Nutritional Care of the Preterm Infant: International Guidelines

Miami Neonatology 2022—46th Annual International Conference

Presented by
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Learning Objectives

- Define adequate nutrient intakes to meet physiological requirements for growth, health, and development in the individual preterm infant

- Recognize the importance of early introduction of nutrition in preterm infants through fortification of human milk formula that includes DHA and ARA

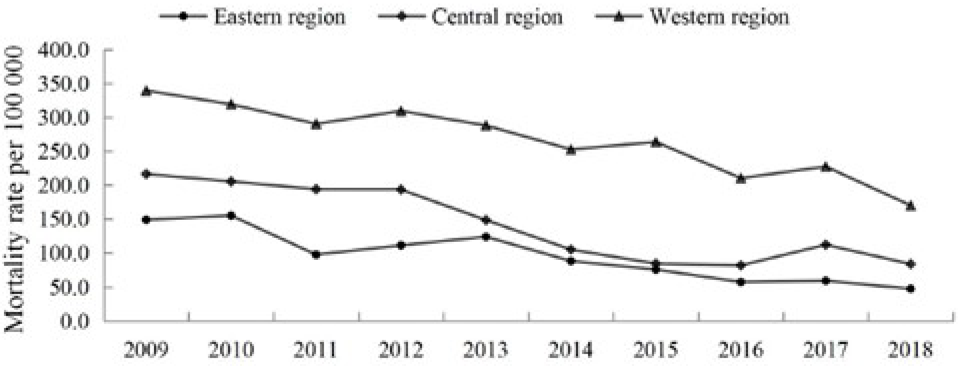
Increased attention to preterm nutritional care

- **Improved survival** of preterms globally *(partic. very/extremely preterms)*

➔ **Long-term outcome** gets greater attention

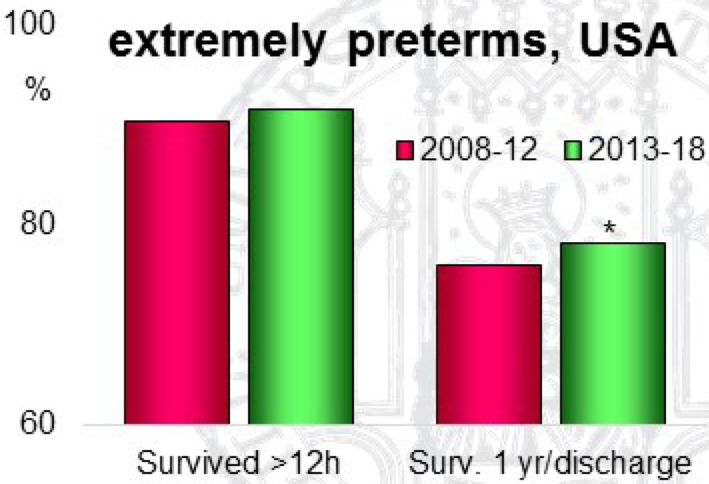
➔ **Greater focus on nutritional care** *which markedly affects outcome*

Preterm mortality declines, China



Yu X et al, PLoS One 2021;16(12):e0260611.

Increased survival of extremely preterms, USA



Bell EG et al, JAMA 2022;327(3):248-63

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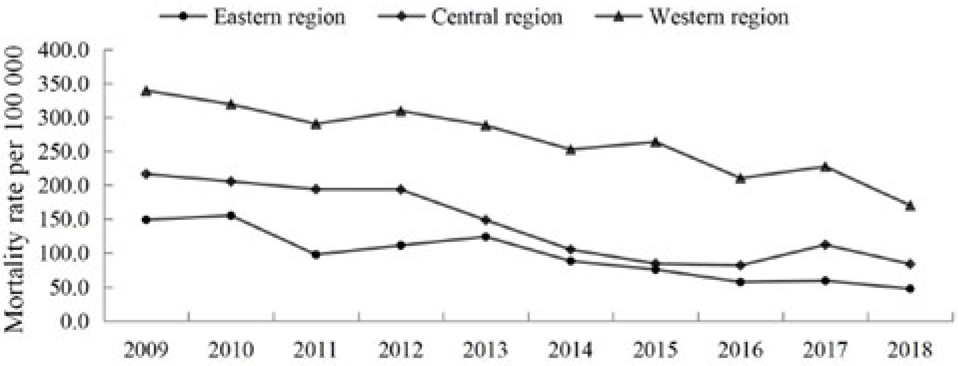

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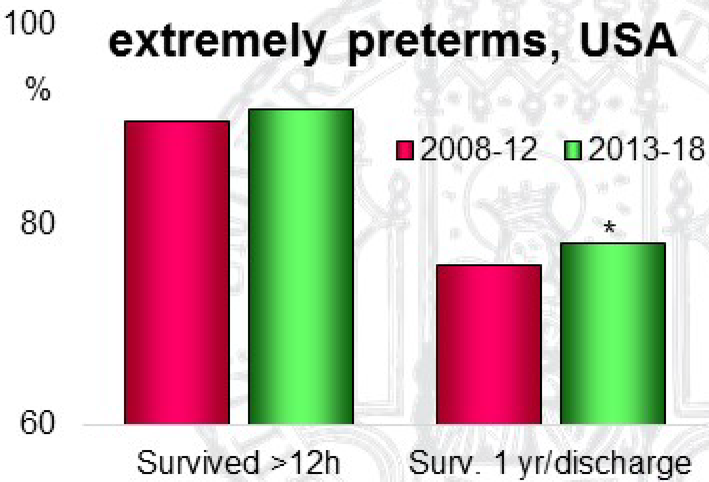

Bell EG et al, JAMA 2022;327(3):248-63

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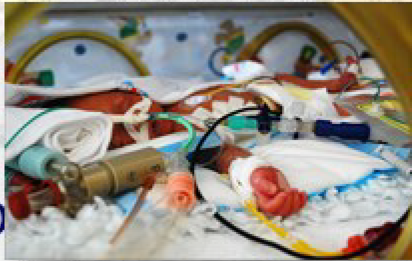
New / revised recommendations, e.g.

- Practice parenteral nutrition (PN) from day 1 with more amino acids & phosphorus
- Early lipid emulsion / higher supply of long chain PUFA
- More emphasis of meeting protein needs
- Prioritize own mother‘s milk with fortification
- More attention to feeding after discharge, and mo



Defining recommended nutrient intakes

- Goal: meet physiological requirements to maintain normal growth, health and development
- Systematic review of scientific evidence: for several nutrients lack of conclusive studies ⇨ uncertainties on adequate intakes
- For several nutrients, needs are related to weight gain velocity

Body weight	Desired weight gain (g/kg &d)
< 1500 g	17-21
1500-2000 g	14-17
2000-2500 g	12-14
2500-3000 g	10-13

Koletzko B et al, Defining nutritional needs of preterm infants. In: Koletzko B et al (eds). Nutritional Care of Preterm Infants, Karger, Basel, 2nd. ed. 2021, World Rev Nutr Diet 122.

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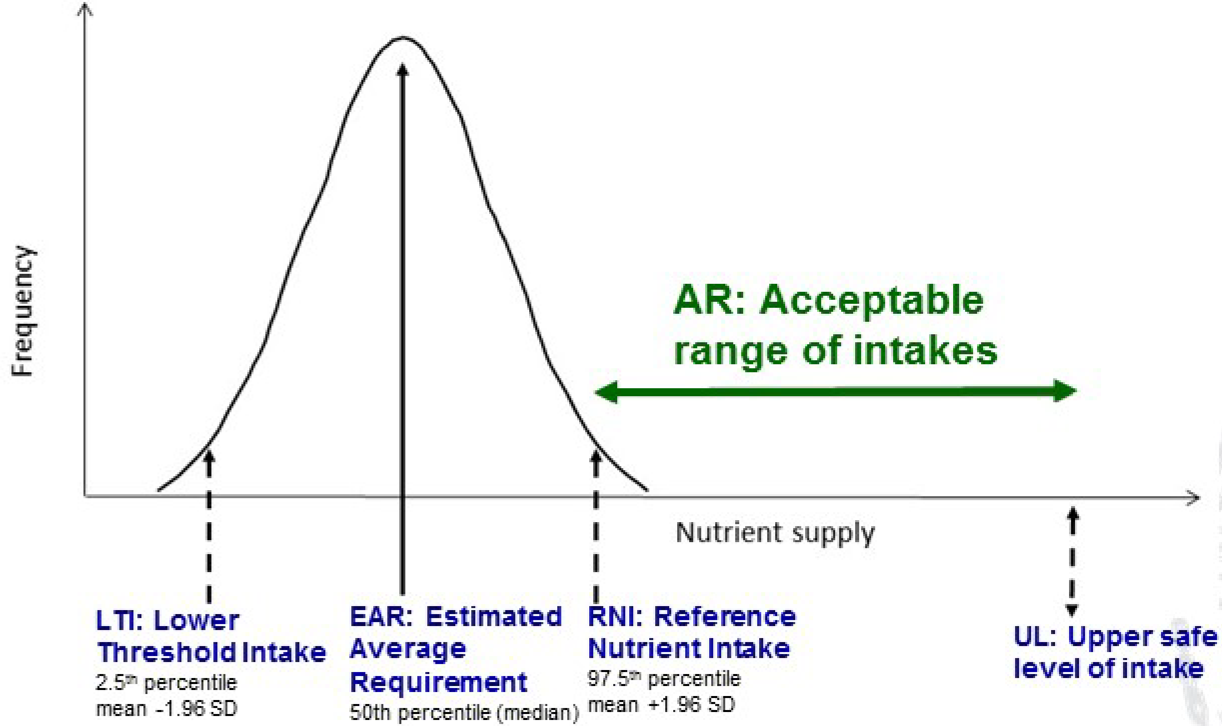
Nutrient intake recommendations refer to preterm populations, not individuals



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Take-home messages: RNI

- Reference nutrient intakes (RNI) refer to stable growing preterm infant populations, based on current body weight categories
- For most nutrients, needs are proportional to growth rates *(few exceptions e.g. water, fat)*
- Nutrient intakes below RNI may be ok during the early postnatal phase prior to full feeding, and during critical illness
- Needs of individual preterm infants may markedly deviate from population reference intakes

Koletzko B et al, Defining nutritional needs of preterm infants. In: Koletzko B et al (eds). Nutritional Care of Preterm Infants, Karger, Basel, 2nd. ed. 2021, World Rev Nutr Diet 122.

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Research opportunities: RNI

- Great opportunities to reduce knowledge gap on nutrient needs in different subgroups of preterm infants
- Application of current methods and technologies can limit the burden on infants participating in such studies
- Neonatologists, researchers & funding agencies should invest in studies to advance solid knowledge on optimal nutrition of preterms, to support their optimal health and development

Koletzko B et al, Defining nutritional needs of preterm infants. In: Koletzko B et al (eds). Nutritional Care of Preterm Infants, Karger, Basel, 2nd. ed. 2021, World Rev Nutr Diet 122.

