Spenderinnenmilch - pro und contra.

Eine Bestandsaufnahme

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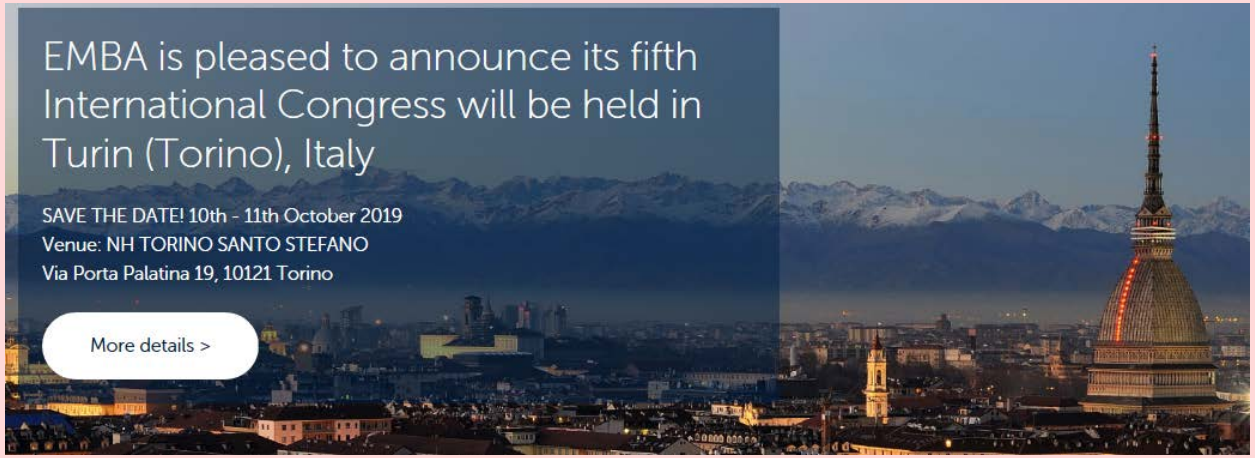
Interessenskonflikte

- Keine Interessenskonflikte

FRAUENMILCHBANK-INITIATIVE | F M B I

emba European Milk Bank Association

event emba



Interessenskonflikte

FRAUENMILCHBANK-INITIATIVE | F M B I

VLKKD: Vorstand

GNPI: Vorstand

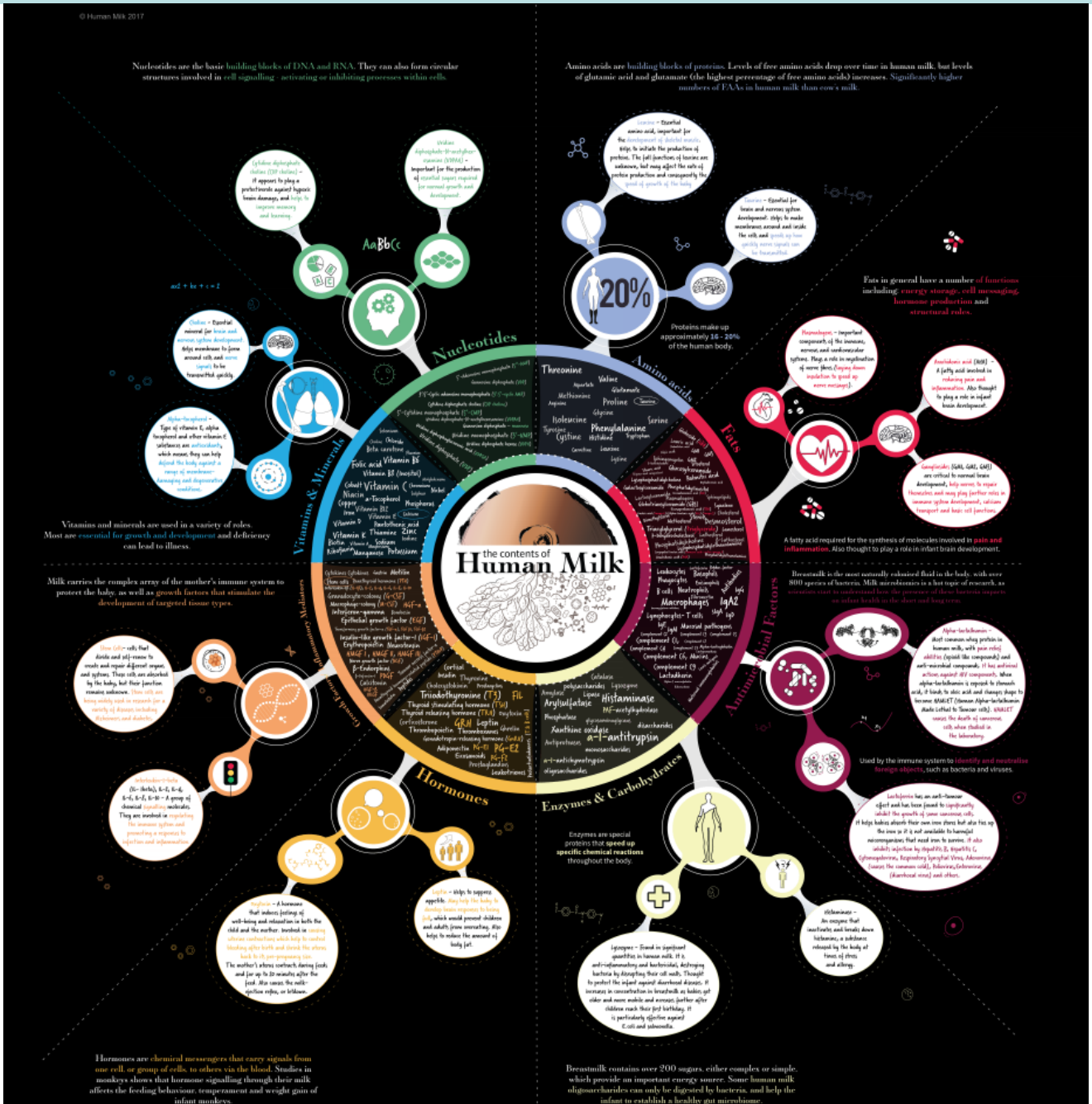
I have no relevant financial relationship of commercial interest in regard to this presentation; advisory role and speaker with Nestle, Milupa(Danone), Mead Johnson, Abbott, Humana, Baxter, Fresenius, Ikaria, Medela, Prolacta, Heinen & Loewenstein, Hamilton Medical. I received an unrestricted research grant from Prolacta.

Milch der eigenen Mutter als optimale Nahrung für Früh- und Neugeborene:

- Frauenmilch ist der Muttermilch ähnlicher als jede andere erhältliche Nahrung
- Formulanahrung auf Kuhmilchbasis
- Zutaten in Frühgeborenen-Formula:

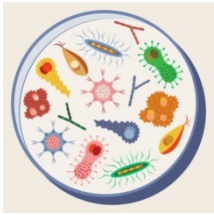
MILCHZUCKER, Maltodextrin, hydrolysiertes **MOLKENEIWEISS**, pflanzliche Öle (Sonnenblumenöl, Rapsöl), pflanzliche Fette (Palmfett, Kokosfett), Calciumorthophosphate, Kaliumhydroxid, Magnesiumchlorid, Kaliumorthophosphate, Algenöl, Öl aus Mortierella alpina, Natriumhydroxid, Kaliumchlorid, Cholintartrat, Vitaminmischung (Vitamin C, Vitamin E, Vitamin A, Pantothensäure, Niacin, Vitamin D, Vitamin K, Vitamin B1 (Thiamin), Vitamin B2 (Riboflavin), Vitamin B6, Folsäure, Vitamin B12, Biotin), Calciumchlorid, Inositol, L-Arginin, Säureregulator Citronensäure, Taurin, Eisensulfat, Milchsäurebakterien (mit Bifidobacterium lactis), Zinksulfat, L-Carnitin, Nukleotide (Cytidin-5-monophosphat, Uridin-5-monophosphat, Adenosin-5-monophosphat,Guanosin-5-monophosphat), Kupfersulfat, Kaliumjodid, Mangansulfat, Natriumselenat.

Humane Milch: biologisch aktive Substanz



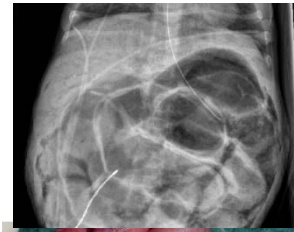
Benefit für Frühgeborene

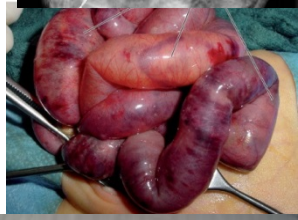
- Immunmodulation (lebende Zellen, IgA, Zytokine, Laktoferrin, Nukleotide)
- Priming des unreifen Darms (Wachstumsfaktoren, Hormone…)
- hoher Gehalt an bioaktiven Faktoren in Kolostrum, Förderung der intestinalen Barrierebildung, Antioxidantien, Pro- und Prebiotika, intestinales Microbiom
- Fehlen von schädlichen Antigenen (natives Kuhmilchprotein)

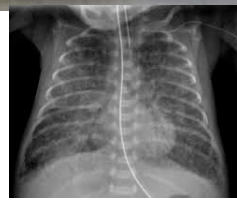


- Reduktion des Auftretens schwerwiegender Ereignisse kurz- und langfristig

  - nekrotisierende Enterokolitis (NEC)
  - Nahrungsunverträglichkeit
  - nosokomiale Infektionen
  - bronchopulmonale Dysplasie, Retinopathie
  - Langzeitverlauf in Bezug auf kardiovaskuläre Risikofaktoren







Boyd 2007, Quigley 2007, McGuire 2003, Gross 1983, Lucas 1984, Lucas 1987, Schanler 2005, Singhal 2001, Singhal 2004

Kontra #1

Spendermilch erhoeht das Risiko fuer Wachstumsretardierung

Donor milk has an inbuilt risk of providing insufficient nutrient intake

In the systematic review by Quigley and McGuire,[11] infants randomized to receive donor milk had slower growth than infants randomized to receive formula; however, only 2 of 9 trials included in their analyses used donor milk fortified with nutrients. Although no statistically significant differences in growth between groups were observed in the present study, results showed a 0.5- to 1.0-SD decline in weight for age and length for age during the intervention, suggesting that growth and likely nutritional intake were suboptimal in both groups of infants.

11. Quigley M, McGuire W. Formula versus donor breast milk for feeding preterm or low birth weight infants. *Cochrane Database Syst Rev*. 2014;4(4):CD002971.

Preterm infants on donor milk experience growth retardation

Providing very preterm infants with donor human milk led to faster breastfeeding rates but worse biometric gains

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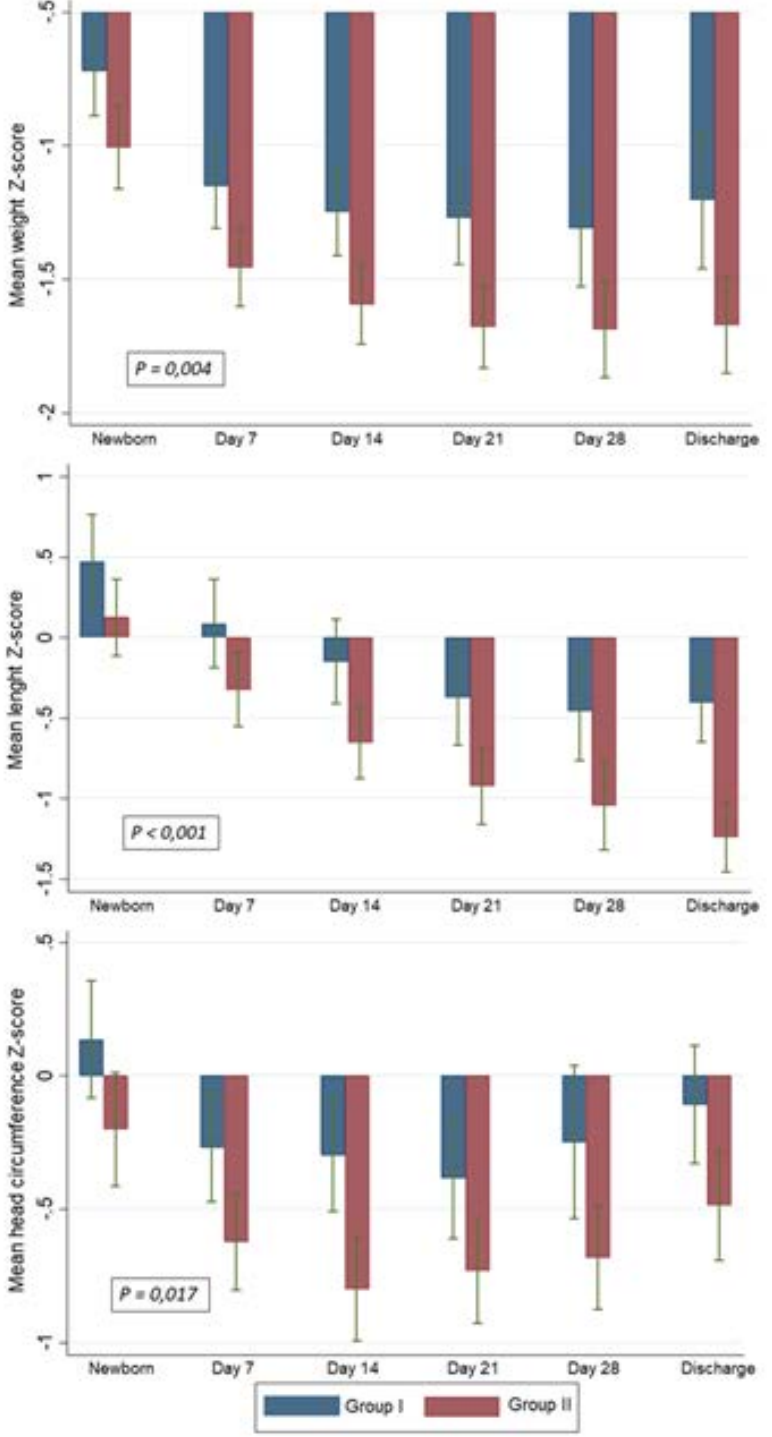
ACTA PÆDIATRICA
NURTURING THE CHILD

Before-after trial(retrospective design)

Table 1 Comparison of infants who did not and did have the opportunity to receive donor human milk

	No donor human milk (July 2011-June 2014)	Donor human milk available (July 2014-June 2017)	p value
Number of infants	52	78	
Maternal age (years)	36 (33-40.5)	35 (32-37)	0.039
Gestational age (weeks)	31.2 (30.1-31.7)	31.5 (30-32.7)	0.218
Birthweight (g)	1430 ± 262	1343 ± 233	0.052
Birth length (cm)	41 (39-42)	40 (38.5-41.5)	0.153
Hours starting enteral nutrition	36 (24-8)	20 (15-25)	<0.001
Hours starting own mother's milk	36 (26-60)	33 (21-57)	0.124
Hours achieving 24 mL/kg/day	72 (49-96)	46 (39-57)	<0.001
Hours achieving 100 mL/kg/day	147 (142-204)	132 (118-174)	<0.001
Hours achieving 150 mL/kg/day	288 (228-336)	194 (179-239)	<0.001
Type of enteral nutrition started, n (%)			
Own mother's milk	34 (65.4)	26 (33.3)	<0.001
Donor human milk	0 (0.0)	51 (65.4)	
Preterm formula	18 (34.6)	1 (1.3)	
Donor human milk independent of enteral feeding	0 (0.0)	16 (20.5)	
Type of nutrition at discharge, †n (%)			
Exclusive breastfeeding	20 (40.0)	37 (48.7)	0.349
Mixed breastfeeding	17 (34.0)	27 (35.5)	
Formula feeding	13 (26.0)	12 (15.8)	

Results are expressed as n (%), mean ± SD or median (p25; p75).
†Sample size was 51 in Group I and 76 in Group II, due to patients' transfers.



