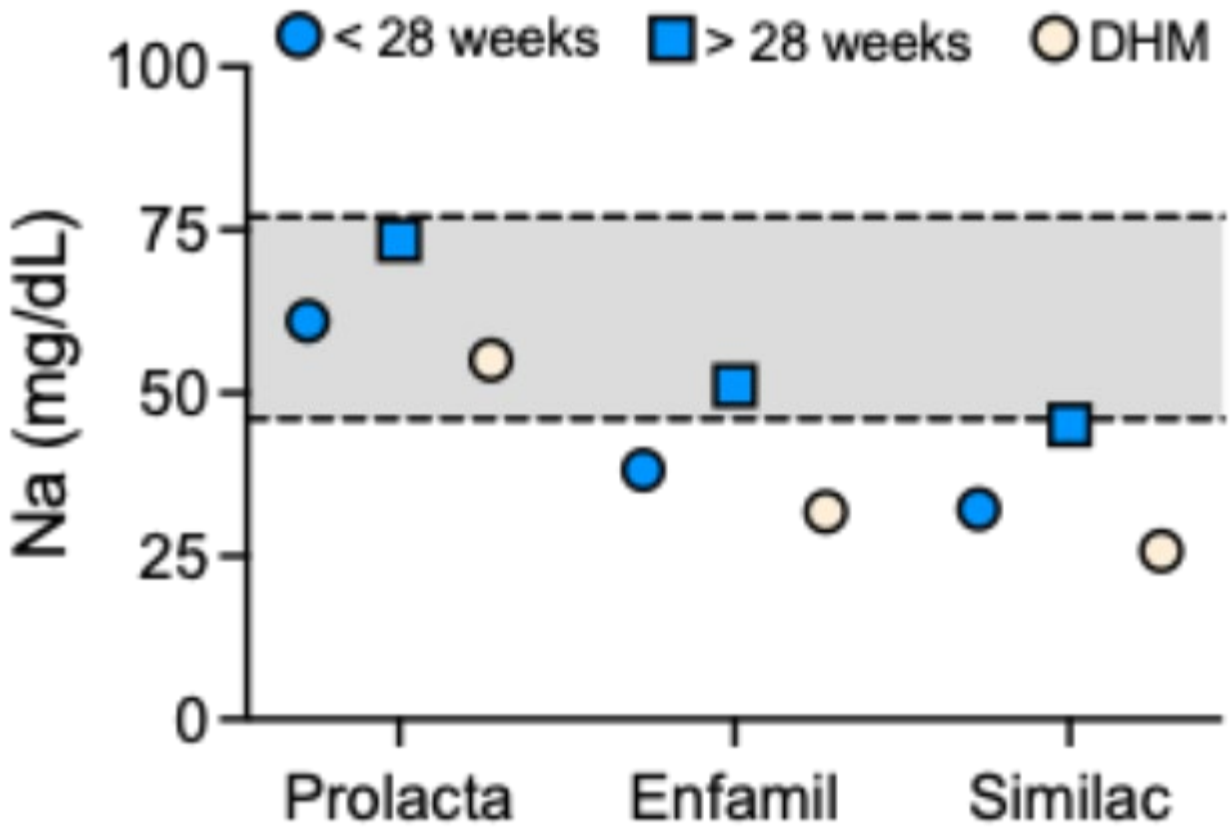