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Margarita: a nutritional emergency

- Born preterm, 28 wks, 1000 g birthweight
- Her body consists of:
  - Water 850 g
  - Protein 100 g
  - Lipid 20 g *(structural lipid, no subcutanous fat)*
  - Glycogen absent
- No utilizable energy stores ⇨ without immediate feeding
  ⇨ high loss of body protein for energy production
  ⇨ nutritional emergency

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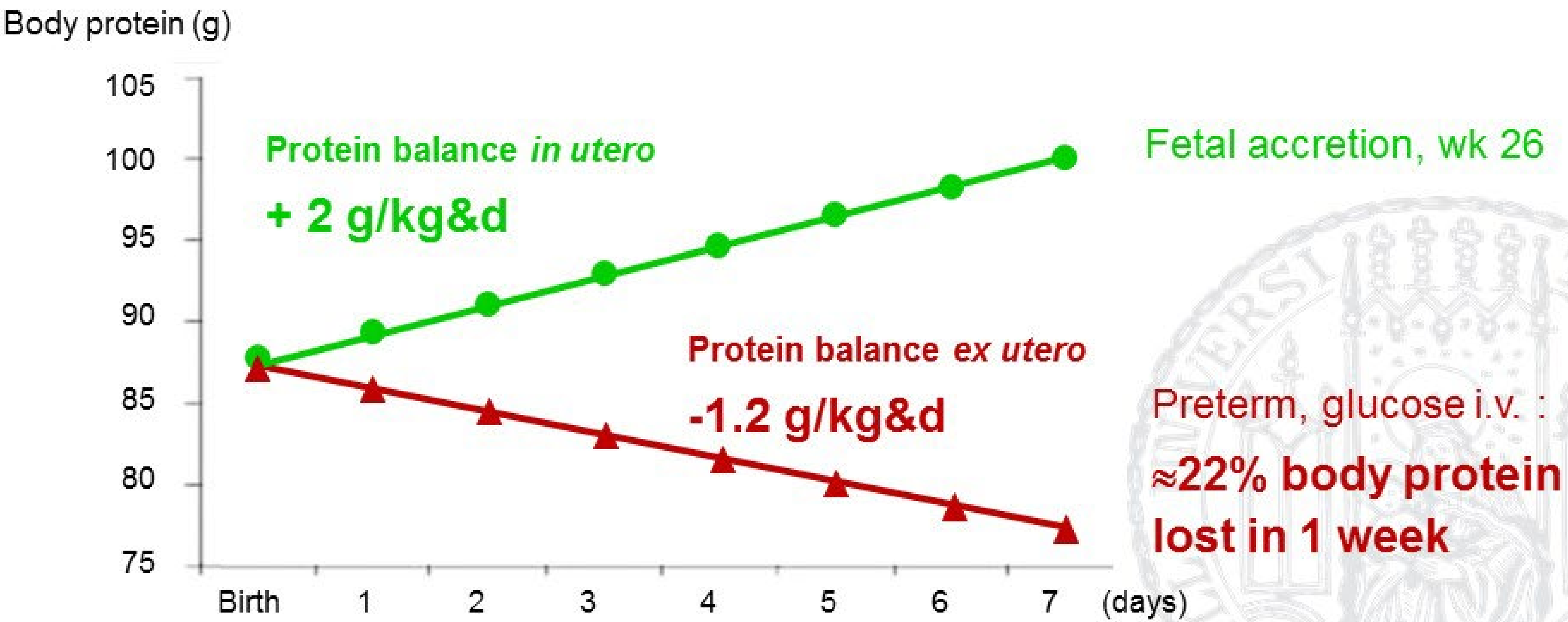
Importance of early supply

Fetal amino acid supply via the placenta ≈3.5-4.0 g/kg&d



Denne SC & Poindexter BB, Sem Perinat 2007; Embleton ND & v d Akker CHP, Sem Perinat 2019

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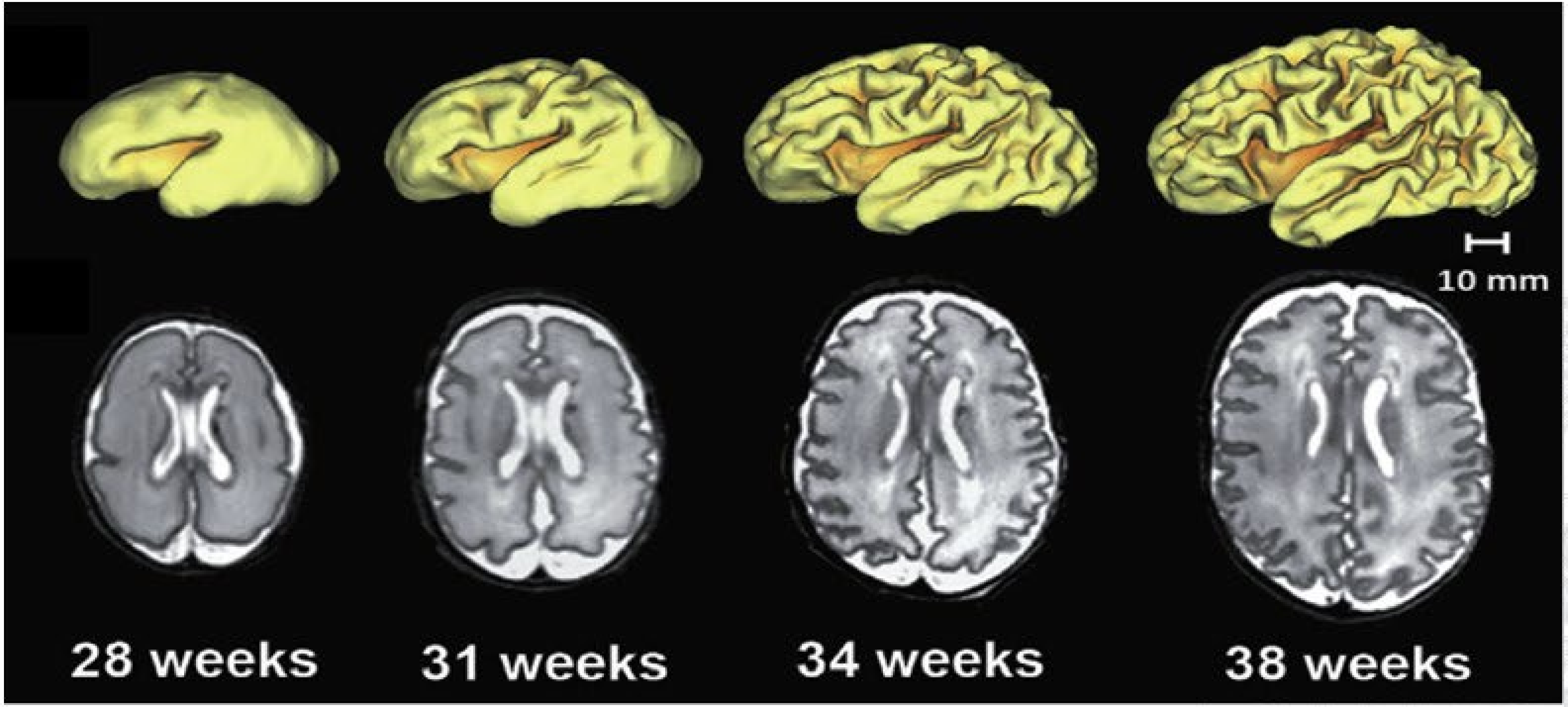
Brain growth needs substrates incl. amino acids



28 wks ≈140 g

term birth ≈400 g

Smyser et al, J Paediatr Child Health 2012.

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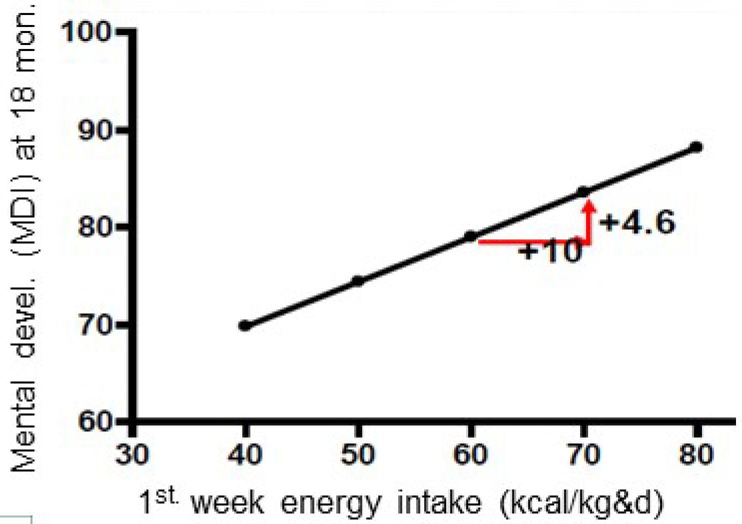
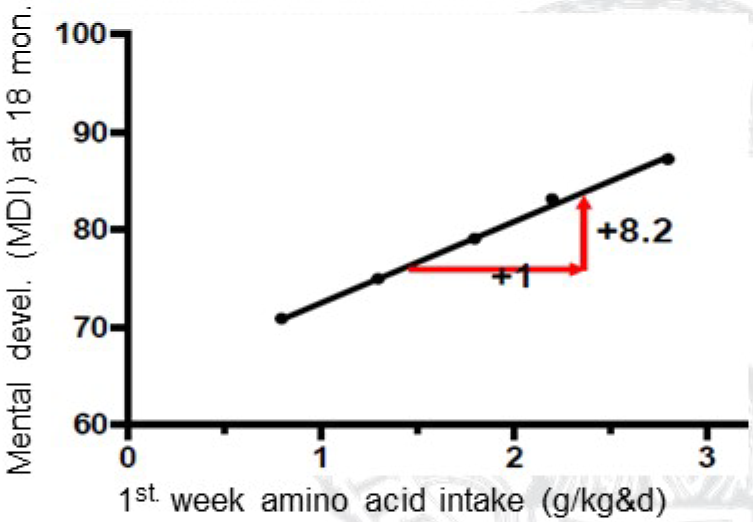
1st. week of life energy & amino acids ⇨ ↑ MDI

Week 1 energy & protein intakes in 124 ELBWI, adj. for confounders, each independently associated with Mental Development Index (MDI) at 18 mon.

- plus 10 kcal/kg& d ⇨ ↑ **4.6 points MDI**
- plus 1 g amino acids/kg&d ⇨ ↑ **8.2 points MDI**





Stephens BE et al. Peds. 2009.

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Lean body mass in very preterms predicts brain volume and white matter microstructure

- 85 infants born <33 wks' GA: each unit Z-score **lean mass** predicts larger total **brain volume** (10.5 cc, 95% CI 3.8-17.2), **cerebellum volume** (1.2 cc, 95% CI 0.5 to 1.9), **white matter** (4.5 cc, 95% CI 0.7 to 8.3); and **white matter microstructure** *[greater fractional anisotropy of white matter tracts in the left cingulum (0.3%, 95%CI 0.1% to 0.6%), right uncinate fasciculus (0.2%, 95% CI 0.0% to 0.5%), and right posterior limb of internal capsule (0.3%, 95% CI 0.03% to 0.6%)]*
- Z-scores **fat mass not associated** with any outcome.

Bell KA, Arch Dis Child Fetal Neon 2022; doi: 10.1136/archdischild-2021-321653.

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Human milk protein & energy in hospital predicts preterm brain growth until term

Effect on brain volume @term (cm³)	Total brain volume	Cortical grey matter	Deep grey matter	White matter
Protein intake >80 th. perc. vs. ≤80 th. perc	**+ 36.0** (7.1, 64.8) p=0.02	**+ 22.2** (6.7, 37.8) p=0.006	**+ 1.5** (0.1, 2.9) p=0.04	18.8 (-10.0, 47.6) n.s.
Energy intake >80 th. perc. vs. ≤80 th. perc	**+ 30.9** (5.5, 56.4) p=0.02	**+ 15.3** (0.8, 19.9) p=0.04	1.0 (-1.0, 3.2) n.s.	**+ 22.9** (12.2, 33.4) p<0.001

50 preterms born 28.2±2.4 wks GA fed excl. or predominantly MOM with standard dose multicomponent bovine milk fortifier, with analysis of ≥10 milk samples (MIRIS) during hospitalization and brain MRI at term equivalent (Boston, MA, USA). Data analysis adj. for GA at birth, sex, birthweight SDS, postmenstrual age @MRI, composite variable for comorbidities representing NEC, sepsis, PDA, respiratory support at 36 wks, & postnatal steroids; and accounted for non-independence of twins

Bell KA et al, Children 2022;9:969.
doi: 10.3390/children9070969.

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Protein & energy supply to match fetal growth

Weight (g)	500-1000	1000-1500	1500-2200	2200-3000
Fetal wt gain (g/kg&d)	19.0	17.4	16.4	13.4
Protein (g/kg&d)	**4.0**	**3.9**	**3.7**	**3.4**
Energy (kcal/kg&d)	106	115	123	130
Protein/100kcal (g/100 kcal)	**3.8**	**3.4**	**3.0**	**2.6**

Ziegler, World Rev Nutr Diet. 2014

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Cochrane: aim at >2 - 3 g amino acids/kg&d i.v.