Dose dependent effects of donor milk exposure

Donor milk may differ from mom's milk for preterm infant needs-growth

Median (IQR)	Percentage of maternal milk intake in diet			
	< 20% mm (n=20)	**20-80% mm (n=11)**	**>80% mm (n=17)**	**p value**
Weight at study entry, g	1126 (996, 1240)	1180 (1050, 1300)	1240 (1143, 1320)	0.17
Weight at end of study, g	1385 (1235, 1455)	1460, (1360, 1510)	1490 (1430, 1510)	0.012*
Weight gain, g/kg/d	11.4 (9.9, 14.5)	15.0 (13.3, 16.1)	15.6 (12.6, 19.3)	0.016**
Length gain cm/wk	0.9 (0.7, 1.1)	0.9 (0.5, 1)	0.9 (0.7, 1.2)	0.91

*difference between <20% and >80%
** difference between <20% and 20-80%

- Compared to >80%, infants fed <20% grew **5.1 g/kg/d slower** than those fed >80%, adjusted for GA at birth, day of first feeding, feeding tolerance, and weight at the first day of full feeding, prenatal steroids, and duration of study . **<20% MM means >80% DM**

Adapted from *Montjaux et al, Acta Peadiactrica 2011, vol 100 pg 1548-54*

Growth Outcomes by Type of Human Milk

	Type of Human Milk			P value
	>75% DM n= 23	>75% MM n= 51	Mixed MM/DM n=14	
Discharge weight, g median (IQR)	2330 (2070, 2720)	2710 (2480, 3050)	2875 (2500, 3200)	0.07
Discharge weight z score median (IQR)	-1.36 (-1.83, -0.48)	-1.04 (-1.43, -0.26)	-0.68 (-1.2, -0.17)	0.24
SGA at discharge	56% (13/23)	35% (18/51)	21% (3/14)	0.08
Human milk fortification, highest level used				
24 kcal/oz	13% (3/23)	20% (10/51)	7% (1/14)	0.82
27 kcal/oz	57% (13/23)	53% (27/51)	57% (8/14)	
30 kcal/oz	30% (7/23)	27% (14/51)	36% (5/14)	
Discharge head circumference, cm n = 56 median (IQR)	32 (31.5, 33.5)	33.5 (32.5, 34.75)	33.25 (32.25, 34.25)	0.23
Discharge head circumference z score median (IQR)	-0.7 (-1.4, -0.2)	-0.4 (-1, 0.4)	-0.9 (-1.15, -0.25)	0.11
Change in weight z score, birth to discharge median (IQR)	-0.84 (-1.09, -0.25)	-0.56 (-0.89, -0.03)	-0.45 (-1.2, -0.15)	0.54

- Low rates of SGA status at discharge for all groups compared to previous studies
- All infants had decrease in wt z score over hospitalization
- Donor milk infants had a non-significantly greater negative change in weight z score
- Growth with donor milk may be compromised?

Kontra #2

Spendermilch ist – wie Muttermilch allgemein - sehr unterschiedlich zuammengesetzt.

Protein content of breast milk: term vs. preterm
Effect on donor milk (Fenton systematic review)

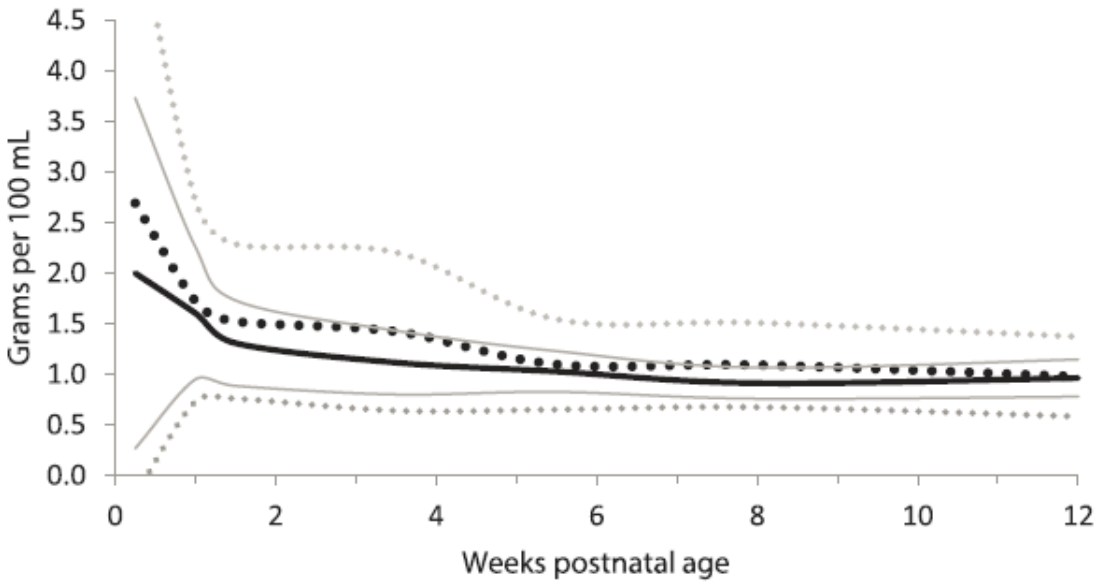
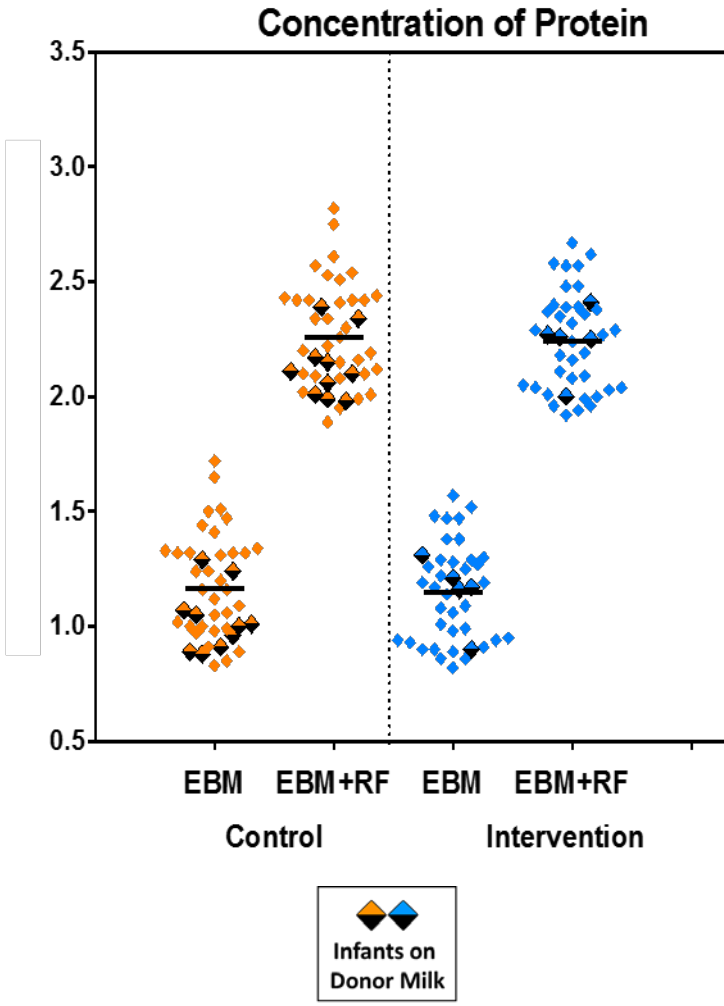
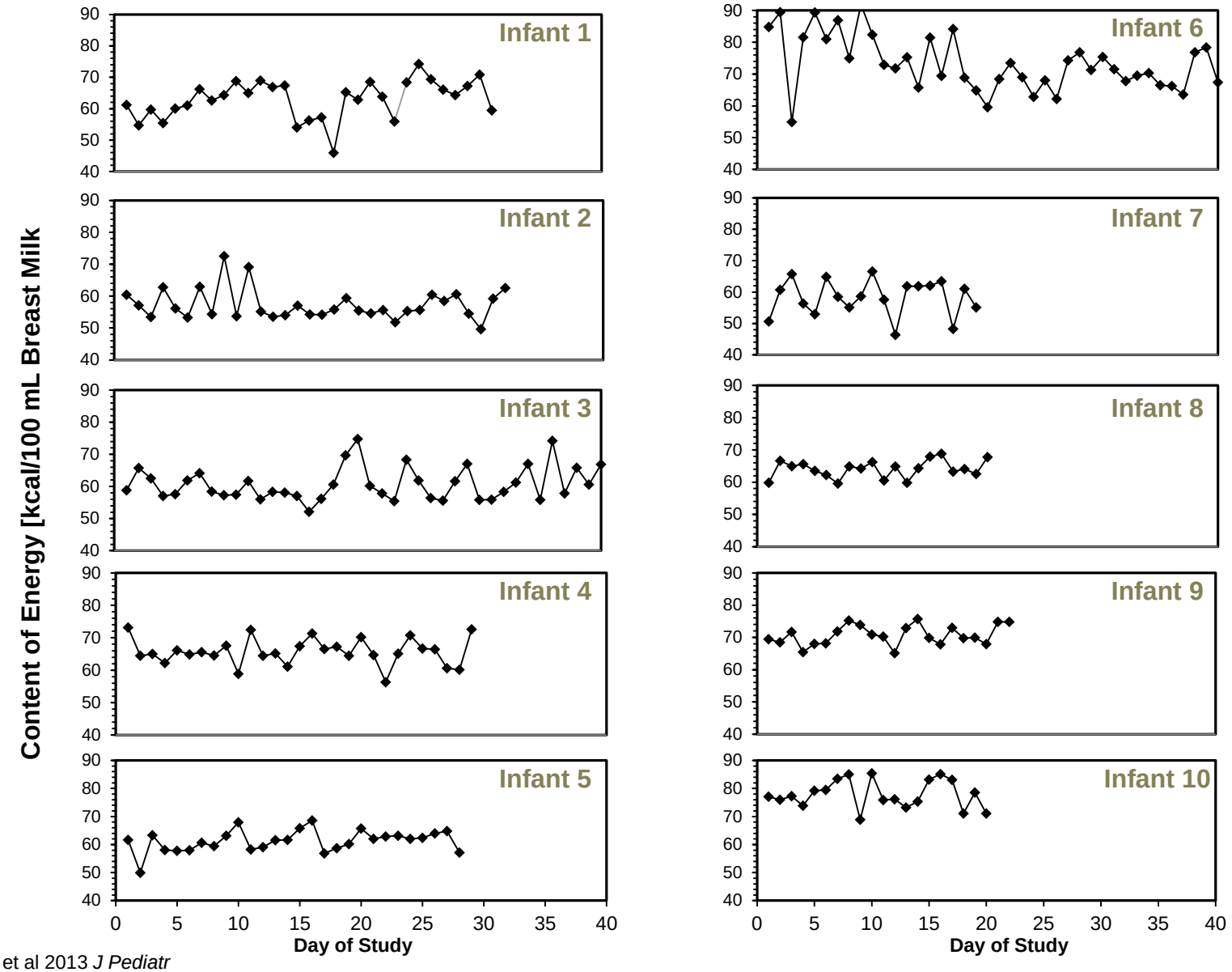


Figure 4 True Protein content distribution of preterm and term breast milk in by postnatal age over the first 12 weeks of lactation, weighted mean and 95% reference interval. Preterm milk ···· Term milk —— : mean +/- 2 standard deviations.

