Nutrition & Growth in Premature Infant

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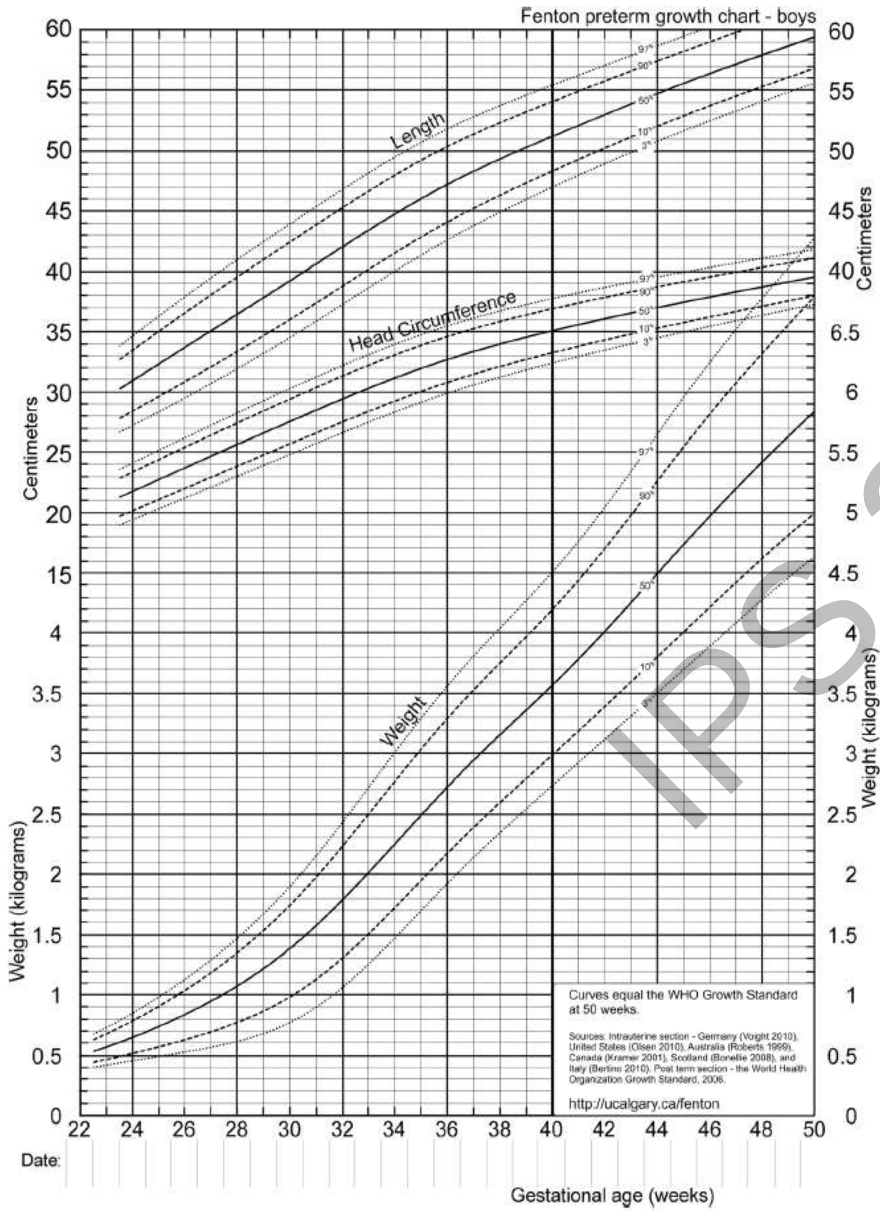
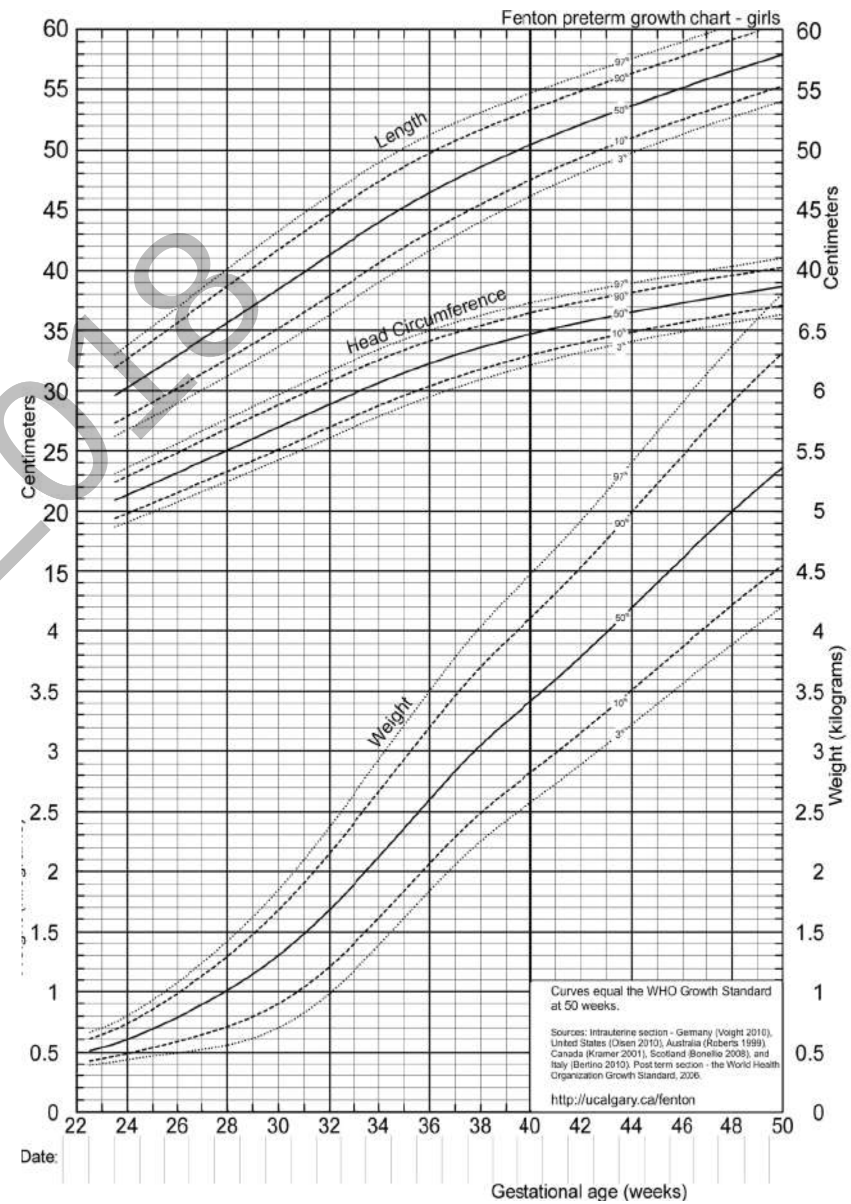
PART ONE : THE GROWTH OF THE PREMATURE INFANT ARE WE ON THE RIGHT TRACK ?

REFERENCE CHART GROWTH FOR PREMATURE





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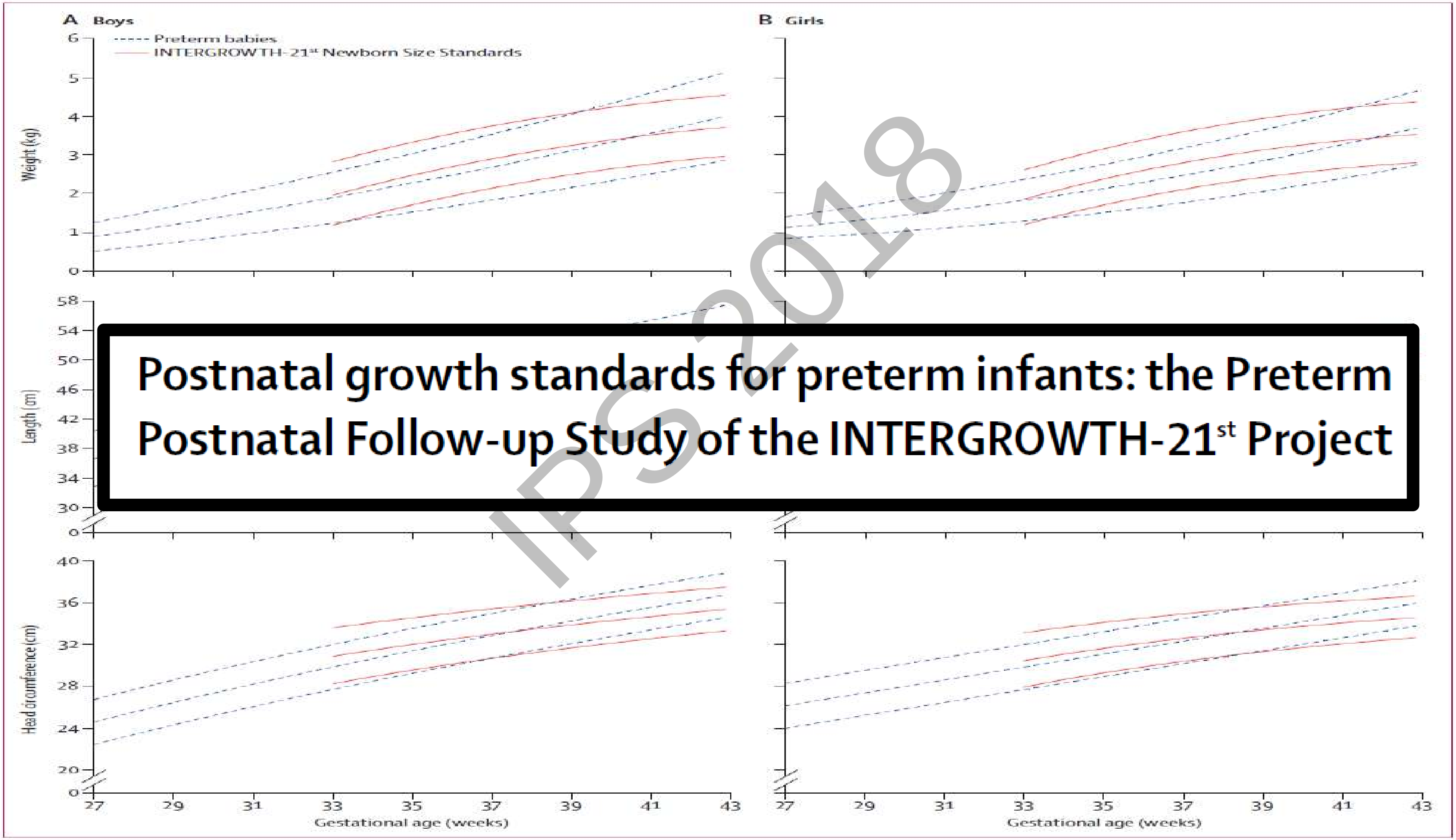
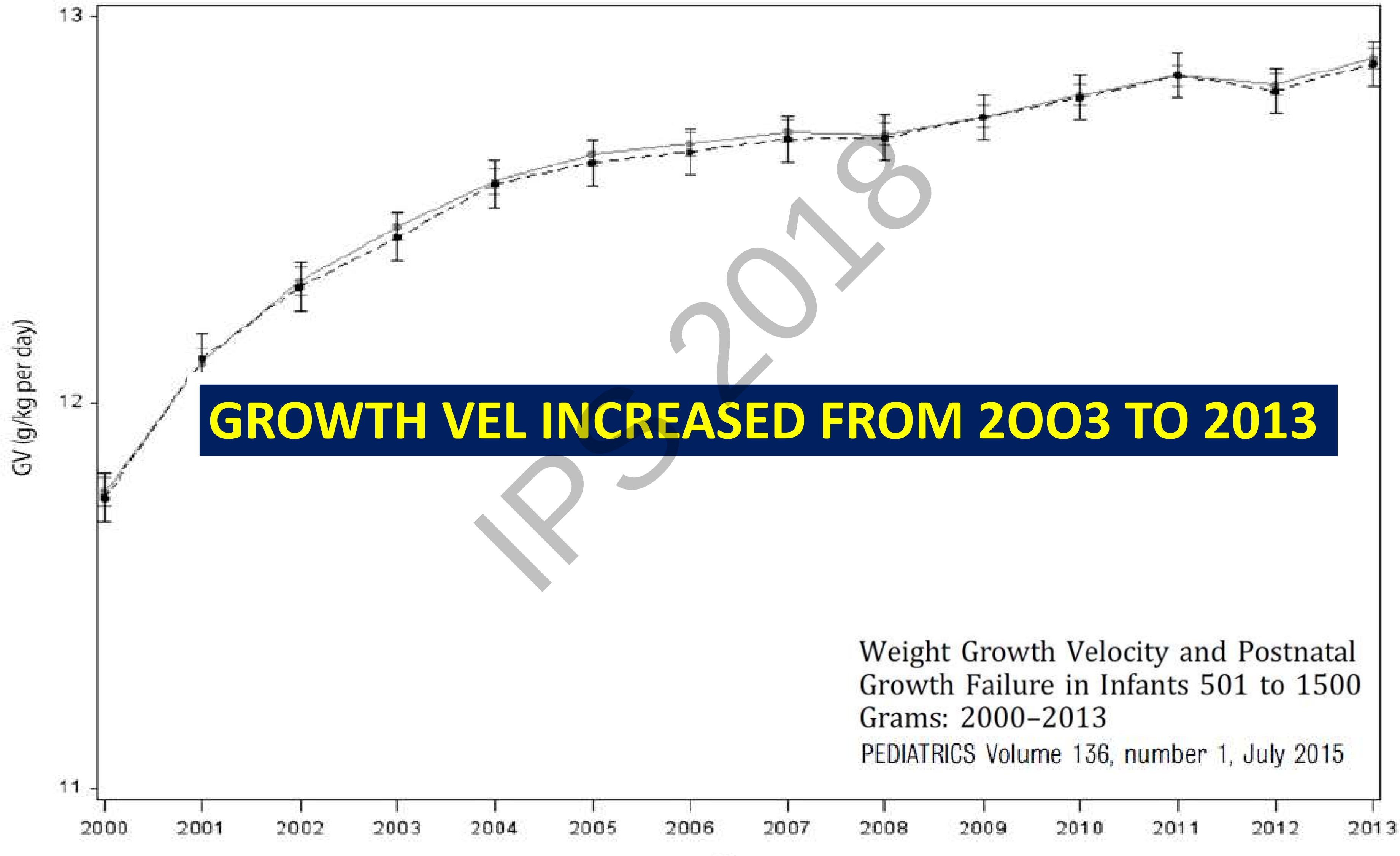


Lancet Glob Health 2015; 3: e681–91

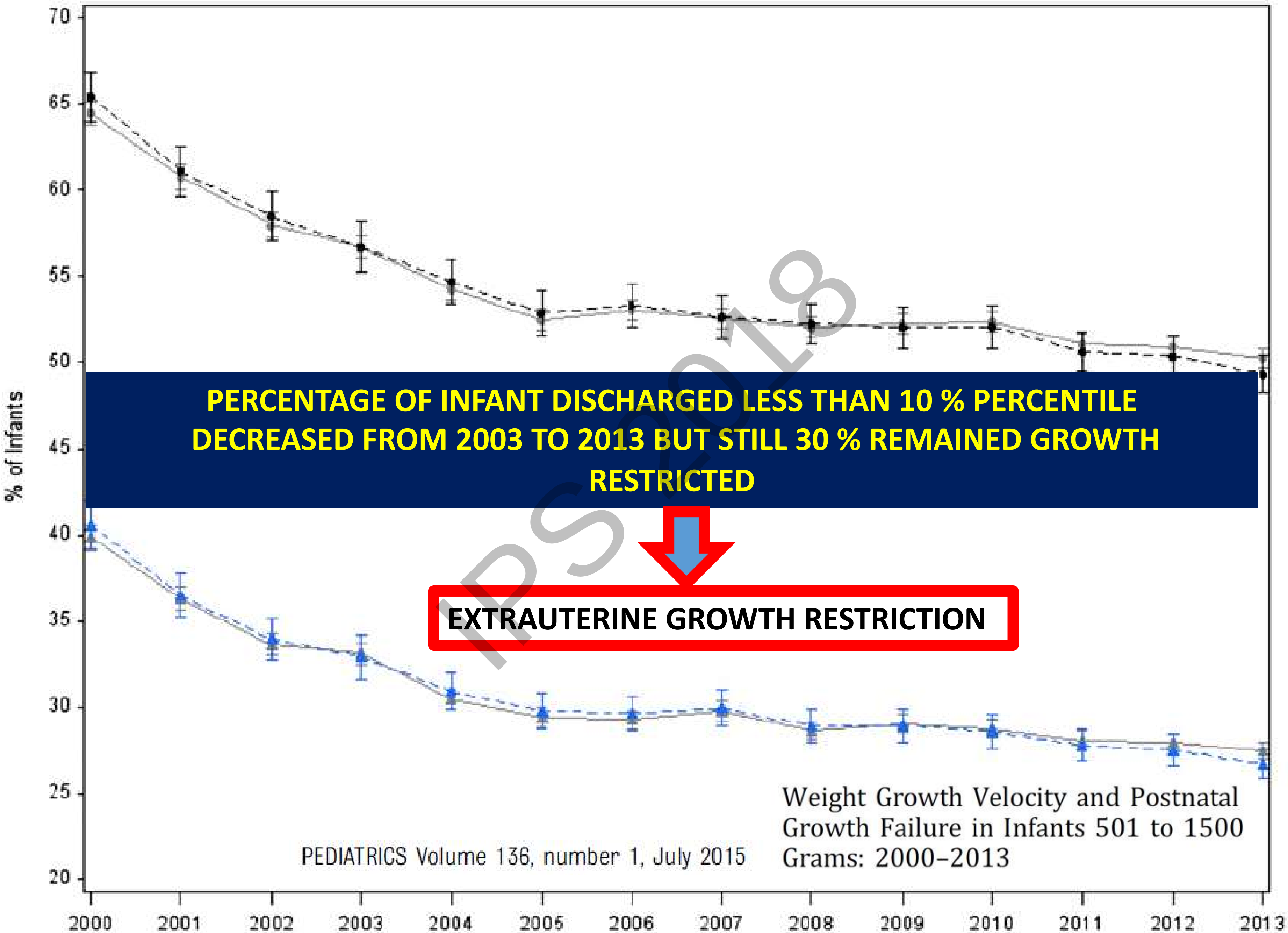
WHAT ABOUT PREMATURE IN NICU ?