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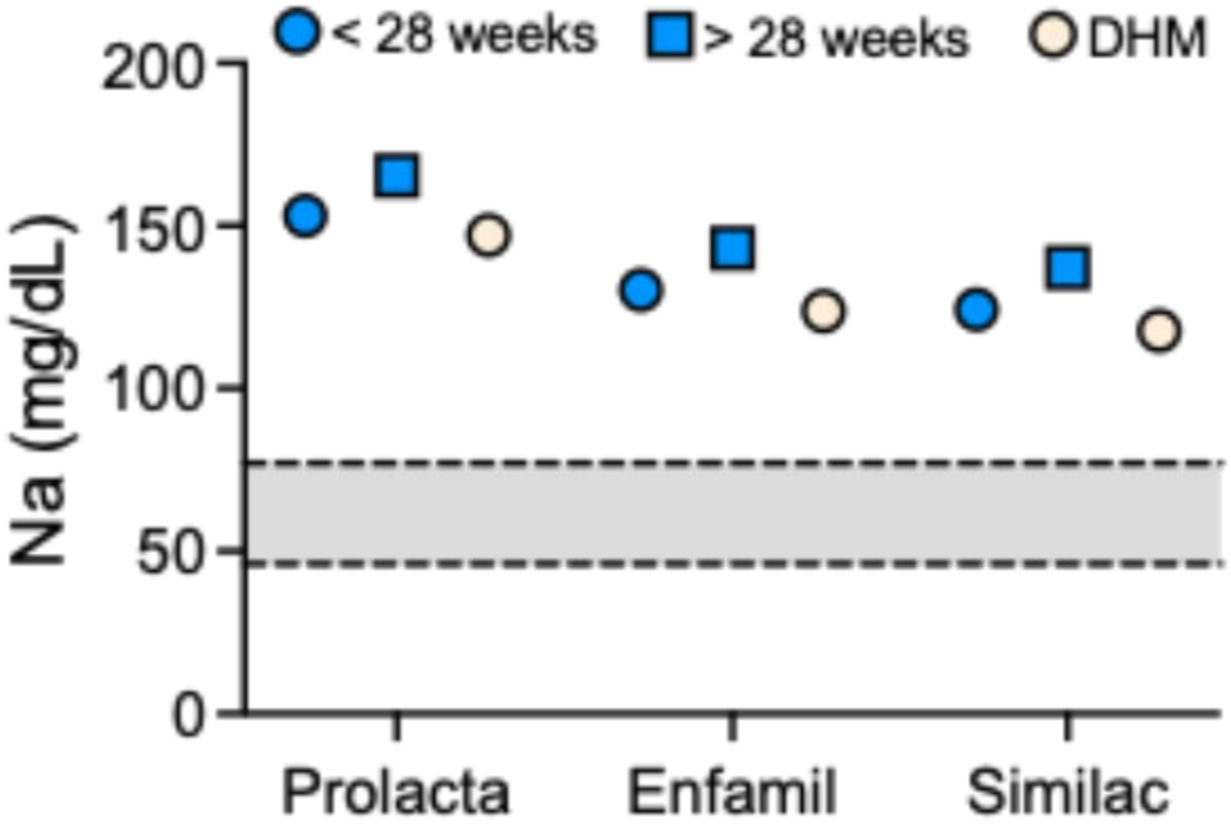