Own data: target fortification study

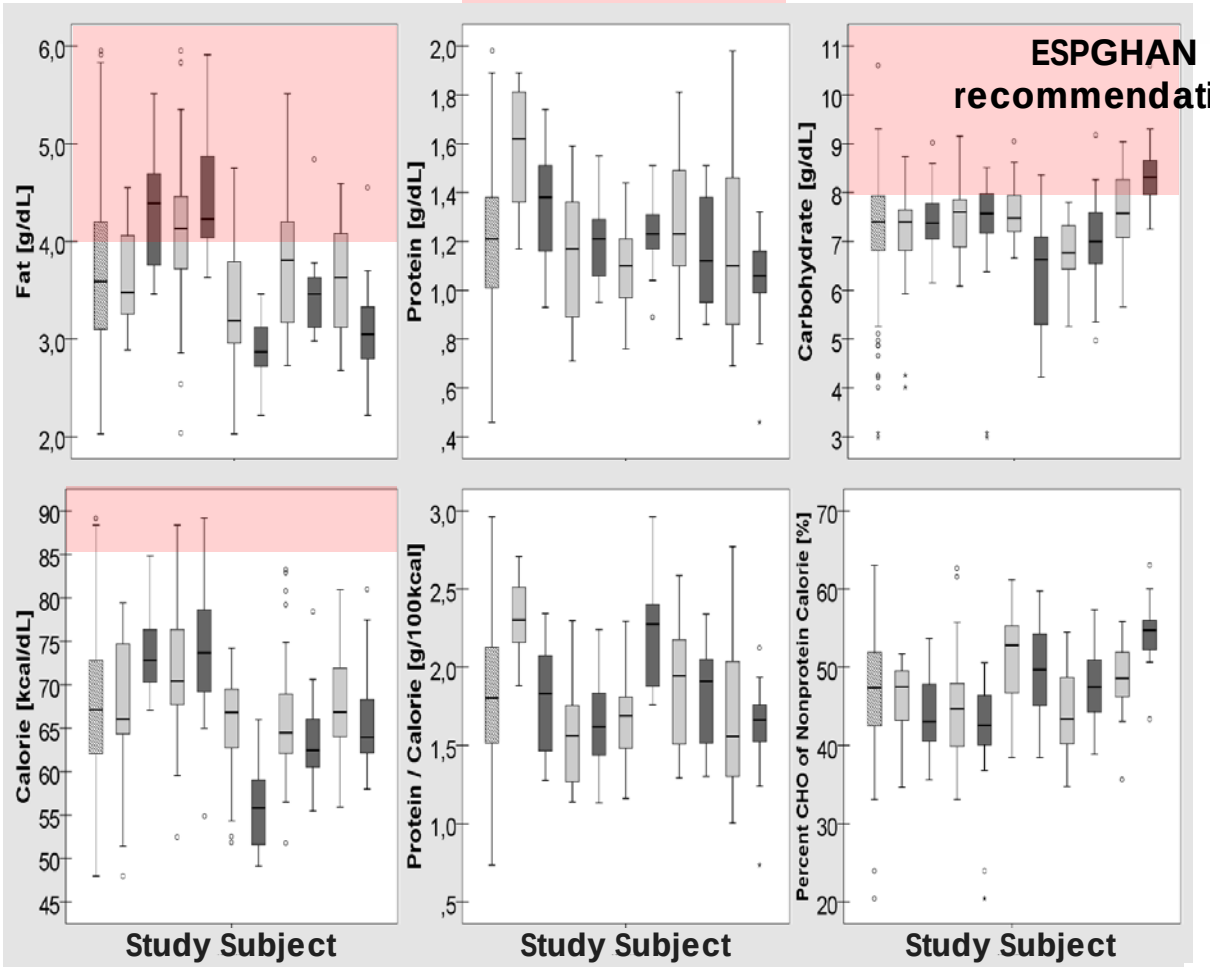


Variation between individuals, from day-to-day an between lactation periods is considerable



Rochow et al 2013 *J Pediatr*

Inter- and Intra-individual Variation of Breast Milk Composition in Unfortified 12h Batches; 10 mothers, 850 samples



No Correlation Between Macronutrient Levels (Wet Lab Chemistry)

Colour: 40 mothers of term and preterm infants
fore, mid and hind milk (n = 3 x 40; 120)

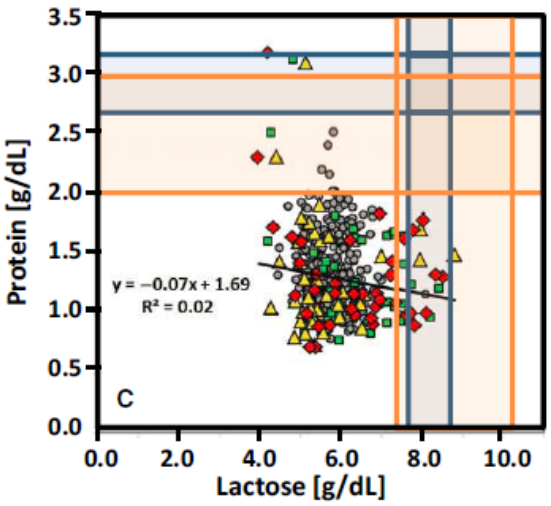
Grey: 10 mothers of preterm infants; on average 85 batches used for feeding (n = 850)

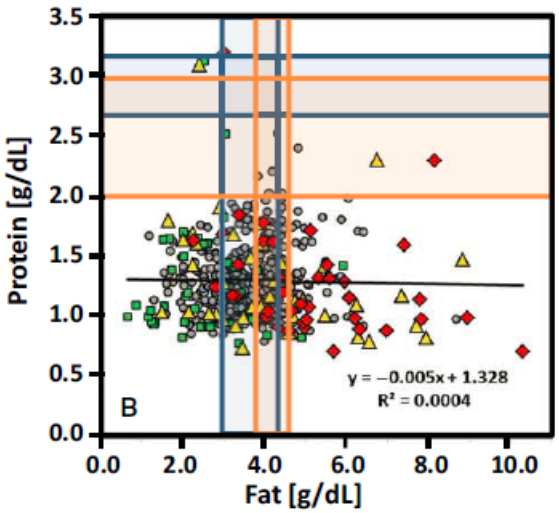
Green: **fore milk**
Yellow: **mid milk**
Red: **hind milk**

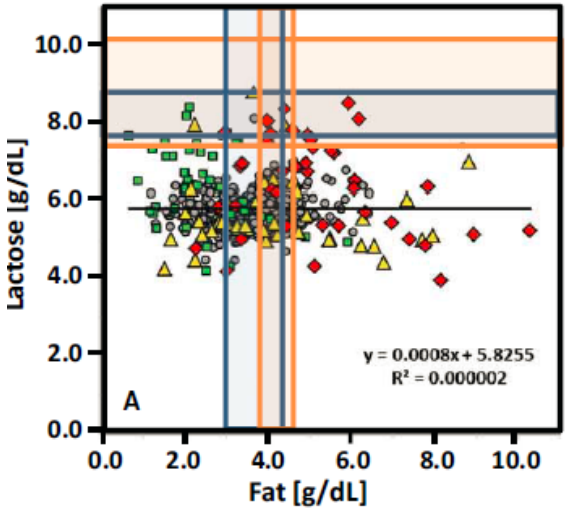
Grey: **batches**

ESPGHAN guideline

commercially available formula: **Enfamil premature, Similac Advance, Preemie SMA 24, Beba, Prematil, Humana 0-VLB**







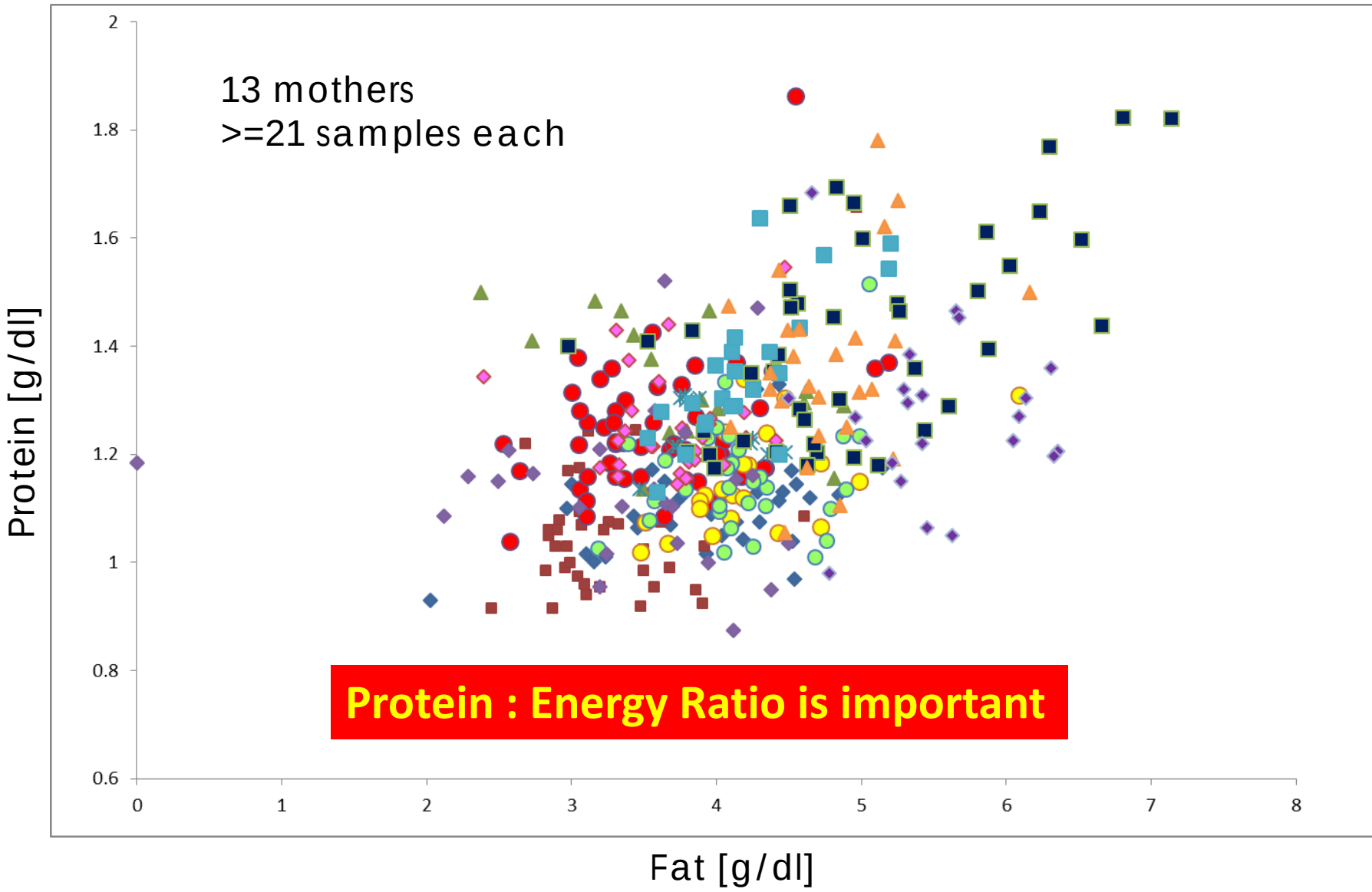
REGULAR ARTICLE

Target fortification of breast milk: levels of fat, protein or lactose are not related

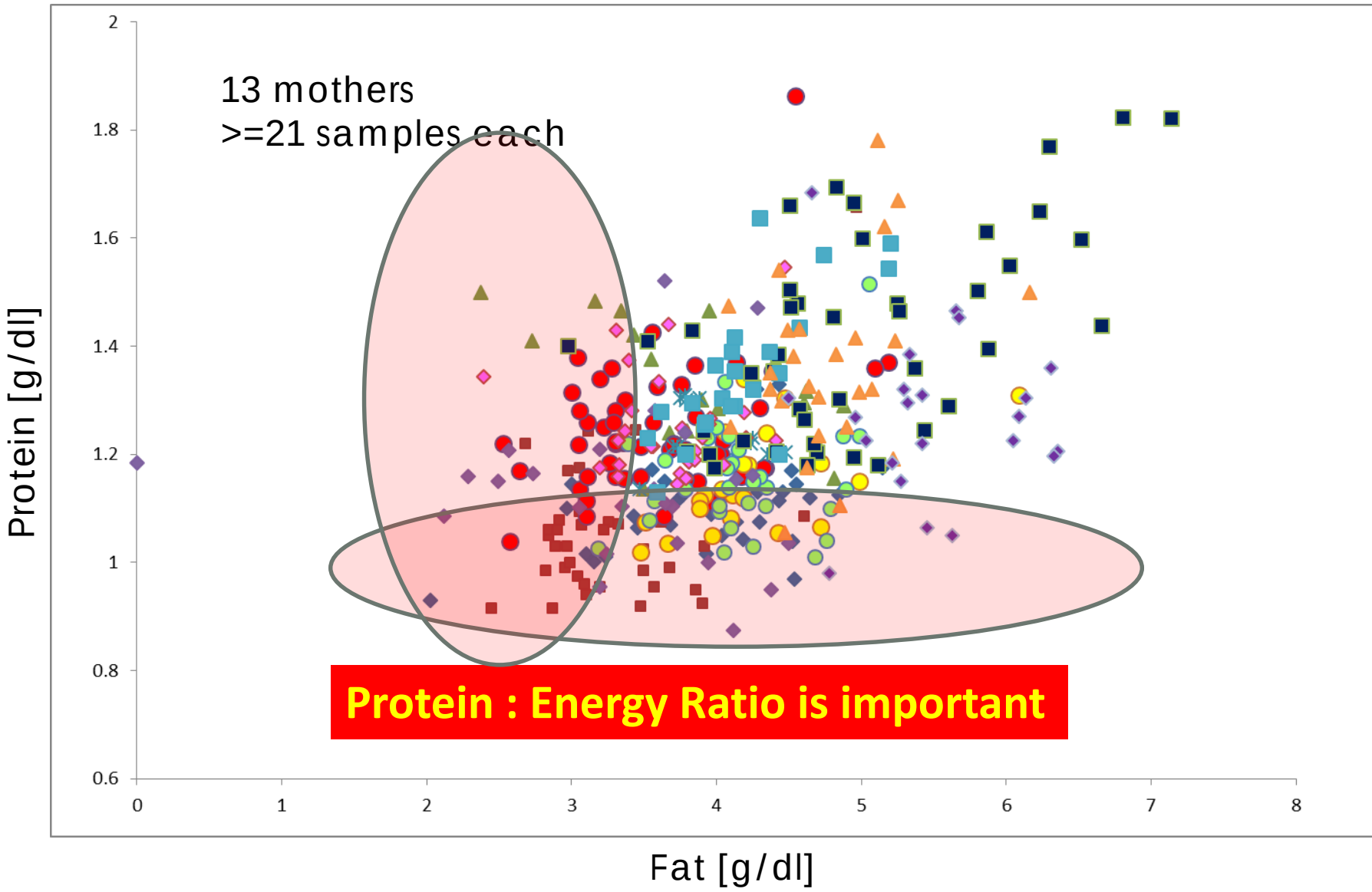
Gerhard Fusch, Souvik Mitra, Niels Rochow, Christoph Fusch (fusch@mcmaster.ca)
Division of Neonatology, Department of Pediatrics, McMaster University, Hamilton, ON, Canada

