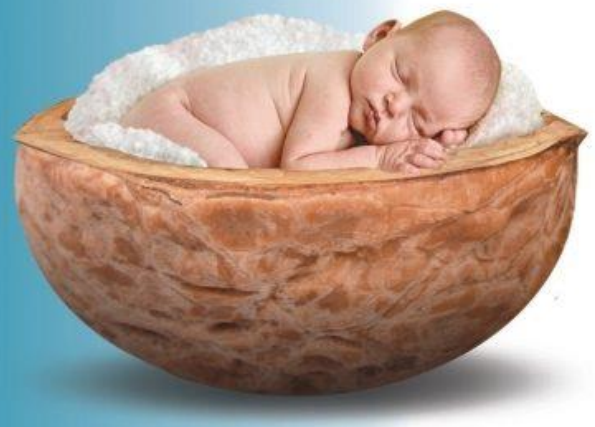
NEONATUS
2018

Międzynarodowa Konferencja
Naukowo-Szkoleniowa
27-28 września 2018



IMPROVED GROWTH and OUTCOME in VLBW INFANTS OPTIMIZING NUTRITION

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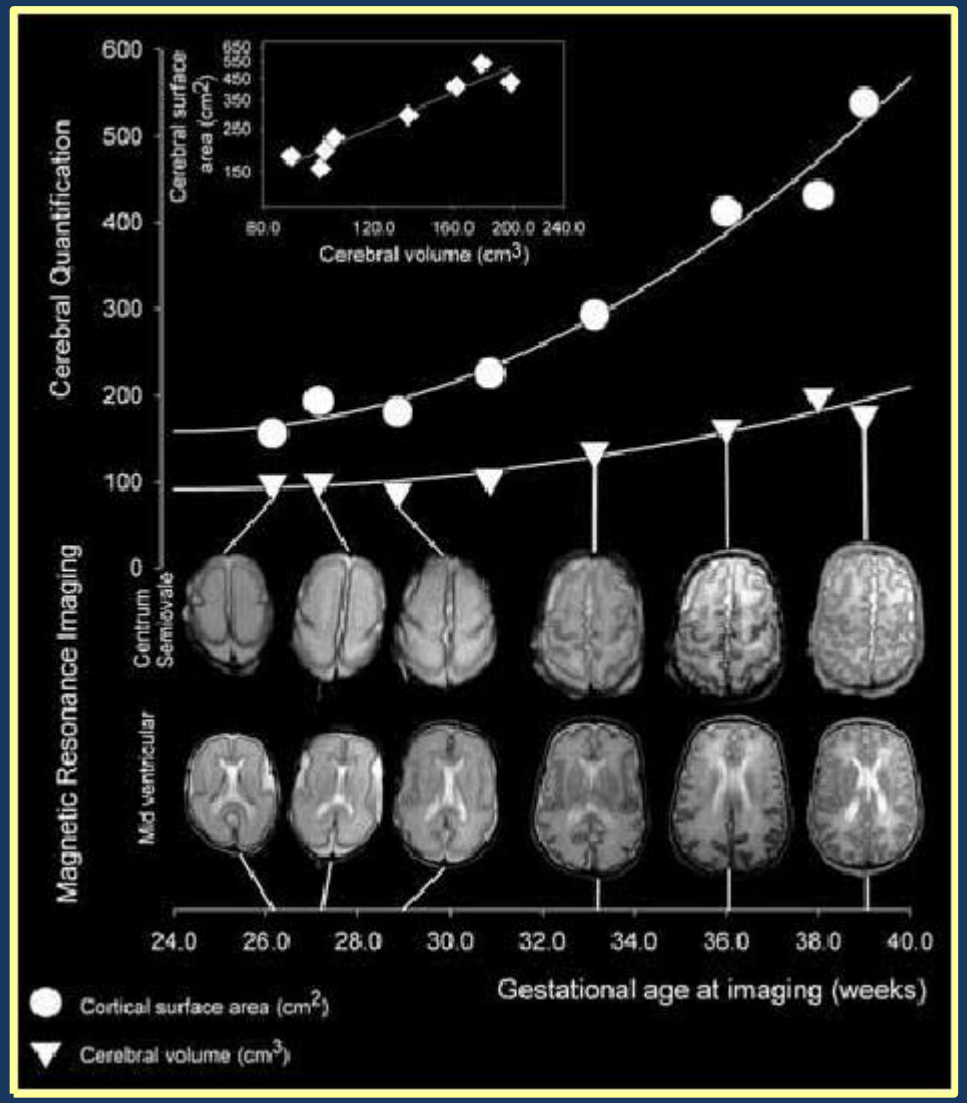
INFANT BRAIN GROWTH- Importance of Nutrition