5 – 7
meq/kg/day

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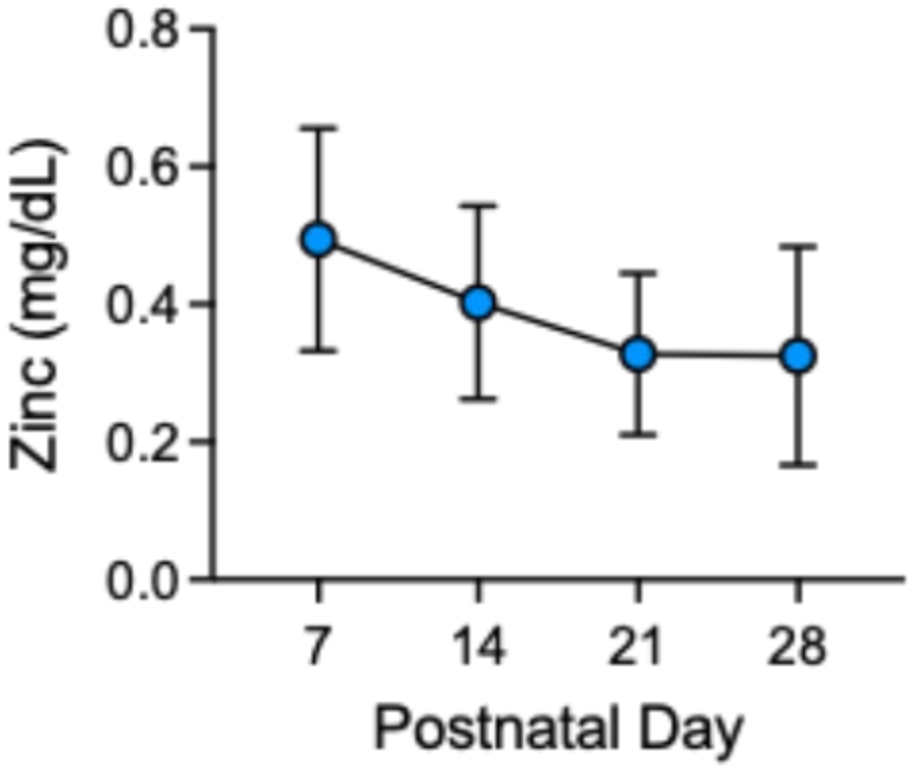
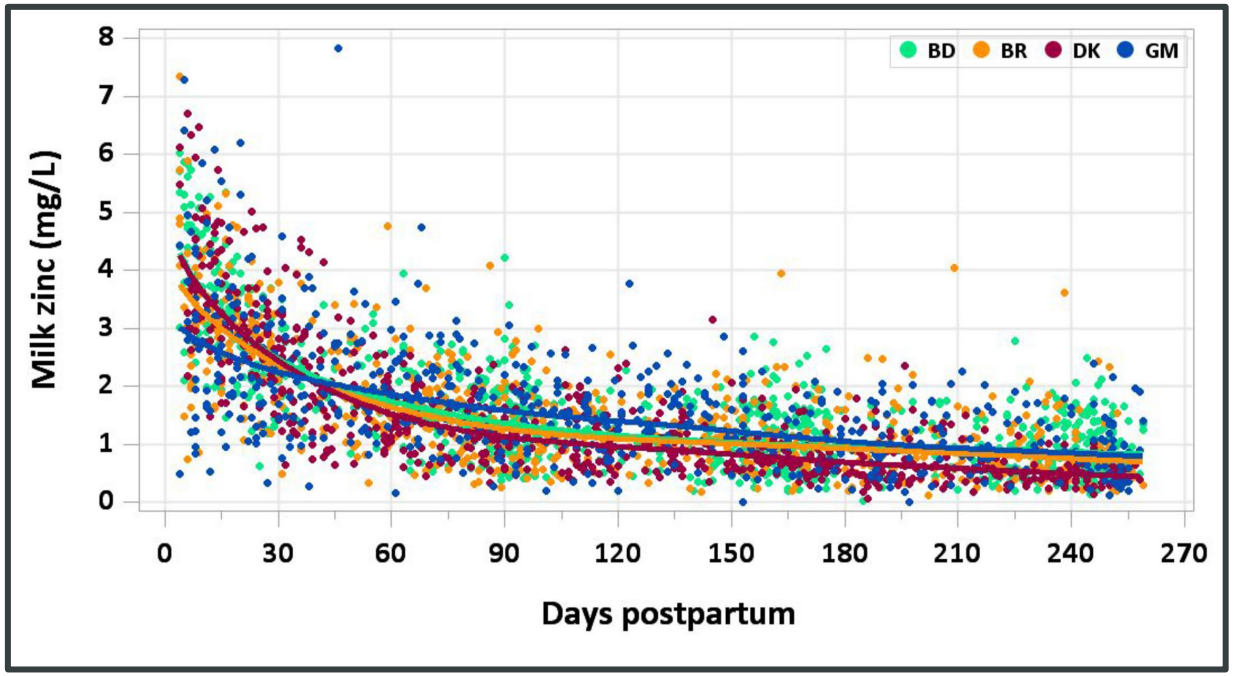
PRETERM MOM: ZINC



MILQ Consortium



Allen et al. *Adv Nutr.* 2025; Gates A et al. *Am J Clin Nutr.* 2021;114(5):1719-1728.