Acta Paediatrica, 2015

Interindividual clusters of macronutrient content in native breast milk



Interindividual clusters of macronutrient content in native breast milk

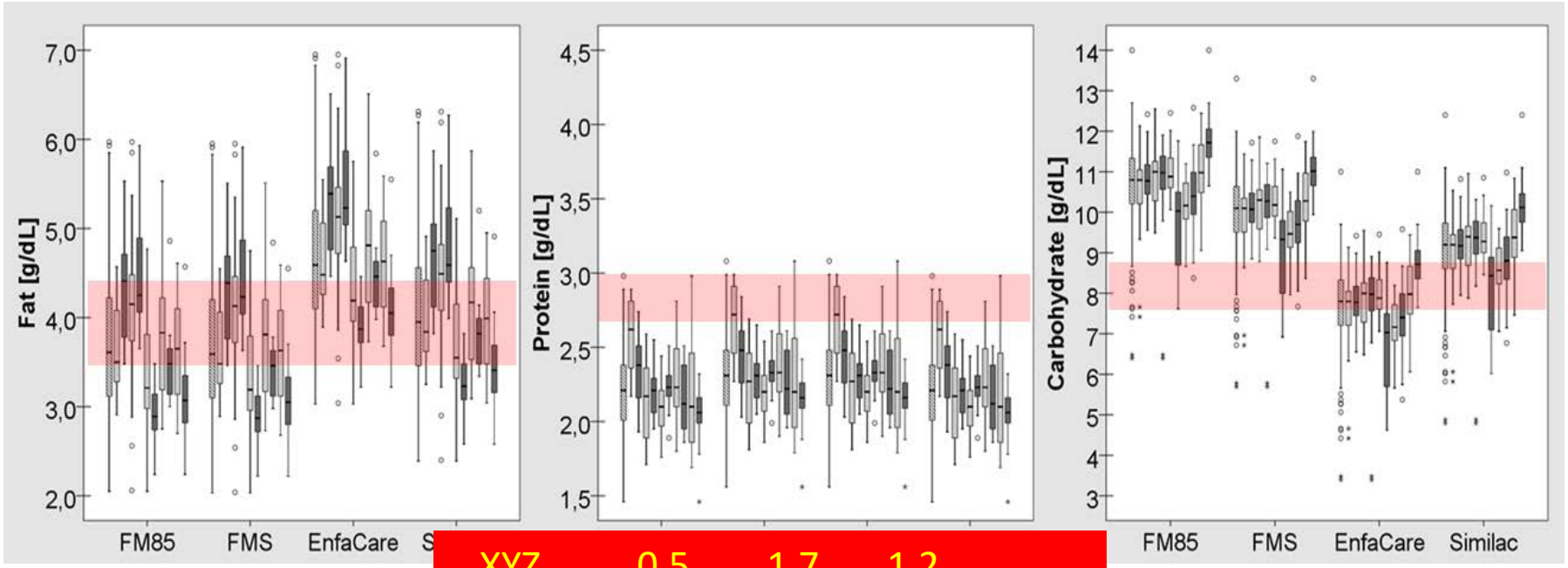


Fortifier (cow's milk), standard

+	-
• Increases nutrient intake protein, calories, minerals	cow's milk protein reduces NEC-protective effect of breast milk
• adds about 1 -1.1 gm protein/dL adds about 14 -18 kcal/dl	optimum composition of non-protein calories (F : CHO) unknown
•	osmolality ^^
•	Variability of MN composition still present
•	adequate growth for all? assumption of standard composition of all BM

Impact of different fortifier strategies on nutrient content of HM

+0,5 1,7 +1,2

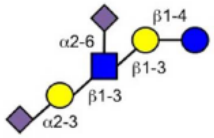


XYZ 0,5 1,7 1,2

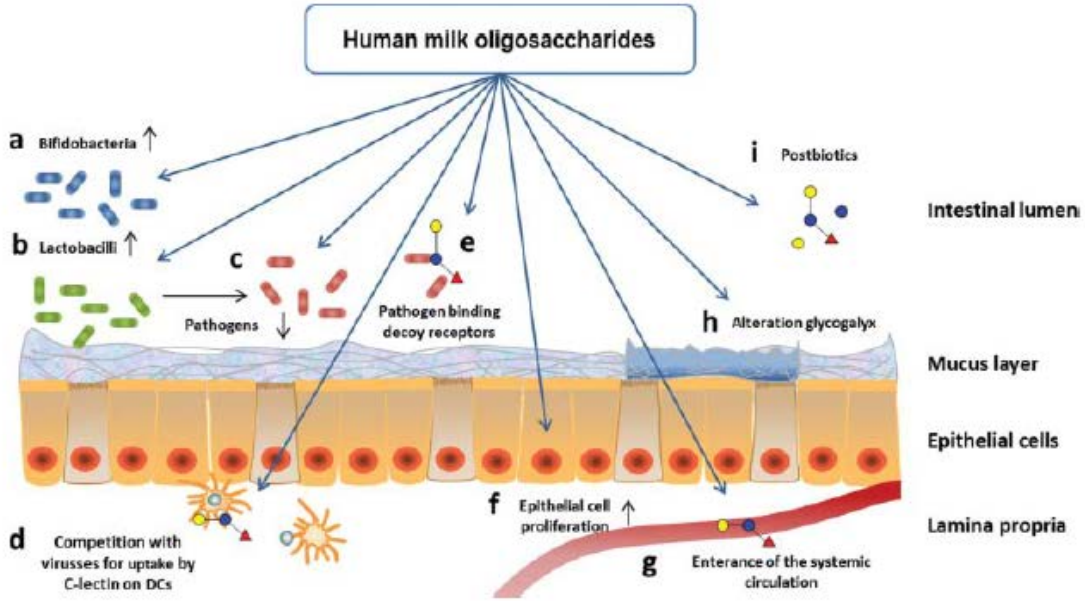
Routine Fortifier	Fat [g/dL]	Protein [g/dL]	Lactose [g/dL]	Energy [kcal/dL]
Nestle® - FM 85	0.02	1.0	3.4	17.8
Milupa® - FMS	0	1.1	2.7	15.2
Mead Johnson® - EnfaCare	1	1.1	0.4	15.0
Abbott® - Similac	0.36	1.0	1.8	14.4

Humane Milcholigosaccharide (HMOs)

DSLNT



- HMOs drittgrößte Komponente der menschlichen Milch (10-25 g/l)
- Mehr als 150 verschiedene HMOs beschrieben
- HMOs sind nicht in Formulanahrung enthalten
- DSLNT (Disialyllacto-N-Tetraose) bei Ratten protektiver Effekt bzgl. NEC



Autran et al., Human milk oligosaccharide composition predicts risk of necrotising enterocolitis in preterm infants. Gut 2018;67:1064–1070
Akkerman et al. Non-digestible carbohydrates in infant formula as substitution for human milk oligosaccharide functions: Effects on microbiota and gut maturation, Crit Rev Food Sci Nutr, 2018 Jan 15:1-12

Kontra #5

Das Potential der Spender/Muttermilch wird durch zusaetzliche notwendige Schritte reduziert

- Pasteurisierung
- Fortifizierung mit KM-Protein

The “universe” of proteins and bio-factors in human milk

REVIEW / SYNTHÈSE Appl. Physiol. Nutr. Metab. Vol. 36, 2011

Effect of pasteurization on immune components of milk: implications for feeding preterm infants

Julia B. Ewaschuk, Sharon Unger, Sarah Harvey, Deborah L. O'Connor, and Catherine J. Field

Table 1. Bioactive components of milk.

Adiponectin	IL-2, -4, -5, -6, -8, -10, -12, -13, -16, -18
α-Lactoglobulin	Insulin
Antisecretory lectins	κ-Casein
α-Tocopherol	Lactadherin
Ascorbate	Lactoferrin
β-Carotene	Lactoperoxidase
B-cells	LCFA–DHA, AA
β-Defensin-1	Leptin
Bifidogenic peptides (hLACFR-la)	Leukocytes
Bifidus factor	Lysozyme
Bombesin	Macrophages
Catalase	MCFA
Complement (C3, C4)	MCP-1
Complement receptors (CF2, CD21)	Mucins
Cortisol	*N*-Acetyl-glucosamine
Cysteine	Nucleotide-hydrolyzing antibodies
EGF, HB-EGF	Neurotensin
Erythropoeitin	Neutrophils
Estrogen, progesterone	NGF
Fibroblast growth factor	Nucleotides
Free secretatory protein	Oligosaccharides
Gangliosides	Osteoprotegerin
Gastrin	Peptide YY
Ghrelin	Platelet activating factor acetylhydrolase
GIP	Prebiotics
Gonadotropin	Prolactin
Glutathione peroxidase	Protease inhibitors
Granulocyte-colony stimulating factor	RANTES
GRP	sCD14
Haptocorrin	Somatostatin
Hepatocyte growth factor	Substance P
Human-chorionic gonadotropin	T-cells
Hypothalamus-related hormones	TGF-α
IFN-γ	TGF-β
IGF-1	Thyroid hormones
IGF-II	TLRs
IL-1 receptor agonist	TNF-α
IL-1b	Vasoactive intestinal peptide

Bio-factors and cellular components in breast milk Caveats

- We do not exactly know about the biological function of these newly reported human milk bio-factors/signals that are orally ingested by the infants.
- Currently, we do not know whether these factors are simple components of body fluids (as components of plasma, appearing by transsudation/passive transport/ultrafiltration) or
  whether **these substrates** are actively secreted into breast milk and serve a true biochemical/nutritional function
- Currently we do not know what effects alteration of these molecules will have on growth and health of infants fed pasteurized human milk.

Table 1. Effect of the pasteurization process on breastmilk components

Component	Maintained (>90%)	Maintained (50–90%)	Maintained (10–50%)	Abolished (<10%)
Macronutrients	Carbohydrate (Lactose, Oligosaccharides)	Protein Total fat		
Micronutrients	Calcium Copper Magnesium Phosphorus Potassium Sodium Zinc	Iron		
Vitamins	Vitamin A	Folate Vitamin B6 Vitamin C		
Biologically active (immune)	IL-8, IL-12p70, IL-13 TGF-α	IgA, sIgA IgG IGF-1, IGF-2 IGF-BP2,3 IFN-γ IL-1β, IL-4, IL-5, IL-10 TGF-β Gangliosides	CD14 (soluble) Il-2 Lactoferrin-iron binding capacity Lysozyme	IgM Lymphocytes
Biologically active (metabolism)	Epidermal growth factor Heparin-binding growth factor	Adiponectin Amylase Insulin	Erythropoeitin Hepatocyte growth factor	Bile salt-dependent lipase Lipoprotein lipase

Bioactive components are impacted to varying degrees by Holder pasteurization; some components remain intact, while cellular components are completely abolished. Ig, immunoglobulins; IGF, insulin-like growth factor; IFN-γ, interferon-γ; IL, interleukin; TGF, transforming growth factor.

Table 3
Summary of main effects of low time low temperature ("Holder") pasteurization on milk components

Component	→	↑	↓	∅	Ref.
Proteins					
Total protein content	X	—	—	—	84,85
Protein quality					
Available lysine	—	—	X[a]	—	86,87
Free amino acids					
Cystine, taurine, methionine,	X	—	—	—	88,89
Arginine, leucine, glutamine	—	X	—	—	88,89
Aspartate	—	—	X	—	89
Bioactive peptides	X	—	—	—	26
Enzymes					
Amylase	—	—	X	—	68,87,90
Lipase, LPL, alkaline phosphatase	—	—	—	X	90
Immunoglobulins					
IgA, IgAs, IgG, IgM IgG4	—	—	X	—	77,82,91–95
Lactoferrine	—	—	X[a]	—	79,80,83,92,93,95
Lyzozyme and lyzozyme activity	—	—	X[a]	—	68,74,76,77,80,82,83,92,95,96
Lipids					
Total fat	X	—	—	—	30,34,84,85,90,97
Free fatty acids	—	X	—	—	30
Fatty acids 18:1, 18:3, 12:0, 14:0, 18:0	X[a]	—	—	—	34,35,89,90,98–101
Other fatty acids	X	—	—	—	30,98,100,101
Saccharides					
Glucose	X[a]	—	—	—	94,102
Lactose, oligosaccharides, GAG	X	—	—	—	84,85,94,97,102–104
Vitamins					
E, B2, B3, B5, B12, Biotin	X	—	—	—	93,105
C, D, B6	—	—	X	—	99,106,107
A, C, α-γ-δ-tocopherols	—	—	X[a]	—	35,94,97,100,108
Zinc, Copper, Iron	X	—	—	—	97,109
Growth factors					
EGF, TGF-ß1, TGF-ß2, MCP-1	X	—	—	—	20,94,110
GM-CSF	—	X	—	—	94
EPO, HB-EGF, IGF-1, IGF-BP~2 & ~3	—	—	X[a]	—	97,100,108
Hormones					
Leptine	X	—	—	—	79
Insuline, adiponectine	—	—	X	—	111
Cytokines					
IL-2, -4, -5, -12, -13, -17	X	—	—	—	35,94,100
IL-8, -7	—	X[a]	—	—	94,100
IL-1ß, -6, -10, TNF-α, INF-γ	—	—	X[a]	—	35,94,108

(*continued on next page*)

Significant body of evidence about integrity of bio-factors

Human Milk—Treatment and Quality of Banked Human Milk

Jean-Charles Picaud, MD, PhD[a,b,c,d,e,*], Rachel Buffin, MD[a,b]

Clin Perinatol 44 (2017) 95–119
http://dx.doi.org/10.1016/j.clp.2016.11.003

Table 3
(*continued*)

Component	→	↑	↓	∅	Ref.
Oxidative stress markers					
Malonedialdehyde	X	—	—	—	112
Glutathione, GPA, TAC	—	—	X	—	112
Bactericial activity	—	X	—	—	113
Cells					
Lymphocytes	—	—	X	—	91
Macrophages	—	X	—	—	96
Electrolytes and minerals	X	—	—	—	78
Osmolality	X	—	—	—	78

Abbreviations: →, No/minor change; ↑, increase; ↓, decrease; ∅, Destruction; GAG, glycaminoglycans; GPA, glutathione peroxidase activity; LPL, lipoprotein lipase; TAC, total antioxidant capacity; TNF, tumor necrosis factor.