- **Higher i.v. amino acids** >2 to ≤3 g/kg&d vs. ≤2 g/kg&d *(32 studies)*:
- **Less SGA at discharge** RR 0.74 (95%CI 0.56-0.97)
- **Regain birth weight faster** -1.14 d (95%CI -1.73 - -0.56)
- **Head circumference** gain +0.09 cm/week (95%CI 0.06 -0.13)
- **Less hyperglycaemia** >8.3 mmol/L/150 mg/dL, RR 0.69 (95%CI 0.49-0.96)
- **Less ROP** RR 0.44 (95%CI 0.21-0.93)
- No adverse effects (mortality, late-onset sepsis, NEC, chronic lung disease, intravent. haemorrhage, periventricular leukomalacia)

THE COCHRANE COLLABORATION

TWL Cochrane.png by Wikipedia Pages, screenshots by Ocaasi licensed under CC BY_SA 3.0

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Osborn et al, Cochrane Database Syst Rev 2018.

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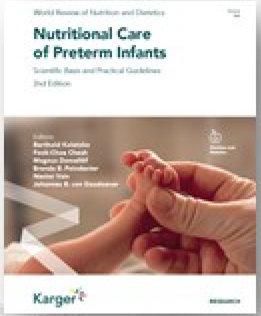
Very preterms: parenteral amino acids from day 1



- Start i.v. amino acids **from birth at 1.5-2.5 g/kg&d**
- Increase within few days **to 3.5-4 g/kg&d**
- Aim at providing **>65 kcal/kg&d** *(limit amino acid oxidation)*
- Provide phosphate (equimolar with Ca)
- Do not taper i.v. amino acids prior to EN ≈75 ml/kg&d

Amino acid supplies >4 g/kg&d are not recommended (no demonstrated benefits, no sufficient documentation of safety e.g. plasma amino acids, BUN, acidosis)

van den Akker CHP et al, in: Koletzko B et al, Nutritional Care of Preterm Infants, 2nd. ed. 2021, World Rev Nutr Diet 122.

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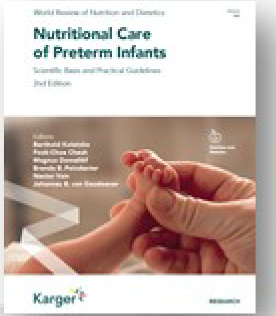
Increased amino acids ⇨ increase P



- Higher initial amino acid (AA) supply enhances tissue uptake of P and Ca turnover
- Higher early AA supply induces greater need for P
- **Early parenteral AA ⇨ early P supply**

	mmol/kg&d	mg/kg&d
PN, first days	**1 – 2**	31 – 62
PN, stable growth	**1.25 – 3**	39 – 93
Enteral feeding	**2.3 – 3.9**	70 – 120

Taylor SN, in: Koletzko B et al, Nutritional Care of Preterm Infants, 2nd. ed. 2021, World Rev Nutr Diet 122.

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How long PN? Delaying enteral feeds?

Cochrane review, 14 RCTs (1551 very preterm/VLBWI),

delayed (≥4 d after birth) vs. **earlier** introduction of progressive enteral feeds

	RR	95%CI
NEC	0.82	0.58-1.14
Mortality to discharge	0.97	0.7-1.36
Feed intolerance	0.81	0.68-0.97
Invasive infection	**1.44**	1.15-1.8

Delayed enteral feeding

⇨ **NEC & mortality unchanged**

⇨ **More invasive infections**

THE COCHRANE COLLABORATION

TWL Cochrane.png by Wikipedia Pages, screenshots by Ocaasi licensed under CC BY_SA 3.0

Young L et al, Cochrane Database Syst Rev 2022 Jan 20;1(1):CD001970.

What to feed to preterms

- Mother's own milk (MOM)
- Donor human milk
- ~~Informally shared human milk~~
- Human milk fortifier
- Preterm formula
- ~~Term formula~~

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Feeding human milk reduces NEC risk

- 12 RCTs or quasi-RCTs comparing feeding formula vs. donor human milk in 1879 preterm or LBW infants
- Formula feeding (vs. human milk):

RR NEC: 1.87 *(95% CI 1.23, 2.85)*

NNT for 1 NEC case: 33 *(95% CI 20, 100)*

THE COCHRANE COLLABORATION

TWL Cochrane.png by Wikipedia Pages, screenshots by Ocaasi licensed under CC BY_SA 3.0

Quigley M et al, Cochrane Database System. Rev. 2019.

Mother's own milk & neurodevelopment at 7 yrs

586 preterm infants, 29.6±2.3 wks GA, neurodevelopment @7 yrs adj. for mat. education & occupation, # adults & children in the home, mat. smoking & alcohol use, parity, race, birth weight, GA, plurality, antenatal steroids, DHA suppl., and center

- **Higher MOM intake** during neonatal hospital stay: higher performance **IQ** (+0.67 points/25 mL/kg&d), **reading** scores (+1.14 points/25 mL/kg&d), **math** scores (+0.76 points/ 25 mL/kg&d), **fewer ADHD** symptoms (-1.08 points/25 mL/kg&d)

- Longer duration of MOM intake: better reading (+0.33 points/mon), spelling (+ 0.31 points/mon), and math (+0.30 points/mon)

- Stronger associations in infants born <30 wks (interaction *P* <.01)

Belfort MB, et al, JAMA Netw Open. 2022;5(7):e2221608. doi:10.1001/jamanetworkopen.2022.21608.

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Mother's own milk & neurodevelopment at 5 yrs

2467 VLBWI, German neonatal network, median 27.9 (26.1-29.4) weeks GA, 980 (745-1220) g, breastfed < 3mon (n=298) or >3 mon (n=2169). @≈5 yrs DQ & Wechsler III IQ adj. for confounders incl. mat. education, GA, BPD & cerebral palsy

Breastfeeding ≥3 mon. vs. < 3 mon.	**Adjusted effect** (95 % CI)
Full scale IQ	**+2.2** (0.45, 3.97)
Conduct problems	**-0.25** (-0.47, - 0.03)
Hyperactivity / inattention	**-0.46** (-0.81, -0,10)

Härtel C et al, Nutrients 2020;12:3278. doi:10.3390/nu12113278.

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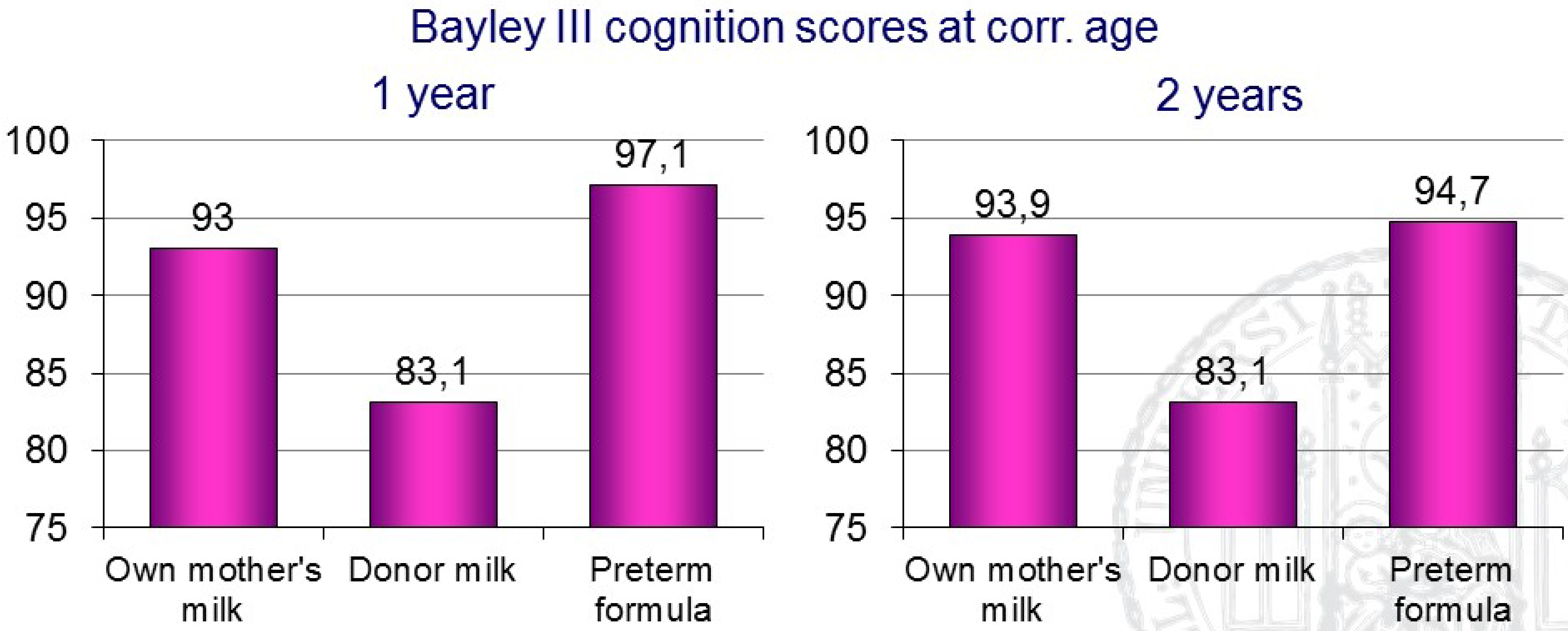
Cognition: donor vs. own mother's milk differ



81 preterms, GA 27,1 wks, Tufts Med Center Boston. Donor milk from Mother's Milk Bank of New England

Madore et al, Clin Ther 2017.

Donor milk $\neq$ mother's own milk (MOM)

Preterms 22-36 wks PCA before (n=139) vs. after (183) donor human milk bank

	No donor milk	Donor milk	P
Time to full enteral feeds, d	21.0 (14.5–31.0)	20.0 (14.0–28.0)	n.s.
Time to regain birthweigth, d	**11.0** (8.0–14.0)	**8.0** (3.0–11.0)	<0.001
SDS weight @37 wks/discharge	**−1.5** ± 0.8	−1.9 ± 0.7	<0.001

Donor milk ⇨ **less weight gain**

Wu T et al, Mat Child Nutr. 2002. doi: 10.1111/mcn.13319.

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MOM vs. donor milk: growth differs

- Single-center retrospective study, 314 infants ≤32 wks GA or ≤1800 g with NICU stay ≥7 days fed fortified human milk

- Per **+10% more donor human milk** vs. own mothers' milk **-0.17 g/kg&d weight gain** to 36 weeks GA or NICU discharge

- Per **+10% more donor human milk** vs. own mothers' milk **-0.01 cm/wk** adjusted **head circumference**

Donor milk ⇨ **less weight & head circumference gain**

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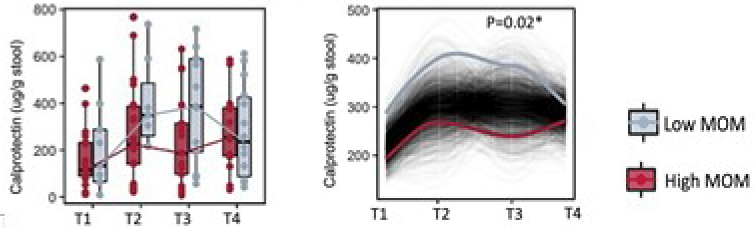
Brownell et al, JPGN 2018;67:90-6. doi: 10.1097/MPG.0000000000001959.