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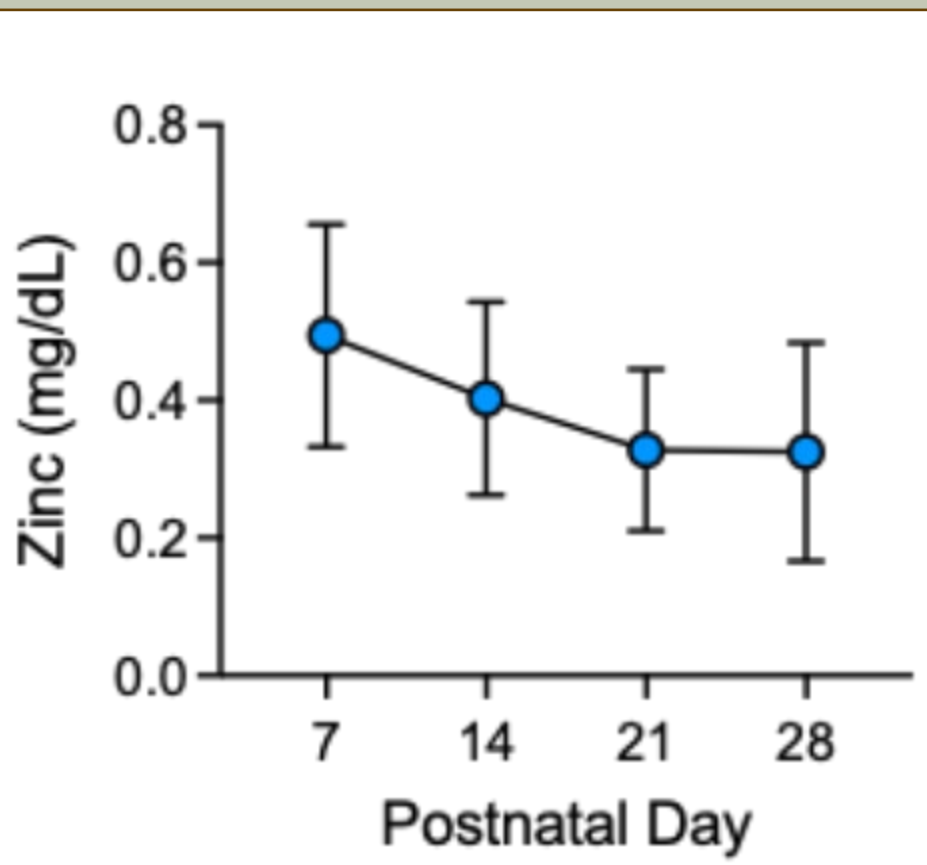