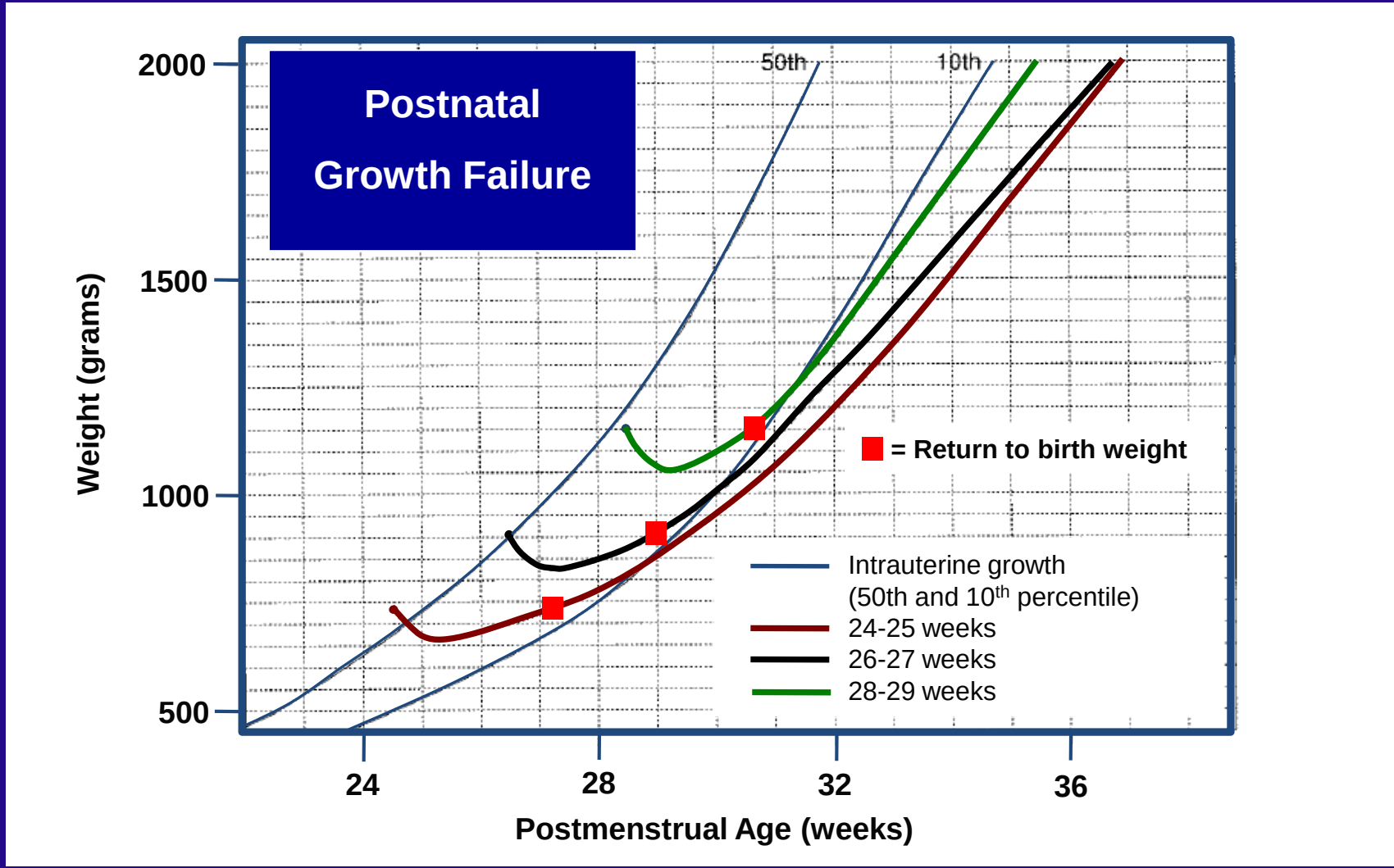


Brain growth over next 8 weeks:

At 28 wks.	100% Increase
At term	40% Increase
At 3 mo.	25% Increase

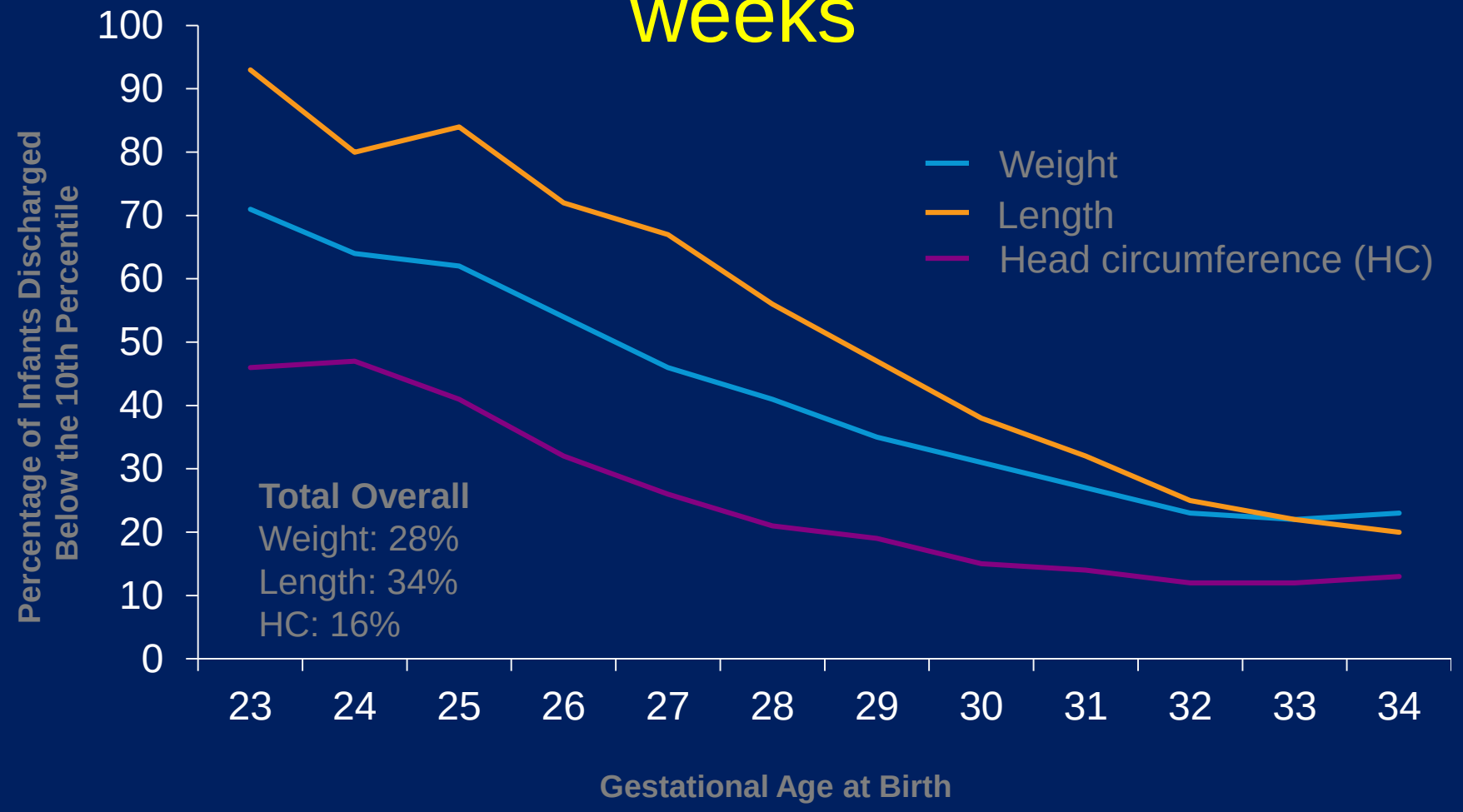
Kapellou O, et al. PLoS Med 2006;3(8):e265.

NICHD Growth Observational Study



Ehrenkranz RA, et al. *Pediatrics* 1999;104:280-9.