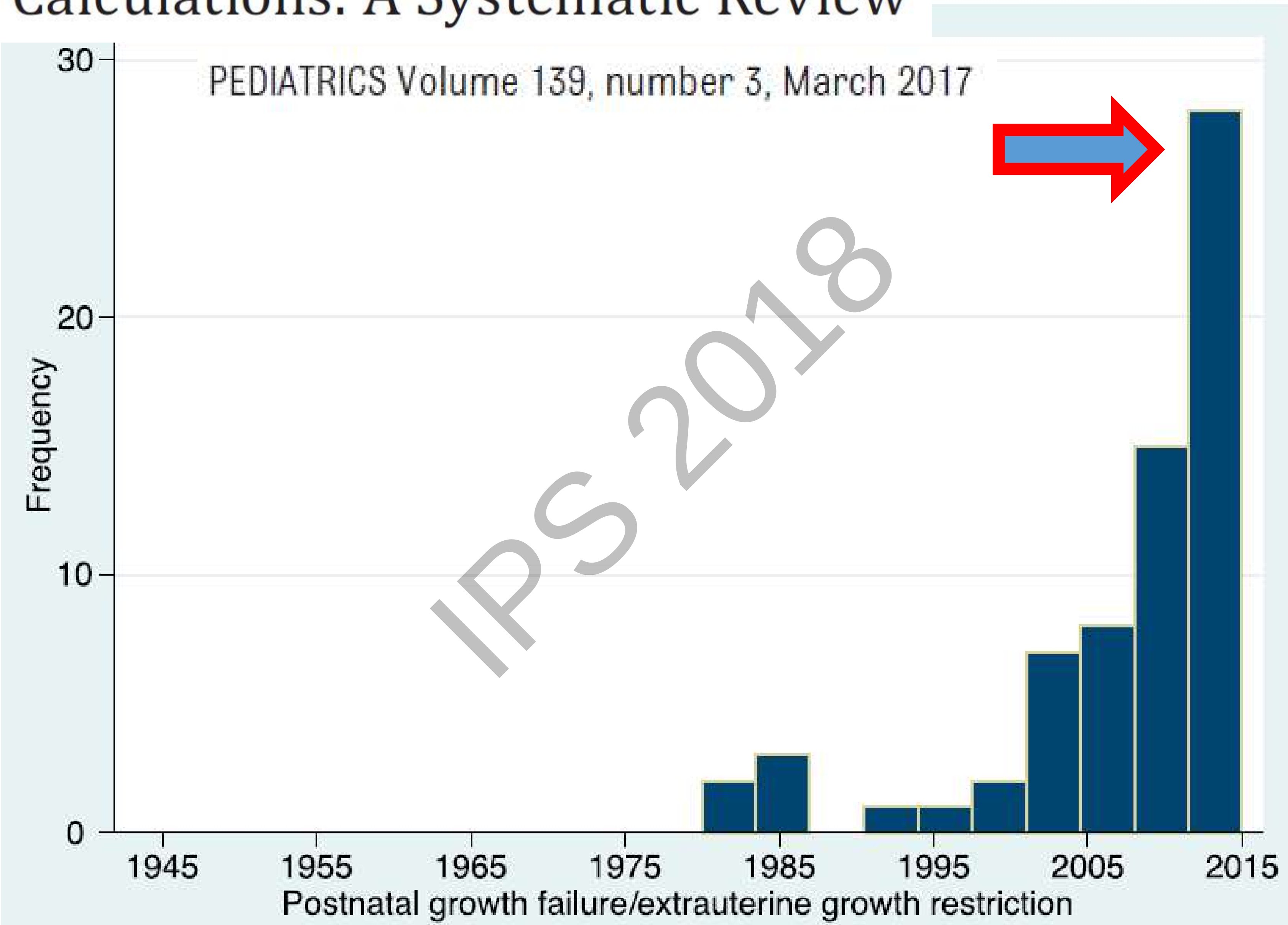
GROWTH VEL INCREASED FROM 2OO3 TO 2013

Weight Growth Velocity and Postnatal Growth Failure in Infants 501 to 1500 Grams: 2000–2013

PEDIATRICS Volume 136, number 1, July 2015

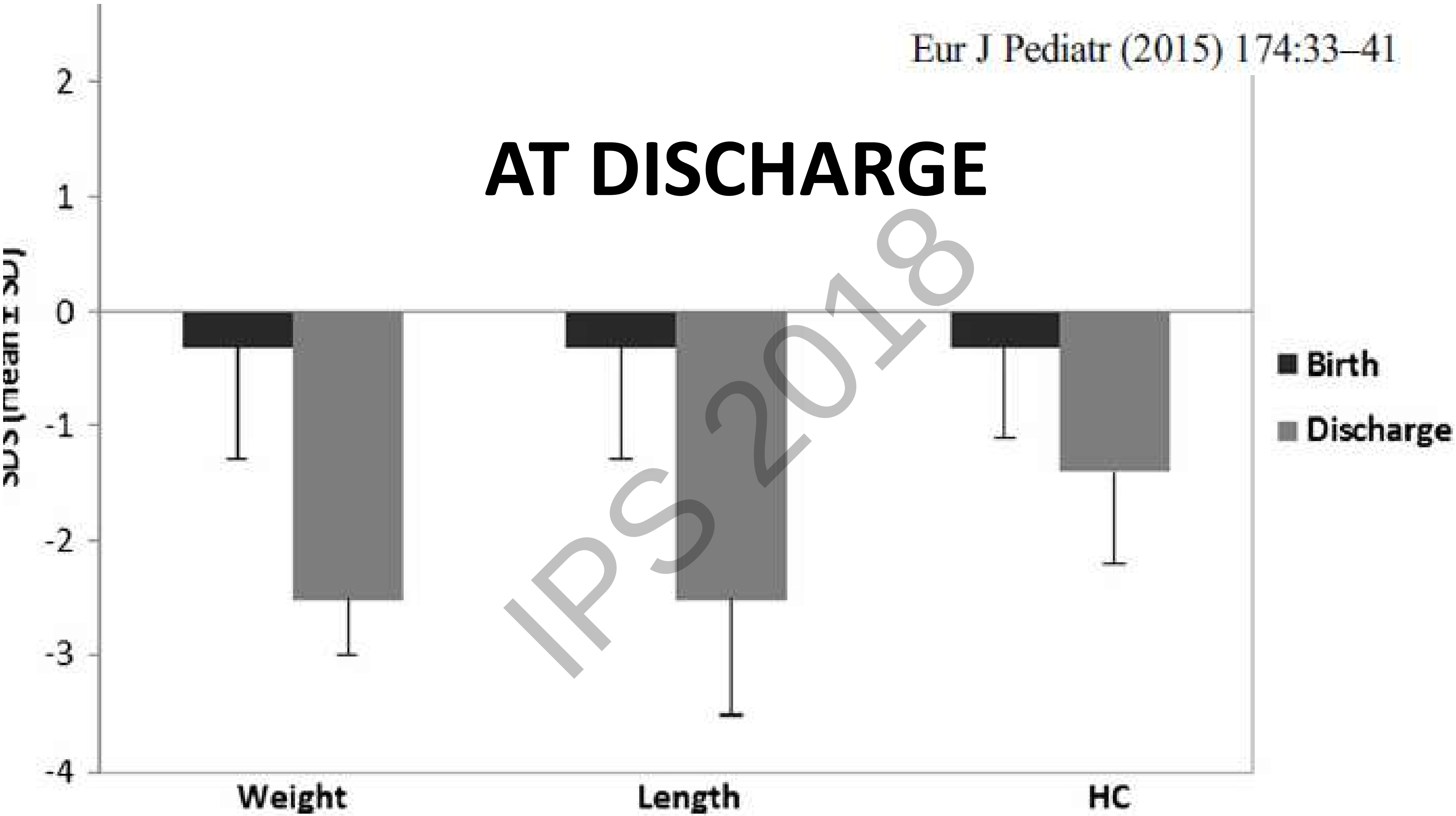

% of Infants
70
65
60
55
50
45
40
35
30
25
20
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
PERCENTAGE OF INFANT DISCHARGED LESS THAN 10 % PERCENTILE DECREASED FROM 2003 TO 2013 BUT STILL 30 % REMAINED GROWTH RESTRICTED
EXTRAUTERINE GROWTH RESTRICTION
PEDIATRICS Volume 136, number 1, July 2015
Weight Growth Velocity and Postnatal Growth Failure in Infants 501 to 1500 Grams: 2000–2013

Preterm Infant Growth Velocity Calculations: A Systematic Review



Preterm infants with severe extrauterine growth retardation (EUGR) are at high risk of growth impairment during childhood

Eur J Pediatr (2015) 174:33–41



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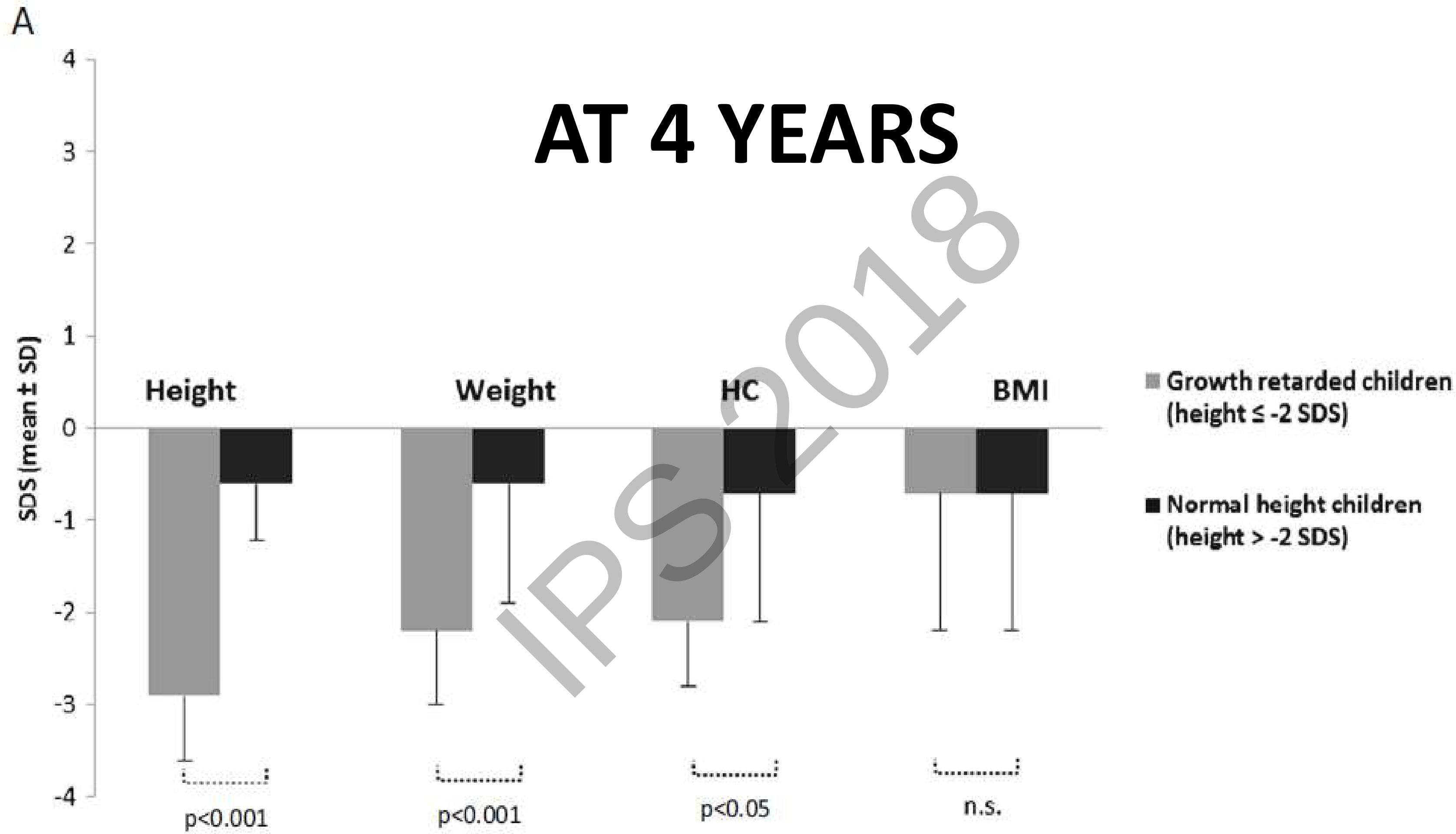
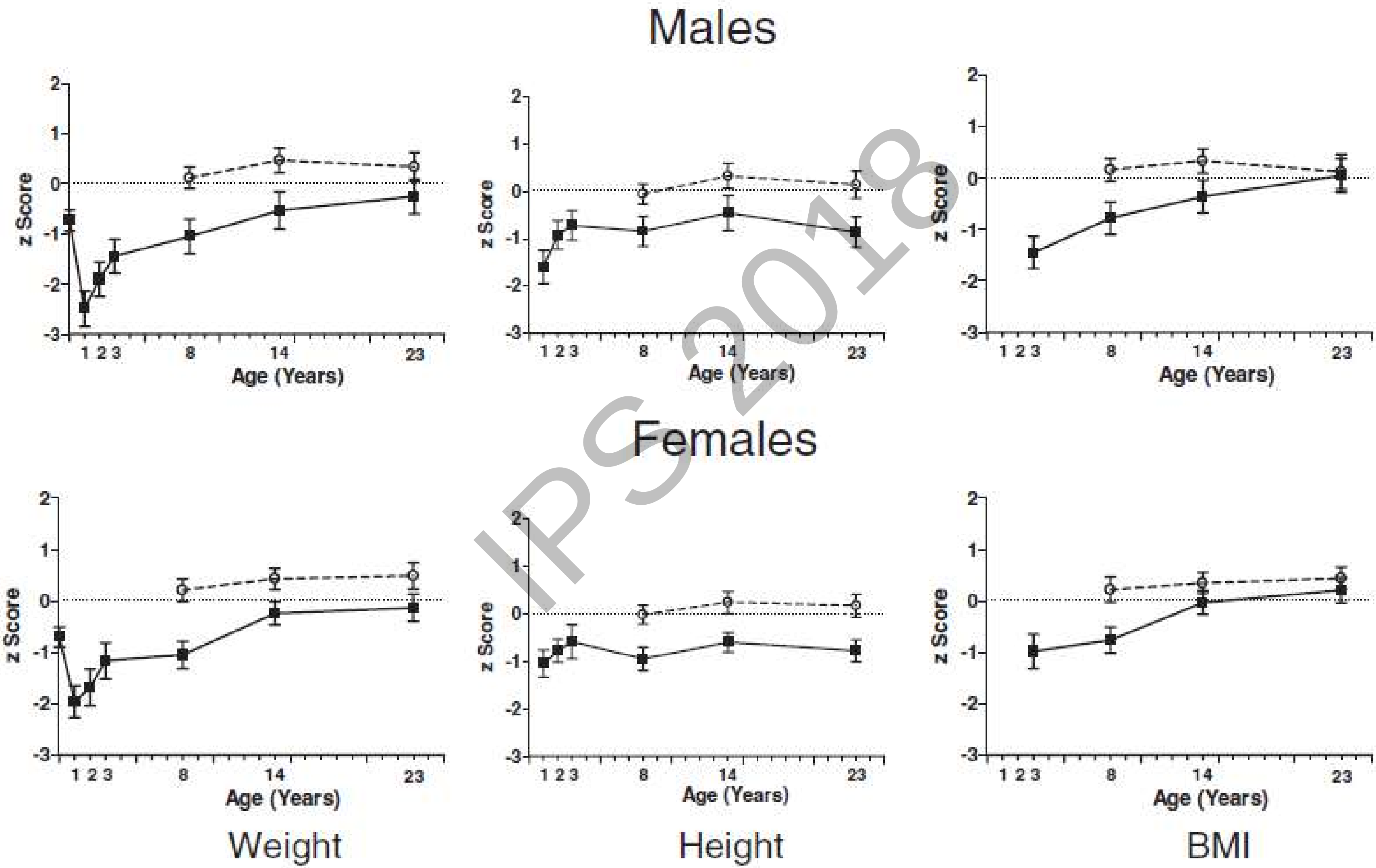


AT 23 YEARS

SAIGAL *ET AL.*
(*Pediatr Res* 60: 751–758.



TAKE HOME MESSAGE ONE

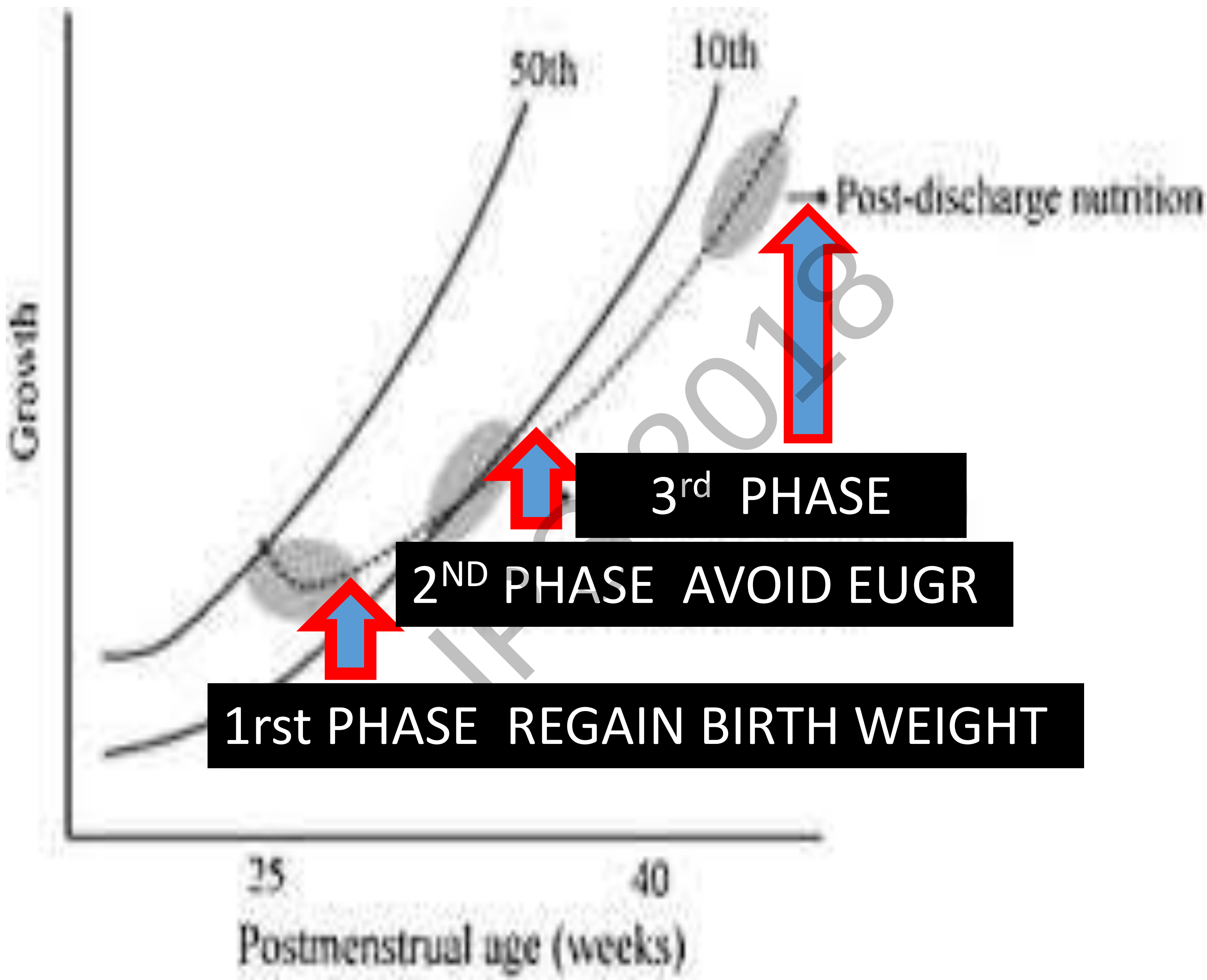
PREMATURITY +
INTRAUTERINE GROWTH RESTRICTION +
EXTRAUTERINE GROWTH RESTRICTION

↓

GROWTH IMPAIRMENT +
NEURODEVELOPMENTAL DELAY +
METABOLIC SYNDROM

PART TWO : THE OPTIMAL NUTRITION FOR A PREMATURE INFANT

TO AVOID EXTRA UTERINE RESTRICTION



50th
10th
Post-discharge nutrition
Growth
3rd PHASE
2ND PHASE AVOID EUGR
1rst PHASE REGAIN BIRTH WEIGHT
25
40
Postmenstrual age (weeks)

1rst PHASE REGAIN BIRTH WEIGHT

*DECREASE INSENSIBLE WATER LOSS

*DECREASE INSENSIBLE INTRACELLULAR FLUID LOSS

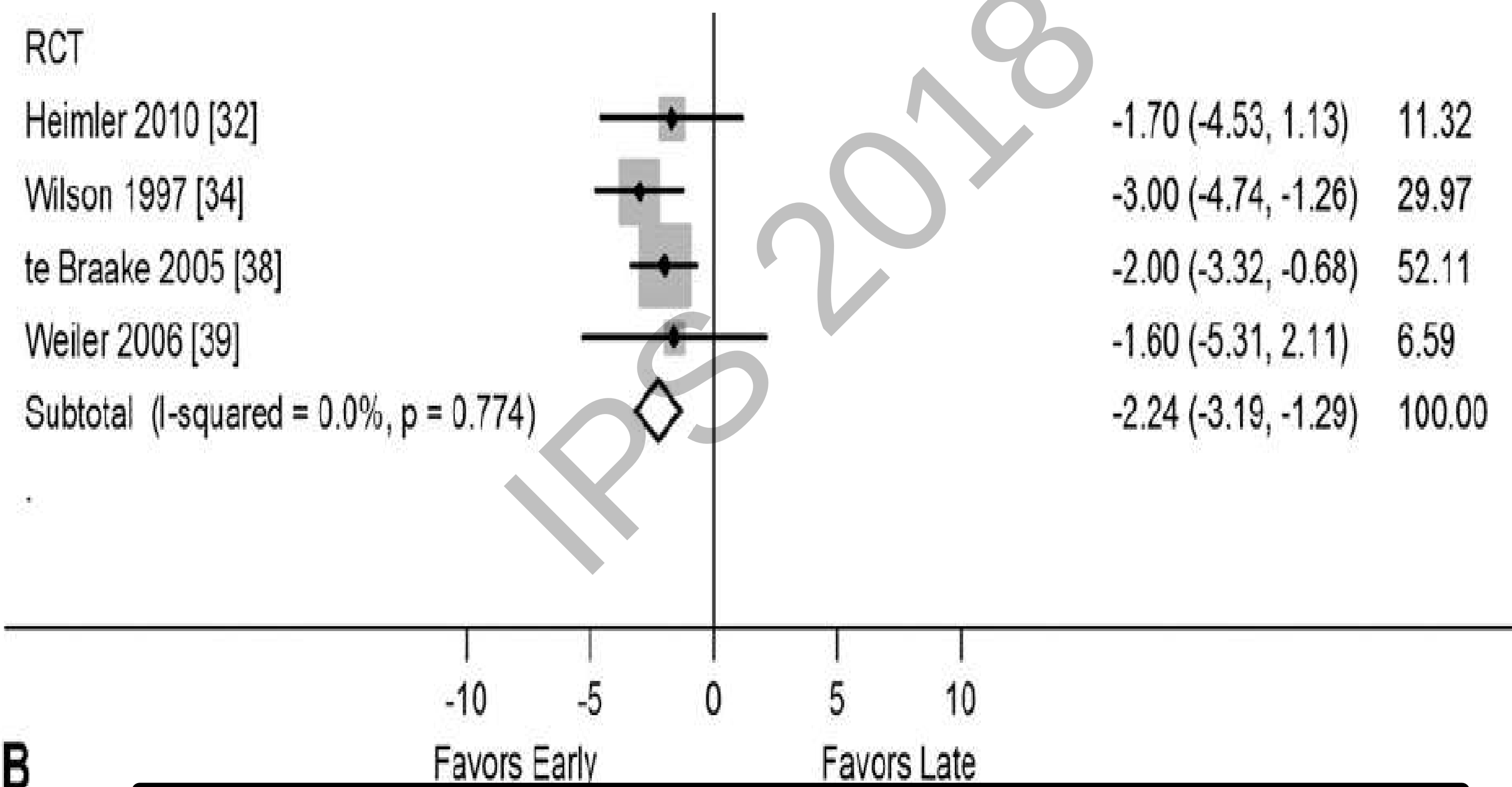
*EARLY POSITIVE NITROGEN BALANCE

***EARLY PARENTERAL NUTRITION**

***MINIMAL ENTERAL NUTRITION**

Clin Nutr 2013;97:816–26.