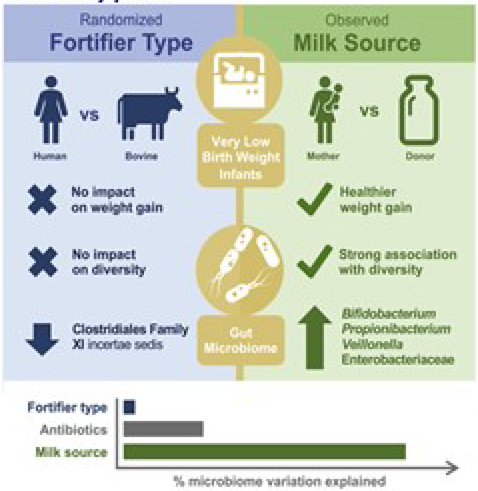
MOM vs. donor milk: different growth, microbiota & inflammation

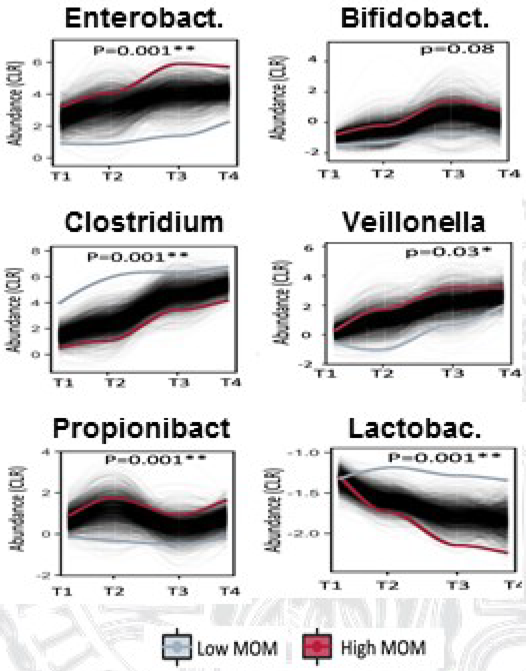
- 30 preterms, 26-30 wks GA, ≤1250 g bw, fed MOM and/or donor milk & randomized to bovine of human milk based fortifier
- **High MOM intake: higher weight gain** *vs. donor milk:* @35 wks GA/discharge weight f age -0.8 SDS *(IQR -1.1, -0.5)* vs.-1.7 *(-1.9, -1.4)*, p<0.001, *but no effect of fortifier type*
- **High MOM: lower Calprotectin & changed microbiota**

no effect of fortifier type

Fecal Calprotectin







Kumbhare SV et al, Cell Rep Med 2022;3:300712
doi: 10.1016/j.xcrm.2022.100712

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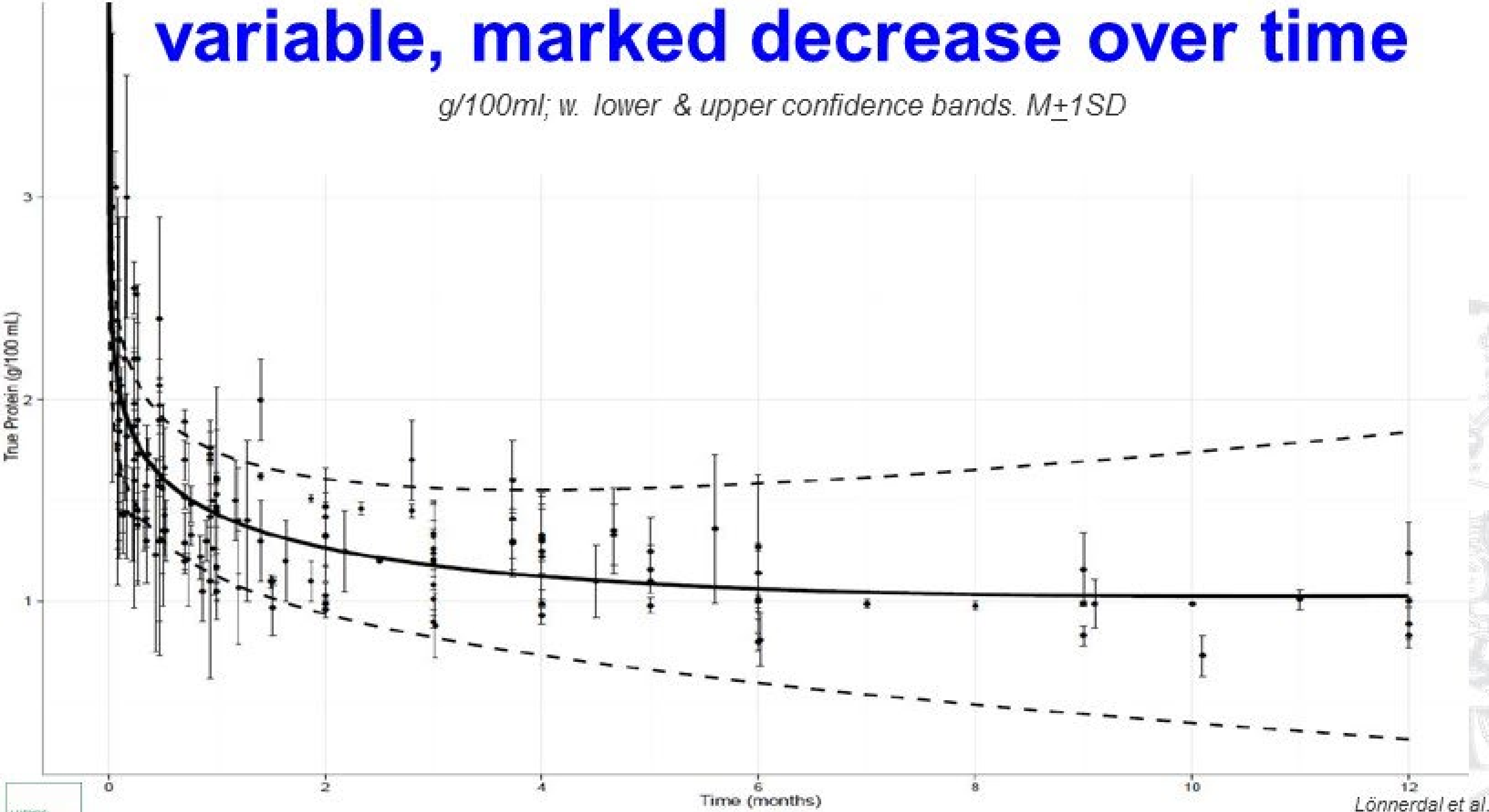
Human milk protein too low for preterms, variable, marked decrease over time

g/100ml; w. lower & upper confidence bands. M+1SD



Lönnerdal et al. 2016.

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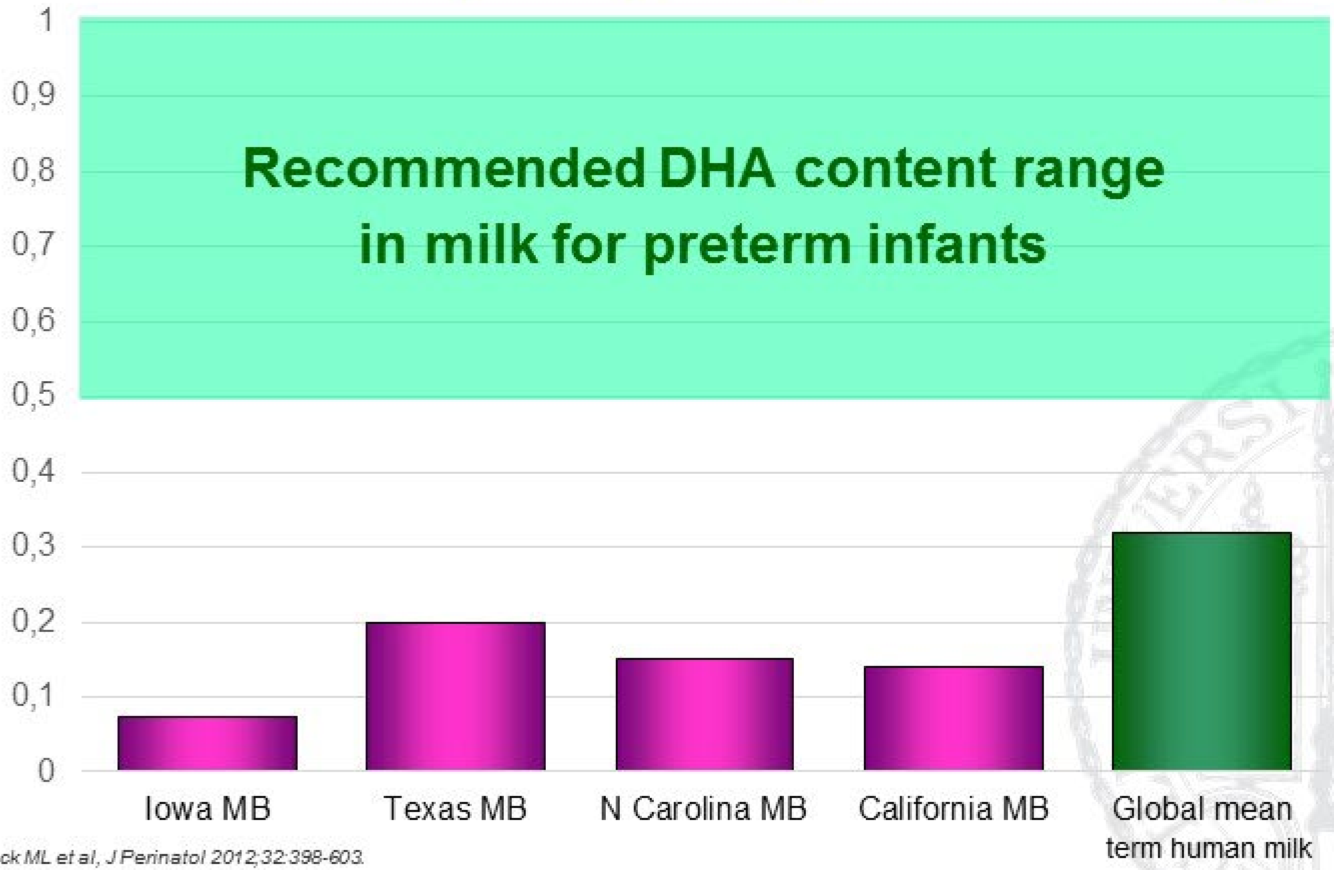
Donor human milk (USA) very low in omega-3 DHA



Baack ML et al, J Perinatol 2012;32:398-603.
Brenna JT et al. AJCN 2007;85:1457-64
Koletzko B & Lapillonne A. World Rev Nutr Diet 2021;122.