[a] Discordant results: requires further studies.

Nekrotisierende Enterokolitis (NEC)
pasteurisierte Frauenmilch

- *Quigley-M, 2014:* Systematischer Review und Metaanalyse aus 6 Studien: MM/FM vs. Formula:
  - Formulanahrung: Risiko für NEC doppelt so hoch, für Nahrungsunverträglichkeit 5 mal so hoch
  - Schätzung: **ein extra NEC-Fall bei jedem 25. FG, das Formulanahrung erhält**
  - Vorteil bleibt erhalten auch bei Fortifier-Zusatz
- **Deutsches Frühgeborene-Netzwerk** (GNN): ausschließlich Formulanahrung: höheres Risiko für NEC (OR 12,6)

- Der Effekt ist dosisabhängig. *(Sisk, 2007; Chowning, 2016)*

Parameter	*Human milk for < 50% of LOS*	*Human milk for ⩾ 50% of LOS*	*P-value*
N	260 (47.3%)	290 (52.7%)	—
Birth weight (kg)	1.03 ± 0.29[a]	1.08 ± 0.28	0.03
PMA at birth (weeks)	28.1 ± 2.7	28.6 ± 2.5	0.02
Weight gain (g kg^{-1} day^{-1})	14.6 ± 4.2	14.8 ± 2.9	0.56
Change in weight z-score	− 1.19 ± 1.13	− 1.33 ± 0.86	0.096
Head circumference gain (cm per week)	0.74 ± 0.17	0.72 ± 0.16	0.095
Change in head circumference z-score	− 0.55 ± 1.05	− 0.60 ± 0.80	0.52
Mortality rate	4.2%	1.0%	0.017
NEC rate (⩾ Bell Stage II)	13.5%	3.4%	< 0.001
Surgical NEC rate	4.2%	2.1%	0.14
Length of stay (days)	81.4 ± 52.8	64.0 ± 29.8	< 0.001
Days of human milk	16.8 ± 15.8	48.7 ± 22.8	< 0.001

Abbreviations: LOS, length of stay; NEC, necrotizing enterocolitis; PMA, post-menstrual age. [a]Mean ± s.d.

Einführung von Frauenmilch führt zur Reduktion der NEC-Rate

NEC-Rate vor und nach Einführung von FM, FG < 1500 g GG

Kantorowska-A, Pediatrics, 2016

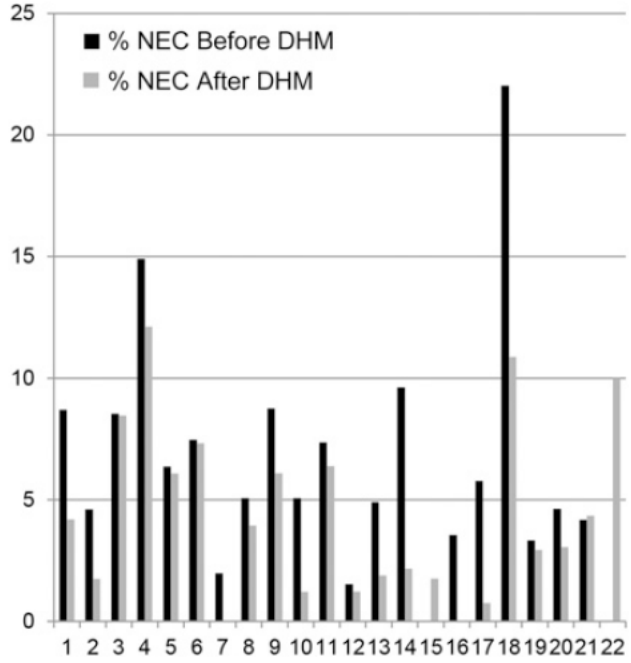
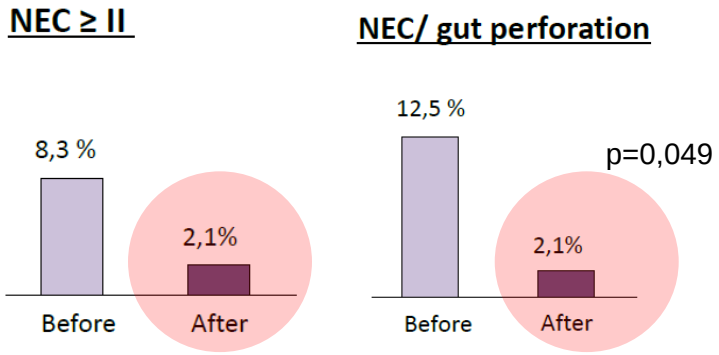


FIGURE 3
Paired NEC rates: comparison of hospital rates of NEC among VLBW infants before/after the transition to having DHM available. Each point on this graph's x-axis represents one of the 22 hospitals that underwent a clear change from not having DHM to having DHM available.

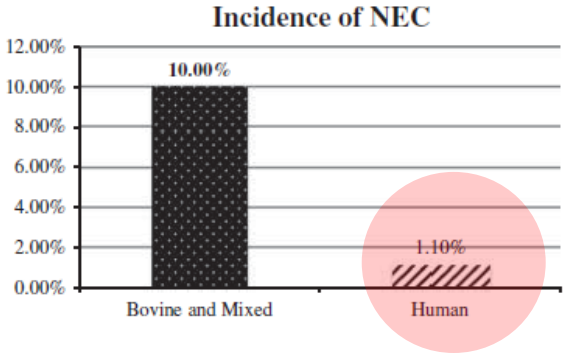
NEC-Rate vor und nach Eröffnung einer FMB, FG < 32 SSW

Vazquez-Roman, An Pediatr., 2014



NEC-Inzidenz unter Ernährung mit ausschließlich humaner Milch, FG ≤ 28 SSW, ≤ 1500 g, 2009-2014

Assad, 2016

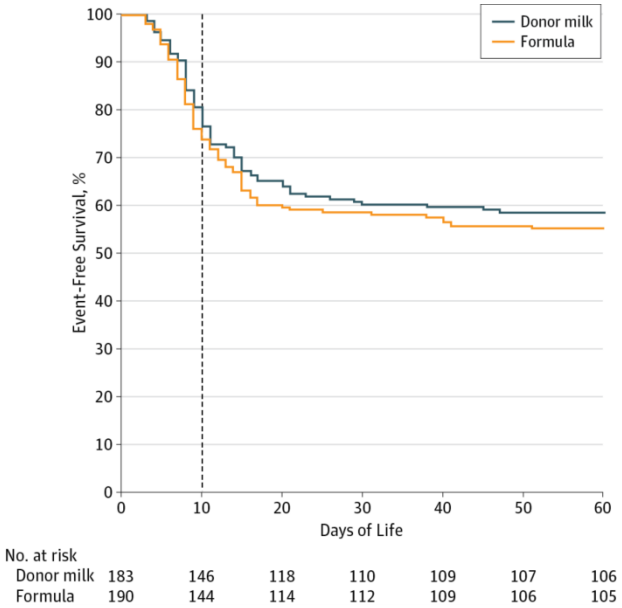


Effect of Donor Milk on Severe Infections and Mortality in Very Low-Birth-Weight Infants: The Early Nutrition Study Randomized Clinical Trial

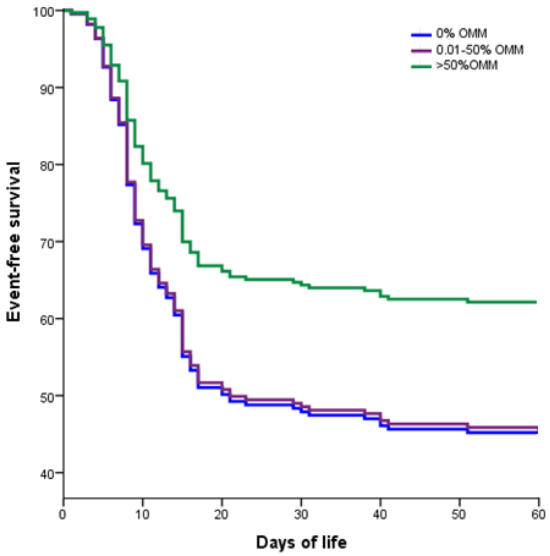
- N= 373, FG <1500 g GG
- Einsatz von **Formula oder Frauenmilch (past.)** als Supplement zur Muttermilch in den **ersten 10 Lt**.: **kein signifikanter Unterschied der NEC-Inzidenz**: 8,9% (F) vs. 9,3% (FM)

10 Tage?

- **kein signifikanter Unterschied von Infektion/NEC/Tod**: 44,7% (F) vs. 42,1% FM



- Anteil der MM >50% an der Nahrung führt in beiden Gruppen zu einer Verbesserung der ereignisfreien Zeit



JAMA Pediatr. 2016;170(7):654-661. doi:10.1001/jamapediatrics.2016.0183

Klinischer Benefit: Retinopathie (ROP)

Deutsches Frühgeborenennetzwerk
N=1433, FG < 32 SSW

Humane Milch: MM und FM

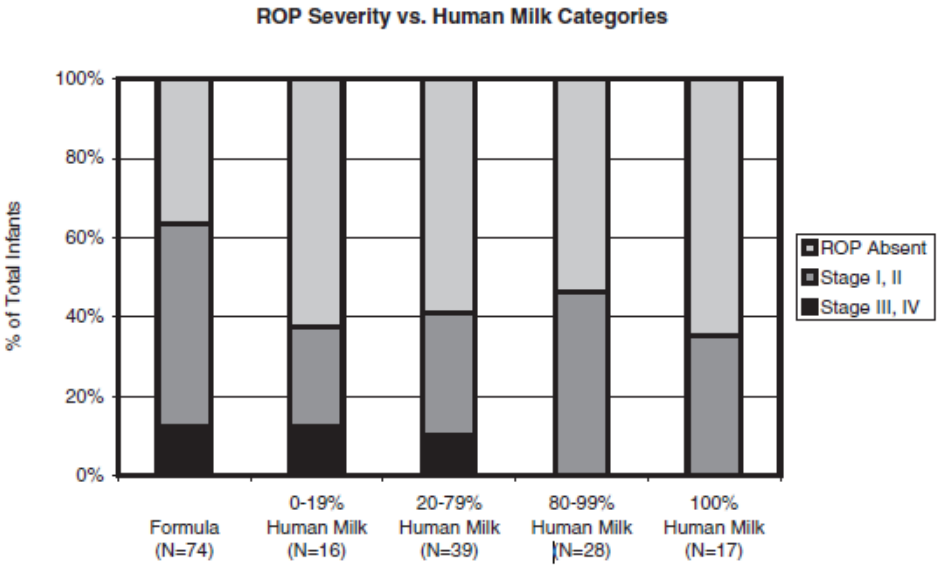
Table II. Logistic regression of exclusive formula or mixed feeding on inflammatory complications of prematurity compared with to exclusive breastmilk

	OR	(CI 95%)
BPD		
Exclusive formula	2.59	(1.33-5.04)
Mixed feeding	1.61	(1.15-2.25)
NEC		
Exclusive formula	12.86	(2.84-58.29)
Mixed feeding	3.59	(1.68-7.63)
ROP		
Exclusive formula	1.80	(1.05-3.11)
Mixed feeding	1.34	(1.02-1.76)

Spiegler-J et al., J Pediatr. 2016; 169:76-80;

Hylander-A, 2001

N=174 FG, GG < 1500 g, GA 27,8 SSW, 1992-1993
MM mit Fortifier, Formula



Hylander-A et al., Journal of Perinatology 2001; 21:356 – 362

Kontra #3

Kein Hinweis, dass das Langzeit-Outcome durch Spendermilch verbessert wird

Tufts BSID III scores at 2 years

Madore, et al; Clin Therapeutics 39(6): 1210-1220; 2017

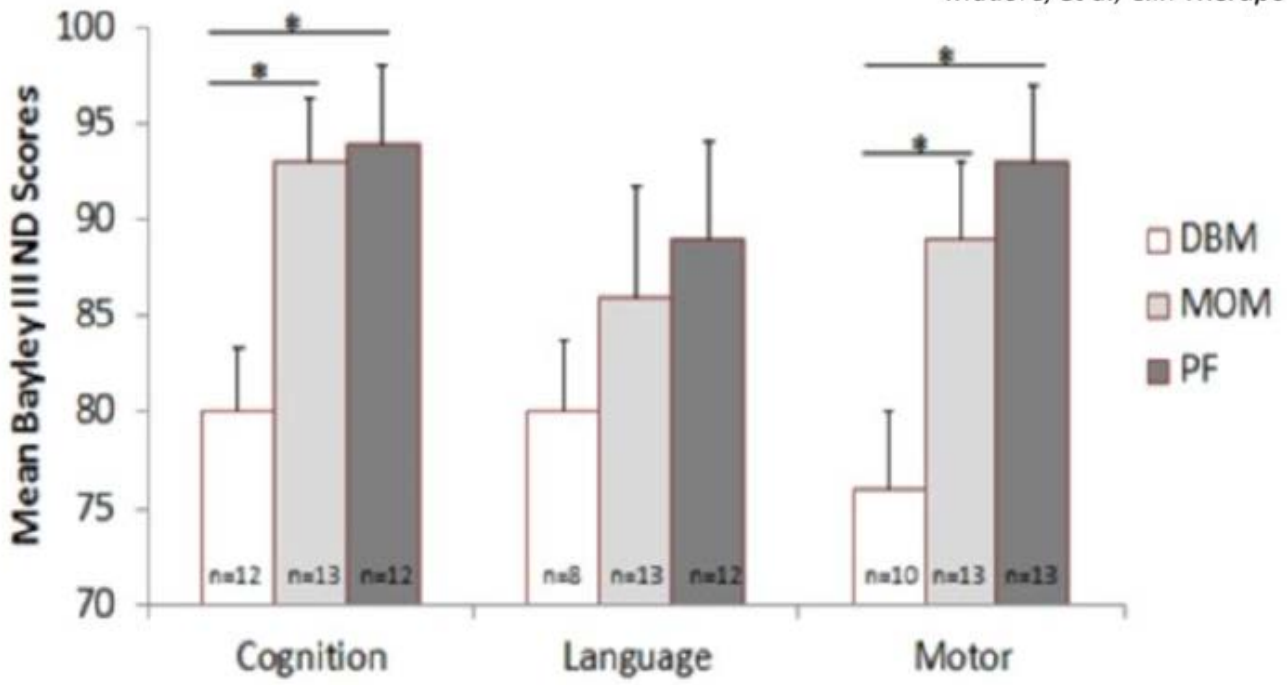


Figure1: Comparison of mean Bayley III neurodevelopmental scores at two-years corrected age between feeding groups ± standard error. Statistical analysis through ANOVA with multiple comparisons. * indicates p value <0.05.