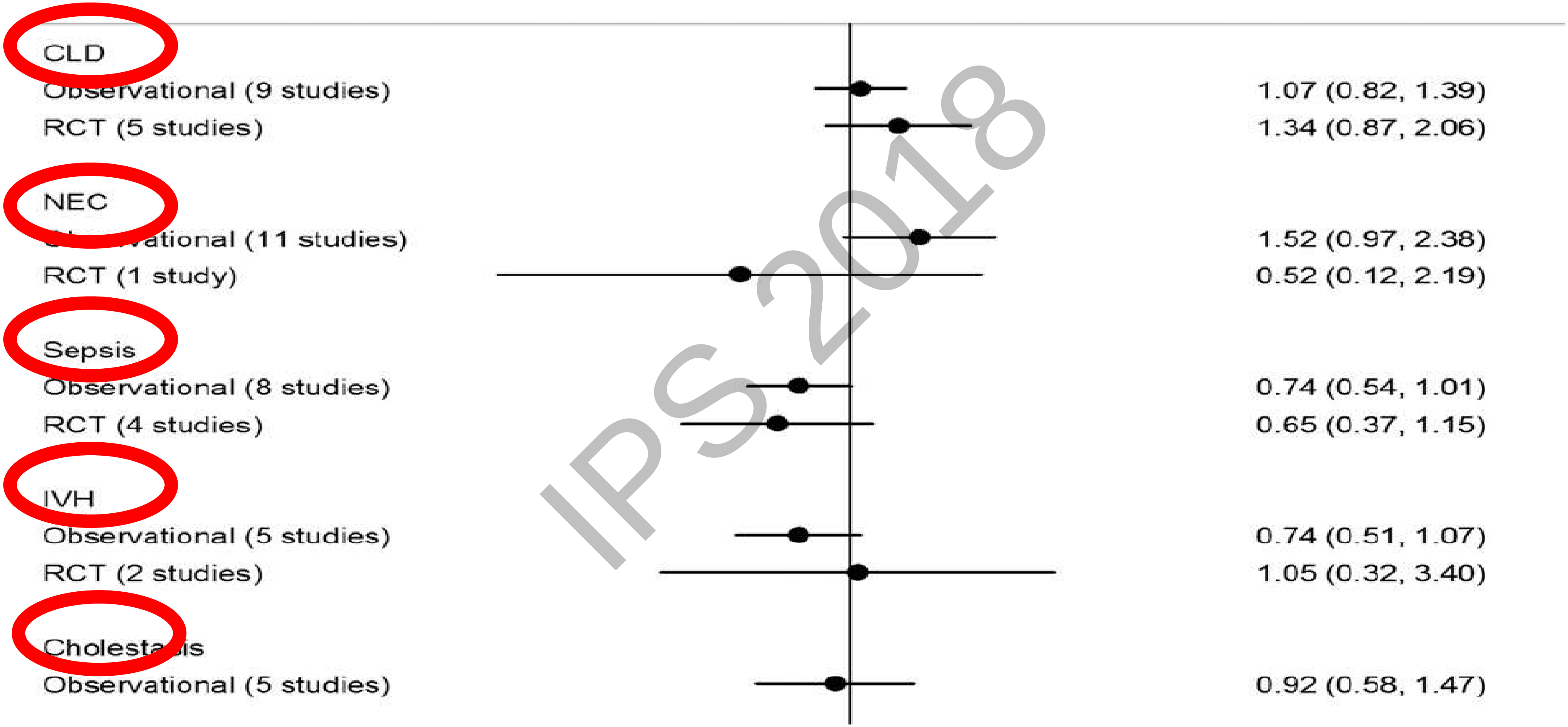
EARLY PARENTERAL NUTRITION



TIME TO REGAIN BIRTH WEIGHT

Clin Nutr 2013;97:816–26.

EARLY PARENTERAL NUTRITION



NO INCREASES IN MORTALITY OR MORBIDITY

EARLY PARENTERAL NUTRITION

Pediatrics and Neonatology (2014) 55, 5–13

Table 1 Evidence-based early nutritional practice for VLBW infants: recommendations and evidence quality.

Practice	Strength of recommendation*	Evidence quality†
Prompt provision of energy:	Recommended	B
Glucose infusion providing about 6 mg/kg/min		
Increase to about 10 mg/kg/d by 7 days of age		
Maintain blood sugar 50–120 mg/dL		
Prompt provision of parenteral amino acids:	Recommended	B
Initiate 3.0 g/kg/d within hours of birth		
Advance to 4.0 g/kg/d by 0.5–1.0 g/kg/d steps		
Initiate lipid emulsion within the first 24 to 30 h of birth	Recommended	B
Start 0.5–1.0 g/kg/d		
Advance to 3.0–3.5 g/kg/d by 0.5–1.0 g/kg/d steps		
Initiate trophic feedings by 5 days of age	Recommended	B
Provide about 10 mL/kg/d (human milk if possible)		
Begin advancing to ~150 mL/kg/d by 10–20 mL/kg/d steps within the next several days		

Suggested intakes of vitamins for premature infants receiving parenteral nutrition

Vitamin	Current regimen based upon pediatric multivitamin formulation* (unit/kg/day)	Estimate based upon the needs of premature infants (unit/kg/day)	Maximum not to exceed term infant (unit/day)
Fat-soluble vitamins			
A (microg)¶	280	500	700
E (mg)Δ	2.8	2.8	7
K (microg)	80	80	200
D (microg)◊	4	4	10
Water-soluble vitamins			
C, Ascorbic acid (mg)	32	25	80
B1, Thiamin (mg)	0.48	0.35	1.2
B2, Riboflavin (mg)	0.56	0.15	1.4
B6, Pyridoxine (mg)	0.4	0.18	1
Niacin (mg)	6.8	6.8	17
Pantothenate (mg)	2	2	5
Biotin (microg)	8	6	20
Folate (microg)	56	56	140
Vitamin B12 (microg)	0.4	0.3	1

Early trophic feeding versus enteral fasting for very preterm or very low birth weight infants (Review)

Cochrane Library

Comparison 1. Effects of trophic feeding versus enteral fasting

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Days to reach full enteral feeding	6	556	Mean Difference (IV, Fixed, 95% CI)	-1.05 [-2.61, 0.51]
2 Incidence of necrotising enterocolitis	9	748	Risk Ratio (M-H, Fixed, 95% CI)	1.07 [0.67, 1.70]
3 Mortality	8	558	Risk Ratio (M-H, Fixed, 95% CI)	0.66 [0.41, 1.07]
4 Days to regain birth weight	5	518	Mean Difference (IV, Fixed, 95% CI)	-0.01 [-0.96, 0.95]
5 Incidence of invasive infection	3	237	Risk Ratio (M-H, Fixed, 95% CI)	1.06 [0.72, 1.56]
6 Duration of phototherapy (days)	3	170	Mean Difference (IV, Fixed, 95% CI)	0.35 [-0.29, 0.99]
7 Days of hospital stay	4	341	Mean Difference (IV, Fixed, 95% CI)	-3.85 [-11.54, 3.84]

Advantages of gastrointestinal priming (trophic feeding) in preterm infants

Shortens time to regain birth weight
Improves feeding tolerance
Reduces duration of parenteral nutrition
Enhances enzyme maturation
Reduces intestinal permeability
Improves gastrointestinal motility
Matures hormone responses
Improves mineral absorption and mineralization
Reduces duration of phototherapy
Lowers incidence of cholestasis

↓ ADVANCING AGE ↓

	Birthweight ≤1000 g		Birthweight 1001 to 1500 g		Birthweight 1501 to 1800 g	
	Ideal schedule*		Ideal schedule*		Ideal schedule*	
Oropharyngeal colostrum¶	DOL 0 to 9	Swab on buccal mucosa every 3 hours	DOL 0 to 6	Swab on buccal mucosa every 3 hours	DOL 0 to 4	Swab on buccal mucosa every 3 hours
Trophic feeds (20 cal/oz)Δ	DOL 1 to 3	15 mL/kg/day for 3 days	DOL 1 to 2	20 mL/kg/day for 1 to 2 days	DOL 1	25 mL/kg/day for 1 day
Feeding advancement (mL/kg added each day)	DOL 4 to 9	Start increasing DOL 4; add 15 mL/kg each day	DOL 3 to 6	Start increasing DOL 3; add 20 mL/kg each day	DOL 2 to 4	Start increasing DOL 2; add 25 mL/kg/day each day
Start fortified feeds (24 cal/oz)◊	DOL 10	Start fortifying day after feed volume reaches 80 mL/kg/day	DOL 7	Start fortifying day after feed volume reaches 80 mL/kg/day	DOL 5	Start fortifying day after feed volume reaches 80 mL/kg/day
Further feeding advancement (start increasing day after fortifying feeds)	DOL 11 to 15	Next day, start adding 15 mL/kg each day	DOL 8 to 11	Next day, start adding 20 mL/kg each day	DOL 6 to 9	Next day, start adding 25 mL/kg each day
Target feeding volume	DOL 15 and thereafter	160 mL/kg/day	DOL 11 and thereafter	160 mL/kg/day	DOL 9 and thereafter	160 mL/kg/day

TAKE HOME MESSAGE TWO

TO REGAIN BIRTH WEIGHT AS SOON AS POSSIBLE WITHIN 10 TO MAX 15 DAYS

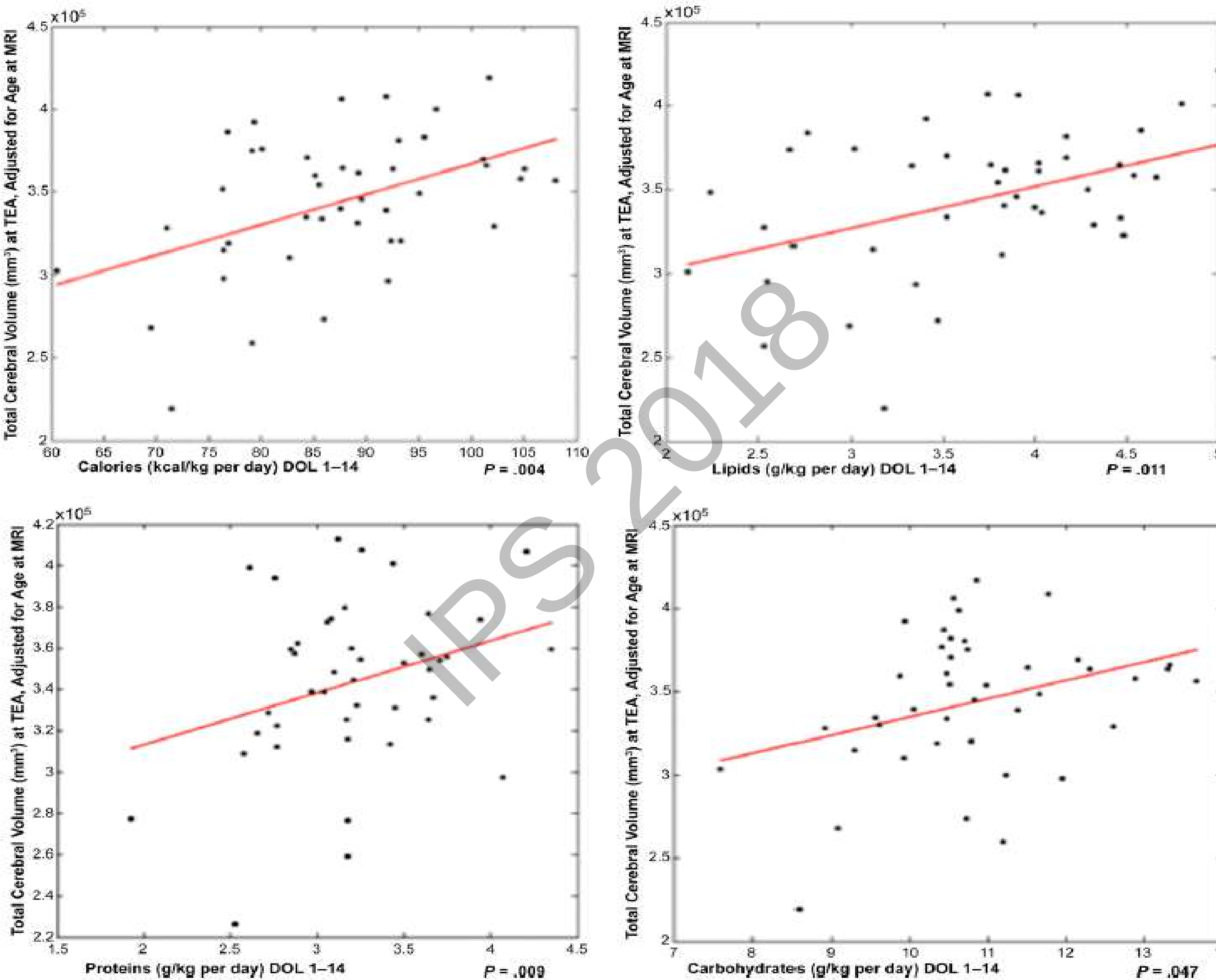
↓

***EARLY PARENTERAL NUTRITION**

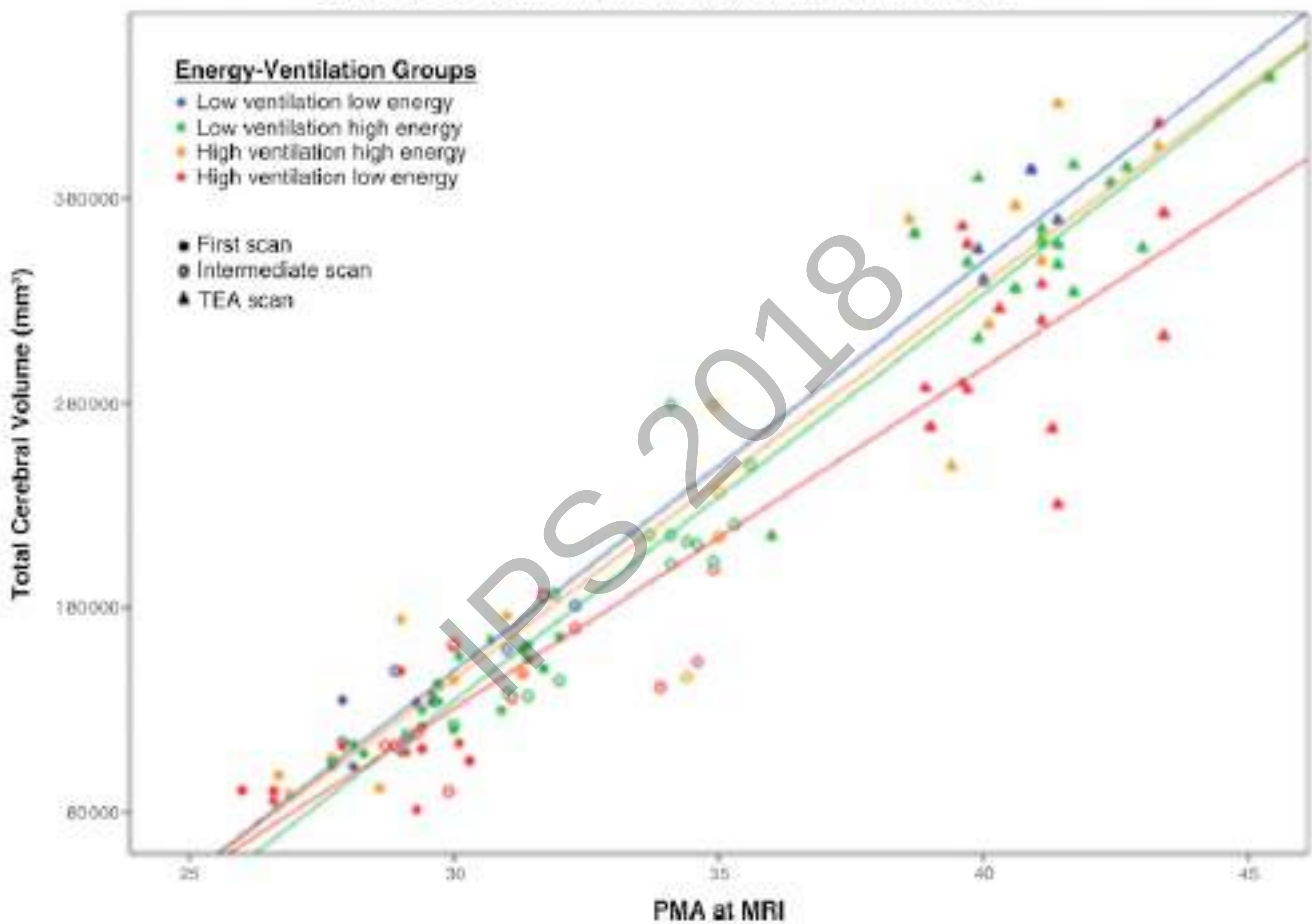
***MINIMAL ENTERAL NUTRITION**

Nutrient Intake in the First Two Weeks of Life and Brain Growth in Preterm Neonates

Nutritional intake per d (DOL 1–14), median (IQR)			
Energy total (kcal/kg per d)	77.6 (74.5–83.4)	93.1 (89.5–101.3)	—
Parenteral	45.8 (28.4–62.3)	41.3 (35.9–56.3)	.847
Enteral	31.7 (15.2–45.2)	52.9 (39.1–60.1)	.001
Lipids total (g/kg per d)	3.0 (2.6–3.5)	4.2 (3.8–4.5)	—
Parenteral	1.0 (0.8–1.8)	1.3 (1.0–1.8)	.405
Enteral	1.8 (0.9–2.7)	3.0 (2.2–3.3)	.001
Carbohydrates total (g/kg per d)	9.9 (9.1–10.5)	11.1 (10.3–12.1)	—
Parenteral	6.7 (4.8–8.7)	6.4 (4.4–7.9)	.448
Enteral	3.1 (1.4–4.2)	5.0 (3.6–6.1)	<.001
Proteins total (g/kg per d)	2.8 (2.6–3.1)	3.2 (2.9–3.5)	—
Amino acids, parenteral	2.0 (1.4–2.7)	1.8 (1.5–2.4)	.502
Proteins, enteral	0.8 (0.3–1.0)	1.3 (0.9–1.6)	<.001
Percentage human milk to total enteral intake, % (IQR)	99 (97–100)	95 (77–98)	.015