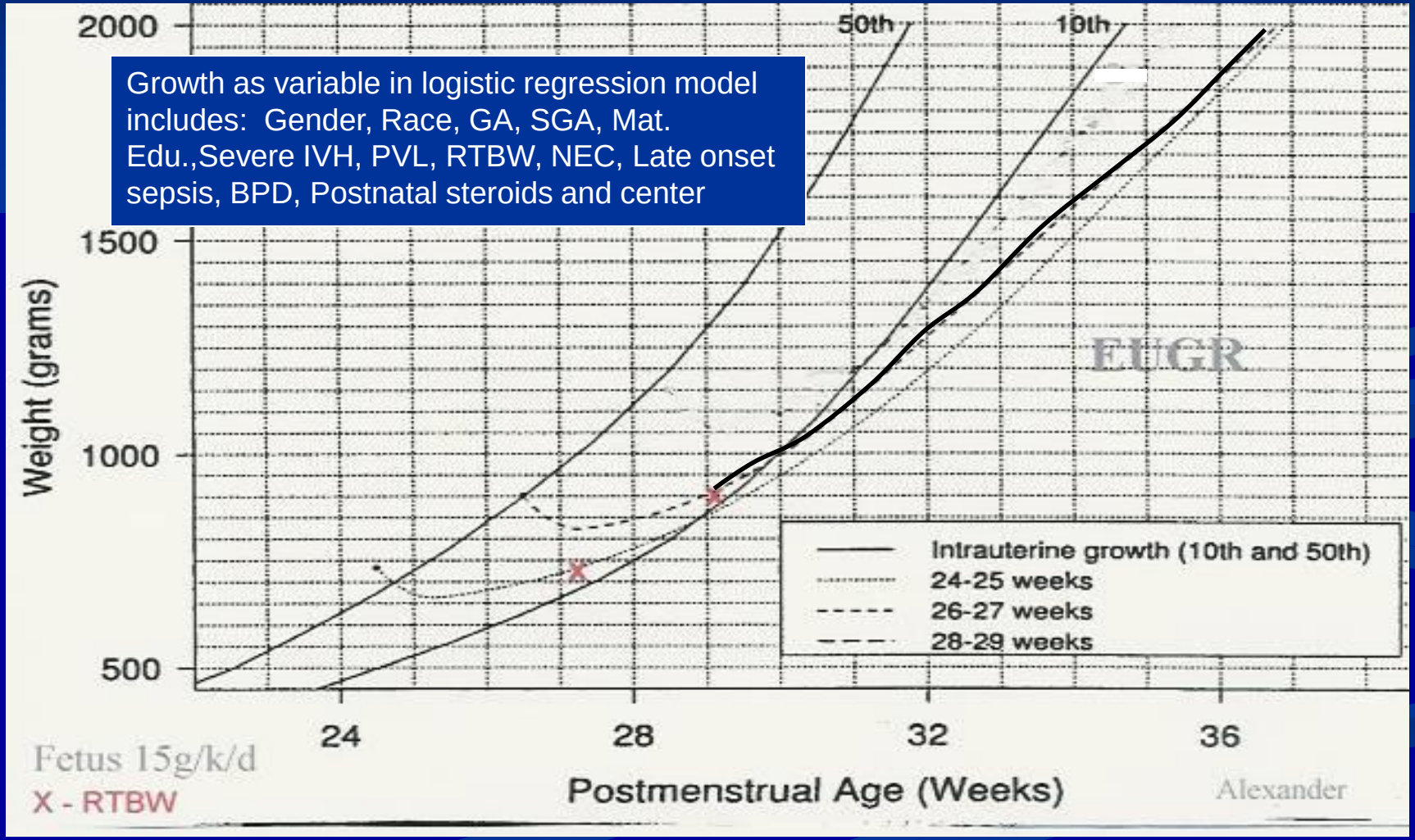
Incidence of Growth Restriction* at Discharge by Gestational Age at Birth Pediatrix 24k infants < 34 weeks



*Defined as weight/length/HC≤10th percentile.

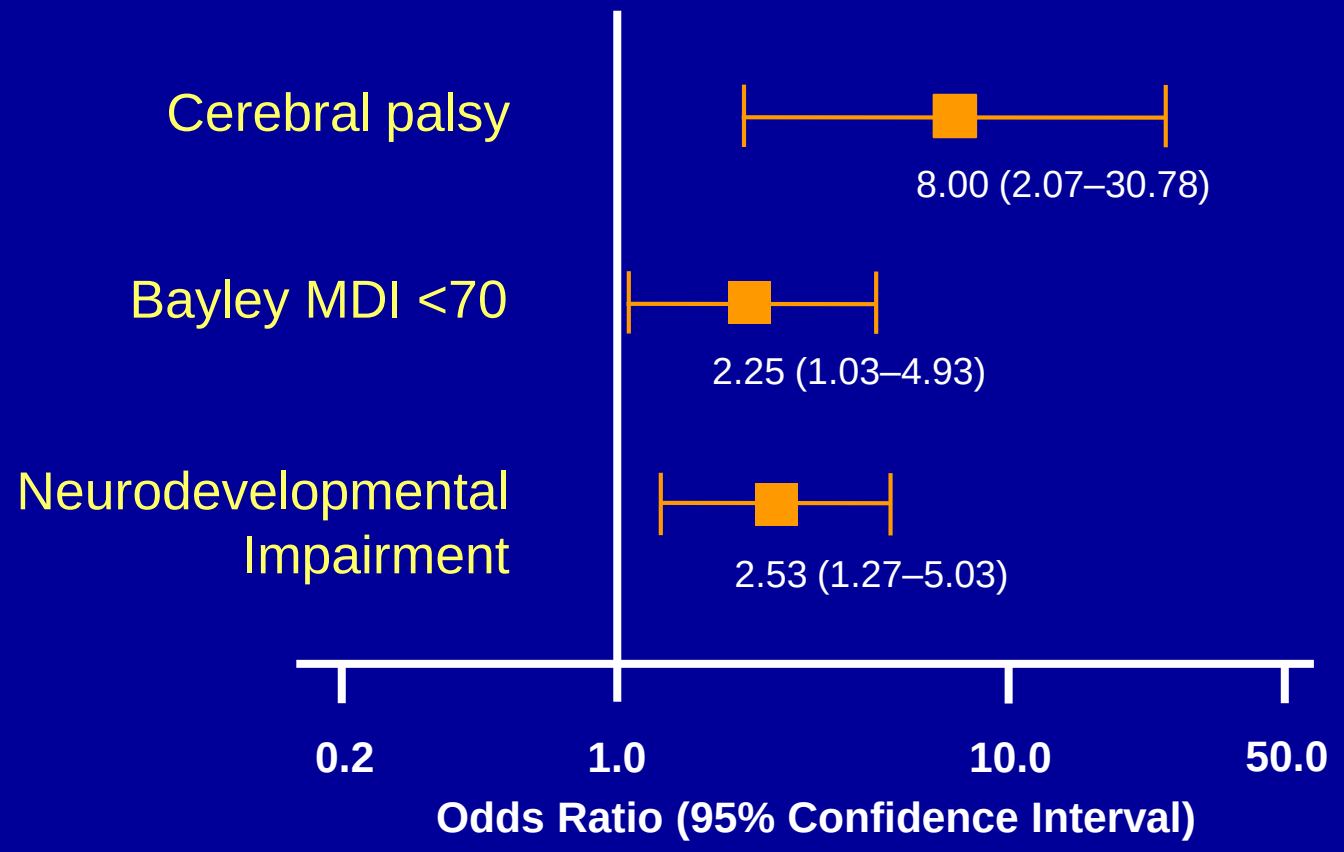
Clark RH, et al. *Pediatrics.* 2003;111:986-990.