Highlights the importance of ongoing randomized trials being completed

- Infants fed DM grew more poorly in the first month of life than those fed MM or PF

DOMINO trial

Lower NEC rates, but no improvement in neurodevelopmental outcomes

From: **Effect of Supplemental Donor Human Milk Compared With Preterm Formula on Neurodevelopment of Very Low-Birth-Weight Infants at 18 MonthsA Randomized Clinical Trial**

JAMA. 2016;316(18):1897-1905. doi:10.1001/jama.2016.16144

Table 2. Neurodevelopment at 18 Months' Corrected Age Assessed by the Bayley Scales of Infant and Toddler Development, Third Edition[a]

Characteristic	Adjusted Mean (95% CI)[b] Donor Milk (n = 151)	Adjusted Mean (95% CI)[b] Preterm Formula (n = 148)	Adjusted: Model 1[c] Effect (95% CI)	Adjusted: Model 1[c] P Value	Adjusted: Model 2[d,e] Effect (95% CI)	Adjusted: Model 2[d,e] P Value
Composite scores[f]						
Cognitive-primary outcome	92.9 (89.8 to 95.9)	94.5 (91.4 to 97.5)	−1.6 (−5.5 to 2.2)	.41	−2.0 (−5.8 to 1.8)	.31
Language	87.3 (83.8 to 90.8)	90.3 (86.7 to 93.9)	−3.0 (−7.5 to 1.5)	.19	−3.1 (−7.5 to 1.3)	.17
Motor	91.8 (88.8 to 94.9)	94.0 (91.0 to 97.0)	−2.2 (−6.0 to 1.7)	.27	−3.7 (−7.4 to 0.09)	.06
	Donor Milk, No./Total (%)	Preterm Formula, No./Total (%)	Adjusted Risk Difference, % (95% CI)	P Value		
Neuroimpairment score <85						
Cognitive	41/151 (27.2)	24/148 (16.2)	10.6 (1.5 to 19.6)	.02		
Language	70/150 (46.7)	54/145 (37.2)	9.3 (−1.8 to 20.3)	.10		
Motor	38/149 (25.5)	30/147 (20.4)	3.7 (−5.2 to 12.6)	.41		
Disability score <70						
Cognitive	14/151 (9.3)	12/148 (8.1)	−1.2 (−8.4 to 6.1)	.75		
Language	29/150 (19.3)	22/145 (15.2)	1.6 (−7.0 to 10.2)	.72		
Motor	18/149 (12.1)	13/147 (8.8)	2.2 (−3.8 to 8.3)	.47		

[a] Standardized mean is 100 (SD, 15). Continuous variables were analyzed by analysis of covariance, with adjustment as indicated. All models were tested for treatment interactions, and except where indicated none were found to be statistically significant. Analyses were rerun without nonstatistically significant interactions in the models. Categorical variables were analyzed by logistic regression analysis with adjustment as indicated.

[b] Adjusted using covariates from model 1.

[c] Adjusted for recruitment center and birth weight group (<1000 g, 1000-1499 g).

[d] Adjusted for recruitment center, birth weight group, maternal education (high school or less, college or vocational diploma, baccalaureate degree, postbaccalaureate degree), and percentage of total enteral feeds for each infant consumed as mother's milk. For the motor composite score, a statistically significant interaction was found with maternal education ($P = .01$), and this interaction was retained in the model.

[e] Logistic regression analyses of the proportion of participants with scores indicative of neuroimpairment or disability were not performed using model 2 adjustments because of insufficient sample size.

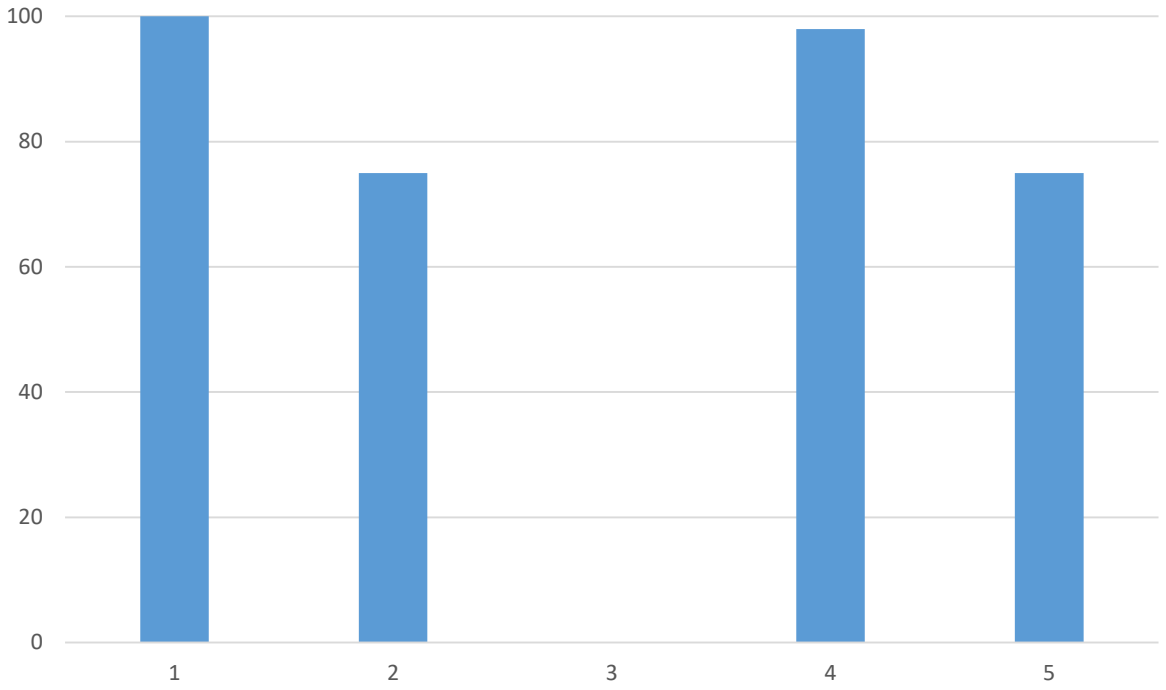
No difference in BSID III scores

Increased risk of Cog < 85

No difference in Risk of Cog < 70

Neurodevelopmental Outcome

NEC	Standard		DM	
	-	+	-	+
	148	10	151	3



14800 + 750 = 15550

98,4

14798 + 225 = 15023

97,6

15100 + 225 = 15325

99,5

DOMINO trial: balance of outcome parameters

Taking Stephens data (8.2 MDI per 1 g Protein/kg/d)

===> **ΔMDI** of 2 ≈ 0.24 g P/kg/d !!! !

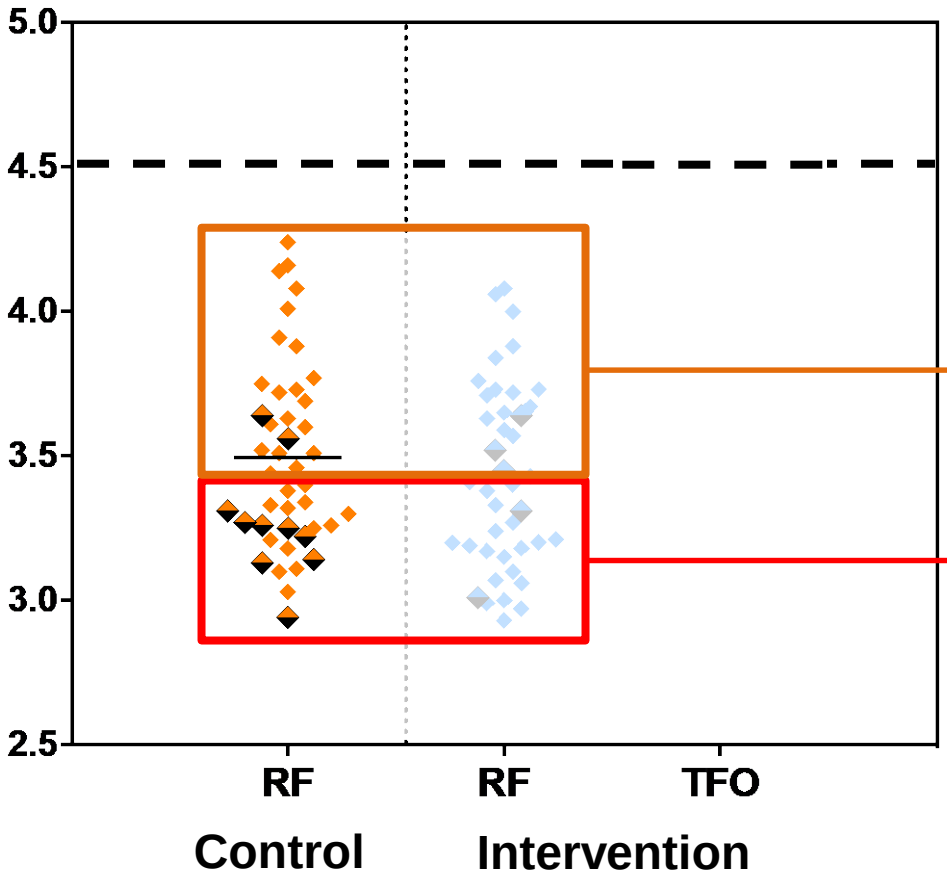
===> **Δ**P of DM vs MM: 0.3 – 0.5 g/kg/d

===> **Δ**P of 0.24 g/kg/d ≈ **Δ**growth rate of 1.5 g/kg/d

- Study possibly not powered (2-tailed) not powered to detect differences in growth rates of 1-2 g/kg/d

McMaster Children's Hospital
NEONATAL NURSERIES

TFO improves intake of Protein



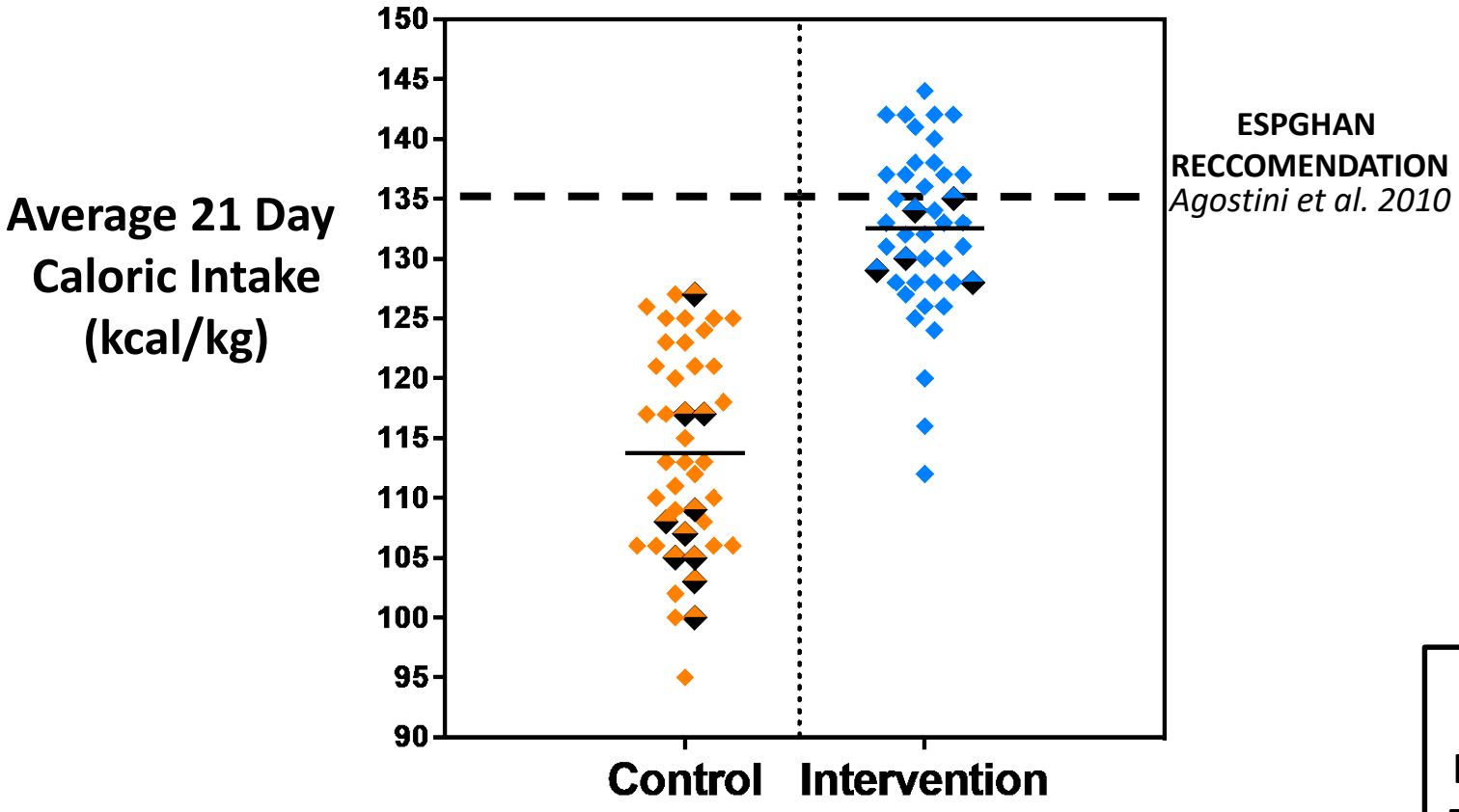
ESPGHAN RECCOMENDATION
Agostini et al. 2010