Total Cerebral Volume (mm³) at TEA, Adjusted for Age at MRI
Calories (kcal/kg per day) DOL 1–14
P = .004
Lipids (g/kg per day) DOL 1–14
P = .011
Proteins (g/kg per day) DOL 1–14
P = .009
Carbohydrates (g/kg per day) DOL 1–14
P = .047
IPS 2018

Cerebral Development and Energy-Ventilation Interaction



Nutrient Intake in the First Two Weeks of Life and Brain Growth in Preterm Neonates

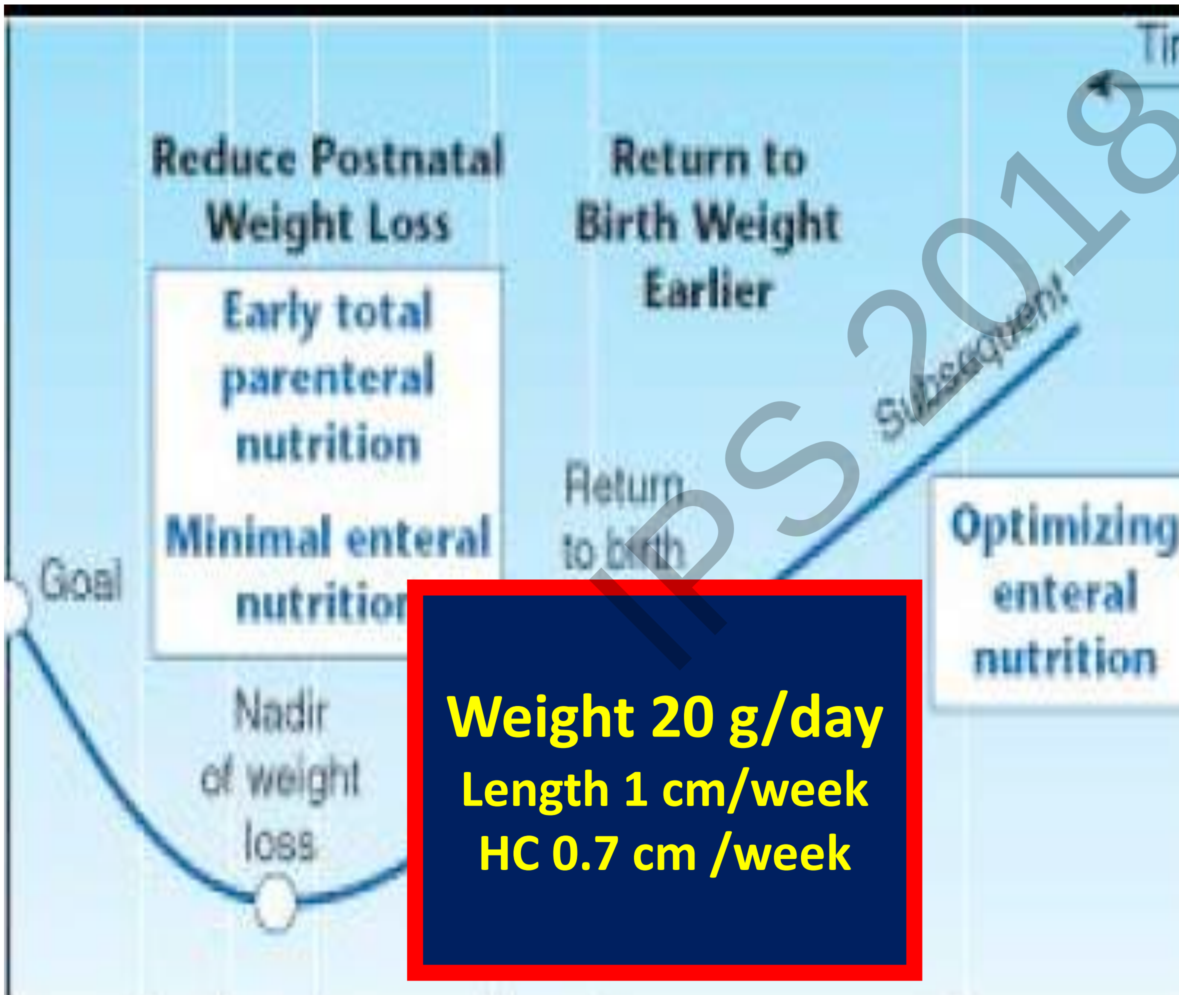
CONCLUSIONS: In preterm neonates, greater energy and enteral feeding during the first 2 weeks of life predicted more robust brain growth and accelerated WM maturation. The long-lasting effect of early nutrition on neurodevelopment may be mediated by enhanced brain growth. Optimizing nutrition in preterm neonates may represent a potential avenue to mitigate the adverse brain health consequences of critical illness.

TAKE HOME MESSAGE TWO BIS

TO ENSURE A BETTER BRAIN GROWTH DURING THE FIRST 15 DAYS

***EARLY PARENTERAL NUTRITION**
***MINIMAL ENTERAL NUTRITION**
***HIGH ENERGY INTAKE**
***BREAST MILK**

2ND PHASE OPTIMIZING ENTERAL NUTRITION



Weight 20 g/day
Length 1 cm/week
HC 0.7 cm /week

MEET ENERGY REQUIREMENT FOR GROWTH TO AVOID Extra Uterine Growth Retardation

GAIN WEIGHT > 20 G/DAY IS THE BEST FOR A BETTER DEV

Outcomes at 18 to 22 Months' Corrected Age According to Weight Gain Quartile

Outcome[a]	Quartile 1 (n = 124)	Quartile 2 (n = 122)	Quartile 3 (n = 123)	Quartile 4 (n = 121)	P[b]
Weight gain, mean (SD), g/kg per d	12.0 (2.1)	15.6 (0.8)	17.8 (0.8)	21.2 (2.0)	—
Normal neurologic examination	70	77	76	86	<.01
CP, %	21	13	13	6	<.01
MDI	75.7 (18)	77.7 (18)	79.7 (18)	80.9 (15)	.32
MDI < 70, %	39	37	34	21	<.01
Neurodevelopmental impairment, %	55	49	41	29	<.001
Weight <10th percentile, %	58	61	51	46	.03
Length <10th percentile, %	47	43	29	28	<.001

Growth in the Neonatal Intensive Care Unit Influences Neurodevelopmental and Growth Outcomes of Extremely Low Birth Weight Infants

PEDIATRICS Volume 117 Number 4 April 2006

Estimated daily energy requirements for growing premature infants

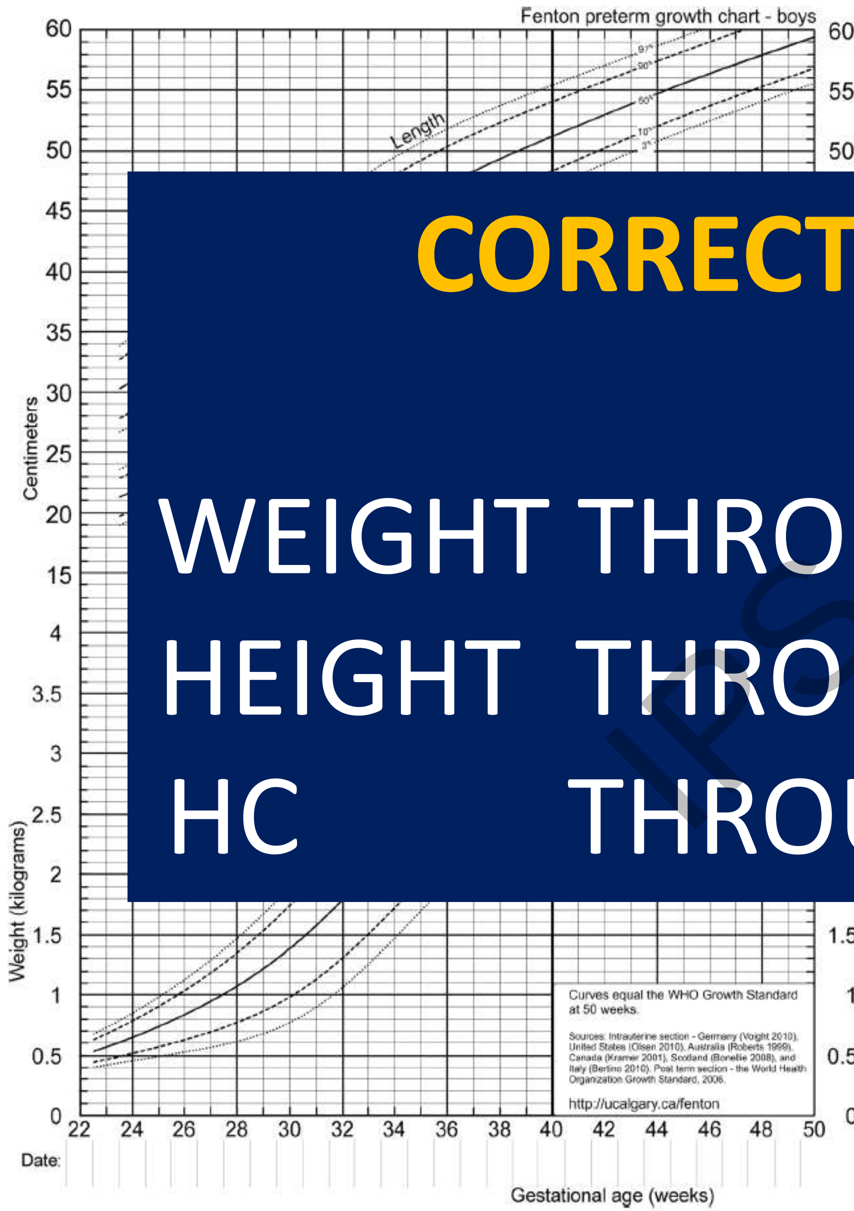
Factor	Kcal/kg	Comment
Resting energy expenditure	50	Resting metabolic rate
Activity	15	30 percent above resting
Cold stress	10	Thermoregulation
Synthetic effect of feeding	8	Dietary thermogenesis
Fecal loss	12	10 percent of intake
Growth	25	Calories stored
Total caloric requirement	**120**	

Adapted from: Sinclair JC. Clin Obstet Gynecol 1971; 14:840.

3RD PHASE THE CATCH UP GROWTH

POST DISCHARGE NUTRITION TO ENSURE A THOUROUGH FOLLOW UP ON GROWTH

FOLLOW UP ON GROWTH



CORRECTION FOR GA

WEIGHT THROUGH 24 MONTHS

HEIGHT THROUGH 40 MONTHS

HC THROUGH 18 MONTHS

Nutritional assessment of the VLBW infant

Assessment	Frequency
Fluid intake	
Parenteral	Daily
Enteral	Daily
Nutrient intake	
Energy	Daily
Protein	Daily
Specific nutrient	Daily
Anthropomorphic measurements	
Body weight	Daily at same time
Length	Weekly
Head circumference	Weekly
Laboratory values	
Hemoglobin, hematocrit	After full feeds are achieved, measure every 2 to 3 weeks until it is clear that the results are stable.
Calcium, phosphorus	As above
Alkaline phosphatase	As above
Blood urea nitrogen (BUN)	As above. If values are abnormal, also measure prealbumin
Serum electrolytes	In selected infants (receiving diuretics, or feeds of unfortified human milk, or limited intake, or slow growth)

VLBW: very low birthweight (birthweight ≤1500 g).

Adapted from: Schanler RJ. The low birth weight infant: Perinatal nutrition. In: Nutrition in Pediatrics: Basic Science and Clinical Applications, Walker WA, Watkins JB (Eds), B.C. Decker Inc., Hamilton, Ontario, Canada 1996. p.387.

Clinical criteria of feeding intolerance in preterm infants

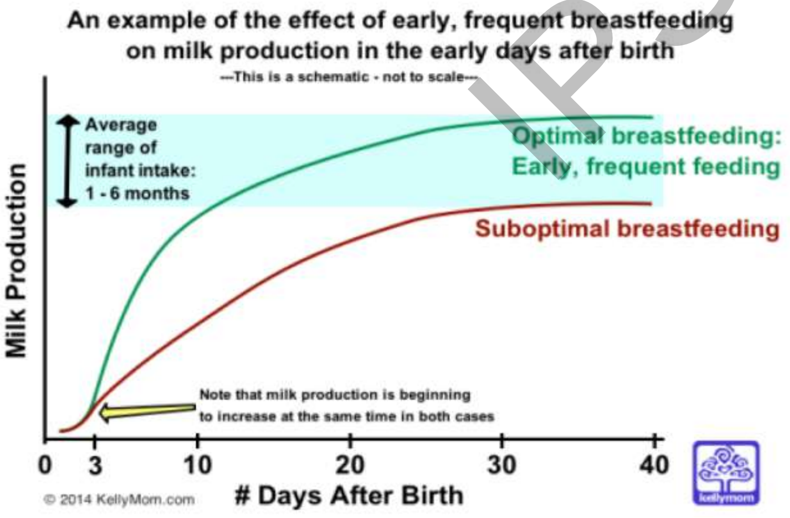
Abdominal examination
Distension
Tenderness
Change in bowel sounds (eg, increased or absent)
Emesis
Gastric residual volume
Greater than 2 mL/kg of body weight
Greater than half the volume of feeds over prior three hours
Any change in quantity of fluid volume (usually increase)
Gastric residual fluid characteristics
Change in color
Green: Bile
Red or brown: Blood
Stools
Any change in frequency
Presence of blood or guaiac positive stools
Clinical status
Any change in clinical status, eg, increased episodes of apnea and bradycardia, diminished oxygen saturation (desaturation events), and lethargy

Laboratory monitoring of infants receiving parenteral nutrition (PN)

Laboratory test	Frequency
Blood	
Electrolytes: sodium, potassium, chloride, bicarbonate	Daily until stable, then serially as indicated
Glucose	Daily until stable, then serially as indicated
Blood urea nitrogen (BUN), creatinine, calcium, phosphorus, magnesium, alkaline phosphatase, bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST)	After the first week and then serially on an alternate week schedule as indicated

PART 3 : ENTERAL NUTRITION OF THE PRETERM
WHAT IS THE BEST ?

BREAST FEEDING



FORMULA ENRICHED OR NOT

BREAST MILK IS THE BEST FOR NUTRITION OF PREMATURE INFANT

IMMUNITY

COGNITION

BREAST MILK IS THE BEST FOR NUTRITION OF PREMATURE INFANT

IMMUNITY

BREAST MILK IS A MUST

IMMUNITY

Suggested benefits of human-milk feeding for preterm infants

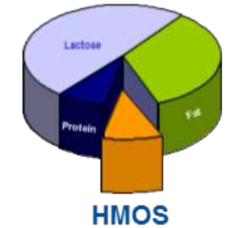
- Dose-related decreases in NICU length of stay and lower morbidity including risk of the following:
  - Sepsis
  - Necrotizing enterocolitis
  - Urinary tract infection
- Benefits persist beyond NICU stay
- Improved gastrointestinal function and integrity via the following:
  - Decreased gastric pH
  - Increased gastrointestinal motility
  - Accelerated mucosal immunity
  - Improved gut microflora
  - Decreased mucosal permeability leading to reduced bacterial translocation
- Improvement in indexes of neurodevelopment that persists into adolescence