Growth in NICU Influences Neurodevelopment and Growth of ELBW Infants (NICHD 2006)



Poor Weight Gain Increases Odds for Poor Outcomes

ELBW infants, in-hospital growth: **12.0** vs **21.2** g/kg/day



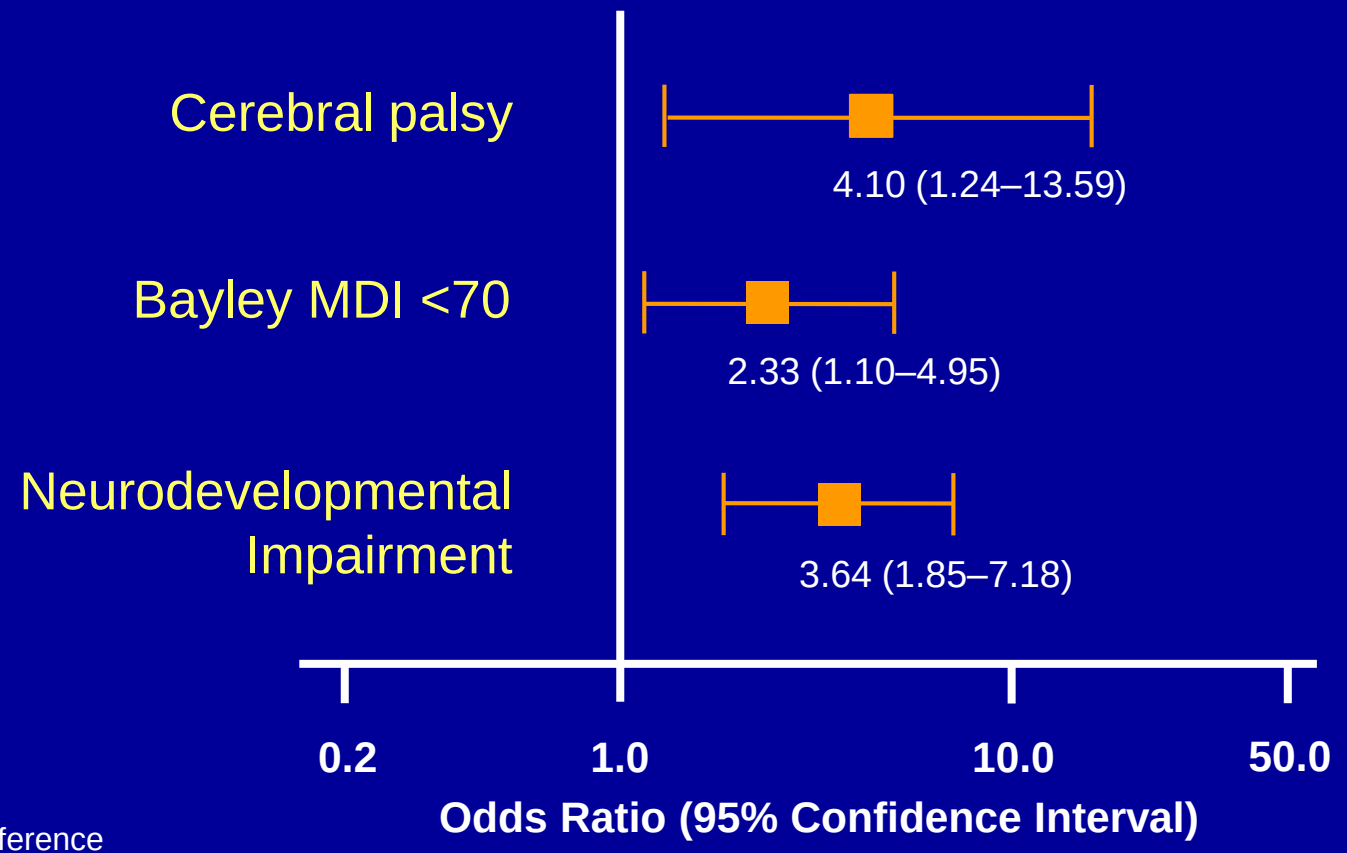
MDI=Mental Development Index

Ehrenkranz RA, et al. *Pediatrics* 2006;117:1253-61.