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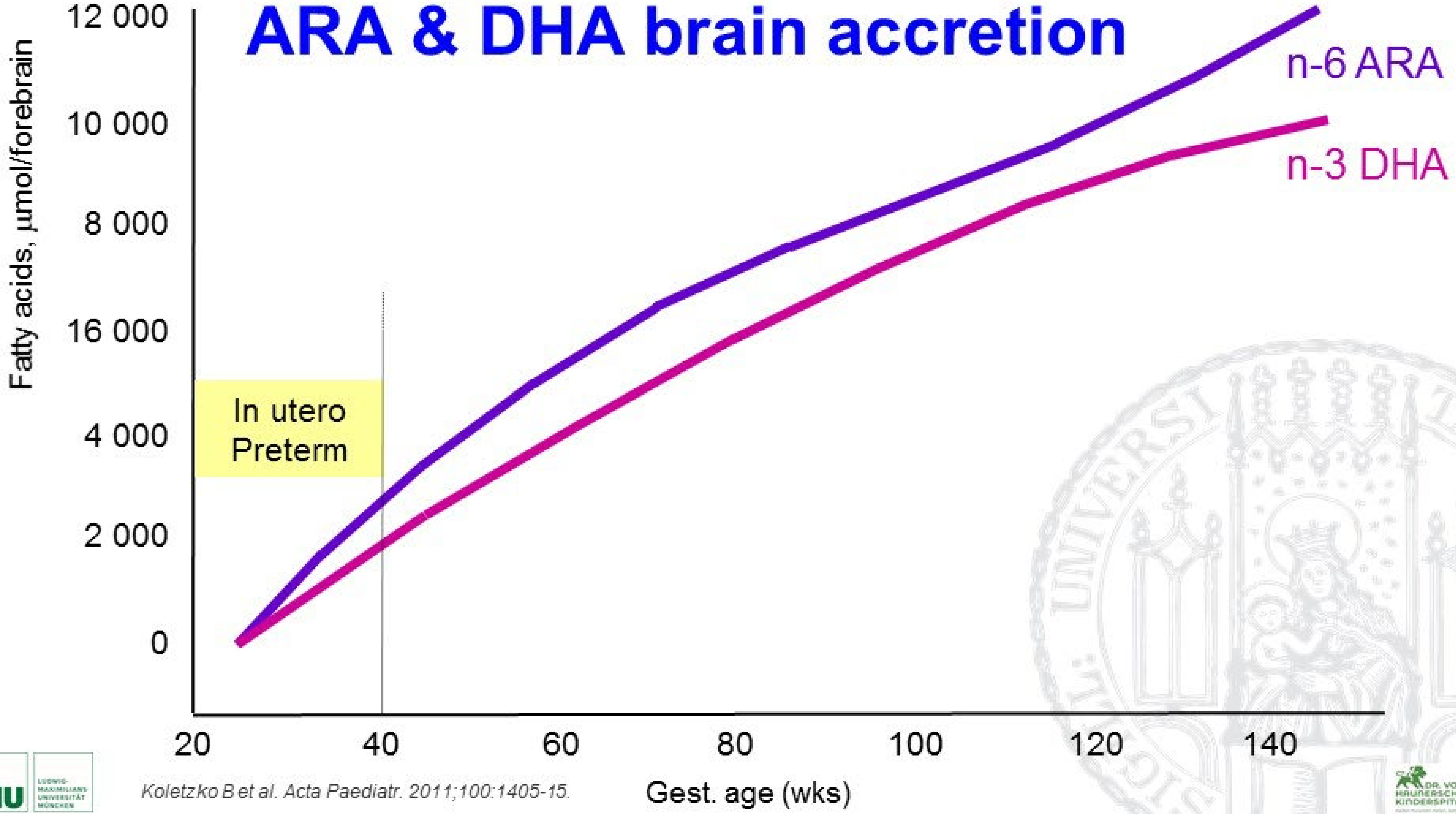
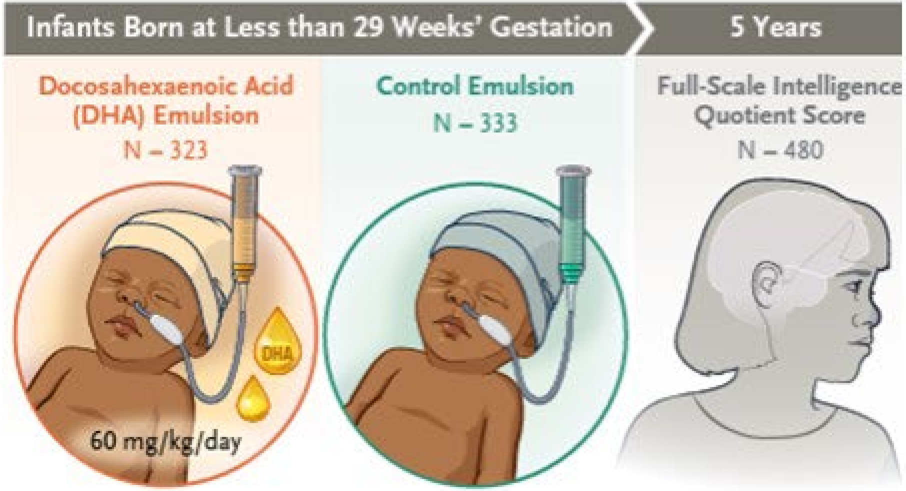
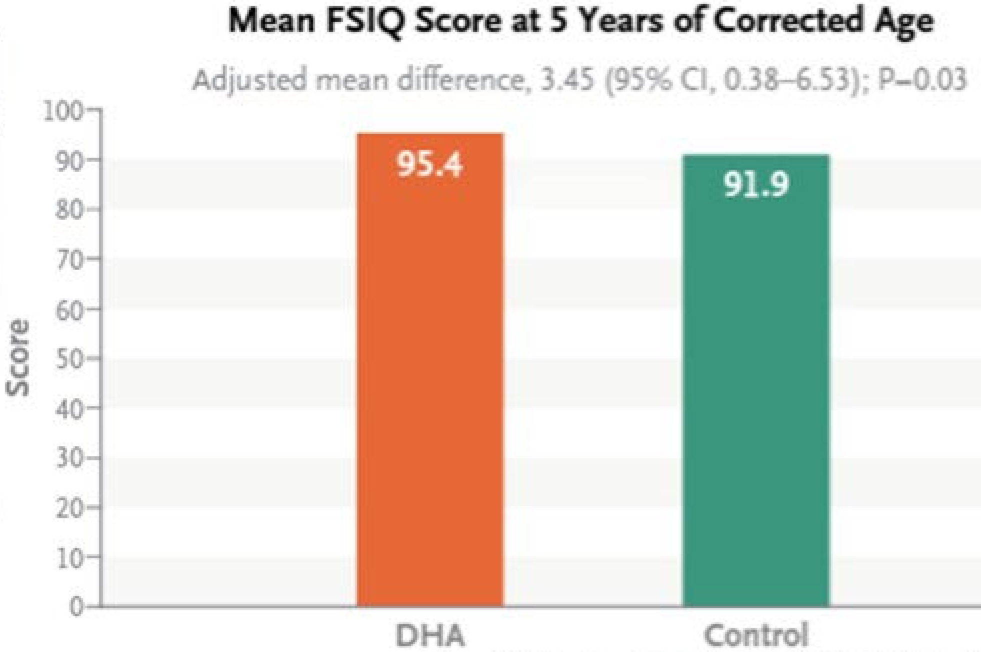
ARA & DHA brain accretion



Koletzko B et al. Acta Paediatr. 2011;100:1405-15.

RCT: +60 mgDHA/kg&d ⇨ ↑ IQ @ 5 yrs





No difference in adverse events

Gould JF et al, NEJM 2022;387:1579-88.

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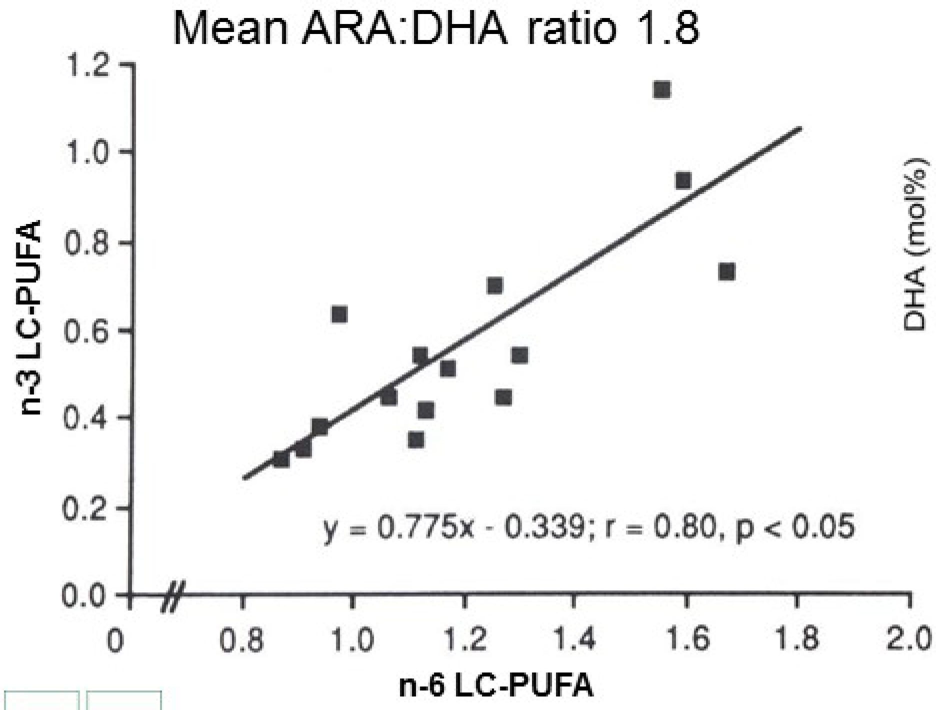
Human milk provides both n-6 ARA & n-3 DHA

Human milk for term infants

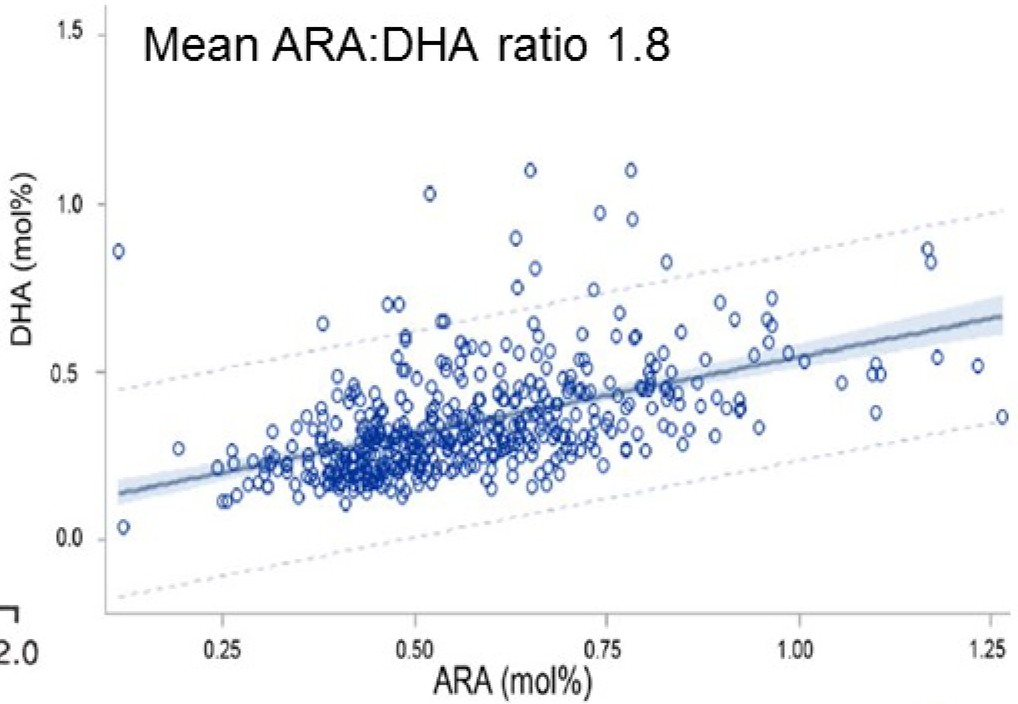
Germany



Koletzko B et al, Am J Clin Nutr 1988;47:954-9.

Human milk for preterm infants

Canada



Hopperton KE et al, Lipids. 2022. doi: 10.1002/lipd.12338

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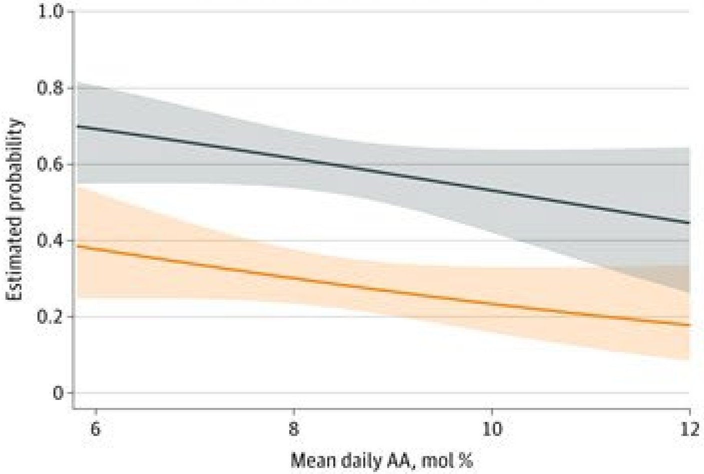
RCT: DHA + ARA supply reduces ROP risk

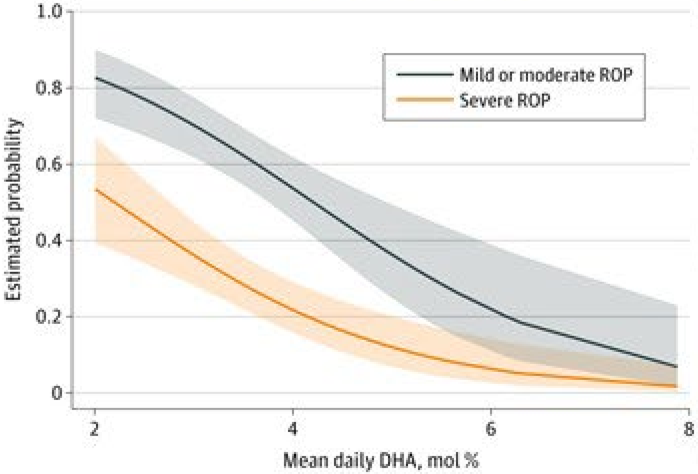
enteral ARA (100 mg/kg&d) + DHA (50 mg/kg&d)

Less severe ROP: adj. RR 0.50 *95%CI 0.28-0.91, P=0.02*

Serum ARA



Serum DHA



175 preterms
<28 gest weeks

Hellström A, JAMA Netw Open 2021;4(10):e2128771. doi: 10.1001/jamanetworkopen.2021.28771.

