Supplemental Online Content

Chinnappan A, Sharma A, Agarwal R, Thukral A, Deorari A, Sankar MJ. Fortification of breast milk with preterm formula powder vs human milk fortifier in preterm neonates: a randomized noninferiority trial. *JAMA Pediatr*. Published online May 10, 2021. doi:10.1001/jamapediatrics.2021.0678

- eTable 1. Composition of breast milk and the two fortifiers used in the study
- **eTable 2.** Additional nutrients added with fortification in the two groups
- **eTable 3.** Nutritional content of the fortified milk preparations considering enteral intake of 180 ml/kg with standardized fortification in the two groups
- **eTable 4.** Comparison of outcomes related to individual components of feed intolerance in the two groups
- **eTable 5.** Composition of preterm formula powders and human milk fortifiers available in India other than those used in the study
- eFigure 1. Intervention overview
- **eFigure 2.** Non inferiority margin and the mean difference in weight gain between two fortification strategies

This supplemental material has been provided by the authors to give readers additional information about their work.

eTable 1. Composition of breast milk and the two fortifiers used in the study

	Expressed breast milk	Preterm formula; Dexolac Special	Human milk fortifier; PreNAN (Nestle and
	(in each 100 mL)	Care, DANONE India	Co., India)
Colorino Konliberta	07	(in each gram)	(in each gram)
Calories, Kcal/kg/d	67	5.00	3.00
Protein, g/kg/d	1.1	0.13	0.30
Fat, g/kg/d	3.6	0.26	0.10
Carbohydrates,			
g/kg/d	6.7	0.55	0.40
Calcium, mg/kg/d	26.0	6.50	15.93
Phosphorus,			
mg/kg/d	13.0	3.25	8.76
Vitamin D, IU/d	2.0	6.00	28.00
Iron, mg/kg/d			0.36
	0.12	0.11	
Vitamin A, IU/kg/d	50.0	68.25	221.60
Vitamin E, IU/kg/d	1.5	0.15	1.12
Vitamin K, mcg/kg/d	0.20	0.90	1.50
Vitamin B6, mcg/kg/d	14.0	10.24	0.02
Vitamin B12,			
mcg/kg/d	0	0.02	0.04
Vitamin C, mg/kg/d	10.6	0.90	3.75
Folic acid, mcg/kg/d	3.3	2.25	7.50
Riboflavin, mcg/kg/d	47.0	7.70	40.00
			30.00
Thiamine, mcg/kg/d	20.0	6.67	
Magnesium, mg/kg/d	3.0	0.50	0.80
Sodium, mEq/kg/d	1.4	0.14	0.32
Potassium, mEq/kg/d	2.4	0.10	0.25
Copper, mcg/kg/d	73.0	4.80	10.00
Manganese,	<u> </u>		
mcg/kg/d	0.60	0.75	1.21
Zinc, mg/kg/d	0.33	0.04	0.19

eTable 2. Additional nutrients added with fortification in the two groups

Additional nutrients	Strength of formulation	Intended Recommended dietary allowance (RDA)	Dose	
Preterm formula powder fortification – Dexolac special care				
Multivitamin drops			0.5 ml PO BD	
Syrup calcium phosphate	16 mg calcium/mL; 8mg phosphorus/mL	120 – 140 mg/kg/day	0.5 ml per feed in 10 feeds	
Drop Iron		2 mg/kg/day	1 drop PO in 2 feeds	
Syrup vitamin D3	400 IU/ml	800 IU/day	1 ml PO BD	
Human milk fortifier – PreNAN				
Syp Vitamin D3	400 IU/ml	800 IU/day	1 ml PO BD	

eTable 3. Nutritional content of the fortified milk preparations considering enteral intake of 180 ml/kg with standardized fortification in the two groups

	RDA (ESPGHAN)	PTF	HMF
Calories, Kcal/kg/d	110-135	156.6	142.2
Protein, g/kg/d	3.5-4.0	2.92	4.14
Fat, g/kg/d	4.8-6.6	8.35	7.2
Carbohydrates, g/kg/d	11.6-13.2	16.02	14.94
Calcium, mg/kg/d	120-140	93.6	161.5
Phosphorus, mg/kg/d	60-90	46.8	86.47
Vitamin D, IU/d	800-1000	46.8	205.2
Iron, mg/kg/d	2-3	1.04	2.81
Vitamin A, IU/kg/d	1330-3300	581.4	1685.5
Vitamin E, IU/kg/d	2.2-11	3.78	10.76
Vitamin K, mcg/kg/d	4.4-28	6.84	11.16
Vitamin B6, mcg/kg/d	45-300	98.93	25.34
Vitamin B12, mcg/kg/d	0.1-0.77	0.14	0.3
Vitamin C, mg/kg/d	11.0-46	25.56	46.08
Folic acid, mcg/kg/d	35-100	22.14	59.94
Riboflavin, mcg/kg/d	200-400	140.04	372.6
Thiamine, mcg/kg/d	140-300	84.02	252.0
Magnesium, mg/kg/d	8.0-15.0	9.0	11.16
Sodium, mEq/kg/d	3.0-5.0	3.53	4.82
Potassium, mEq/kg/d	3.0-5.0	5.04	6.12
Copper, mcg/kg/d	100-132	165.96	203.4
Manganese, mcg/kg/d	<27.5	6.48	9.79
Zinc, mg/kg/d	1.1-2.0	0.87	1.96