Abbott Nutrition

Poor HC Growth Increases Odds for Poor Outcomes

ELBW infants, in-hospital HC growth: **0.67** vs **1.17** cm/wk



HC=Head circumference

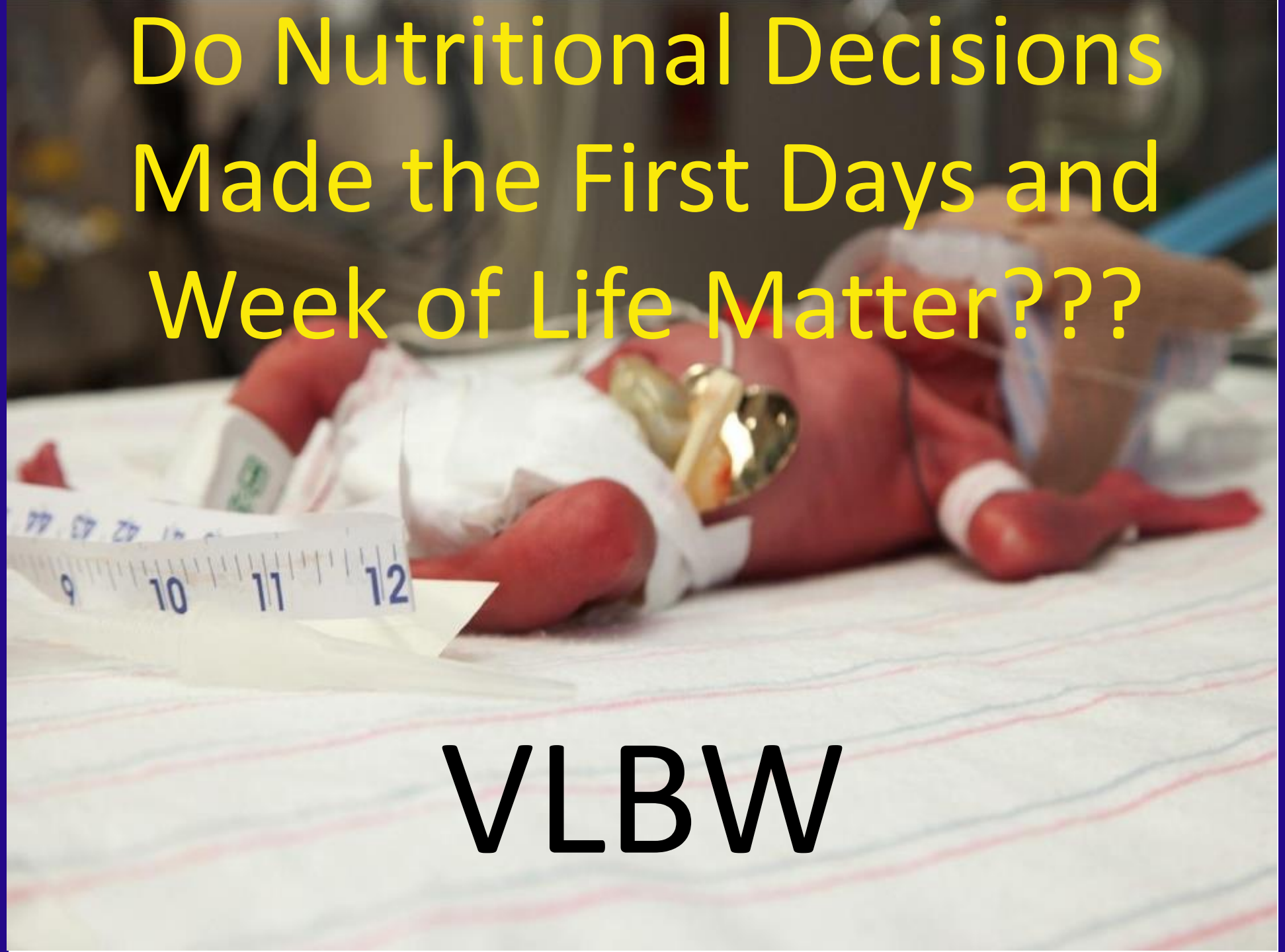
MDI=Mental Development Index

Ehrenkranz RA, et al. *Pediatrics* 2006;117:1253-61.

Abbott Nutrition

Postnatal Growth During Hospitalization is Critical to Neurodevelopmental Outcome

Do Nutritional Decisions Made the First Days and Week of Life Matter???



VLBW

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

Schneider et al Peds 2018

- N=49, 27 wks gest age, MRI scans serially @ 29, 32, and 41 wks PMA

Greater Nutrient Intakes Predicted:

1)Increased Total Brain and Basal Nuclei volumes over the course to Term Equivalent Age

2) Greater fractional anisotropy values in selected WM tracts (increased devt)

3) Brain Growth predicted psychomotor outcomes @ 18 months CA

4)Duration of assisted ventilation was associated with smaller brain volumes which was attenuated by higher energy intake.

Early Nutrition Mediates the Influence of Severity of Illness on ELBW

Ehrenkranz, NICHD Ped Res 2011

N = 1366 (NICHD Glutamine Study)

More critically ill received IMV for mean of 41 days (BW 734g)

Less critically ill 13 days days IMV (BW 842 g)

More critically ill suffered more morbidities and slower growth

More critically ill also received less TPN and enteral energy, delayed initiation of enteral nutrition, total energy (52 cal/k/d vs 42 p <001)

Early Nutritional support was associated with later growth and other outcomes after controlling for critical illness 1st three weeks of life

Morbidities and Death Decreased 2% for each increase 1cal/kg/d of total energy intake first week of life

NEC	BPD
Late Onset Sepsis	DEATH

Take Home Messages For Nutritional Mediation of Severity of Illness ELBW

- Early Nutritional decisions for ELBW are influenced by our perception of severity of illness
- Early aggressive TPN/Enteral support are associated with lower rates of death and short term morbidities and improved growth and neurodevelopmental outcomes
- Early initiation of enteral nutrition was well tolerated and associated with an earlier achievement of full enteral and no increase NEC
- Daily energy intake first 7 days of life mediate the influence of critical illness on risk of adverse outcomes
- Management decisions made within the first several days of life may have long-lasting effects

Optimizing Nutritional Support (ESPGHAN) Rec

N=102, <1250g, 2 year period ~1kg, 28 weeks

Senterre and Rigo JPGN 2011

	Day 1	1 – 7	Birth – Discharge
Prot (g/k/d)	2.4 ± 0.3	3.2 ± 0.5	3.7 ± 0.2
Energy (cal/k/d)	38 ± 6	80 ± 14	122 ± 10

Observations

1) PWL limited to first 3 days. No further decrease Z score after DOL 3 except more immature and most ill (n=25). Maximal wt loss 8± 5%. RTBW 7± 3 days.

2. SGA earlier and higher weight gain and rapid catch-up (16.6 ±1.6 vs 14.4 ±2) $p<0.01$

3) The major Z score change occurred the first three days; inversely correlated with BW Z score (which may be explained by differences in water content and body composition).