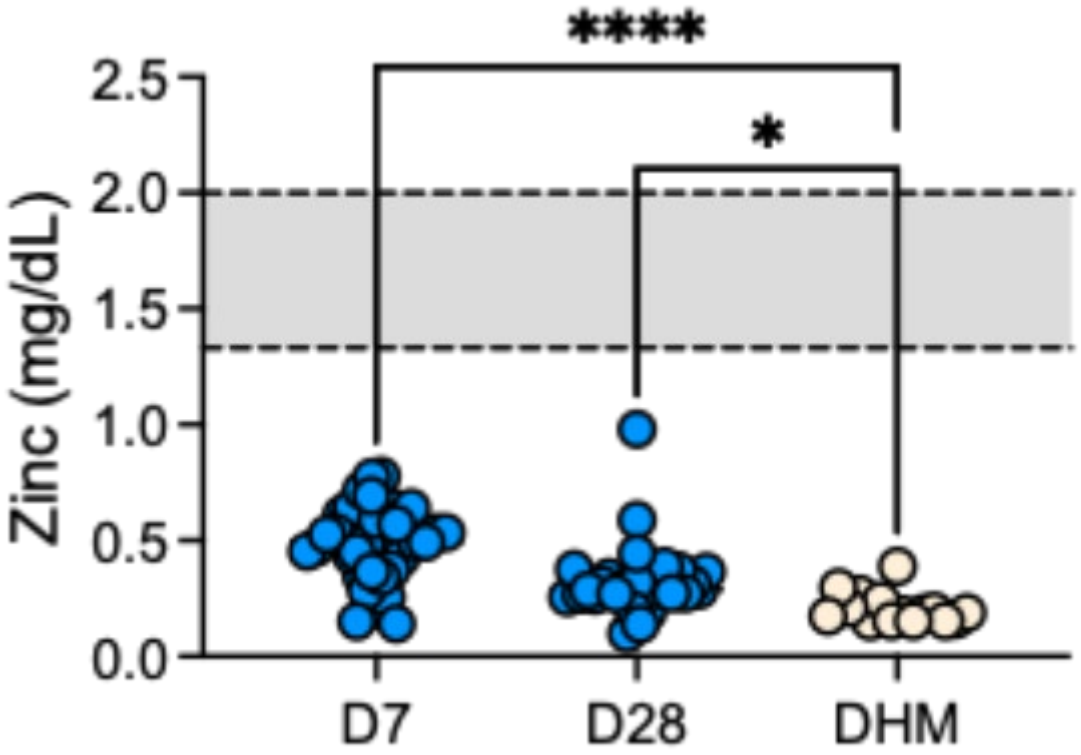

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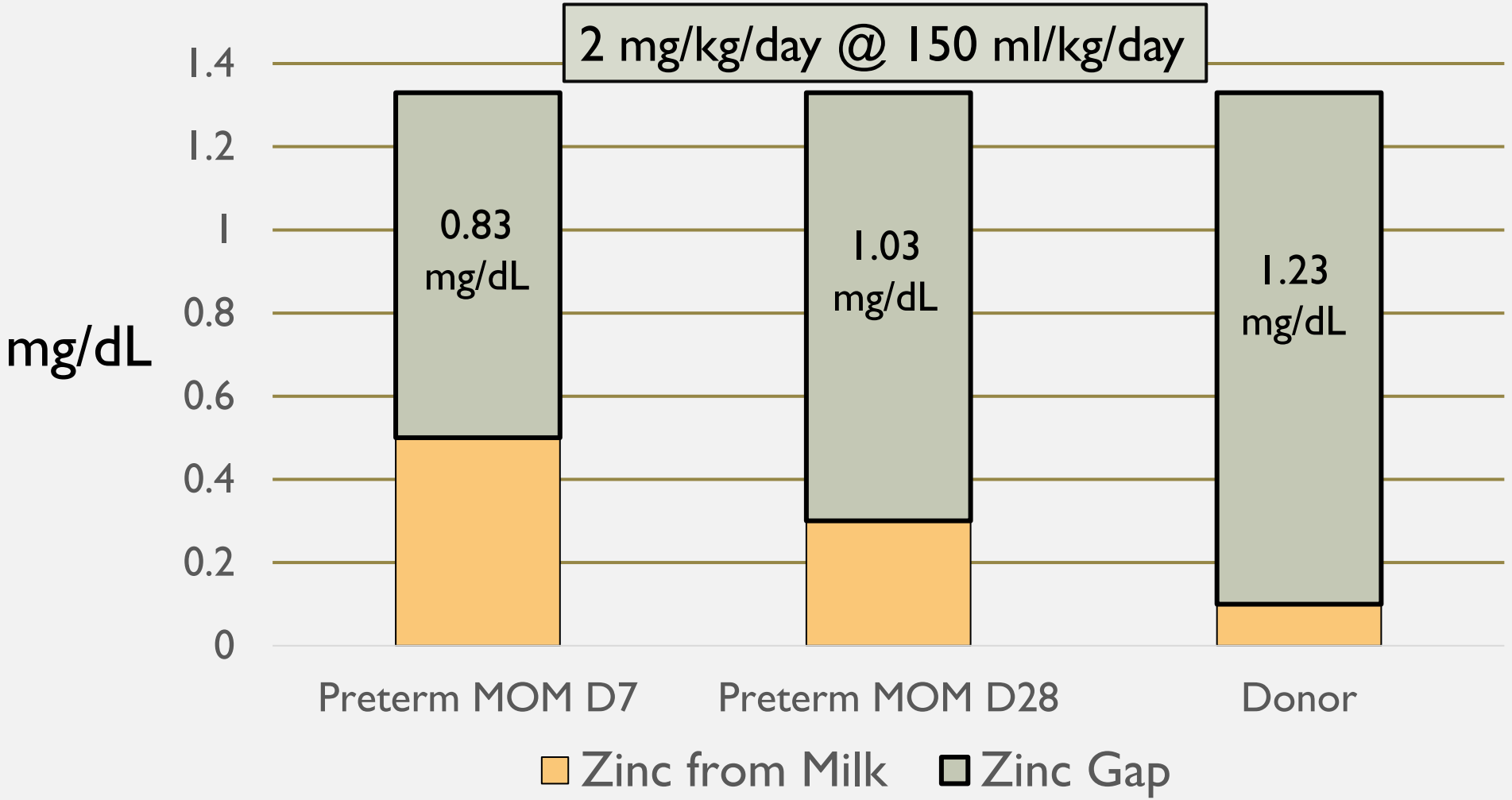
GAPS IN NUTRITION: ZINC