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Preterms need more DHA & ARA than terms

- Preterms deposit much DHA & ARA in brain & other tissues, with functional importance. Fetal accretion **>>** term infants
  ⇨ preterms need per d **≈30-65 mg DHA/kg & 50-130 mg ARA/kg**

- Mothers providing breast milk: **eat oily fish** regularly, take **DHA supplements** (≈600 mg DHA/d)

- Preterm formula should provide **0.5-1 % DHA***
  with **ARA ≥ DHA** *(DHA:ARA ratio of 0.5-1) (*% of fatty acids)*

Koletzko B & Lapillonne A, in: Koletzko B et al, Nutritional Care of Preterm Infants, 2nd. ed. 2021, World Rev Nutr Diet 122.

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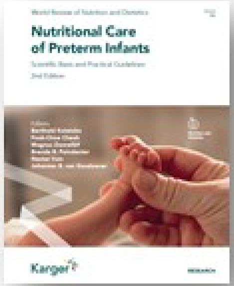
Mother‘s own milk = preferred choice

- **Fortified mother’s own milk** (MOM) = **best option** for preterms
- Donor human milk from a milk bank with established safety standards is the second best choice, but not the same as MOM
- Key benefit: risk reduction for necrotizing enterocolitis (NEC)

Koletzko B, Cheah F-C, Domellöf M, Poindexter BB, Vain N, van Goudoever JB (eds): Nutritional Care of Preterm Infants. Scientific Basis and Practical Guidelines. World Rev Nutr Diet. Basel, Karger, 2021, vol 122, pp 212–224 (DOI: 10.1159/000514733)

Mother’s Own Milk and Donor Milk

Regina Valverde[a] Nestor Alejandro Dinerstein[b] Nestor Vain[c]



Promoting Human Milk and Breastfeeding for the Very Low Birth Weight Infant

American Academy of Pediatrics

Margaret G. Parker, MD, MPH,[a] Lisa M. Stellwagen, MD,[b,c] Lawrence Noble, MD,[d,e] Jae H. Kim, MD, PhD,[f] Brenda B. Poindexter, MD,[g] Karen M. Puopolo, MD, PhD,[h] SECTION ON BREASTFEEDING, COMMITTEE ON NUTRITION, COMMITTEE ON FETUS AND NEWBORN

Valverde R et al, in: Koletzko B et al, Nutritional Care of Preterm Infants, 2nd. ed. 2021, World Rev Nutr Diet 122.
American Academy of Pediatrics. Peds. 2021148:e2021054272.

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Improved LBWI growth with higher enteral protein intake ($\geq$3 vs <3 g/kg&d)

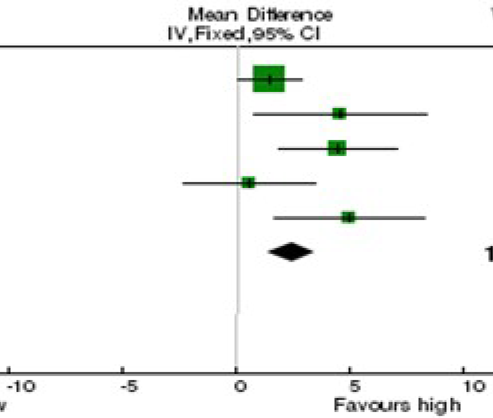
Protein $\geq$3g/kg **enhances weight gain** with **no adverse effects**

(incl. NEC, sepsis, diarrhea)

Study or subgroup	High N	Mean(SD)	Low N	Mean(SD)	Weight	Mean Difference IV,Fixed,95% CI
1 Weight gain (g/kg/d)						
Bhatia 1991	16	20.3 (2.31)	7	18.9 (1.2)	52.7 %	1.40 [-0.04, 2.84]
Hillman 1994	18	17.4 (3.6)	9	12.9 (5.3)	7.4 %	4.50 [0.66, 8.34]
Kashyap 1986	9	18.3 (2.8)	9	13.9 (2.8)	16.3 %	4.40 [1.81, 6.99]
Svenningsen 1982	16	13.8 (4.1)	14	13.3 (3.9)	13.3 %	0.50 [-2.37, 3.37]
Wauben 1995	8	16.45 (3.51)	8	11.54 (3.15)	10.2 %	4.91 [1.64, 8.18]
Subtotal (95% CI)	**67**		**47**		**100.0 %**	**2.36 [1.31, 3.40]**

Heterogeneity: Chi² = 9.25, df = 4 (P = 0.06); I² =57%
Test for overall effect: Z = 4.42 (P < 0.00001)

Test for subgroup differences: Chi² = 17.70, df = 2 (P = 0.00), I² =89%



THE COCHRANE COLLABORATION

TWL Cochrane.png by Wikipedia Pages, screenshots by Ocaasi licensed under CC BY_SA 3.0

Fenton et al, Cochrane Database Syst Rev 2015.

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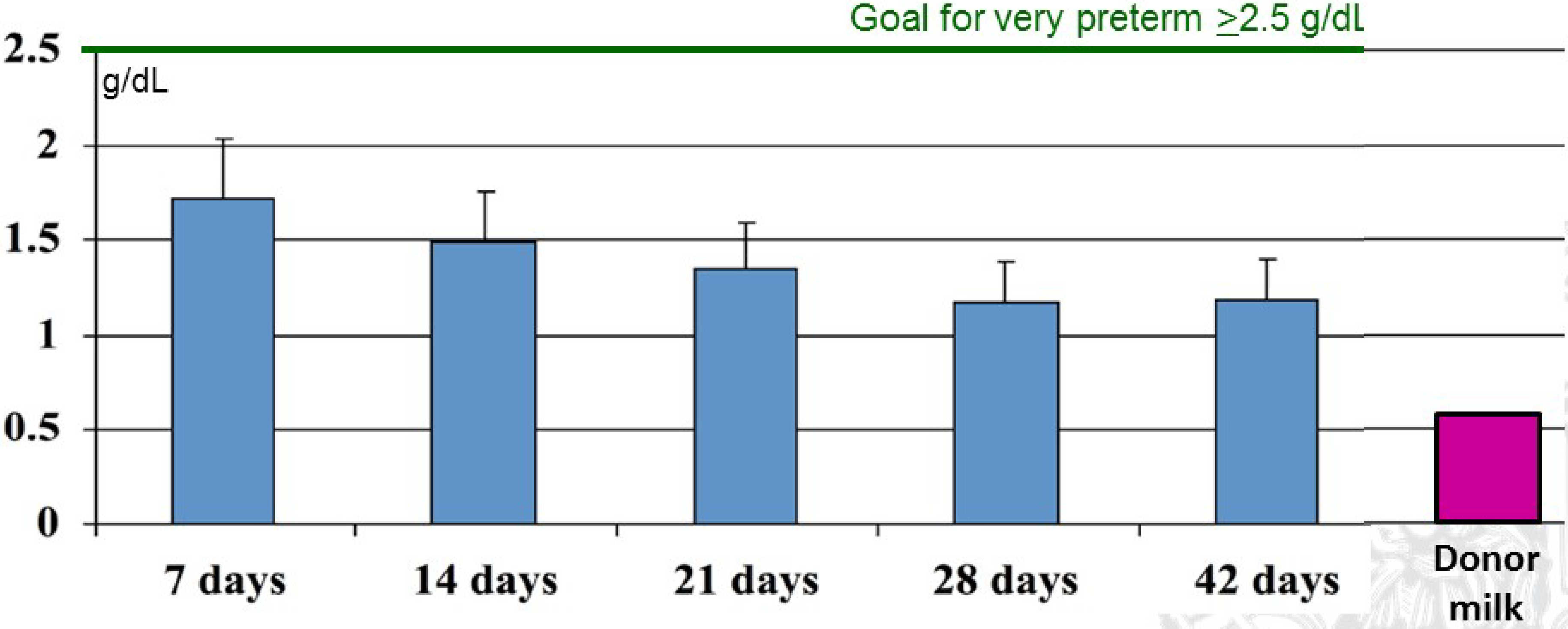
Human milk protein too low for preterms, very variable, decreases over time



Adapted from Ziegler E using data of Lemons et al 1982, in: Koletzko B et al (eds.): Nutritional Care of the Premature Infant, 1st. ed. 2014

Human milk fortification needed to meet protein needs of preterm infants

Current body weight	g/kg&d
500–1500 g	**3.5–4.5** (max. 3.5 i.v.)
1500–2000 g	**3.0–4.0** (max. 3.0 i.v.)
2000–2500 g	**2.5–3.5** (max. 2.5 i.v.)

v d Akker, CHP, et al. Proteins and Amino Acids. In: Koletzko B et al (eds). Nutritional Care of Preterm Infants. Karger. 2021

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Protein fortification of human milk improves growth in preterm infants

Protein fortification of human milk (6 RCTs, 204 preterms)

- Improved gain of **weight** (Δ 3.82 g/kg/day, 95% CI 2.94-4.7), **length** (Δ 0.12 cm/wk, 95% CI 0.07- 0.17), and **head circumference** (Δ 0.06 cm/wk, 95% CI 0.01-0.12)
- NEC risk unchanged (RR 1.11, CI 0.07-17.12)

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Amissae EA et al, Cochrane Database Syst Rev 2018.

For whom & why?

For whom

- Very preterm infants (<32 weeks)
- Preterm infants <1,800 g
- Preterm infants requiring fluid restriction

Why fortify [1]

- Avoid postnatal growth faltering
- Avoid deficits in minerals & micronutrients
- Linear growth & bone mineralization
- Enhance neurocognitive development

Targeted outcomes

- Meet nutrient needs
- Growth rates approaching fetal growth
- Less growth faltering & assoc. adverse effects

Special challenges to be avoided

- Low weight gain ⇨ higher risk of later metabolic disorders and NCDs [2,3]
- Low head growth ⇨ motor / cognitive delay [4,5]
- Postnatal growth faltering [6,7]

1) Arslanoglu S et al. Front Pediatr 2019;7:76; 2) Embleton ND et al. Arch Dis Child 2016;101:1026-31; 3) Barker DJ et al. N Engl J Med. 2005;353:1802-9; 4) Cooke RW et al. Arch Dis Child. 2003;88:482-7; 5) Raghuram K et al. Peds. 2017;140:e20170216; 6) Fenton TR et al. BMC Pediatr. 2013;13:59; 7. Rochow N et al. Pediatr Res. 2016;79:870-9.

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When and How to Start Human Milk Fortification?

When to start?	• No consensus about best time to start fortification, add full-strength at **50-100 ml/kg&d** enteral feeds
Why wait?	• **Don't wait**, delayed start has no benefit, but risk of slower growth
Full strength?	• No demonstrated advantage of starting at less than full-strength fortification
Safe?	• **Safe** when introduced early with enteral feeds, not associated with feeding intolerance

Picaud JC, Vicent M, Buffin R. Human Milk Fortification for Preterm Infants. In: Koletzko B, et al. (eds): Nutritional Care of Preterm Infants. World Rev Nutr Diet. Basel, Karger, 2021, vol 122.

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No evidence for benefit of human milk based over cows‘ milk based fortifiers

- **No benefit** demonstrated for human milk- vs. bovine milk-derived fortifier in human milk-fed preterm infants

- Low-certainty evidence from 1 study in human milk-fed preterm infants suggests **no change in risk of NEC, mortality, feeding intolerance, infection, or growth** with that human milk- vs. bovine milk-derived fortifiers

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Premkumar MH et al, Cochrane Database of Systematic Reviews 2019.

Which Fortification Strategy?