BODY WT @ 3 DAYS (as baseline) is MORE ADEQUATE to evaluate FETAL GROWTH, POSTNATAL NUTRITION, SUBSEQUENT GROWTH than BIRTHWEIGHT.

Conclusions from Optimizing Nutritional Support

First week of life is critical to promote growth.

PWL and PNGR may be limited to the first days of life in most VLBW infants. This emphasizes the importance of early initiation of amino acids.

Subsequent growth also may be optimized with catch-up growth allowing a reduction of postnatal growth failed VLBW infants at D/C

Senterre/Rigo

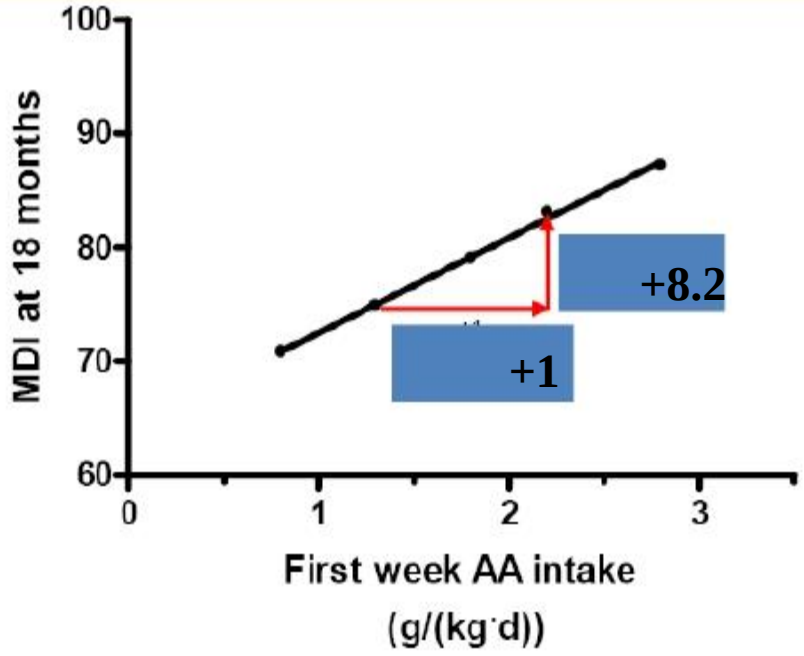
Improved Nutrition in First Week of Life Improves Outcomes at Eighteen Months

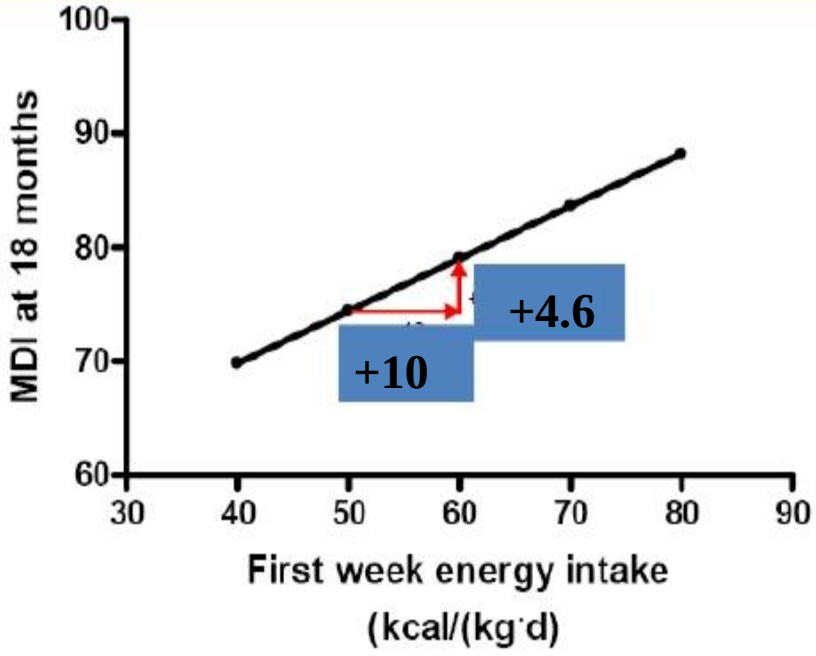
First week protein and energy intakes associated with 18-months developmental outcome in ELBW infants

Day 1 : 0.4 g AA /kg*day and 31 kCal/kg*day

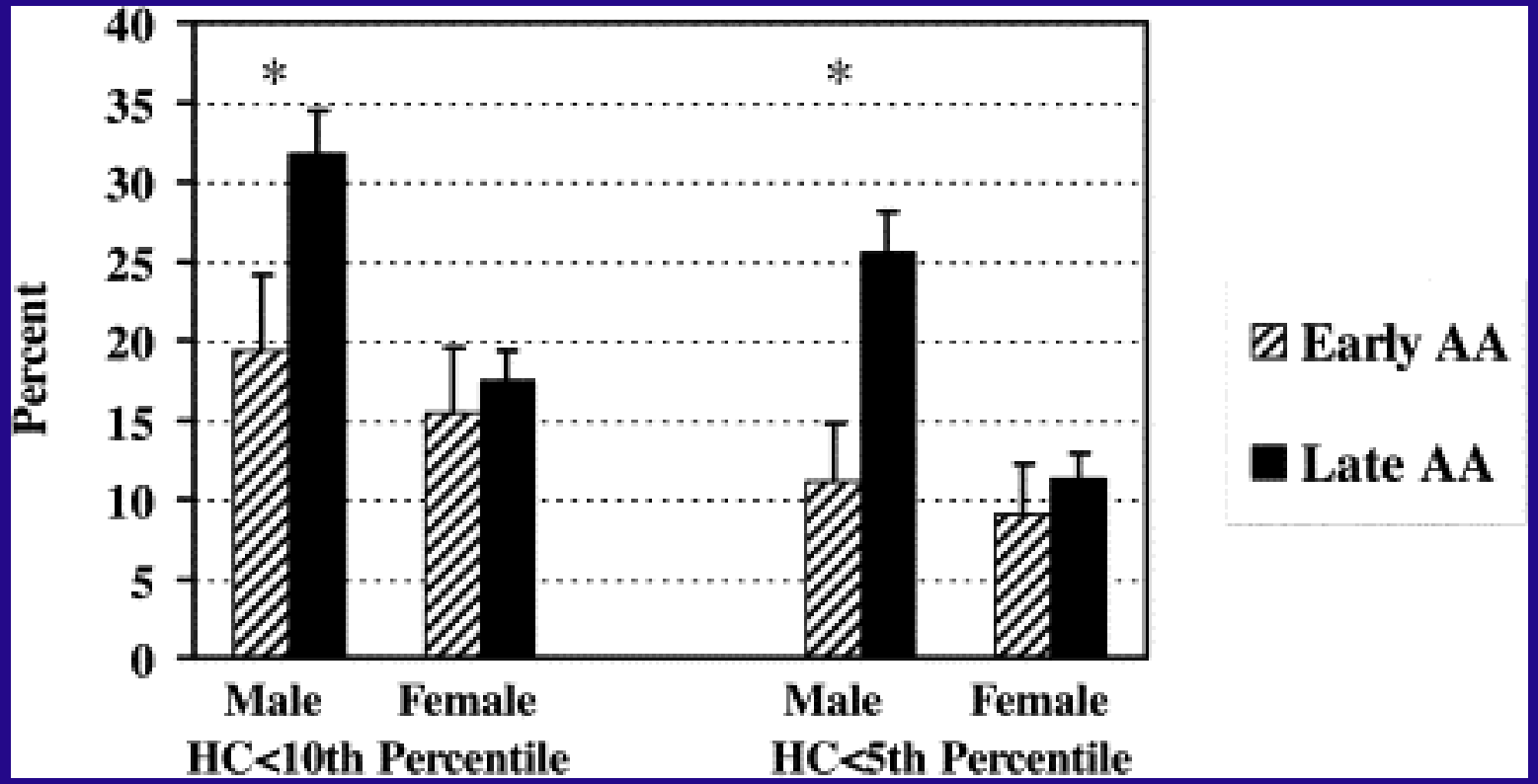
Day 7 : 2.9 g AA /kg*day and 81 kCal/kg*day