<u>High Protein Group</u>
Intake > Median of 3.41 g/kg/day after RF

<u>Low Protein Group</u>
Intake < Median of 3.41 g/kg/day after RF

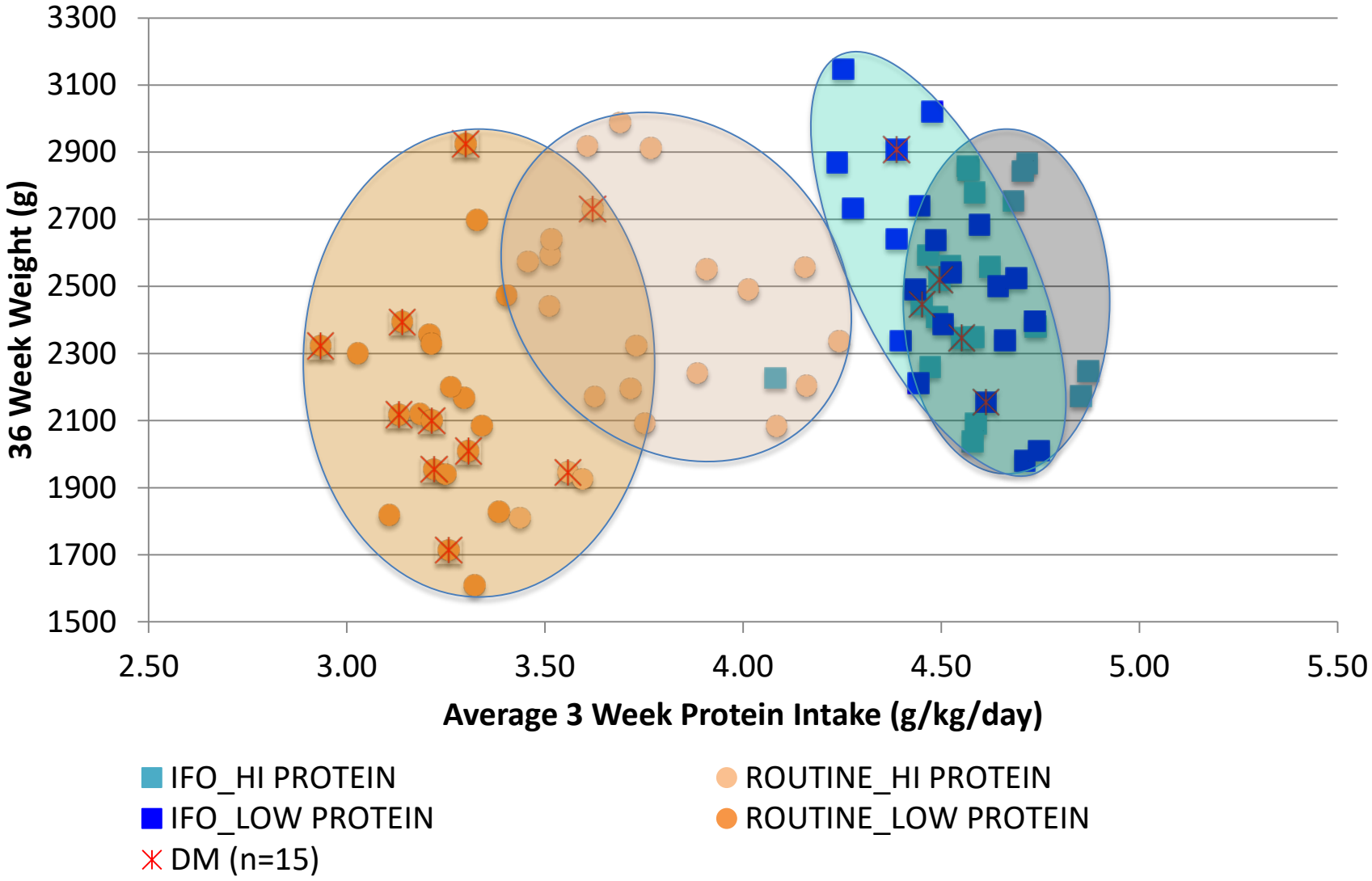
Infants on Donor Milk

TFO increases caloric intake to provide more energy for preterm growth



Infants on Donor Milk

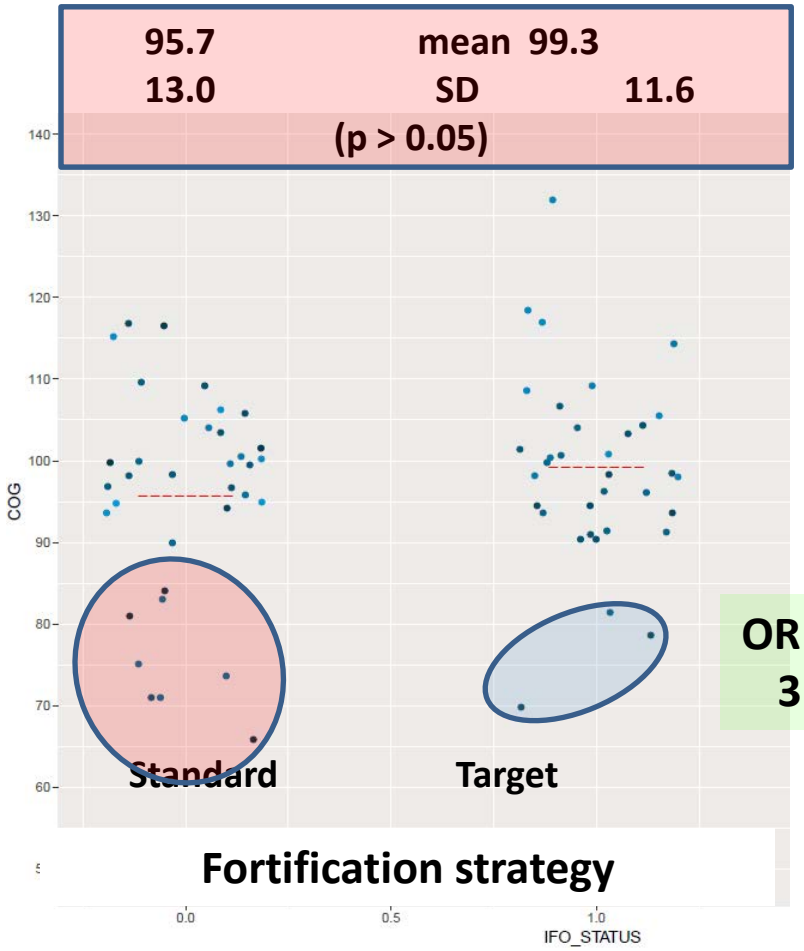
Protein intake vs growth
Influence of Donor milk



Fortification and Neurodevelopment

Cognition – per protocol analysis

Subjects on target fortification do better

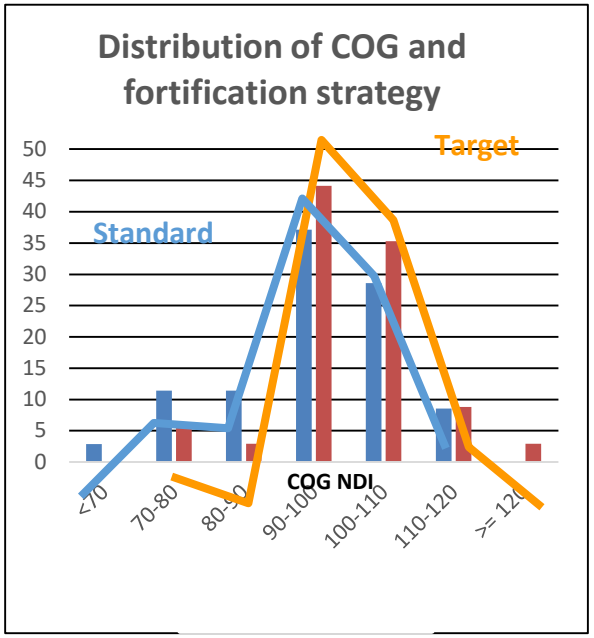


Sample size for
alpha 0.05
beta 0.80
delta ~ 3 - 4
SD ~ 12

n = 180 -240
250 – 300 to
Recriuit for ND-F/U

higher mean (average)
Lower OR for COG<85
Right shift of population

OR for COG < 85
3.1 (p>0.05)



Kontra #4

Der Aufwand ist betraechtlich und die Kosten sind doch sehr hoch
(300 Liter fuer 90.000 Euro) und

es gibt keine Standardisierung.

Leitlinie für die Einrichtung und zur Arbeitsweise von Frauenmilchbanken

Herausgegeben von Skadi Springer

unter Mitarbeit von N.Bannert, M. Boettcher, Chr. Dittmer, W. Handrick, W. Heine, J. Henker,
B. Pustowoit, F.-B. Spencker, Chr. Vogtmann

Mit einem Geleitwort von Friedrich Manz

Guidelines for Germany are missing

Preface

The 13th edition of the *Guidelines for the Establishment and Operation of a Donor Human Milk Bank* provides direction for donor milk banking in North America. This edition was developed after careful review of current research, other tissue banking guidelines, including blood banking, and in consultation with clinical experts. All 11 donor milk banks in Canada and the US, as members of Human Milk Banking Association of North America, contribute to and operate under these guidelines. These donor milk banking guidelines are formally recognized by the states of California, New York and Texas, the only three states to address donor milk banking in statutes, as their standard for human milk banking.

Wide variation of practices when handling human milk

Handling of Breast Milk by Neonatal Units: Large Differences in Current Practices and Beliefs

Daniel Klotz[1], Stefanie Jansen[1], Corinna Gebauer[2] and Hans Fuchs[1]*

[1] Department of Neonatology, Center for Pediatrics, Medical Center - University of Freiburg, Faculty of Medicine, University of Freiburg, Freiburg, Germany, [2] Department of Neonatology, University Children's Hospital, Leipzig, Germany

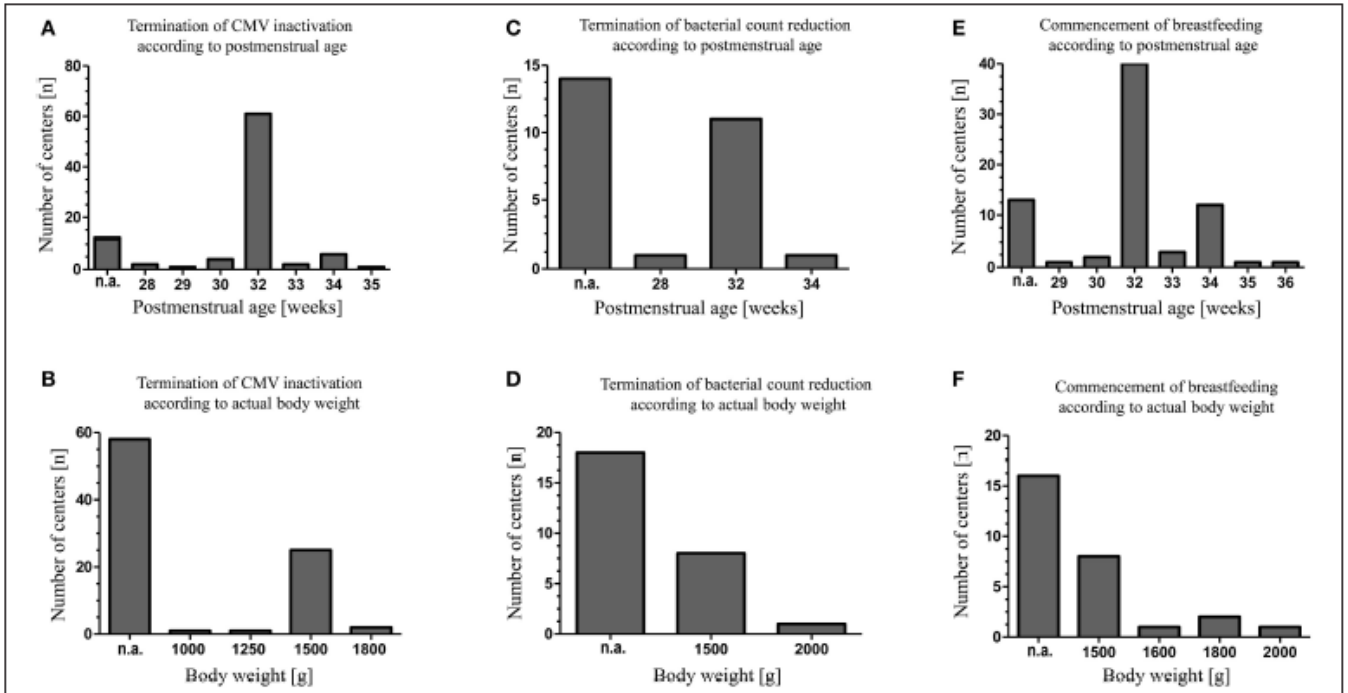
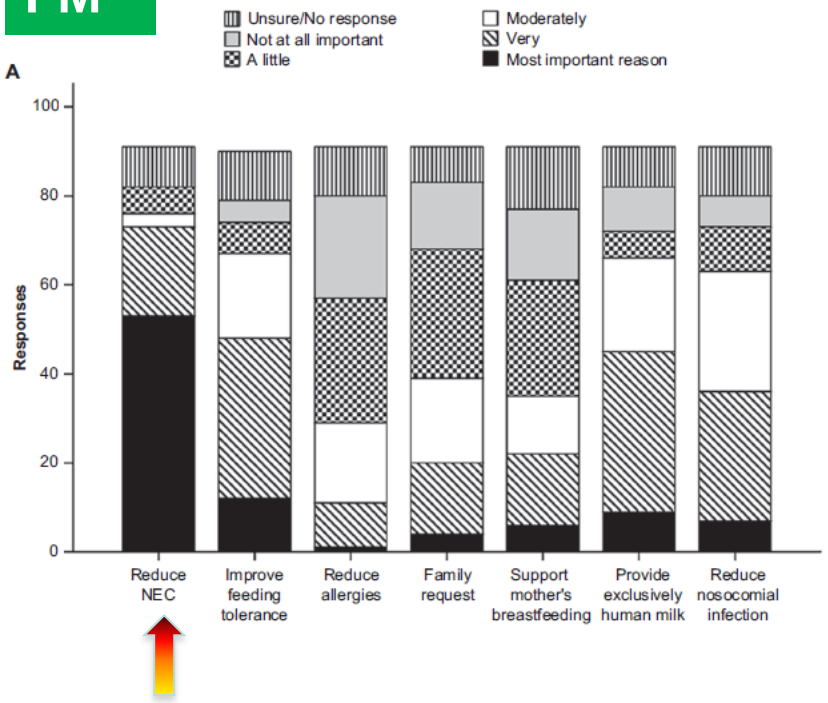