Standardized	• Improves postnatal growth, bone mineralization; but does not achieve adequeate postnatal growth in all very preterm infants
Adjusted Fortification	• Fortifier dose/protein intake adjusted based on weight gain and/or blood urea nitrogen • Studies report higher weight and head circumference gains compared to standardized fortification group (1,2)
Targeted	• Adjust dose to measured HM composition (3–5) • Safe, apparent benefit over standardized fortification (6,7)

Adjusted & targeted human milk fortification promote postnatal growth in very preterm infants compared to standardized fortification - long-term effects still need to be evaluated

1. Arslanoglu S, et al. J Perinatol. 2006;26:614–21; 2. Alan S, et al. Early Hum Dev. 2013;89: 1017–23; 3. Buffin R, et al. J Perinatol. 2017;37:552–7; 4. Fusch G, et al. Clin Perinatol. 2017;44:209–67; 5. de Halleux V, et al. Arch Pediatr. 2007;14 Suppl 1:S5–10; 6. Rochow N, et al. Clin Nutr. 2020;S0261–5614:30202–8; 7. AAP. Breast feeding. In: Kleinman RE, Greer FR, eds, Pediatric nutrition. 7th ed. Elk Grove Village: American Academy of Pediatrics; 2014:41–60.

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Fortification of human milk

- Always fortify human milk for very preterms/preterms <1800 g
- Start full strength fortification @ ≈50-100 ml/kg&d enteral feeds
  (⇨ "early" beneficial but no strong evidence for optimal starting point)
- Standard: Bovine protein multicomponent fortifiers
  (no firm evidence for greater benefit of human milk-based fortifiers)
- Aim at protein intakes >3g/kg/day
- Targeted/adjusted fortification recommended

⇨ In LMIC, formula powders have been used when fortifiers are unavailable/unaffordable

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Pichaud JC et al, in: Koletzko B et al, Nutritional Care of Preterm Infants, 2nd. ed. 2021, World Rev Nutr Diet 122.

Human milk feeding: research needs

- Explore **variability of human milk** composition, predictors, and short and long-term health effects, in concert with maternal and infant biology
- Assess **interventions** in mothers to improve diet/lifestyle, & infant outcomes
- Evalute improving **quality of donor milk**, e.g. donor selection, processing
- Multi-nutrient human milk fortifiers improve in-hospital preterm growth, but data on **later outcome** incl. neurodevelopment are needed
- Better evidence is needed on **optimal timing of introducing fortifier**
- Well designed & powered trials to **compare effects of different fortifiers** e.g. bovine vs. human milk based, intact vs. hydrolysed protein, liquid vs. powder
- Evaluate options and effects of breastfeeding fortification **post-discharge**

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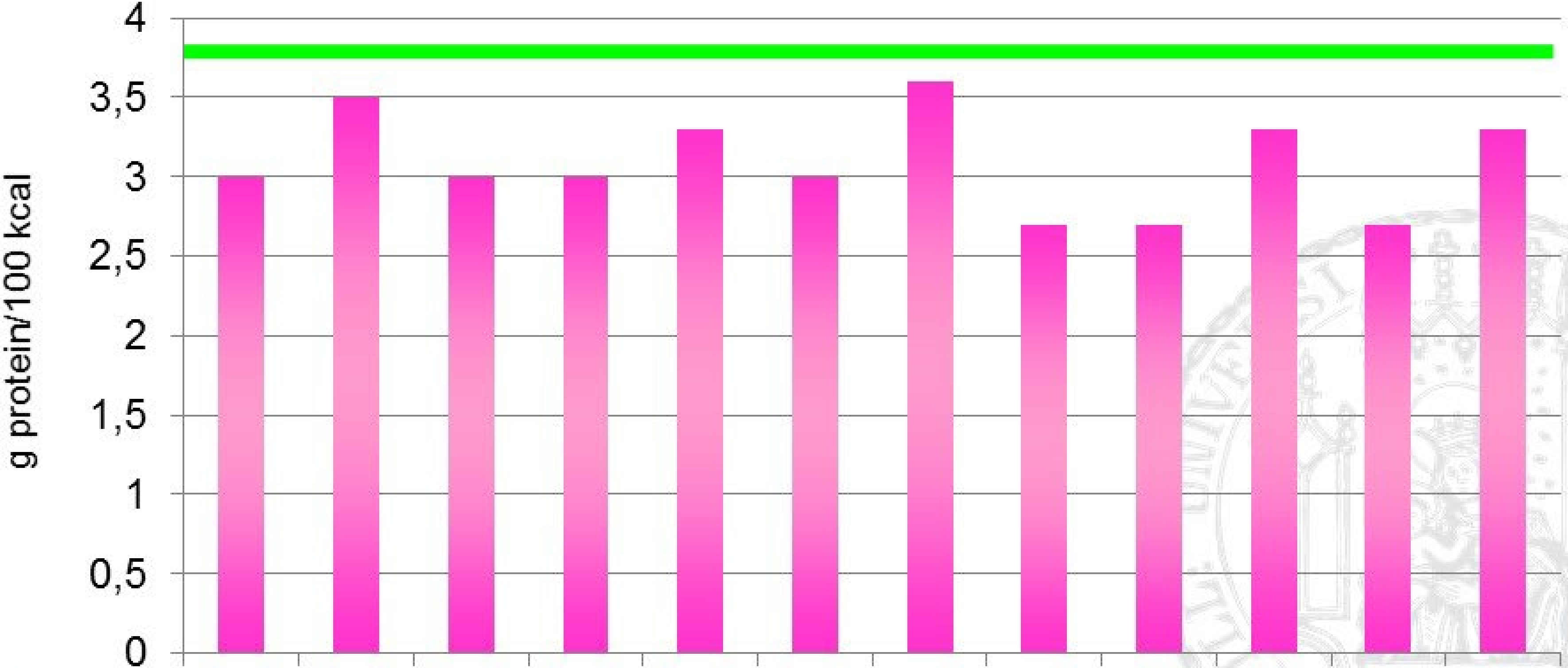
Preterm formula: generally good, but composition varies, e.g. protein



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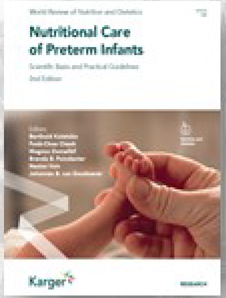
Early enteral nutrition, rapid advancement

- Avoid "total" PN, provide (at least minimal) EN 6-48 h after birth
- Don' t delay EN, also not in IUGR/abnormal fetal circulation
- Rapid EN advancement by 24-36 ml/kg&d possible, RCT evaluated
- No routine evaluation of gastric residuals
- Compare composition of fortifiers & preterm formulas, choose products that best approach meeting the high nutrient needs
- Regular evaluation of weight, length, HC
- Establish written unit policy, motivate & train all staff, audit



Bozzetti V, Martin CR. World Rev Nutr Diet. 2021;122:265. Dorling J et al, NEJM.2019;381:1434. Parker LA et al, J Pediatr. 2020:165.

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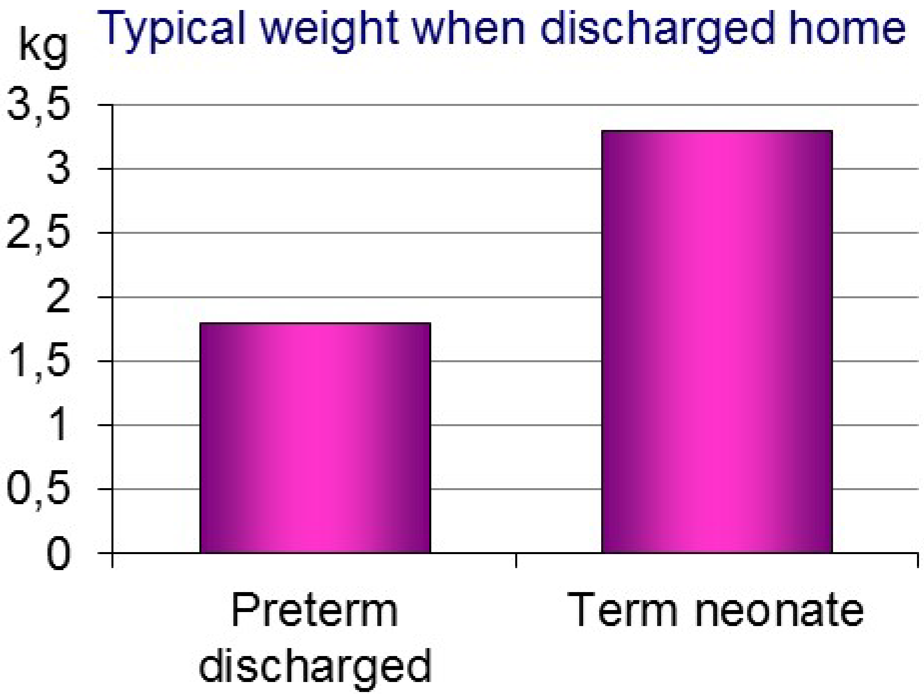
How to feed after discharge?



- Preterms at discharge: ≈55% of term baby's weight
- Lower nutrient stores & higher needs than term infants
  e.g. protein, iron, other micronutrients, LC-PUFA
- Unfortified breastfeeding / standard infant formula meet needs of term infants, but not optimal for preterms

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Growth faltering after hospital discharge

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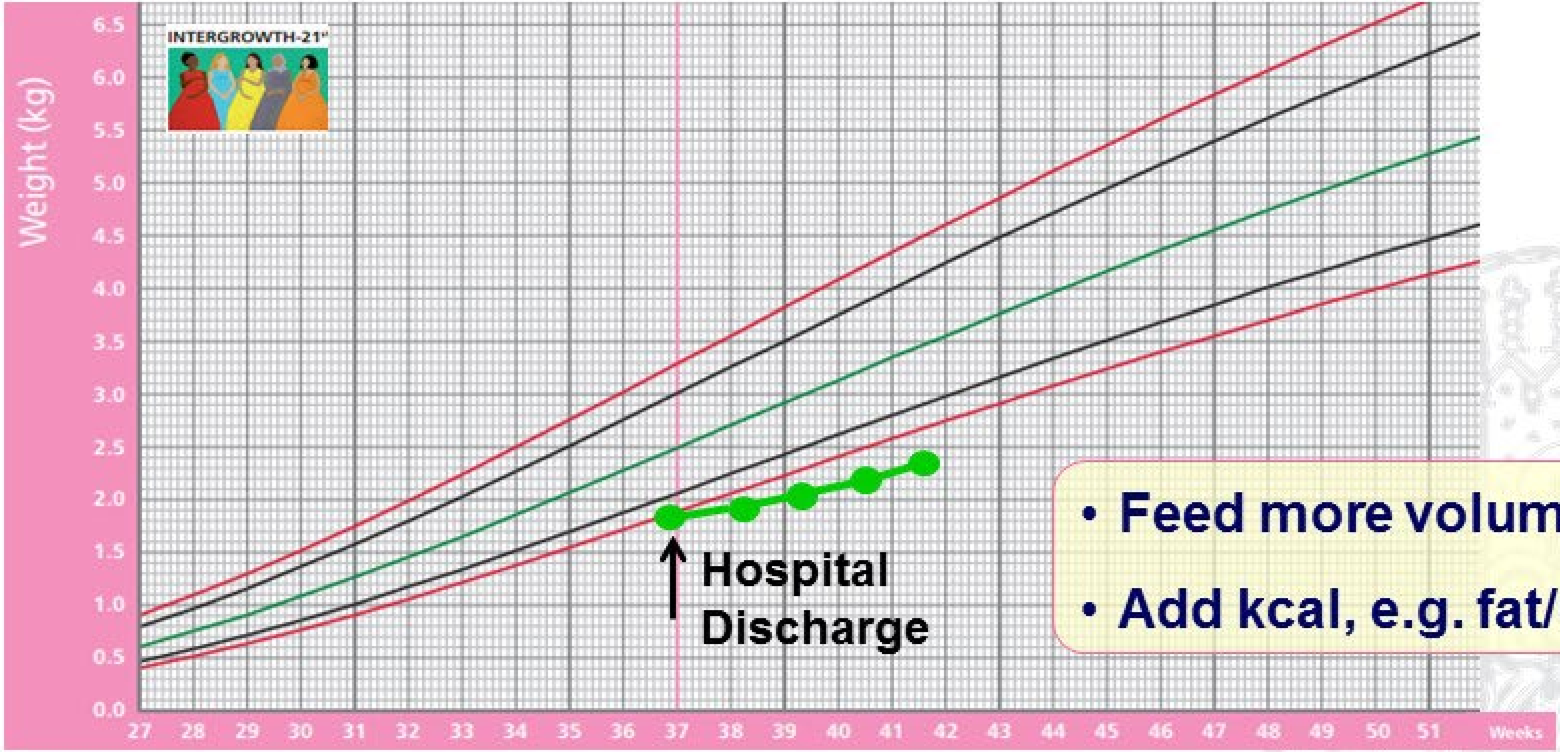
Growth faltering after hospital discharge



- Feed more volume?
- Add kcal, e.g. fat/CHO?