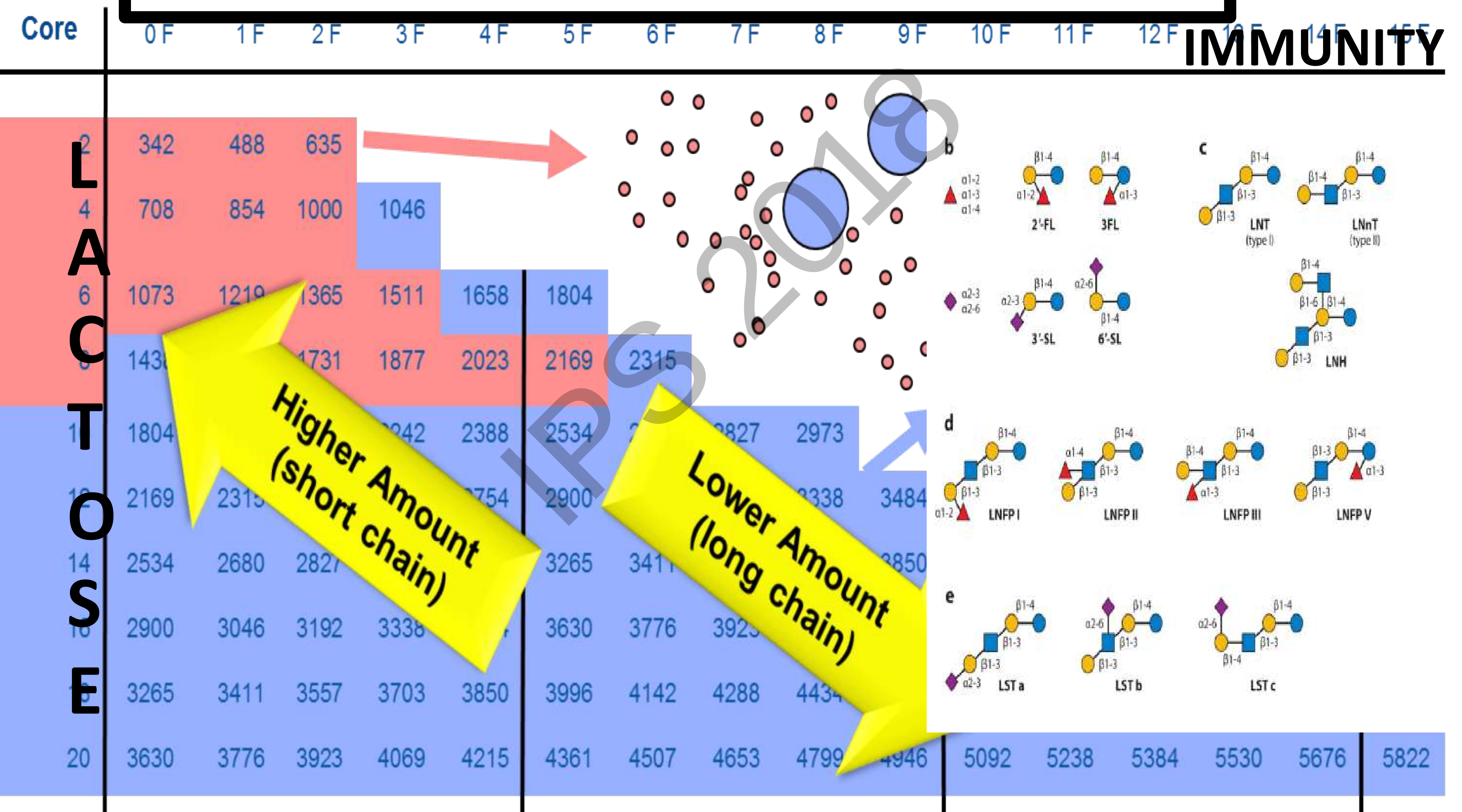
IMMUNITY

an milk proteins

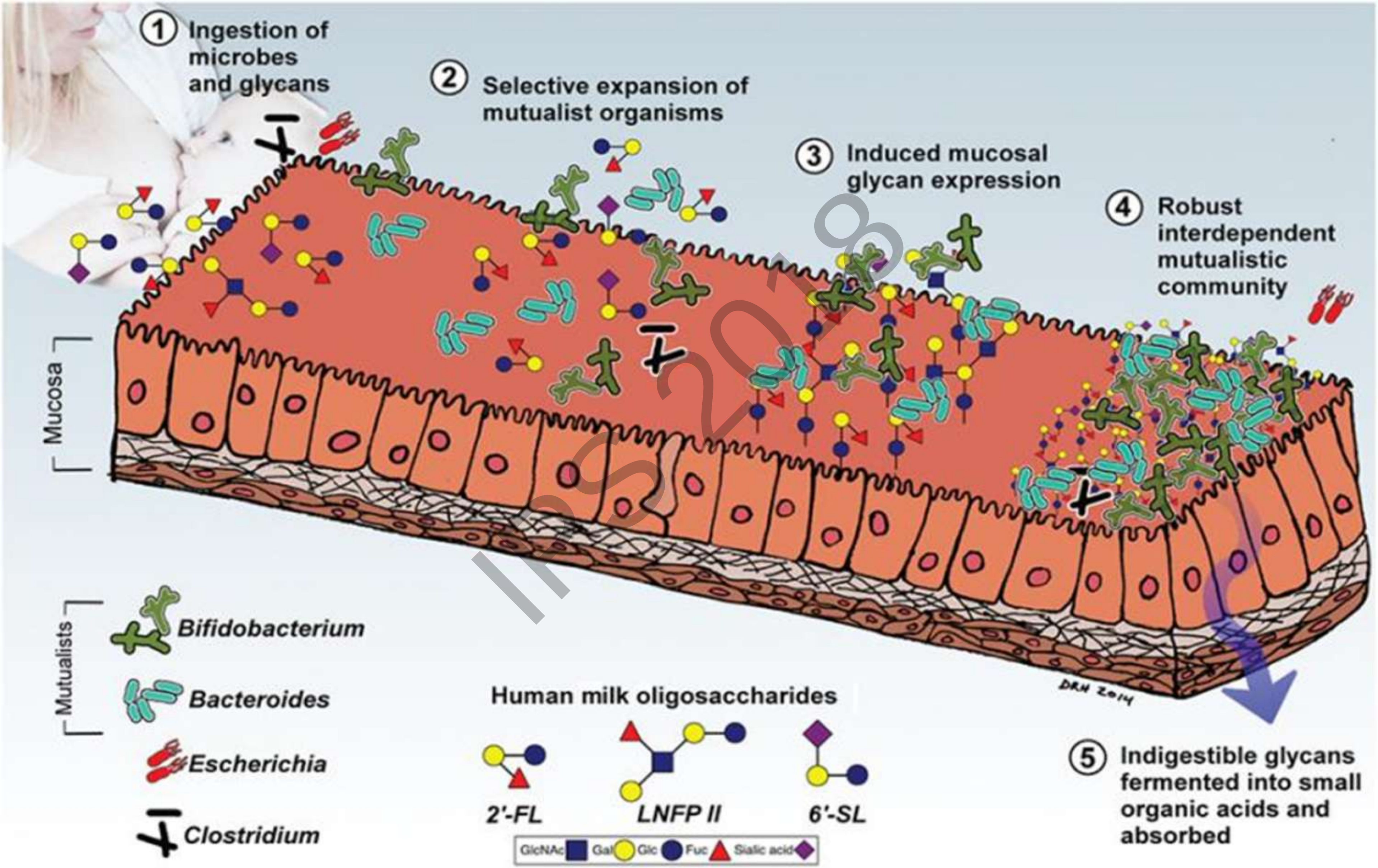
	Bioactivity
	Bacteriostatic; bactericidal; immunomodulatory; cell prolif differentiation
	Prebiotic; antimicrobial; immunostimulatory; enhanced Fe absorption
	Transfer of maternal immunity; antibodies against bacteria
	Antibacterial activity; degradation of bacterial cell wall gly
	Hydrolysis of triglycerides; fat absorption
	Immunomodulatory activity; brain function; intestinal dev
	Vitamin B12 absorption; antimicrobial activity
	Limit/slow down protein digestion
	Opioid activity; enhancing calcium absorption
	Antibacterial activity by acting as structural analogues
es	Antibacterial and antiviral activities

HMO > 200 STRUCTURES SYNTHETHIZED IN MAMMARY GLANDS ONLY DURING LACTATION



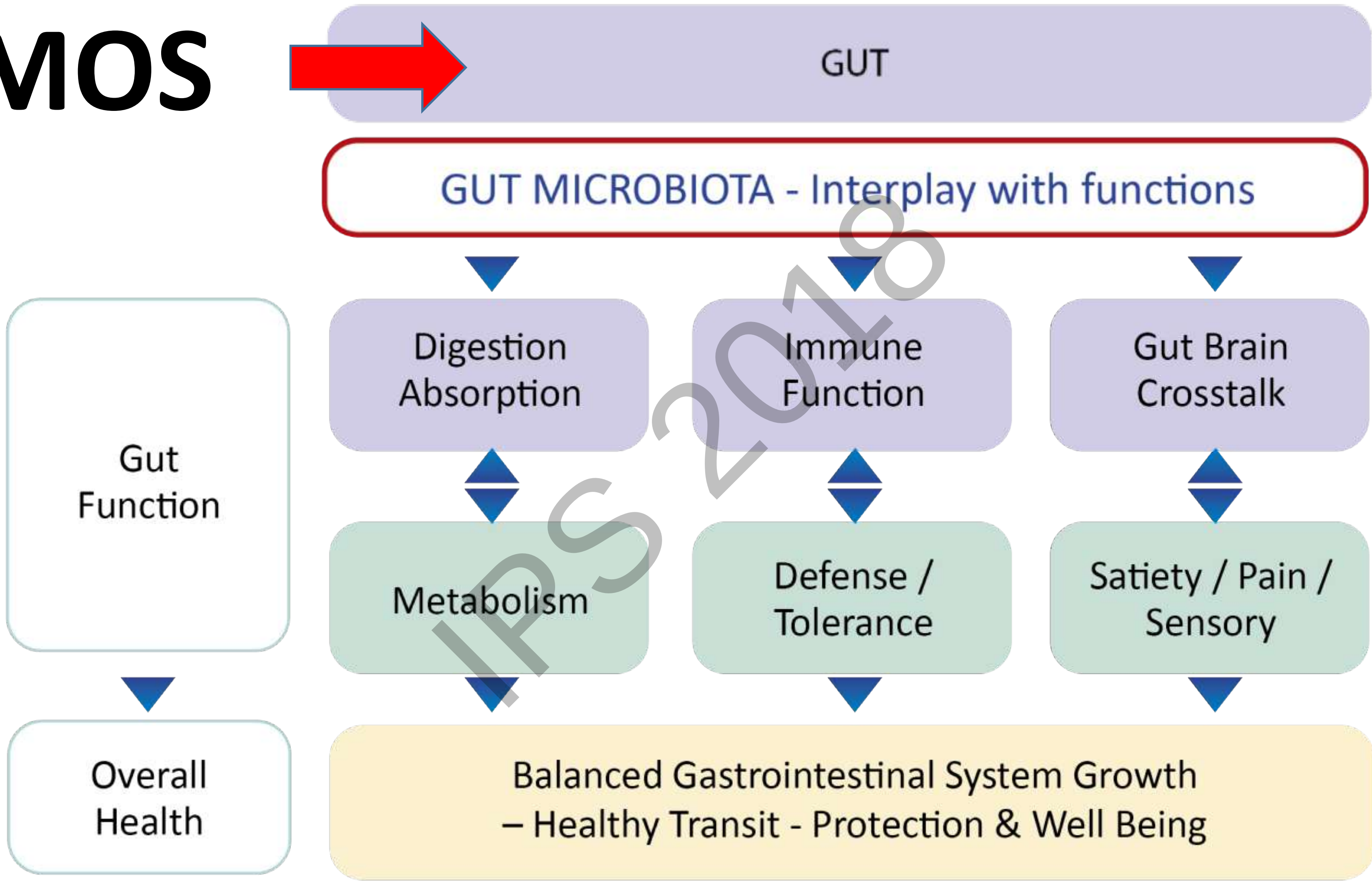


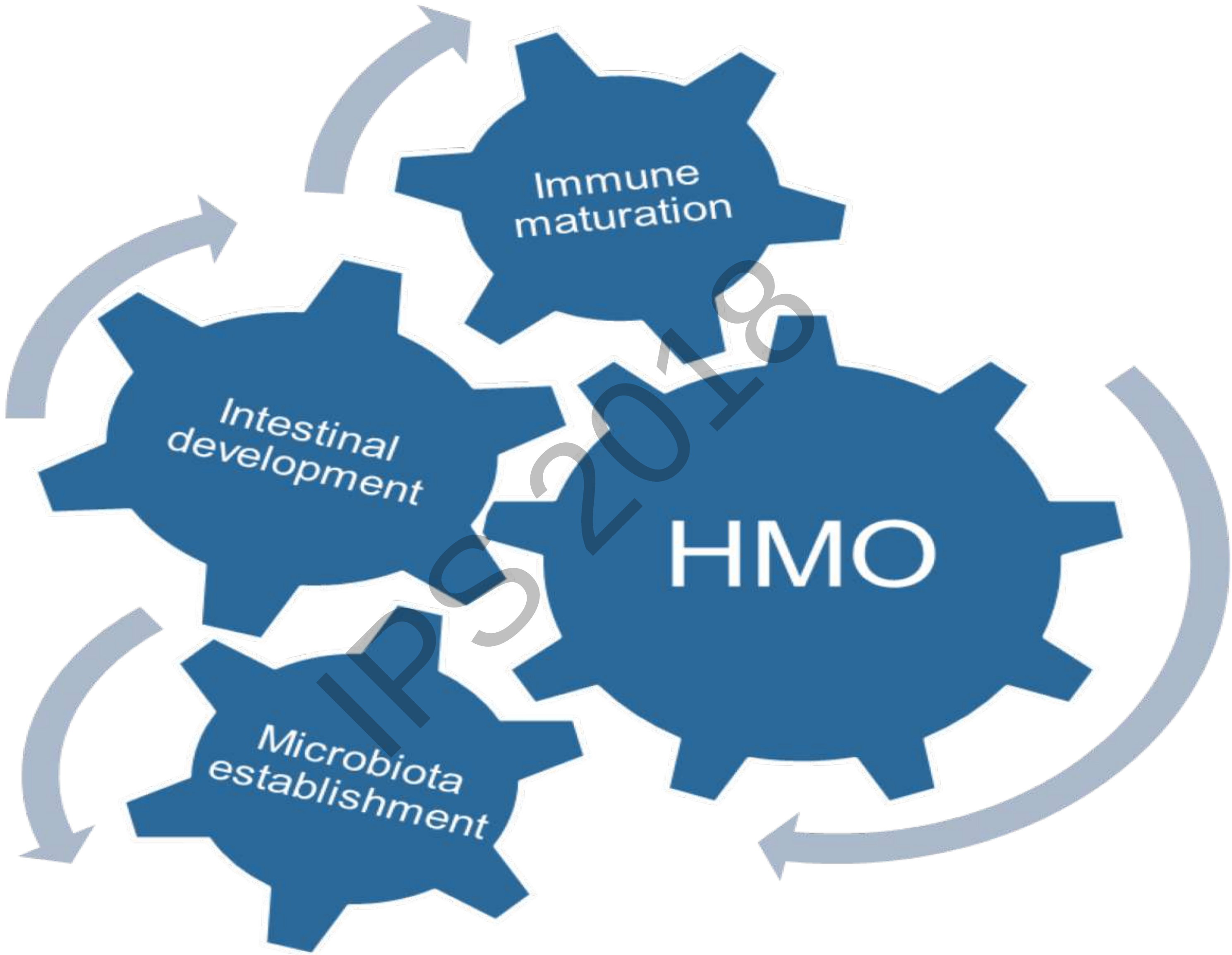
Human Milk OligoSaccharides = Natural PREBIOTIC



IMMUNITY

HMOS




Immune maturation
Intestinal development
HMO
Microbiota establishment

BREAST MILK IS THE BEST FOR NUTRITION OF PREMATURE INFANT

COGNITION

Neurodevelopmental Outcomes of Preterm Infants Fed Human Milk

A Systematic Review

CrossMark

Clin Perinatol 44 (2017) 69–83

Beatrice E. Lechner, MD[a,b,*], Betty R. Vohr, MD[a,b]

NeuroImage 82 (2013) 77–86

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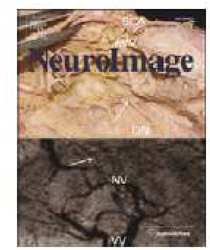
Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg



Breastfeeding and early white matter development: A cross-sectional study

CrossMark

Sean C.L. Deoni[a,*], Douglas C. Dean III[a], Irene Piryatinsky[a,b], Jonathan O'Muircheartaigh[a,c], Nicole Waskiewicz[a], Katie Lehman[a], Michelle Han[a], Holly Dirks[a]

Table 1
Studies during infancy: between newborn and 2 years of age

Author	Population	Birth Years	Age	Test	Outcome						
Feldman & Eidelman,[22] 2003	86 infants <1750 g	1996–1999	At discharge and 6 mo	Bayley II	6m	HM	Substantial	Intermediate	Minimal		*P*
					MDI		94.2 ± 9	91.7 ± 7	90.5 ± 8		<.05
					PDI		85.8 ± 11	78.6 ± 13	78.0 ± 12		<.01
Blaymore Bier et al,[25] 2002	39 infants <2000 g	1996–1999	7 and 12 mo	Bayley II	12m	HM	Formula				*P*
					MDI	100 ± 12	91 ± 10				<.05
Pinelli et al,[26] 2003	148 infants <1500 g	2008–2009	6 and 12 mo	Bayley II	12m	HM	>80%		<80%		*P*
					MDI		98 ± 15		91 ± 12		NS
					PDI		78 ± 15		77 ± 14		NS
O'Connor et al,[27] 2003	463 infants 750–1800 g	1996–1998	12 mo	Bayley II		PHM-T	≥50% HM-T		<50% HM-T		PFF-T
					MDI	93.1 ± 15	95 ± 13		91.6 ± 11		92.9 ± 13
					PDI	86.8 ± 15	84.6 ± 15		86.5 ± 15		88.1 ± 15
Vohr et al,[28] 2006	1035 infants <1000 g	1999–2001	18–22 mo	Pentiles of HM vol. Bayley II		≤20th	20–40th	40–60th	60–80th	>80th	Adjust. *P*
					MDI	74.2	76.9	78.3	90.4	97.3	.004
					PDI	80.2	82.7	84.2	84.4	89.4	.003
					BRS	44.8	52.1	50.1	51.8	58.8	.028
Furman et al,[5] 2004	98 infants <1500 g	1997–1999	20 mo	HM mL/kg/d Bayley II		None	1–24 mL	25–29 mL	≥50 mL		Adjusted *P*
					MDI	80 ± 16	70 ± 14	75 ± 14	85 ± 21		NS
					PDI	80 ± 16	75 ± 19	71 ± 17	76 ± 16		NS

Abbreviations: BRS, Behavior Rating Scale; MDI, Bayley Mental Development Index; NS, not significant; PDI, Psychomotor Development Index; PFF, predominantly formula fed; PHM-T, predominantly HM until term.

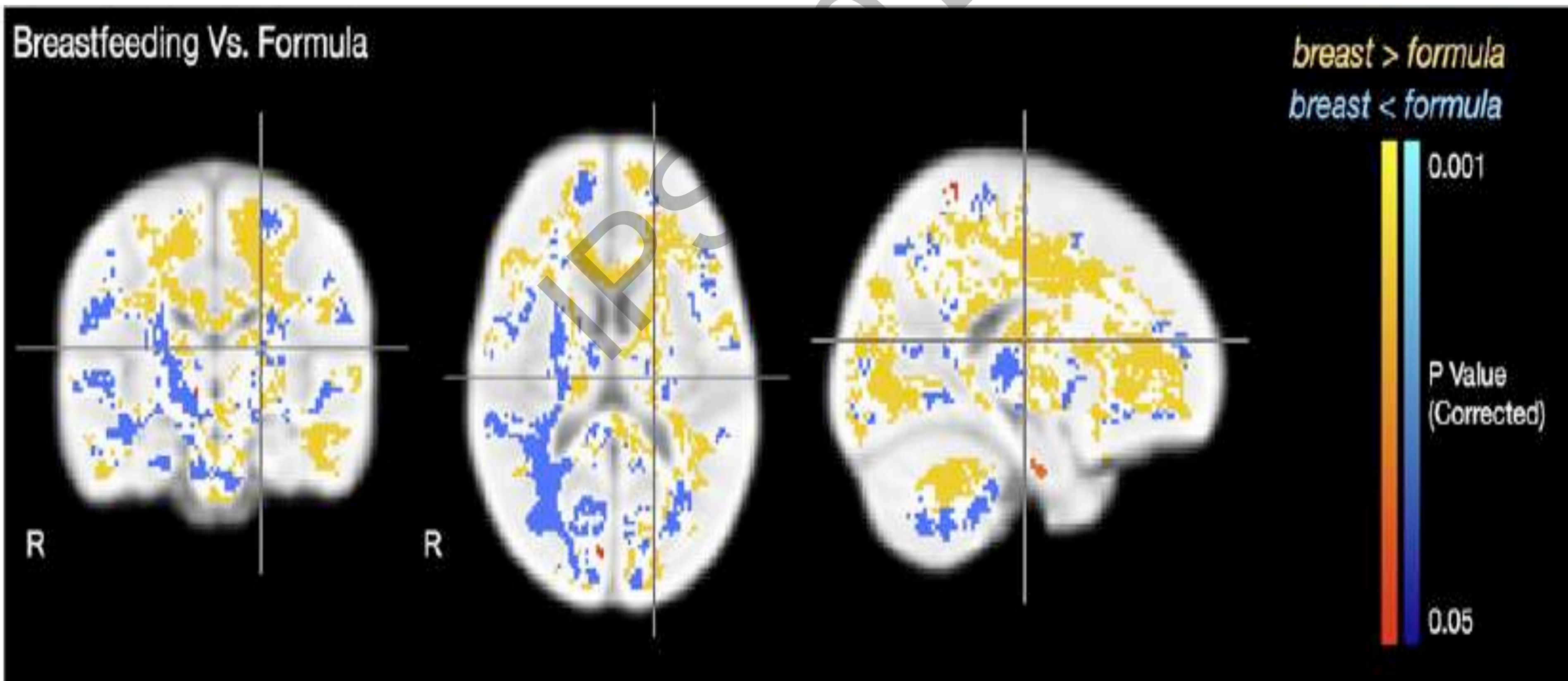
Table 2
Studies in childhood: ages 2 years to 12 years

Author	Population	Birth Years	Age	Test	Outcome		
Vohr et al,[29] 2007	773 infants NICHD 401–1000 g	Oct 1999–Jun 2001	30 m CA	Bayley II	Parameter estimate	Standard error	Adjusted *P* value
				MDI	0.59 pts per 10 mL[a]	0.17	.0005
				PDI	0.56 pts per 10 mL[a]	0.21	.0092
				Total behavioral score	0.99% per 10 mL[a]	0.33	.0028
Rozé et al,[30] 2012	2925 infants LIFT (<33 wk) France	Jan 2003–Jun 2008	2 y	Ages and Stages Questionnaire	Association between breastfeeding at time of discharge and nonoptimal neurodevelopmental performance[b]		
		1997	5 y			OR (95% CI)	*P* value
	EPIPAGE (22–32 wk) France			KABC	LIFT	0.53 (0.39–0.73)	.001
					EPIPAGE	0.44 (0.33–0.60)	.001
Beaino et al,[33] 2011	1503 infants EPIPAGE (22–32 wk) France	1997	5 y	KABC MPC	Breast milk % OR (95% CI)	No breast milk % OR	
				Mild cognitive deficiency[f]	15% 0.54 (0.39–0.76)	23% 1.00[c]	
				Severe cognitive deficiency[g]	4% 0.25 (0.14–0.44)	13% 1.00[c]	
Tanaka et al,[34] 2009	38 infants VLBW Japan	1999–2000	5 y	KABC	Breast milk	Formula	
				MPC	100.9 ± 14.6	94.5 ± 11.8	
				Simultaneous processing	99.3 ± 13.8	94.6 ± 15.9	
				Sequential processing	106.7 ± 14.5	94.7 ± 11.6[c]	
				Day-Night Test	14.1 ± 1.4	11.1 ± 0.9[c]	
				KRISP	17.2 ± 0.8	15.0 ± 1.4[d]	
				Motor Planning Test	18.8 ± 5.3	12.0 ± 3.9[c]	
				SDQ	11.0 ± 1.2	13 ± 3.9[c,e]	

(*continued on next page*)