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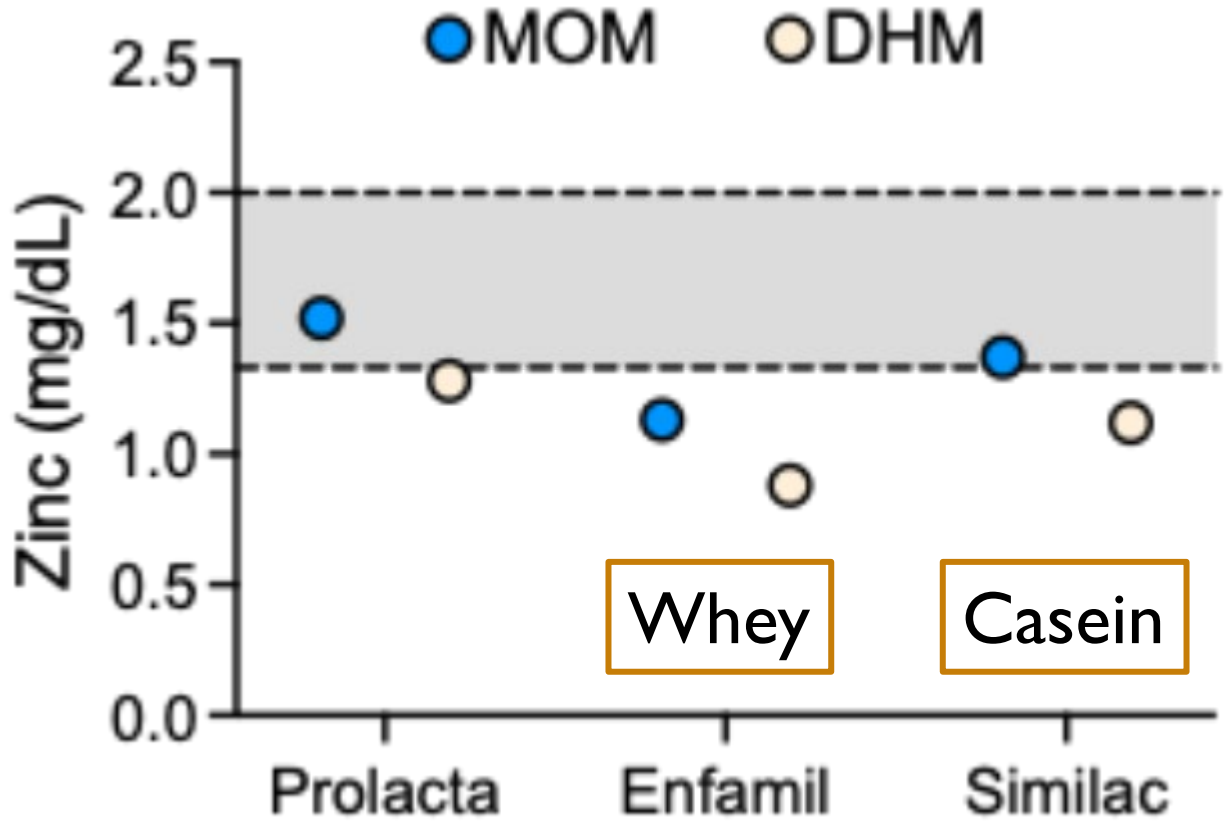
ZINC & HUMAN MILK FORTIFICATION

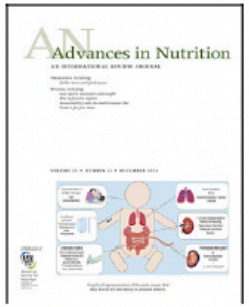


1 mg/day

ZINC SUPPLEMENTATION

American Society for Nutrition
Excellence in Nutrition Research and Practice

Advances in Nutrition
AN INTERNATIONAL REVIEW JOURNAL
journal homepage: https://advances.nutrition.org/



Review

Tracing Zinc's Role in Preterm Infants' Health: A Narrative Review

Alessandra Consales [1], Carlo Agostoni [1,2,*], Roberta Cazzola [3], Roberta Ottria [3], Maria Lorella Giannì [1,4]