Abbreviations: ESPGHAN, European Society for Paediatric Gastroenterology Hepatology and Nutrition; HMF, human milk fortifier; PTF, preterm formula; RDA, recommended dietary allowance

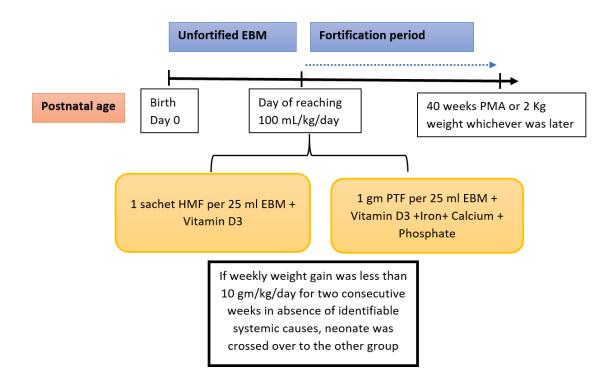
eTable 4. Comparison of outcomes related to individual components of feed intolerance in the two groups

Variables	Preterm formula fortification (n = 59)	Human milk fortifier (n = 63)	Relative risk (95% CI)	P value
>2 episodes vomiting, No.(%)	23 (39)	30 (48)	0.82 (0.54 to 1.23)	0.34
Abdominal distension(> 2 cm), any episode, No. (%)	6 (10)	10 (16)	0.64 (0.25 to 1.65)	0.35
Prefeed aspirate >50%, No. (%)	0	0	-	-
Bilious vomiting, No. (%)	1 (2)	2 (3)	0.53 (0.05 to 5.73)	0.59
Altered blood in vomitus, No. (%)	0	3 (5)	-	0.49
At least one episode of feed intolerance, No. (%)	2 (3)	9 (14)	0.24 (0.05 to 1.05)	0.06
Need to withhold fortification for 24 hours or more, No. (%)	3 (5)	14 (22)	0.23 (0.07 to 0.76)	0.01

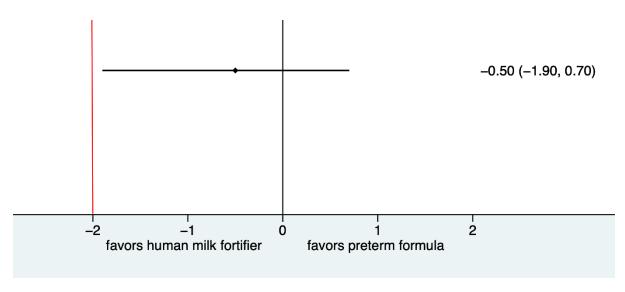
eTable 5. Composition of preterm formula powders and human milk fortifiers available in India other that those used in the study

Composition	Human Milk Fortifier (HMF) powder		Preterm formula powder	
	Lactodex (Raptakos, Brett & Co.Ltd.)	HIJAM (Endocura Pharma)	Lactodex LBW (Raptakos, Brett & Co.Ltd.)	Similac Neosure (Abott)
Calories, Kcal/kg/d	3.37	3.6	4.99	5.17
Protein, g/kg/d	0.27	0.25	0.13	0.13
Fat, g/kg/d	0.04	0.25	0.26	0.28
Carbohydrates, g/kg/d	0.49	0.05	0.535	0.534
Calcium, mg/kg/d	15.8	25	6.5	6.67
Phosphorus, mg/kg/d	7.9	12.5	3.25	3.33
Vitamin D, IU/d	133	100	7	6
Iron, mg/kg/d	0.3	0.36	0.12	0.09
Vitamin A, IU/kg/d	200	155	65	30
Vitamin E, IU/kg/d	1.25	0.62	0.25	0.18
Vitamin K, mcg/kg/d	1.1	0.55	0.71	0.61
Vitamin B6, mcg/kg/d	25	12.5	6.5	5.2
Vitamin B12, mcg/kg/d	0.05	0.025	0.025	002
Vitamin C, mg/kg/d	5	2.5	1.15	1.89
Folic acid, mcg/kg/d	12.5	20	2	1.9
Riboflavin, mcg/kg/d	20	10	10.5	9.75
Thiamine, mcg/kg/d	18.5	6	7.5	9.0
Magnesium, mg/kg/d	1.75	2	0.5	0.61
Sodium, mEq/kg/d	0.082	0.173	0.16	0.1
Potassium, mEq/kg/d	0.23	0.41	0.12	0.16
Copper, mcg/kg/d	14.3	12.5	5	6.16
Manganese, mcg/kg/d	1.7	0.85	0.68	0.51
Zinc, mg/kg/d	0.04	0.04	0.04	0.034

eFigure 1. Intervention overview



eFigure 2. Non inferiority margin and the mean difference in weight gain between the two fortification strategies



95% CI of mean difference of weight gain with preterm formula fortification did not cross the pre-specified non-inferiority margin of 2 g/kg/day indicated by the solid red line.