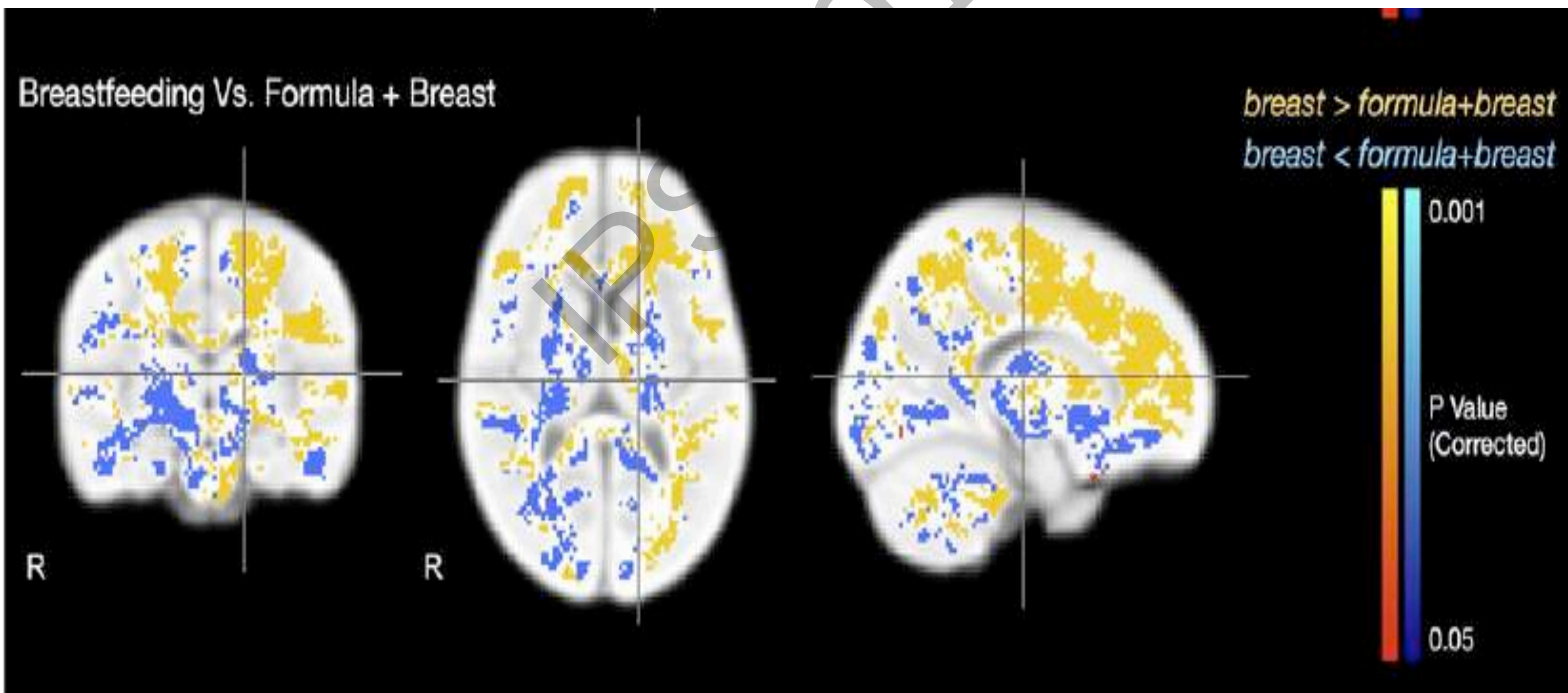
Subset comparison of older members of Group #1 and Group #2

	Group #1 (breastfed)	Group #2 (formula-fed)	p-Value
Participants (n)	21	12	
Age (days)	1287 ± 153	1281 ± 118	0.91
Fine motor	36.8 ± 5.3	34.3 ± 4.8	0.19
Receptive language	41.1 ± 3.3	34.5 ± 5.6	**0.0019**
Expressive language	39.1 ± 3.9	37 ± 5.8	0.28
Visual reception	44.4 ± 4.6	41.6 ± 4.5	0.09



Subset comparison of older members of Group #1 and Group #3

	Group #1 (breastfed)	Group #3 (breast + formula-fed)	p-Value
Participants (n)	21	15	
Age (days)	1287 ± 153	1219 ± 150	0.19
Fine motor	36.8 ± 5.3	32.9 ± 6.4	0.067
Receptive language	41.1 ± 3.3	34.7 ± 5.8	**0.0011**
Expressive language	39.1 ± 3.9	35.2 ± 6.4	0.05
Visual reception	44.4 ± 4.6	38.8 ± 6.1	**0.0056**



Subset comparison of older members of Group #2 and Group #3

	Group #2 (formula-fed)	Group #3 (breast + formula-fed)	p-Value
Participants (n)	12	15	
Age (days)	1281 ± 118	1219 ± 150	0.23
Fine motor	34.3 ± 4.8	32.9 ± 6.4	0.52
Receptive language	34.5 ± 5.6	34.7 ± 5.8	0.91
Expressive language	37 ± 5.8	35.2 ± 6.4	0.45
Visual reception	41.6 ± 4.5	38.8 ± 6.1	0.18

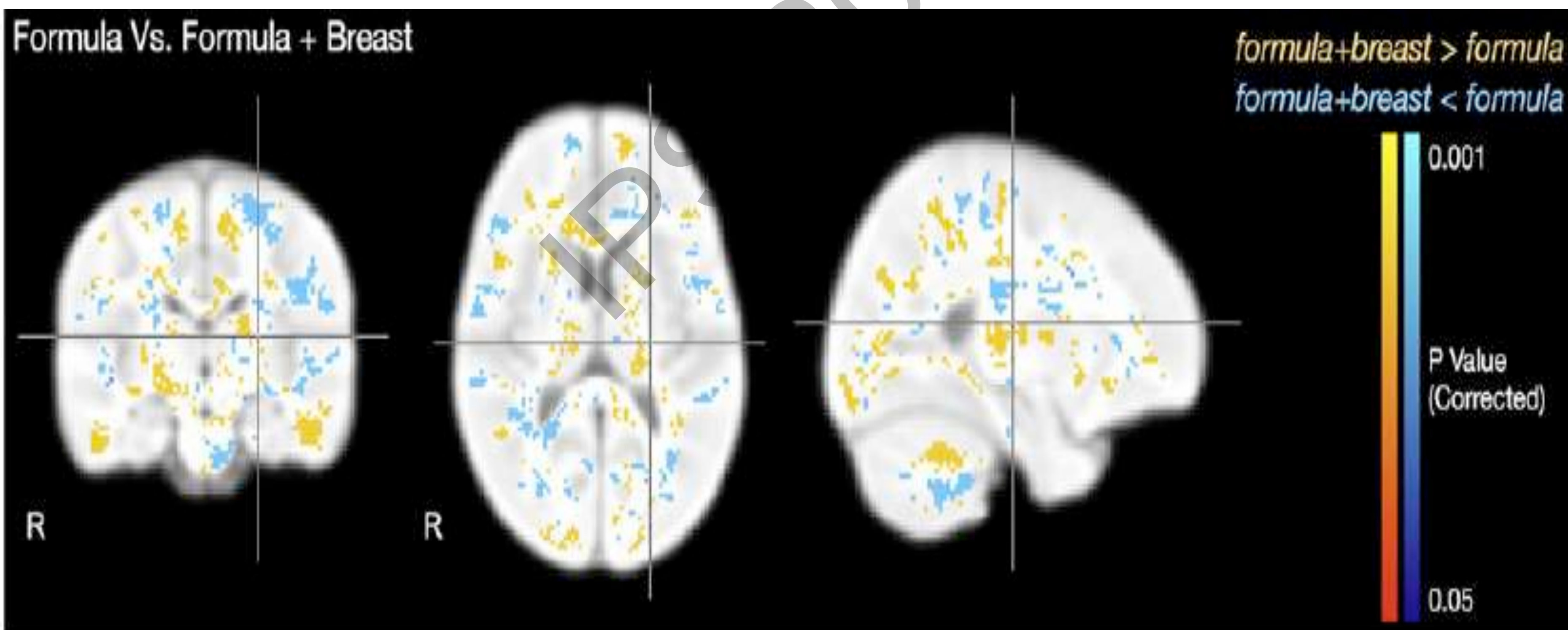
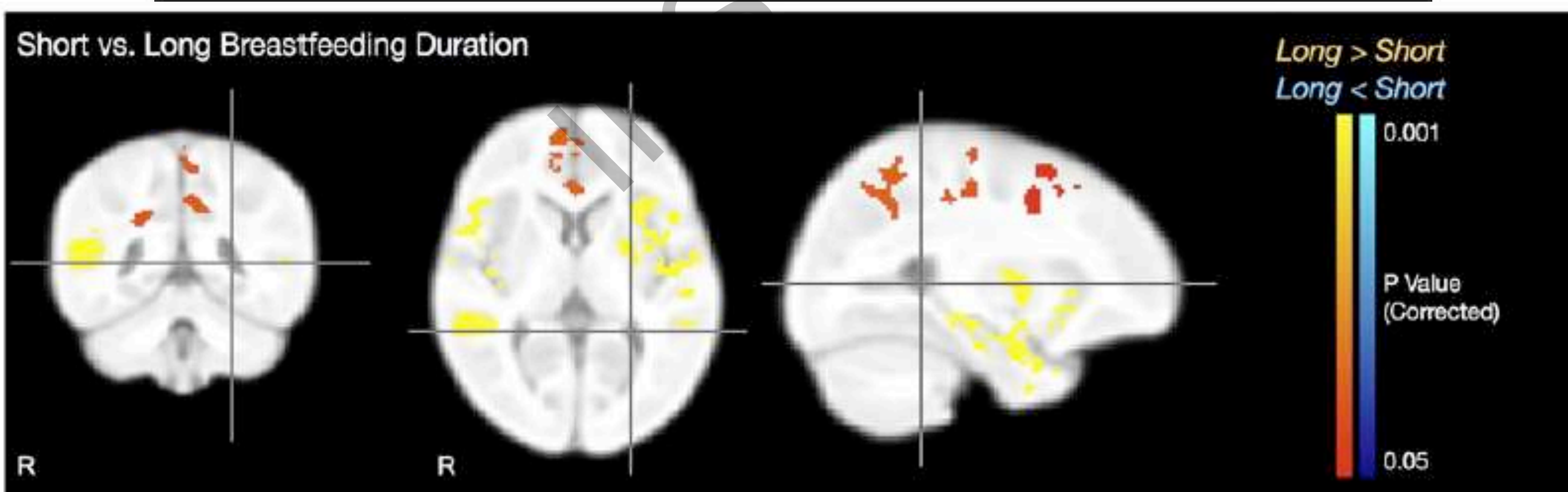


Table 7
Comparison of behavioral test scores for breast-fed children divided into short and long feeding durations. Bold values indicate statistically different scores corrected for type 1 error using Holm–Bonferroni correction.

	Short breast feeding duration	Long breast feeding duration	p-Value
Participants (n)	22	25	
Age (days)	691 ± 324	807 ± 341	0.24
Breast feeding duration	220 ± 81	600 ± 124	
Gross motor	20.41 ± 4.7	23 ± 5	**0.046**
Fine motor	20.4 ± 5.5	25.3 ± 8.6	**0.028**
Receptive language	19.2 ± 8.9	26.7 ± 11.2	**0.015**
Expressive language	16.9 ± 7.9	25.6 ± 10.7	**0.0036**
Visual reception	20.9 ± 9.2	30 ± 11.1	**0.0042**



BREAST MILK IS THE BEST FOR NUTRITION OF PREMATURE INFANT

IS THERE A NEED FOR PHM FORTIFICATION ?

FOR A BETTER GROWTH

IS THERE A NEED FOR PHM FORTIFICATION ?

PROTEIN

DHA

VIT D

IRON

Nutrient Requirement of Premature & LBW FOR PROTEIN

- **Protein (+ kcals) is the principal determinant of growth**
- **Aim is to support intrauterine rate of weight gain**
- **Digestion, absorption and metabolism limited by immaturity of organs**

- **ESPGHAN 2010 Recommendation of two different protein intakes**
- **Preterm babies <1000 g 3.6 – 4.1 g/100 kcal**

  4 -4.5 g/kg/day
- **Preterm babies 1000-1800 g 3.2 – 3.6 g/100 kcal**

  3.5-4 g/kg/day

IS THERE A NEED FOR PHM FORTIFICATION ?

Journal of Neonatal-Perinatal Medicine 6 (2013) 319–323

PROTEIN

Table 1
Macronutrient analysis results (mean ± SD)

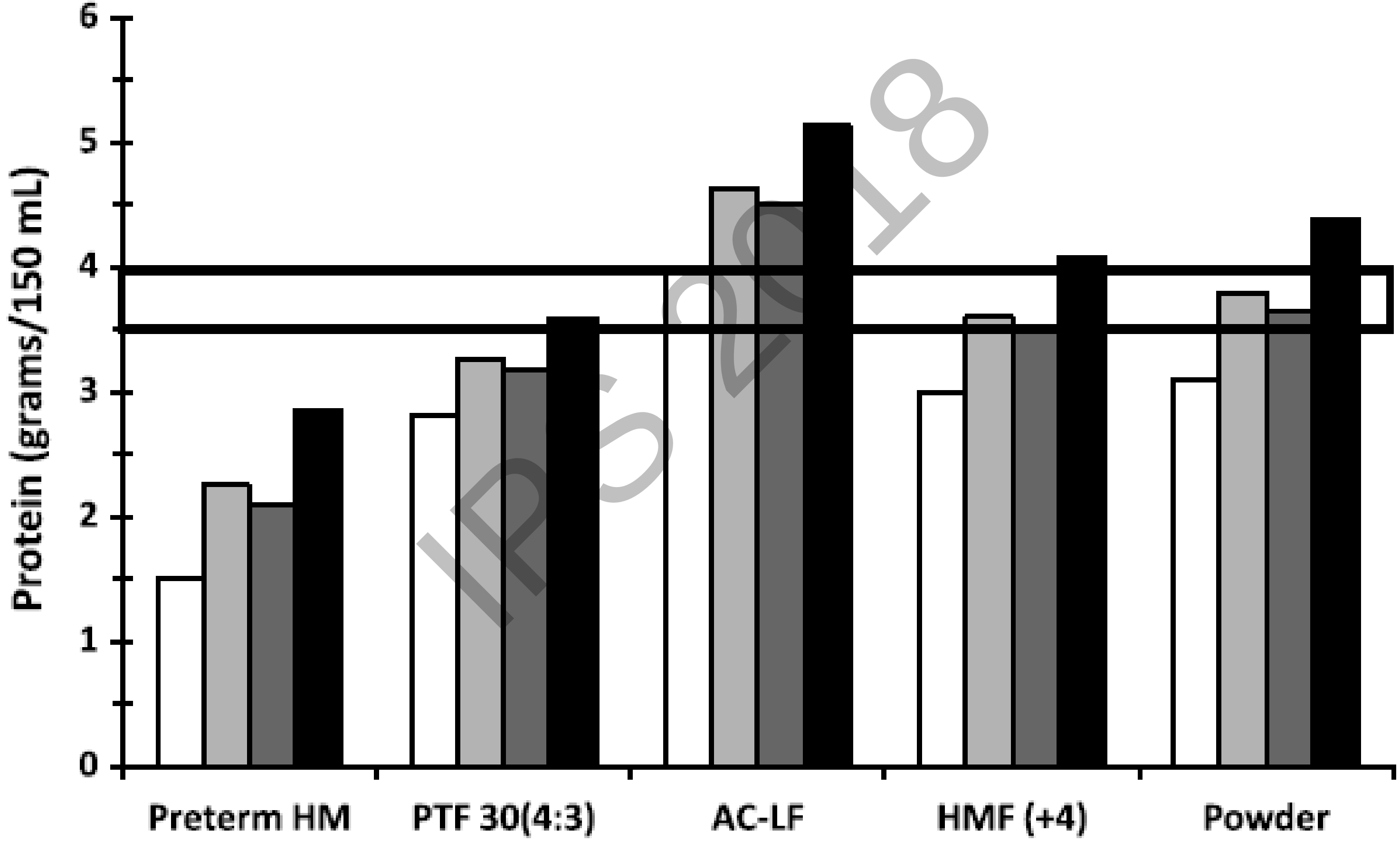
	Stage of lactation				p
	0–2 weeks	2–4 weeks	≥4 weeks	Donor human milk (term)	
Protein (g/dL)	1.7 ± 0.3	1.5 ± 0.2	1.3 ± 0.4	1.0 ± 0.1	<0.02 (DHM vs. all stages)
(range)	1.3–2.8	1.2–2.0	0.9–1.9	0.8–1.1	
Fat (g/dL)	3.0 ± 0.9	3.6 ± 1.1	3.8 ± 0.9	2.5 ± 0.3	≤0.015 (DHM vs 0–2 wks and ≥4 wks)
(range)	1.0–5.7	1.8–6.2	2.1–5.5	2.2–3.0	
Lactose (g/dL)	6.5 ± 0.5	6.6 ± 0.3	6.5 ± 0.2	6.1 ± 0.4	<0.005 (DHM vs. all stages)
(range)	5.1–7.9	6.4–7.5	5.9–7.1	5.5–6.7	
Energy (kcal/oz)	17.2 ± 2.4	18.6 ± 2.9	18.9 ± 2.6	14.6 ± 1.4	0.021 (DHM vs 0–2 wks and ≥4 wks)
(range)	12.4–24.5	13.6–25.7	14.2–23.6	13.1–16.6	

DHM: donor human milk.

IS THERE A NEED FOR PHM FORTIFICATION ?

Journal of Neonatal-Perinatal Medicine 6 (2013) 319–323

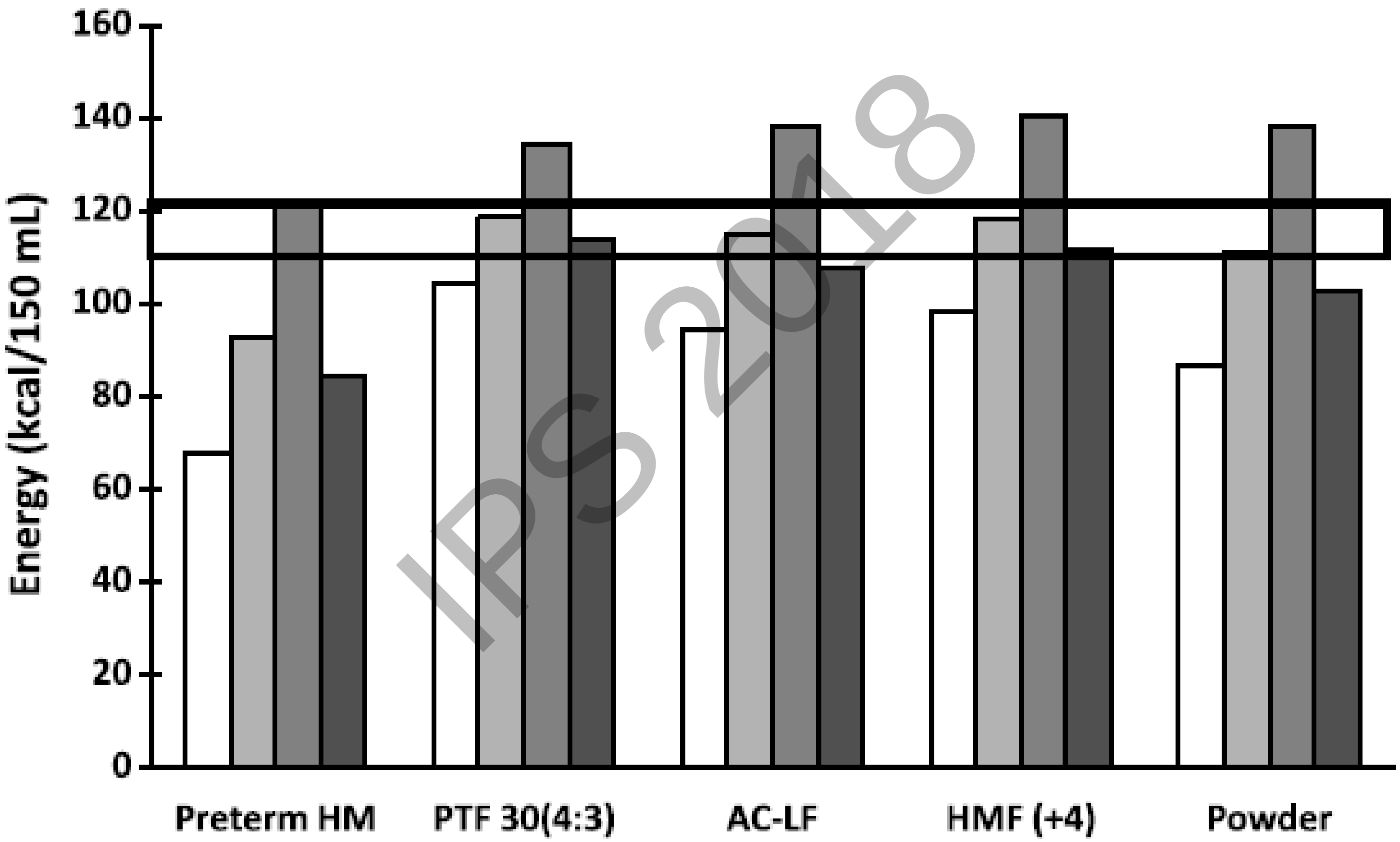
PROTEIN



IS THERE A NEED FOR PHM FORTIFICATION ?