Stephens BE, 2009





Comparison of head circumference at 18 months' CA according to sex and study group; *$P < .05$.



No difference in neurodevelopment

JPed 2006NICHD

Human Milk Feeding For VLBW Infants

Decrease NEC

Improved neurodevelopmental outcomes

Improve gastric motility

Healthy microbiome

Increased immunologic function

Prevent BPD?

Decrease late-onset sepsis

Reduces risk of metabolic syndrome


THE THINKER
BY AUGUSTE RODIN
A GIFT TO THE PEOPLE
OF LOUISVILLE BY THE
HILLMAN – HOPKINS
FAMILY – MCMXLIX

Beneficial Effects of Breastmilk in the NICU on the Developmental Outcome of Extremely Low Birth Weight Infants at 18 Months of Age

n=1035 (<1000g BW)

Nutritional Data
- Parenteral
- Enteral

Prospective, F/U at 18 mos corrected age

Calculated total volume breast milk (ml/k/d) during hospitalization

Analysis of outcomes adjusted for maternal age, marital status, race, ethnicity and other after covarients

No donor milk

Vohr et al NICHD Peds July 2006

“Food for Thought”

The GAP

- 13.1 point difference in Bayley MDI Scores (74.2 – 87.3) between lowest and highest quintiles adjusted for environmental confounders at 18 months!!

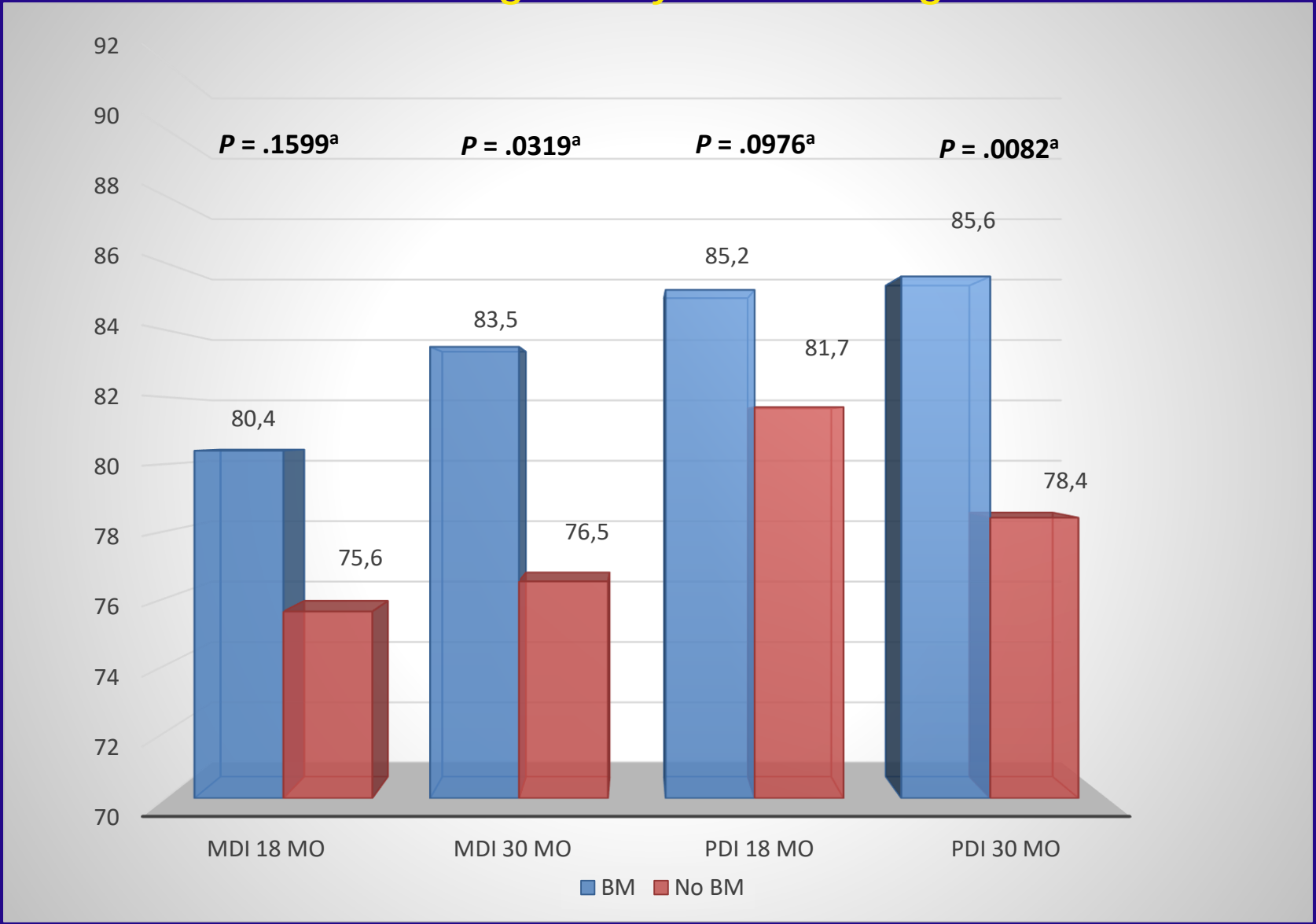
The IMPACT

- Every 10 ml/k/d of breast milk contributes 0.53 points to Bayley MDI. Therefore highest quintile at 110ml/k/d, 10 X 0.53 or 5.3 points