EMERGING DATA: ENTERAL ZINC SUPPLEMENTATION

- In a meta-analysis of 8 RCTs that enrolled 742 preterm infants, **growth benefits of zinc supplementation** included:[1]
  - Increased weight gain
  - Increased linear growth
  - Higher motor development scores

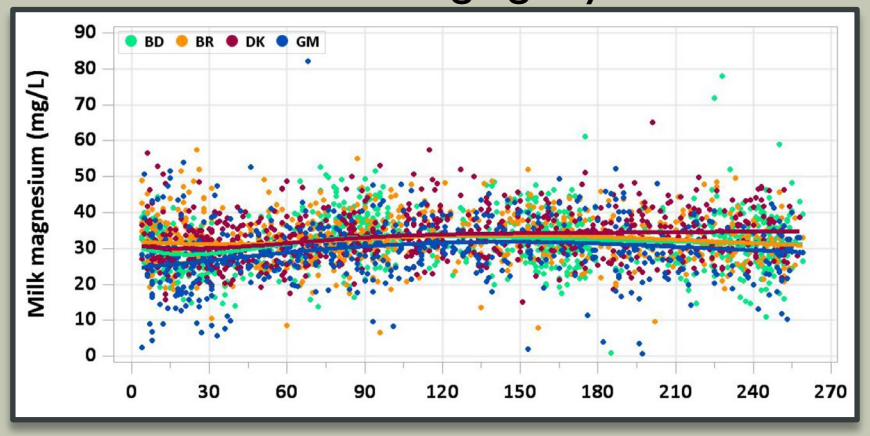
- In a separate meta-analysis of 5 RCTs and quasi-RCTs that enrolled 482 preterm infants, **morbidity and mortality benefits** of zinc supplementation included:[2]
  - Moderate decrease in all-cause mortality
  - No effect on NEC or other common comorbidities

[1]. Alshaikh B et al. *J Perinatol*. 2022;42(4):430-439. [2]. Staub E et al. *Cochrane Database Syst Rev*. 2021;3(3):CD012797.