PROTEIN

Journal of Neonatal-Perinatal Medicine 6 (2013) 319–323

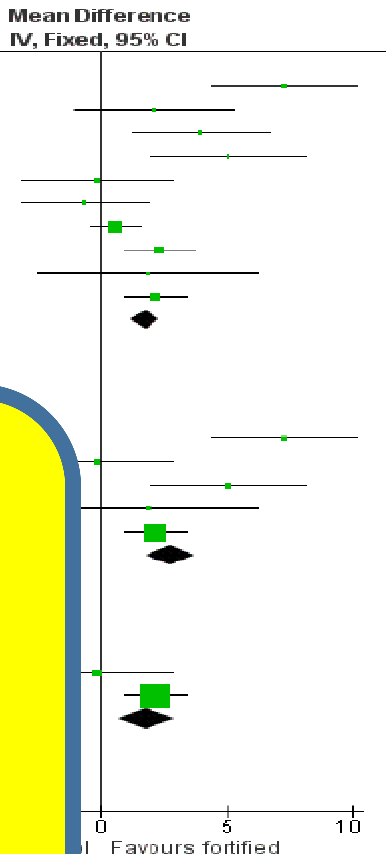


Multi-nutrient fortification of human milk for preterm infants

Figure 3. Forest plot of comparison: 1 Fortified breast milk versus unfortified breast milk, outcome: 1.1 Weight gain (g/kg/d).

Study or Subgroup	Fortified Mean	Fortified SD	Fortified Total	Unfortified Mean	Unfortified SD	Unfortified Total	Weight	Mean Difference IV, Fixed, 95% CI	Year
1.1.1 All trials									
Modanlou 1986	26.7	3.4	8	19.4	2.7	10	4.0%	7.30 [4.41, 10.19]	1986
Gross 1987 (1)	19.9	2.5	10	17.7	4.4	10	3.4%	2.20 [-0.94, 5.34]	1987
Gross 1987 (2)	21.5	3.5	17	17.5	3.3	9	4.6%	4.00 [1.28, 6.72]	1987
Polberger 1989	20.4	2.8	7	15.3	3.2	7	3.4%	5.10 [1.95, 8.25]	1989
Pettifor 1989	16.7	5	29	16.8	6.4	28	3.8%	-0.10 [-3.09, 2.89]	1989
Porcelli 1992	11.4	2.7	10	12	3	10	5.4%	-0.60 [-3.10, 1.90]	1992
Lucas 1996	15.6	4.7	137	15	3.5	138	35.2%	0.60 [-0.38, 1.58]	1996
Wauben 1998	16.6	1.6	12	14.2	2	13	16.9%	2.40 [0.99, 3.81]	1998
Nicholl 1999	15.1	3.3	13	13.2	6.4	10	1.8%	1.90 [-2.45, 6.25]	1999
Mukhopadhyay 2007	15.1	4	82	12.9	4	75	21.5%	2.20 [0.95, 3.45]	2007
Subtotal (95% CI)			**325**			**310**	**100.0%**	**1.81 [1.23, 2.40]**	
Heterogeneity: Chi² = 32.63, df = 9 (P = 0.0002); I² = 72%									
Test for overall effect: Z = 6.12 (P < 0.00001)									
1.1.2 Trials recruiting only very preterm									
Modanlou 1986	26.7	3.4							
Pettifor 1989	16.7	5							
Polberger 1989	20.4	2.8							
Nicholl 1999	15.1	3.3							
Mukhopadhyay 2007	15.1	4							
Subtotal (95% CI)									
Heterogeneity: Chi² = 16.02, df = 4 (P =									
Test for overall effect: Z = 5.58 (P < 0.00									
1.1.3 Trials conducted in low- or midd									
Pettifor 1989	16.7	5							
Mukhopadhyay 2007	15.1	4							
Subtotal (95% CI)									
Heterogeneity: Chi² = 1.94, df = 1 (P =									
Test for overall effect: Z = 3.15 (P = 0.00									

Test for subgroup differences: Chi² = 3



EFFECT ON WEIGHT GAIN

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Multi-nutrient fortification of human milk for preterm infants

Figure 4. Forest plot of comparison: 1 Fortified breast milk versus unfortified breast milk, outcome: 1.2 Length gain (cm/wk).

	Fortified			Unfortified				Mean Difference	
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Fixed, 95% CI**	**Year**
1.2.1 All trials									
Modanlou 1986	0.99	0.4	8	0.81	0.44	10	1.6%	0.18 [-0.21, 0.57]	1986
Gross 1987 (1)	0.89	0.19	10	0.81	0.22	10	7.3%	0.08 [-0.10, 0.26]	1987
Gross 1987 (2)	0.84	0.25	17	0.79	0.12	9	11.8%	0.05 [-0.09, 0.19]	1987
Polberger 1989	1.2	0.17	7	0.83	0.17	7	7.5%	0.37 [0.19, 0.55]	1989
Porcelli 1992	0.6	0.2	10	0.7	0.3	10	4.8%	-0.10 [-0.32, 0.12]	1992
Lucas 1996	0.93	0.47	137	0.96	0.47	138	19.3%	-0.03 [-0.14, 0.08]	1996
Wauben 1998	1.1	0.2	12	0.9	0.2	13	9.7%	0.20 [0.04, 0.36]	1998
Mukhopadhyay 2007	1.04	0.3	82	0.86	0.2	75	38.0%	0.18 [0.10, 0.26]	2007
Subtotal (95% CI)			**283**			**272**	**100.0%**	**0.12 [0.07, 0.17]**	

Heterogeneity: Chi² = 22.71, df = 7 (P = 0.002); I² = 69%
Test for overall effect: Z = 4.80 (P < 0.00001)

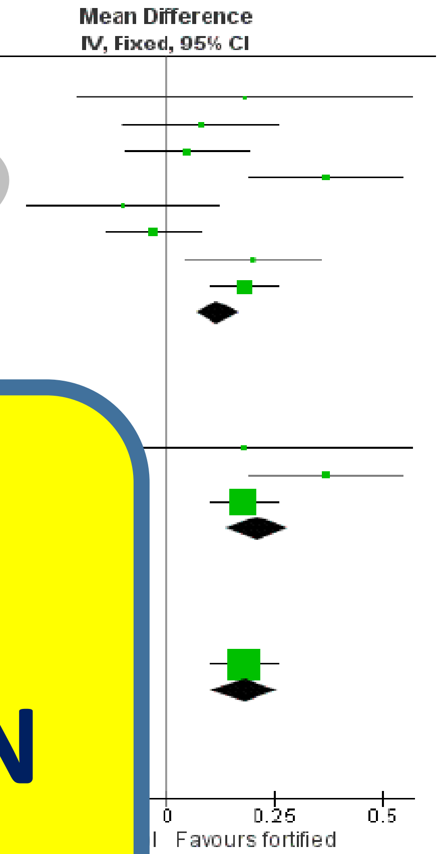
1.2.2 Trials recruiting only very preter			
Modanlou 1986	0.99	0.4	
Polberger 1989	1.2	0.17	
Mukhopadhyay 2007	1.04	0.3	
Subtotal (95% CI)			

Heterogeneity: Chi² = 3.67, df = 2 (P
Test for overall effect: Z = 5.80 (P < 0

1.2.3 Trials conducted in low- or mi			
Mukhopadhyay 2007	1.04	0.3	
Subtotal (95% CI)			

Heterogeneity: Not applicable
Test for overall effect: Z = 4.46 (P < 0

Test for subgroup differences: Chi² =



EFFECT ON LENGTH GAIN

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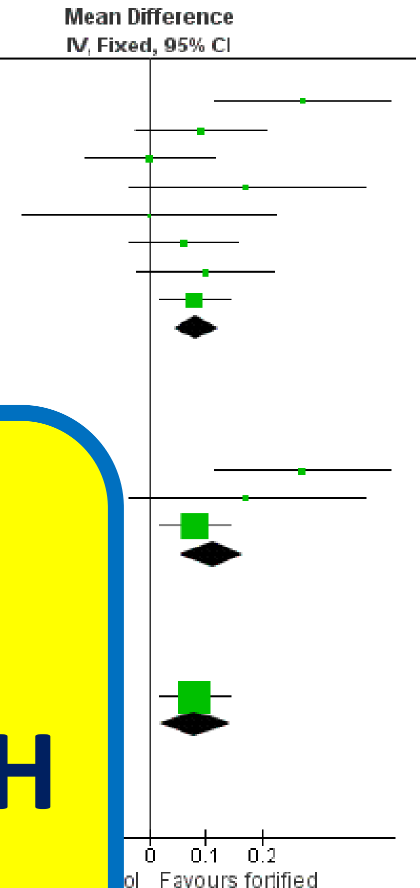
Multi-nutrient fortification of human milk for preterm infants

Figure 5. Forest plot of comparison: 1 Fortified breast milk versus unfortified breast milk, outcome: 1.3 Head growth (cm/wk).

Study or Subgroup	Fortified Mean	Fortified SD	Fortified Total	Unfortified Mean	Unfortified SD	Unfortified Total	Weight	Mean Difference IV, Fixed, 95% CI	Year
1.3.1 All trials									
Modanlou 1986	1.09	0.07	8	0.82	0.24	10	6.2%	0.27 [0.11, 0.43]	1986
Gross 1987 (1)	0.92	0.09	10	0.83	0.16	10	11.7%	0.09 [-0.02, 0.20]	1987
Gross 1987 (2)	0.84	0.21	17	0.84	0.09	9	11.3%	0.00 [-0.12, 0.12]	1987
Polberger 1989	1.11	0.13	7	0.94	0.25	7	3.5%	0.17 [-0.04, 0.38]	1989
Porcelli 1992	0.7	0.3	10	0.7	0.2	10	3.0%	0.00 [-0.22, 0.22]	1992
Lucas 1996	1.01	0.47	137	0.95	0.35	138	15.7%	0.06 [-0.04, 0.16]	1996
Wauben 1998	1	0.1	12	0.9	0.2	13	10.1%	0.10 [-0.02, 0.22]	1998
Mukhopadhyay 2007	0.83	0.2	82	0.75	0.2	75	38.6%	0.08 [0.02, 0.14]	2007
Subtotal (95% CI)			**283**			**272**	**100.0%**	**0.08 [0.04, 0.12]**	
Heterogeneity: Chi² = 8.96, df = 7 (P = 0.26); I² = 22%									
Test for overall effect: Z = 4.21 (P < 0.0001)									
1.3.2 Trials recruiting only very pret									
Modanlou 1986	1.09	0.0							
Polberger 1989	1.11	0.							
Mukhopadhyay 2007	0.83	0							
Subtotal (95% CI)									
Heterogeneity: Chi² = 5.22, df = 2 (									
Test for overall effect: Z = 3.88 (P =									
1.3.3 Trials conducted in low- or									
Mukhopadhyay 2007	0.83	0							
Subtotal (95% CI)									
Heterogeneity: Not applicable									
Test for overall effect: Z = 2.50 (P =									

Test for subgroup differences: Chi



EFFECT ON HEAD GROWTH

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Multi-nutrient fortification of human milk for preterm infants

NO EFFECTS ON

- 7 Mental development index
- 8 Psychomotor development
- 9 Length of hospital stay
- 10 Feed intolerance.
- 11 Necrotising enterocolitis.

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The Use of Multinutrient Human Milk Fortifiers in Preterm Infants

A Systematic Review of Unanswered Questions

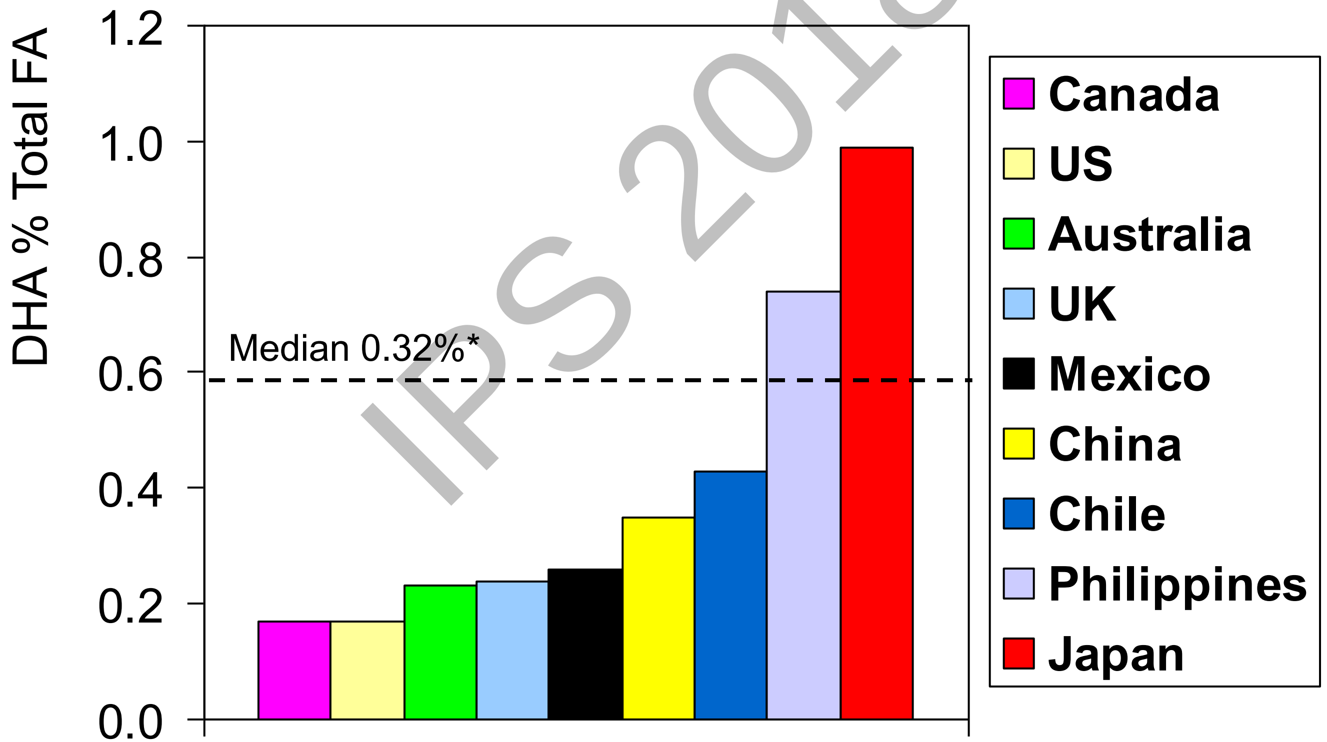
Bovine vs human source fortifier

Early vs late fortification

Clin Perinatol 44 (2017) 173–178

IS THERE A NEED FOR PHM FORTIFICATION ?

Wide Variation in Human Milk DHA Due to Diet

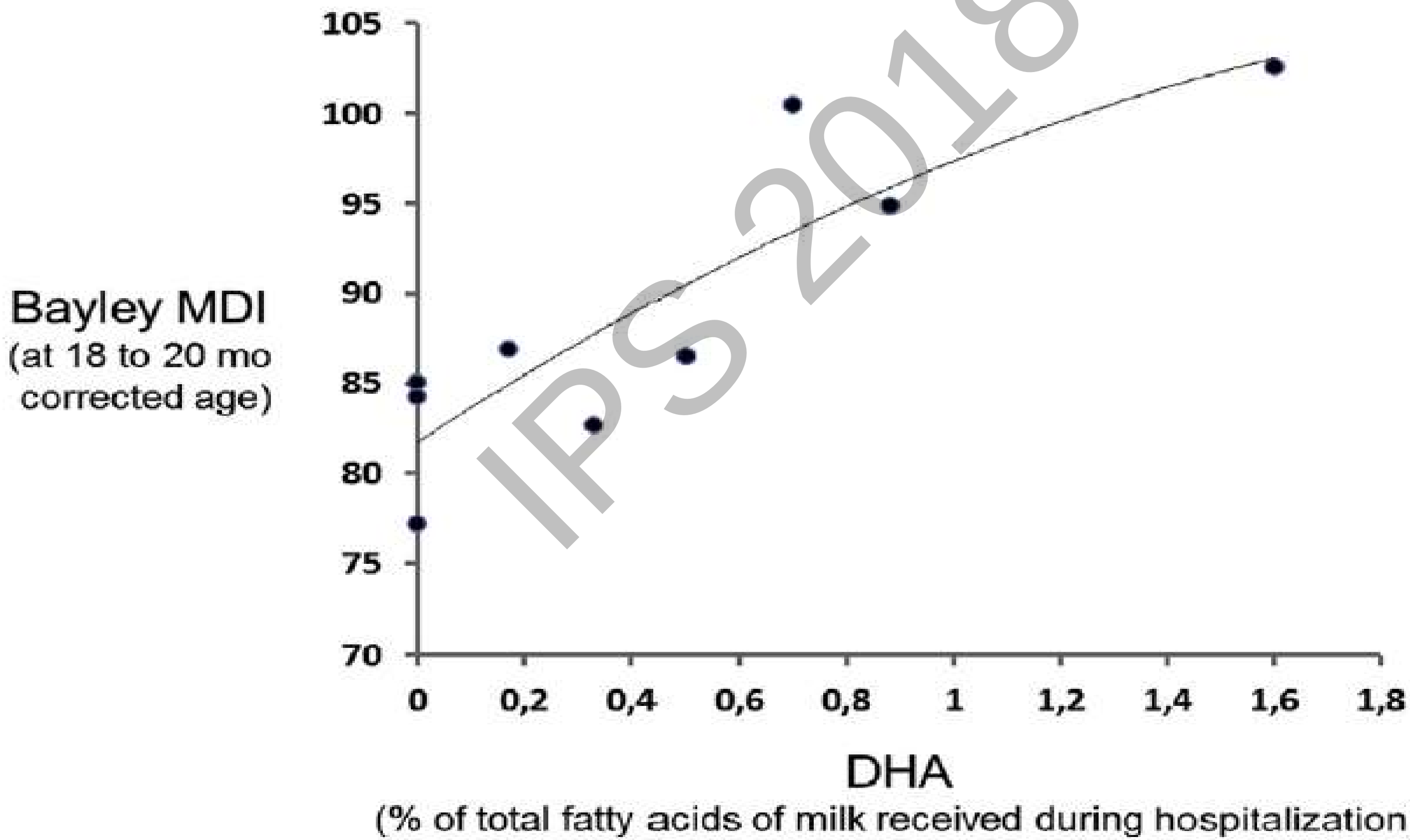


Yuhas R, et al. *Lipids.* 2006;41:851-858.
*Brenna JT et al. *Am J Clin Nutr.* 2007;85:1457-1464.

IS THERE A NEED FOR PHM FORTIFICATION ?

Clin Perinatol 44 (2017) 85–93

DHA



IS THERE A NEED FOR PHM FORTIFICATION ?

DHA

Clin Perinatol 44 (2017) 85–93

Table 1
Providing preterm infants with milk with a higher docosahexaenoic acid dose (about 1% of fatty acids, compared with 0.3%) improved early visual function and reduced markedly abnormal developmental outcomes at age 18 months

	High DHA (≈1%)	Standard DHA (≈0.3%)	Significance
Visual acuity (cycles per degree), aged 4 mo (corrected for gestational age)			
	9.6 (3.7)	8.2 (1.8)	*P* = .025
Mental development index (MDI), aged 18 mo (corrected for gestational age)			
Girls	99.1(13.9)	94.4 (17.5)	*P* =.03
Boys	91.3 (14.0)	91.9 (17.2)	n.s.
Markedly abnormal development index (MDI), aged 18 mo (corrected for gestational age)			
MDI <70	17 (5%)	35 (11%)	*P* = .03
MDI <85	64 (20%)	90 (27%)	*P* = .08

*ADAM.