SOCIETAL IMPLICATIONS [1/3 of a SD in IQ]

- Annually 56k (1.4%) USA VLBW
- 50% (28k) require remedial or special education services at school age
- Hack (NEJM 2002) VLBW survivors with lower academic achievement as adults
- IQ was 87 vs 92 in term controls
- + 5 potentially would optimize outcomes and decrease costs by decreasing number of VLBW children requiring special education services

Mean MDI and PDI scores at 18 and 30 months according to any BM feeding.



[a] Adjusted *P* values.

Pediatrics Vol. 120 No. 4 October 1, 2007 pp. e953 -e959

Does Breastmilk Influence Development of BPD?

- N= 1433 VLBW < 32 weeks (GNN) d/c 2013
- Exclusive Human Milk (n= 223) vs exclusive FF (n = 239)

	HMF	FF	MIX
BPD	11%	21%	20%
NEC	0.9%	6%	2.7%

- Odds Ratio FF Increase risk of BPD (OR 2.6), NEC (0R 12.6), ROP (OR 1.8) after controlling for risk factors

- HUMAN MILK GAIN LESS WEIGHT from BIRTH to D/C SDS, Median - 1.1 vs 0.9

Spiegler J, et al J of Peds 2015

POLICY STATEMENT Organizational Principles to Guide and Define the Child Health Care System and/or Improve the Health of all Children

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

Donor Human Milk for the High-Risk Infant: Preparation, Safety, and Usage Options in the United States

COMMITTEE ON NUTRITION, SECTION ON BREASTFEEDING, COMMITTEE ON FETUS AND NEWBORN

abstract

FREE

The use of donor human milk is increasing for high-risk infants, primarily for infants born weighing <1500 g or those who have severe intestinal disorders. Pasteurized donor milk may be considered in situations in which the supply of maternal milk is insufficient. The use of pasteurized donor milk is safe when appropriate measures are used to screen donors and collect, store, and pasteurize the milk and then distribute it through established human milk banks. The use of nonpasteurized donor milk and other forms of direct, Internet-based, or informal human milk sharing does not involve this level of safety and is not recommended. It is important that health

Summary of Key Points (abbreviated)

- OMM preferred, DHM may be used for high-risk infants when OMM not available or mother cannot provide milk (>1500g)

- Donors should be id and screened using methods by HMBANA or other established commercial milk banks

- DM should be pasteurized according to accepted standards. Post pasteurization testing performed according to internal quality-control guidelines.

Retrospective Analysis of the Impact of Human Milk on Prevention of NEC and Postnatal Growth

- Retrospective chart review: EPOCH 1 2008-2009 Increase NEC with limited use of donor milk vs EPOCH 2 2010-2013--expanded use of donor milk
- Multiple bovine fortifiers used (Preterm Formula added to HM)
- N = 550 VLBW
- Examined NEC and Postnatal Growth related to amount of Own Mothers Milk and amount of Donor milk provided
- Growth rates (Wt g/k/d and HC cm/wk) from RTBW to D/C
- Z scores from birth

Chowning R, et al J of Perinatol 2016

Table 2. Outcomes at Extremes of Human Milk Intakes			
Parameter	No Human Milk	Human Milk for ≥ 90% of days	P value
N (%)	76 (13.8%)	71 (12.9%)	-
Birthweight (kg)	1.15 ± 0.29*	1.16 ± 0.24	0.71
GA at birth (weeks)	29.3 ± 2.8	29.1 ± 2.4	0.52
Weight gain (gm/kg/day)	16.2 ± 5.8	15.2 ± 2.4	0.17
Change in weight z-score	-0.84 ± 1.03	-1.38 ± 0.83	<0.001
Head circumference gain (cm/week)	0.79 ± 0.19	0.70 ± 0.15	0.002
Change in head circumference z-score	-0.25 ± 1.13	-0.74 ± 0.73	0.002
Mortality rate	7.9%	0%	0.016
NEC rate	10.5%	0%	0.005
Surgical NEC rate	7.9%	0%	0.016
Length of stay in days	65.9 ± 60.2	56.5 ± 22.0	0.20
Days of Human Milk	0	53.3 ± 20.3	<0.001

Table 3: Outcomes for Infants with Human Milk at < or ≥ 50% of LOS			
Parameter	Human Milk for < 50% of LOS	Human Milk for ≥ 50% of LOS	P value
N	260 (47.3%)	290 (52.7%)	-
Birthweight (kg)	1.03 ± 0.29*	1.08 + 0.28	0.03
PMA at birth (weeks)	28.1 ± 2.7	28.6 ± 2.5	0.02
Weight gain (gm/kg/day)	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/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

GROWTH

Table 2. Outcomes at Extremes of Human Milk Intakes			
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Length of stay in days	65.9 ± 60.2	56.5 ± 22.0	0.20
Days of Human Milk	0	53.3 ± 20.3	<0.001

Chowning R, et al. J Perinatalogy 2016

Use of Human Milk in Preterm Summary

- Nutrition is critically important for the optimal growth and development of premature babies

- Ideal food for premature infants is
  1. Mother's breast milk that should be fortified for VLBW
  2. Donated breast milk that should be fortified
  3. Premature specialty formula

- Successful use of breast milk requires institutional promotion, lactation support, and maximizing availability

- Standardized feeding approach based on providing mainly human milk.
  In Louisville, there has been a reduction in NEC

- Optimizing growth velocity is challenging but improves with standardized approach