HUMAN MILK: OTHER NUTRIENTS

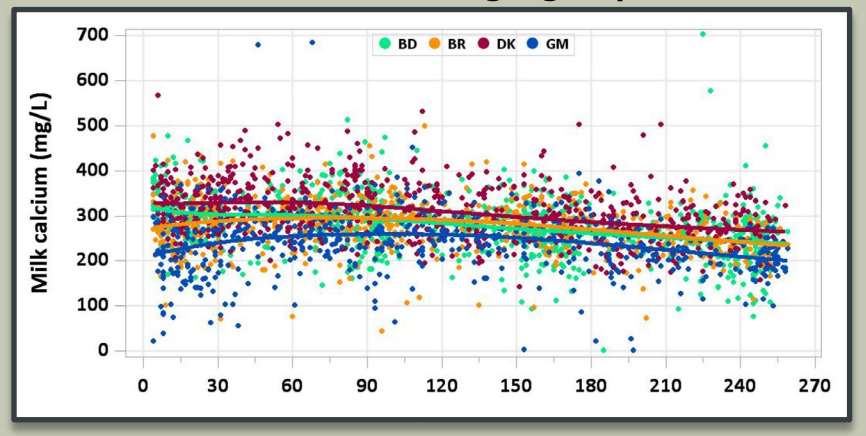
Mg

HMF: 8-9 mg/kg/day



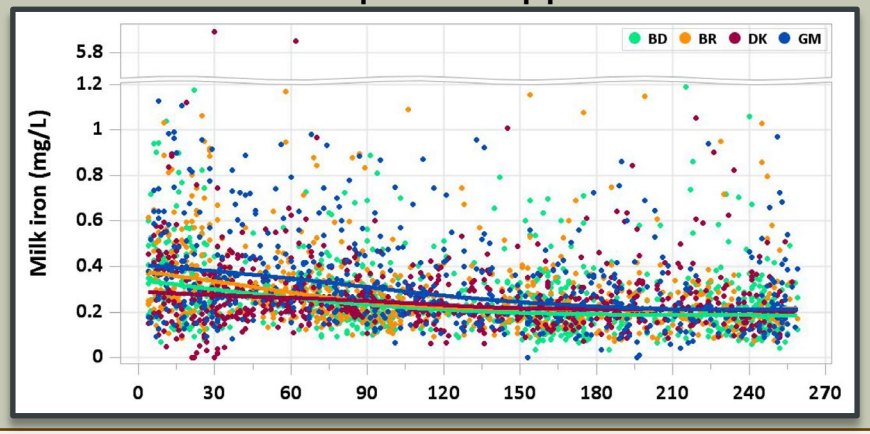
Ca

HMF: 120 mg/kg/day



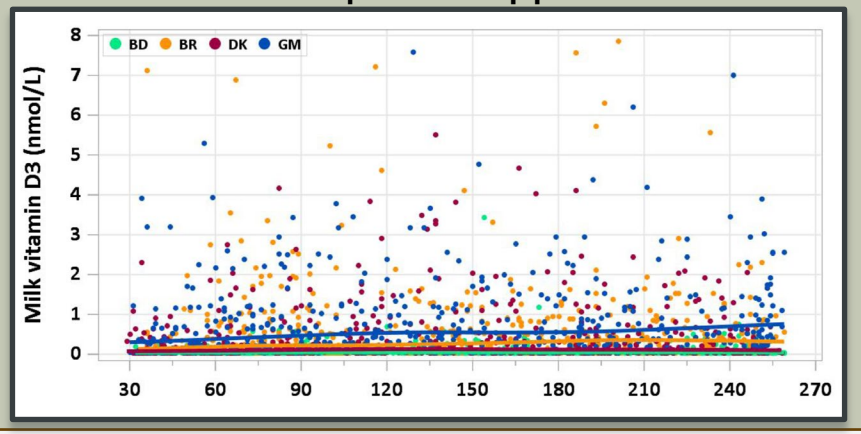
Fe

HMF: Requires Supplement*



D3

HMF: Requires Supplement



Allen et al. *Adv Nutr*. 2024

WHAT DO WE NOT KNOW

- Selenium: Beneficial in preventing late onset sepsis in 2 RCTs (2000 & 2016) providing 5-7 mcg/kg/day or 10 mcg/day, respectively

  Goal: 7-10 mcg/kg/day

  Preterm milk: 1.7 mcg/dL

  HMFs: not a significant source of Se

Lee et al. *Ann Clin Nutr Metabol.* 2023; Darlow et al. *J Pediatr.* 2000; Aggarwal et al. *J Trop Pediatr.* 2016

WHAT DO WE NOT KNOW

- Manganese: Highly concentrated in TPN and accumulates in the basal ganglia of preterm infants with prolonged TPN exposure

  RCT: No Mn in TPN did not alter plasma Mn levels

  Goal: 1-15 mcg/kg/day

  Preterm milk: 0.3-1 mcg/dL

  HMFs: 5-8 mcg/kg/day

Sauberan et al. *Nutr Clin Pract.* 2025

WHAT DO WE NOT KNOW

- Iodine: Important for thyroid hormone production

  RCT: Iodine supplementation (30 mcg/kg/day) was necessary to meet recommended delivery but no difference in T4/TSH values or neuro-developmental outcome

  Goal: 11-55 mcg/kg/day

  Preterm milk: 15 mcg/dL

  HMFs: Human HMF provides 17 mcg/dL but bovine HMFs do not provide iodine

Ares et al. *Eur J Pediatr*. 2021

KEY TAKEAWAYS

MINERAL AND TRACE ELEMENTS

- Sodium Supplementation
  - 1-4 meq/kg/day after 14 days of life
  - Improved growth and prevention of hyponatremia

- Zinc Supplementation
  - 1-2 mg/day
  - Improved growth and reduced mortality
  - Excessive Zn may affect copper

THANK YOU

LEARNING ASSESSMENT QUESTIONS

- All of the following statements regarding sodium are correct except?

a) Sodium supplementation improves weight gain in preterm infants

b) Donor human milk contains ~ 11 mg/dL (0.5 meq/dL) of sodium

c) Sodium content in preterm mother's own milk increases over time

d) When added to donor human milk, some human milk fortifiers may fail to meet the minimum daily sodium intake for preterm infants

LEARNING ASSESSMENT QUESTIONS

- All of the following statements regarding zinc are correct except?

a) The concentration of zinc in human milk declines over time
b) Zinc supplementation improves preterm infant growth
c) Zinc supplementation reduces all-cause mortality in preterm infants
d) Whey protein binds to zinc and reduces its bioavailability