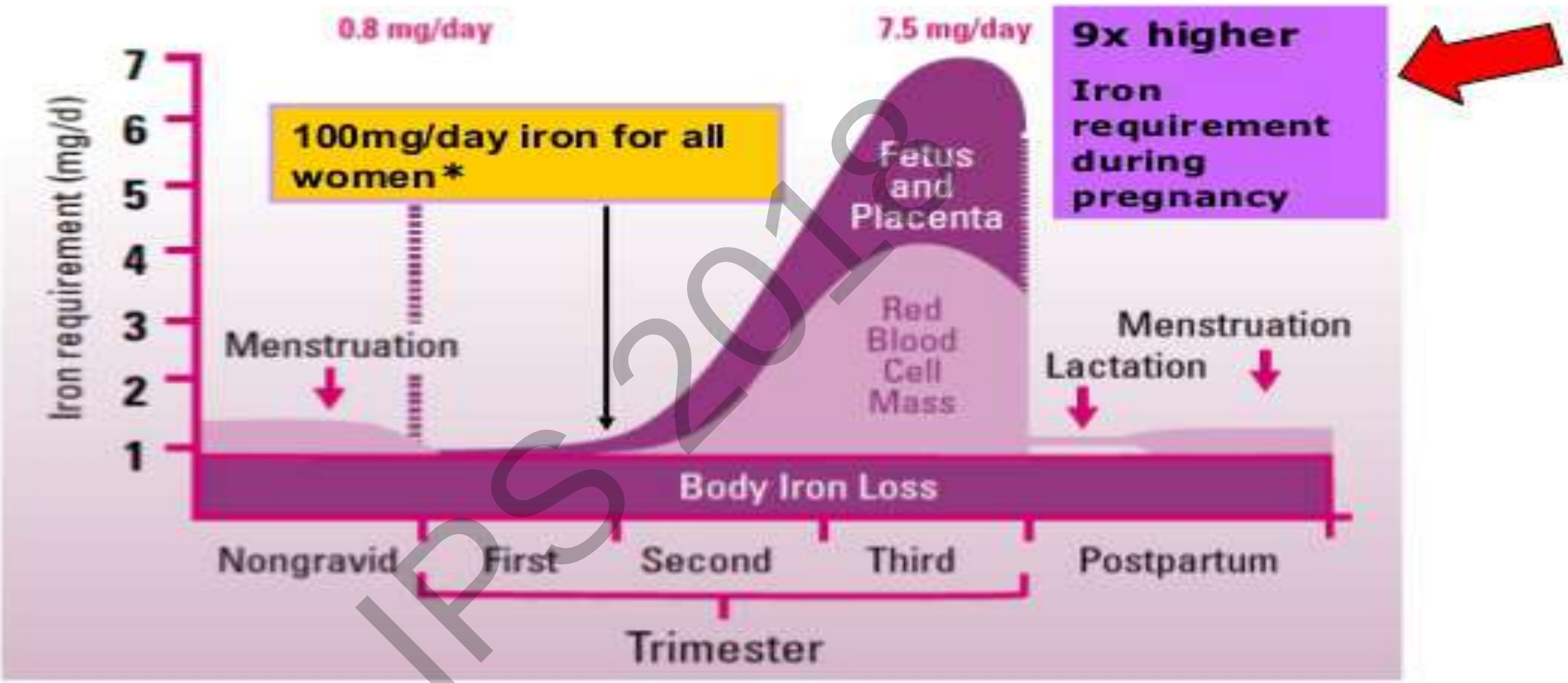
RISK OF OSTEOPENIA

Semin Perinatol 31:89-95 © 2007 I

Table 1 Macronutrient Concentrations (per dL) of Feedings for Preterm Infants at the Time of Discharge

	Human Milk (mature)*	TERM FORMULA		ENRICHED POST DISCH FORMULA	
Calories/dL	69	68	68	75	74
Protein g/dL	1.0	1.4	1.4	2.1	2.1
Fat g/dL	3.9	3.6	3.6	4.1	3.9
CHO g/dL	6.6	7.3	7.3	7.7	7.9
Vit A IU/dL	390	203	203	343	333
Vit D IU/dL	2	40	40	52	59
Vit E IU/dL	1.0	2.0	1.3	2.7	3.0
Ca mg/dL	25	53	53	78	89
P mg/dL	13	28	36	46	49
Fe mg/dL	0.1	1.22	1.22	1.34	1.33

If a baby was born prematurely they may not have had enough time to get iron from their mother during the last few weeks of pregnancy



IRON SHOULD BE SUPPLEMENTED WHEN PREMATURE ARE FED BREAST MILK

TAKE HOME MESSAGE THREE

TO ENSURE AN APPROPRIATE GROWTH IN THE SECOND PHASE

THE USE OF BREAST MILK FORTIFIED BY PROTEINS AND DHA AND VIT D IS RECOMMENDED along with IRON SUPPLEMENTATION

3RD PHASE THE CATCH UP GROWTH

POST DISCHARGE NUTRITION IF BREAST MILK MILK IS NOT AVAILABLE

ENTERAL NUTRITION OF THE PRETERM
THE DEBATE!

FORMULA ENRICHED OR NOT ?

STANDARD FORMULA

PRETERM FORMULA

POST DISCHARGE FORMULA

	PROTEINS	ENERGY
STANDARD FORMULA	1.4-1.7 g/100 ml	66-68 Kcal /100ml
PRETERM FORMULA	2-2.4 g/100 ml	80 K cal /100ml
POST DISCHARGE FORMULA	1.7-1.9 g/100 ml	74 K cal /100ml

Nutrient-enriched formula versus standard formula for preterm infants following hospital discharge (Review)

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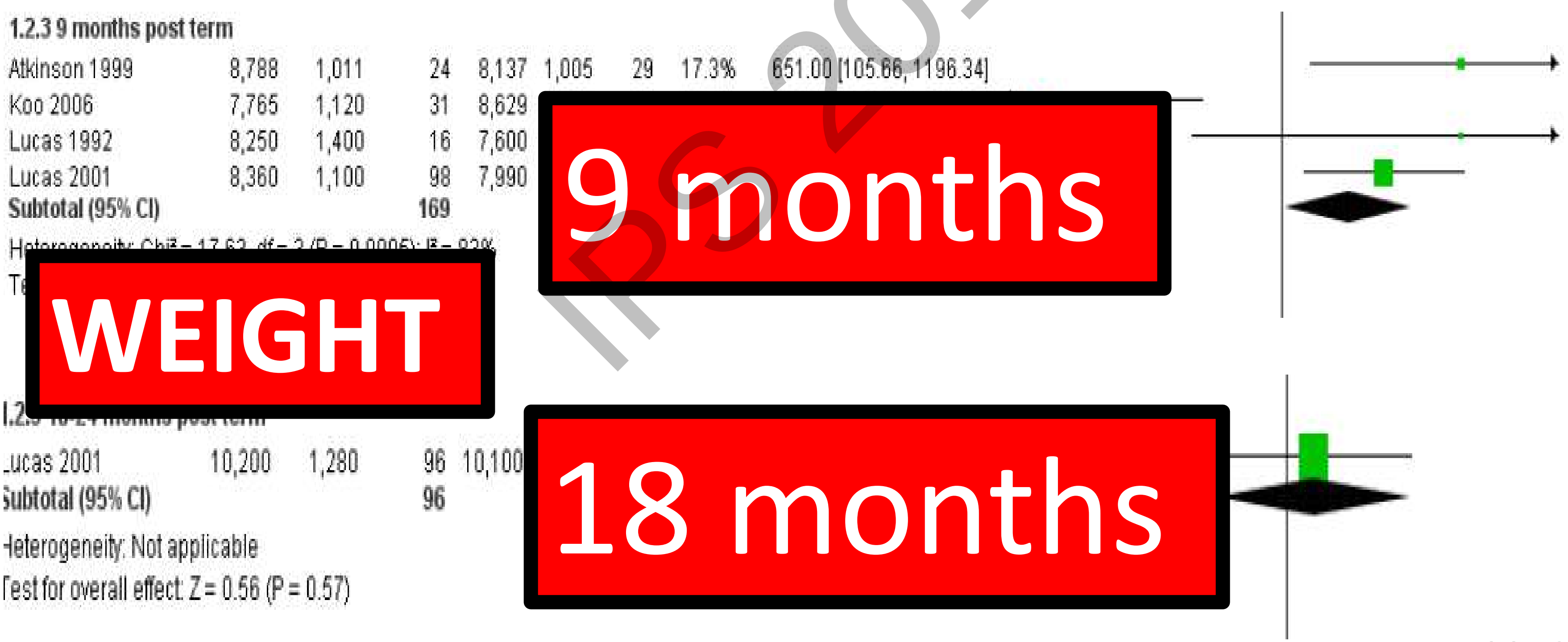
POST DISCHARGE FORMULA

STANDARD FORMULA



2016

Nutrient-enriched formula versus standard formula for preterm infants following hospital discharge (Review)

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POST DISCHARGE FORMULA

STANDARD FORMULA

1.3.3 9 months post term

Atkinson 1999	705	23	24
Koo 2006	668	30.6	31
Lucas 1992	720	18	16
Lucas 2001	709	32	98
Subtotal (95% CI)			**169**

9 months

LENGTH

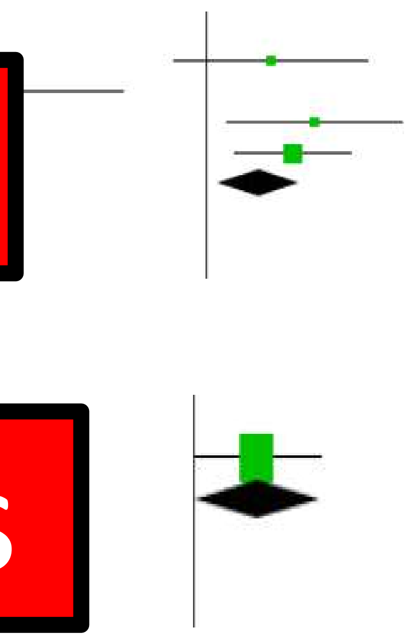
1.3.5 18-24 months post term

Lucas 2001	806	34	96
Subtotal (95% CI)			**96**

Heterogeneity: Not applicable

Test for overall effect: Z = 2.03 (P = 0.04)

18 months



2016

Nutrient-enriched formula versus standard formula for preterm infants following hospital discharge (Review)

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PRETERM FORMULA

STANDARD FORMULA

WEIGHT

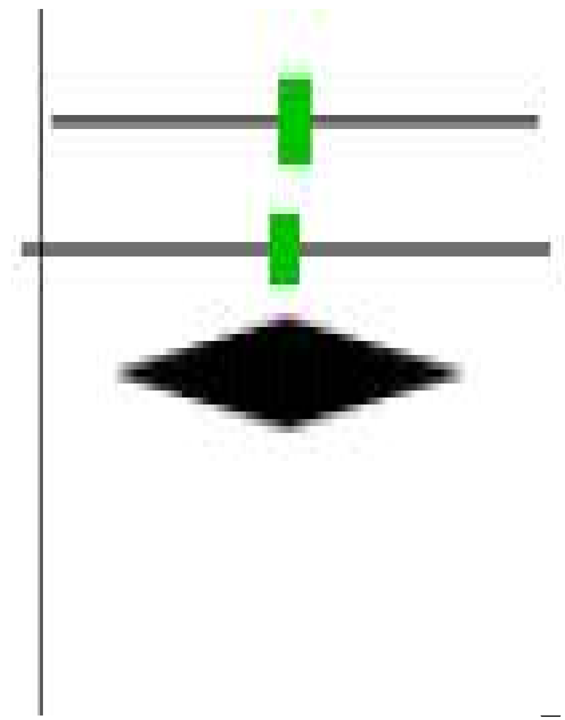
12 & 18 M

LENGTH

18 M

H C

6 to 18 M



CONCERNS ABOUT RAPID GROWTH AND CATCH UP

EARLY GROWTH & LATER MORBIDITIES

TWO SCENARIOS

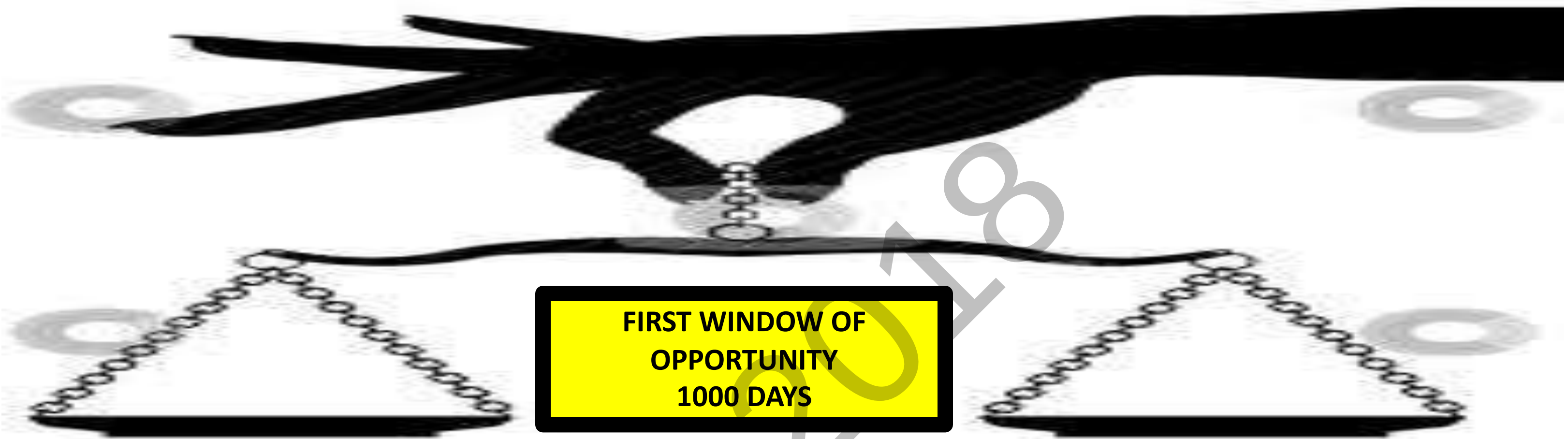
PREGNANCY | **NEONATAL & POST**

BARKER → THE THRIFTY PHENOTYPE HYPOTHESIS

LUCAS -SINGHAL → THE GROWTH ACCELERATION HYPOTHESIS

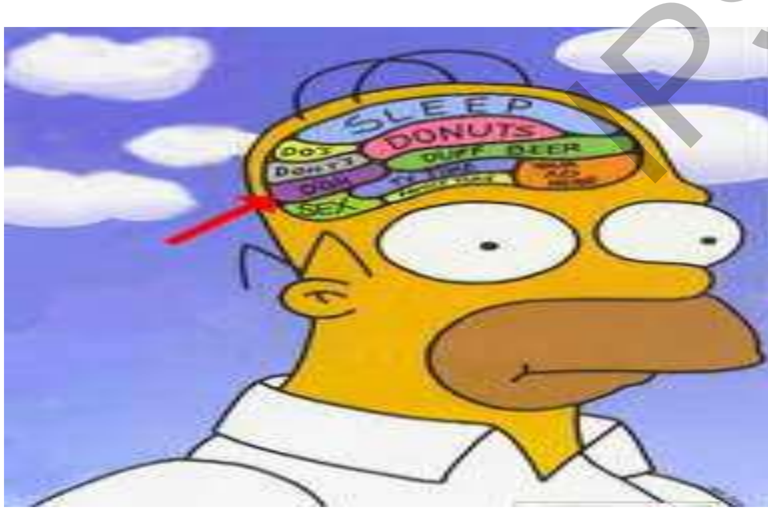
THE METABOLIC SYNDROME

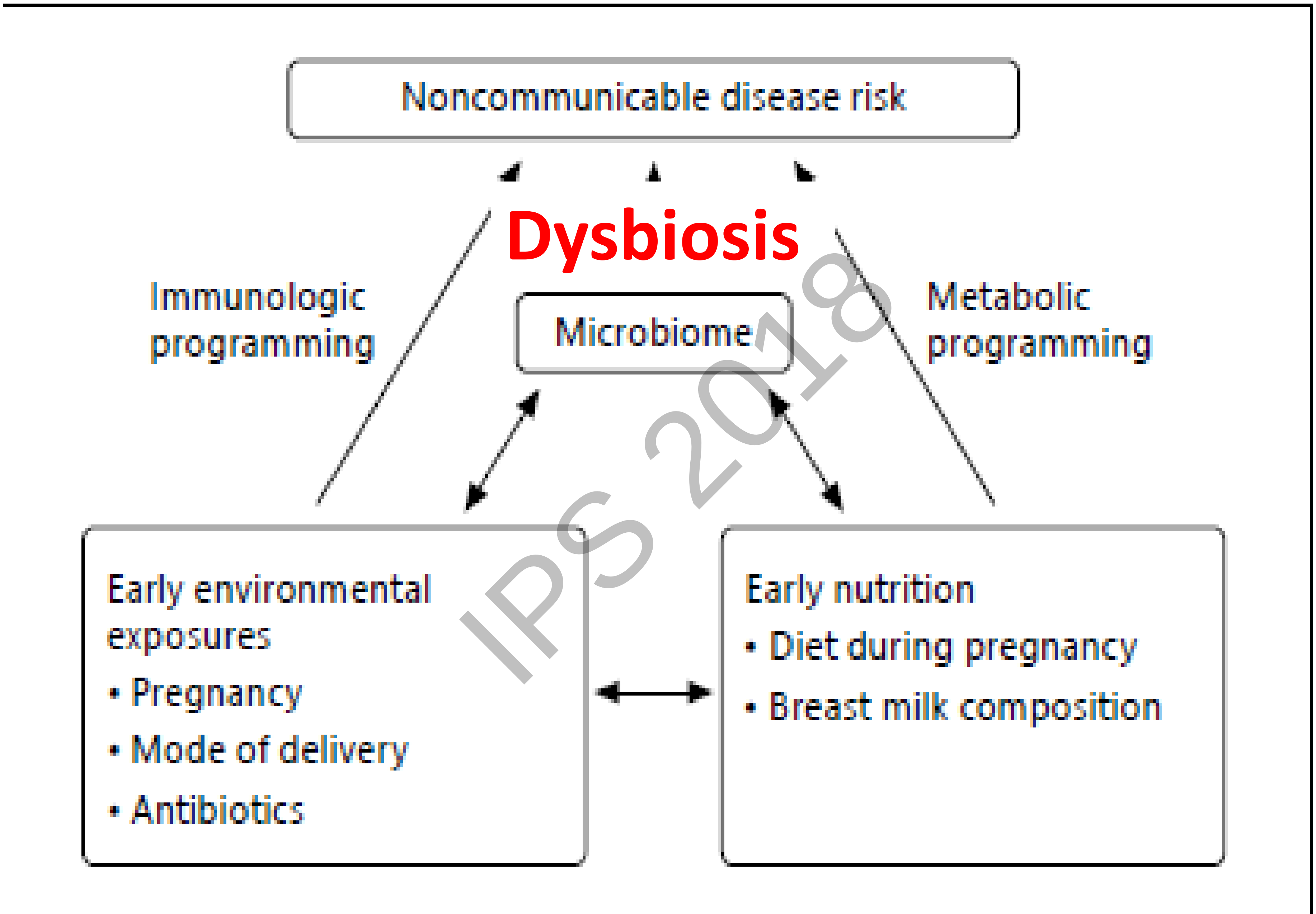
NUTRITION &DEVELOPMENT



FIRST WINDOW OF OPPORTUNITY 1000 DAYS

UNDERNUTRITION **OVER NUTRITION**





Noncommunicable disease risk
Dysbiosis
Immunologic programming
Microbiome
Metabolic programming
Early environmental exposures
• Pregnancy
• Mode of delivery
• Antibiotics
Early nutrition
• Diet during pregnancy
• Breast milk composition
IPS 2018