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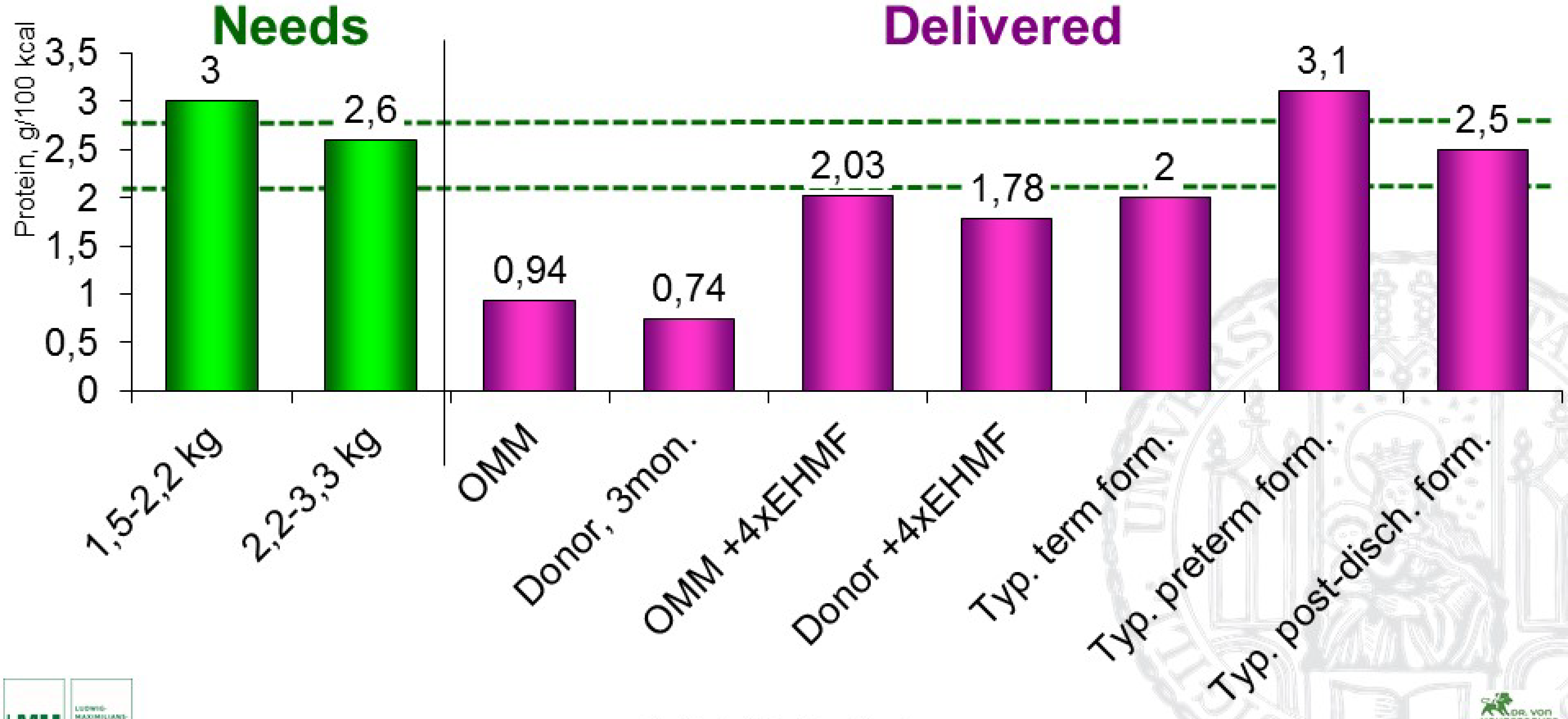
Growth after discharge: no excessive fatness

- Weight gain through excessive fat deposition undesirable
- Avoid overfeeding empty calories *(sugar, starch, dextrinmaltose, fat)*
- Too low protein to energy ratio promotes body fatness
- Support high density of protein and essential nutrients in feeds

Fernando Botero. Niña comiendo helado
Museo Botero, Bogota

Protein/energy ratio after discharge



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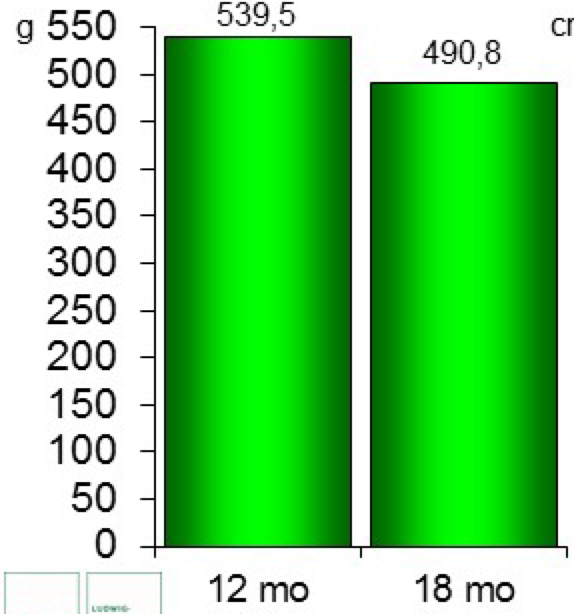
Nutrient-rich formula post discharge: better growth

Cochrane review:16 trials, 1251 preterms: preterm or post-discharge vs. standard formula

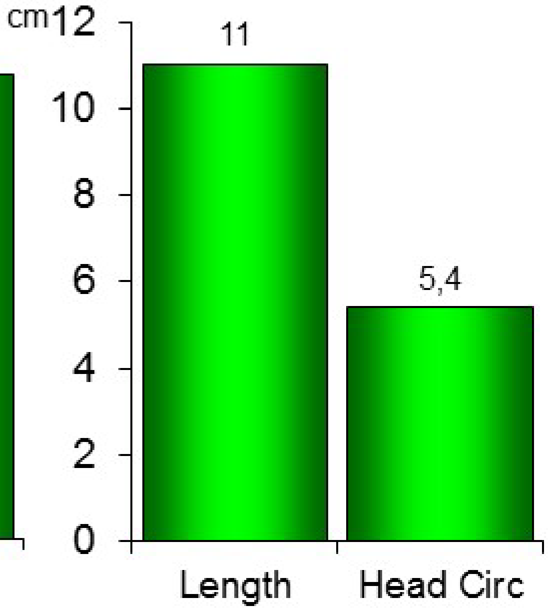
Cochrane Library

Preterm vs. Term Formula

Weight benefit
at 12 &18 mon

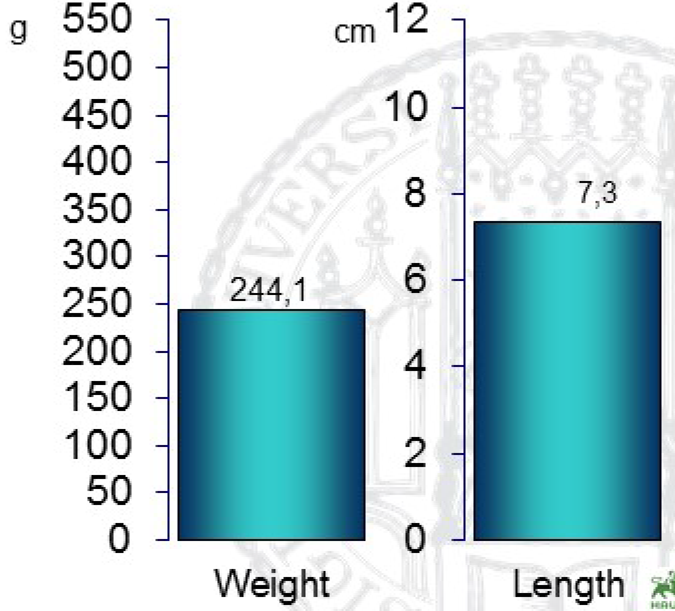


Length & HC benefit
at 18 mon



Post-Discharge vs Term F.

Weight & Length Benefit
at 9 mon



Young et al, Cochrane Database Syst Rev 2016.

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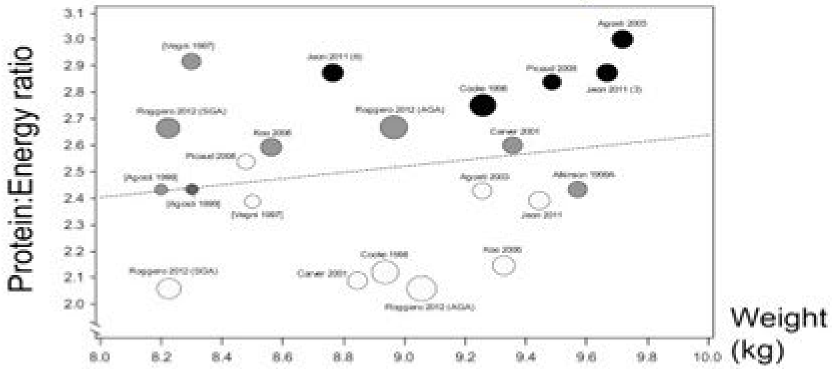
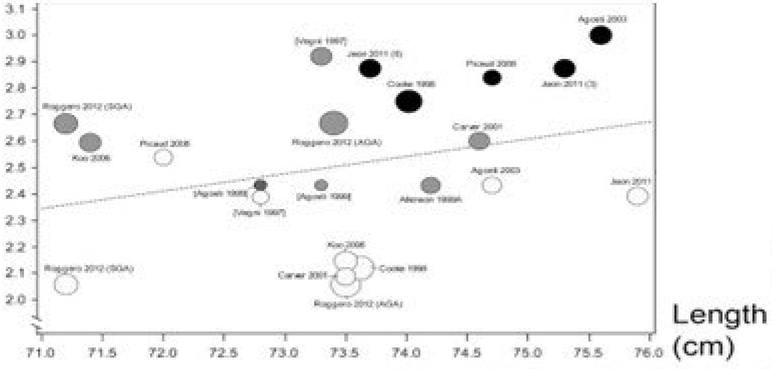
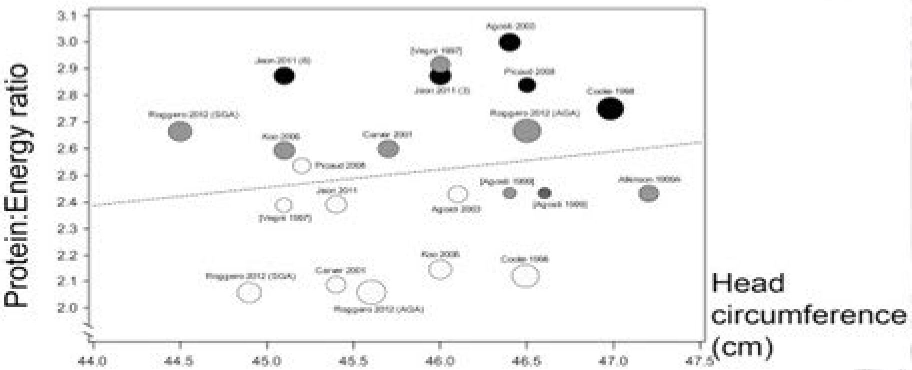
Protein-energy ratio post-discharge predicts weight, length, head circumference & body composition

systematic review, 31 studies







Teller et al, Clin Nutr. 2016

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Nutrition after discharge

- Don't fatten babies, no overfeeding with "empty calories"
- ≈3 g or 2-2.5 g protein/100 kcal at ≈1.5-2 kg or ≈2-2.5 kg bw.
- Support breastfeeding, consider human milk fortification *(partic. with poor growth)*, advise fish / omega-3 DHA intake for breastfeeding mothers *(part. vegetarian)*
- Post-discharge or preterm formula if not/not fully breastfed
- Monitor growth in all, nutrient status by indication (e.g. ferritin)

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Thank you
for your kind attention!
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