FIGURE 1 | Indications of individual neonatal units for CMV inactivation, reduction of bacterial breast milk count and initiation of breastfeeding in case of maternal CMV seropositivity. The decisions to commence breastfeeding, to terminate CMV inactivation or bacterial count reduction were made either depending on the infants postmenstrual age **(A,C,E)** or depending on the infants' actual body weight **(B,D,F)**. N.a., respective criteria were not applied.

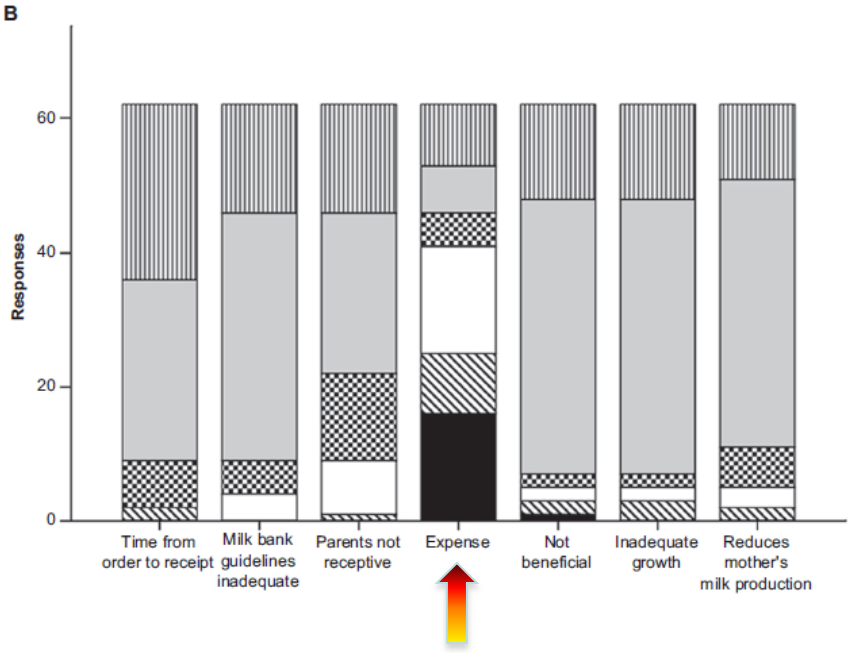
Hohe Kosten: FM / Frauenmilchbank

- Kosten Hauptgrund für Nichtverwendung von gespendeter Frauenmilch (Hagadorn et al., JPEN J Parenter Enteral Nutr. 2016 Mar;40(3):326-33)

FM



keine FM

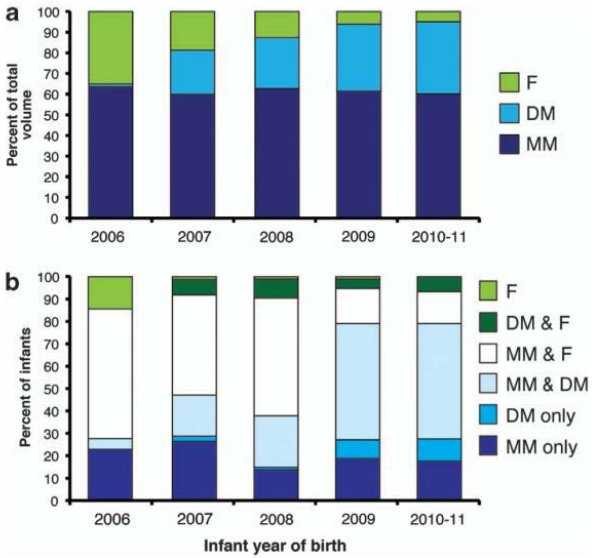


- Einsparung an Kosten durch kürzere Aufenthaltshauer, Verhindern einer NEC, kürzere parenterale Ernährung, geringere Wiederaufnahmeraten (Arnold, 2002; Johnson 2015; Ganapathy, 2012; Assad, 2016)

In der Klinik nach Eröffnung einer Frauenmilchbank….

- sinkender Verbrauch von Formula
  - in den ersten 4 Lebenswochen: 37% vs. 60% *(Utrera Torres-MI, 2010)*
  - in den ersten 15. Lt.: 50% vs. 16% *(Vazquez-Roman, 2014)*

- Anstieg der FM-Gabe von 8% auf 77% der Kinder, MM-Anteil unverändert, Formula-Anteil verdrängt
  (Delfosse-NM, 2013)



- Höherer Anteil an muttermilchernährten ehemaligen FG bei Entlassung in NICUs mit FMB als in solchen ohne:
  - 29,6% vs. 16% (*Arslanoglu-S, 2013)*
  - ca. 10% höher *(Kantorowska-A, 2016)*
  - 54% vs. 40% (Vazquez-Roman, 2014)

Zusammenfassung

- Die Milch der eigenen Mutter ist die beste Nahrung fuer kleine Fruehgeborene.

- Fuer Kinder, deren Muetter nicht ausreichend Muttermilch zur Verfuegung stellen koennen, reduziert die Ernaehrung mit Spendermilch gegenueber handelsueblicher Fruehgeborenen-Nahrung das Risiko fuer NEC, Sepsis, BPD, ROP etc.

- Die Wirkung wird wahrscheinlich durch einer verbesserte Toleranz bei der Einfuehrung enteraler Nahrung (Sepsisrate und assoziierte Konsequenzen), die Ausbildung eines guenstigeren Mikrobioms (Bifidobakterien) durch Oligosaccharide (HMO) sowie einer Reduktion der Exposition von tierischem Casein (Entzuendungspotential) herbeigefuehrt

Zusammenfassung

- Neben den Hauptnaehrstoffen Eiweiss, Fett, Kohlehydraten und HMO’s befinden sich weitere Stoffe in der Muttermilch wie bioaktive Eiweisse, Zellen etc, deren Bedeutung bislang nicht geklaert ist.

- Fruehgeborene, die mit Spendermilch ernaehrt werden, haben ein hoeheres Risiko fuer schlechteres Wachstum.

- Dies liegt wahrscheinlich am niedrigeren Proteingehalt der Spendermilch.

- Dieses Defizit kann durch eine Extra-Fortifizierung behoben werden.

Zusammenfassung

- Da Spendermilch – wie auch die Milch der eigenen Mutter – einer erheblichen Variation der diaetetischen Zusammensetzung unterliegt, empfiehlt sich neben einer angepassten Fortifizierung die Schulung der Mitarbeiter fuer ernaehrungsphysiologische Grundlagen und Zusammenhaenge.

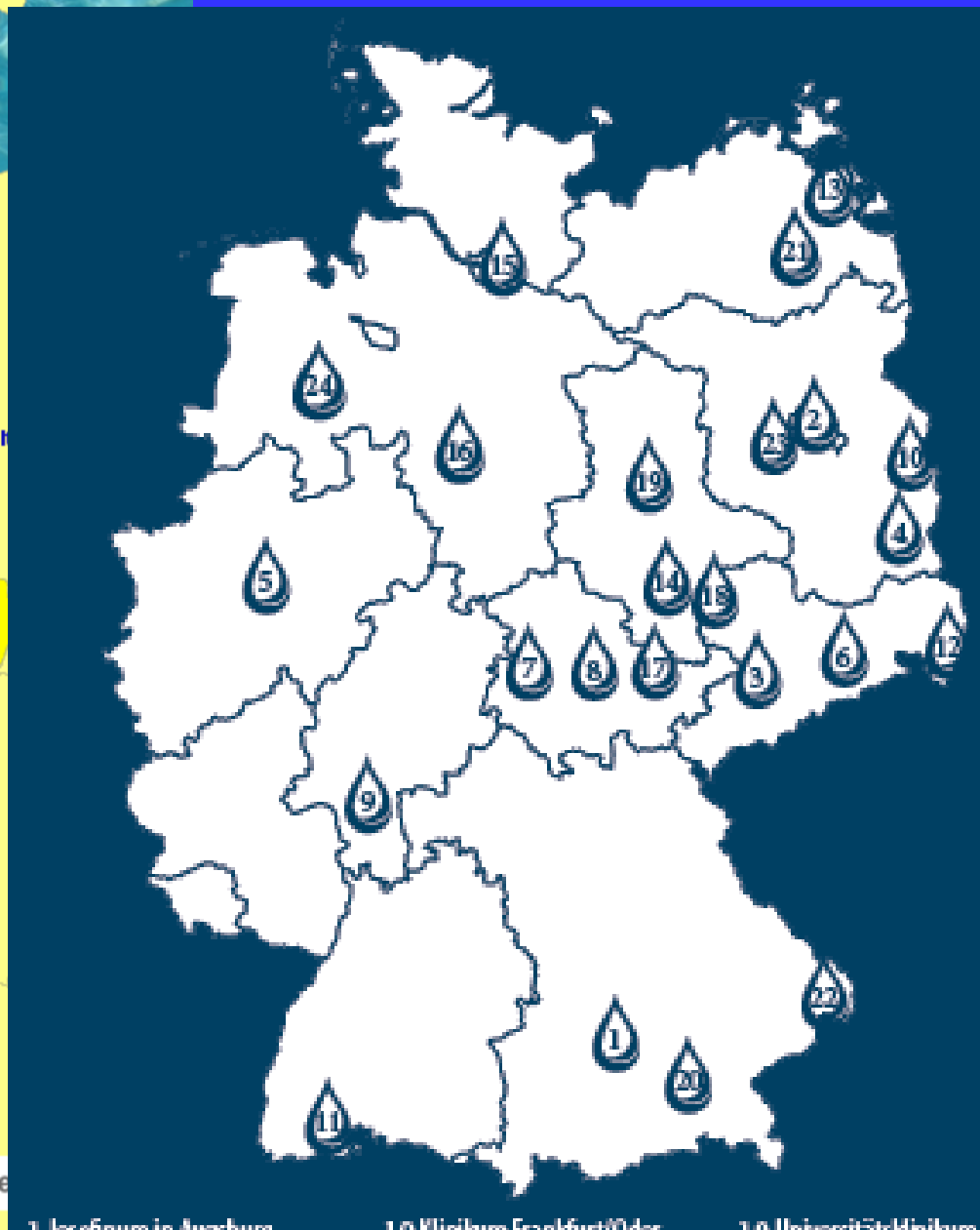
- Es besteht noch Entwicklungsbedarf im Bereich der Pasteurisierung, um den Verlust von bioaktiven Substanzen zu begrenzen.

- Ebenso im Bereich der Naehrstoffanreicherung, da Standardfortifizierung sowie die Exposition gegenueber kuhmilch-basiertem Protein nicht optimal sind


Kiel
Rostock
Hamburg-Schnelsen
Hamburg Moorfleet
Brinkum
Oldenburg
Lüneburg
Großburgwedel
Berlin-Spandau
Osnabrück
Berlin-Tempelhof
Berlin-Waltersdorf
Hannover
Bielefeld
Braunschweig
Essen
Kamen
Duisburg
Dortmund
Kaarst
Düsseldorf
Kassel
Leipzig
Erfurt
Dresden
Köln-Butzweilerhof
Siegen
Chemnitz
Köln-Godorf
Kobelnz
Hanau
Wallau
Frankfurt am Main
Walldorf
Würzburg
Mannheim
Nürnberg/Fürth
Saarlouis
Ludwigsburg
Regensburg
Sindelfingen
Ulm
München-Eching
Augsburg
Freiburg
München-Brunnthal
stepmap.de

IKEA – Standorte in Deutschland

IKEA – Standorte in Deutschland



Richtigstellung

- Prof. Fusch hat im Rahmen diese Vortrages die “advocatus diabolic” Rolle uebernommen.

- Er ist von der positive Wirkung der Mutter- und Spendermilch ueberzeugt und distanziert sich ausdruecklich von der gespielten Kontra-Rolle.

- Wir sind aber ueberzeugt, dass dieser Beitrag zeigt, dass noch viel Forschung vonnoeten ist, um das volle Potential der Ernaehrung mit Spendermilch auszuschoepfen.