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Aggressive Nutrition in Preterm Infants

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Declaration of potential conflicts of interest

Regarding this presentation the following relationships could be perceived as potential conflicts of interest:

- **There are no conflicts of interest to report**

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Declaración de potenciales conflictos de interesesa

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Optimal Nutrition

- Remains to be defined
- No negative impact on growth and development
- Achieve the maximal appropriate weight gain without adverse effect

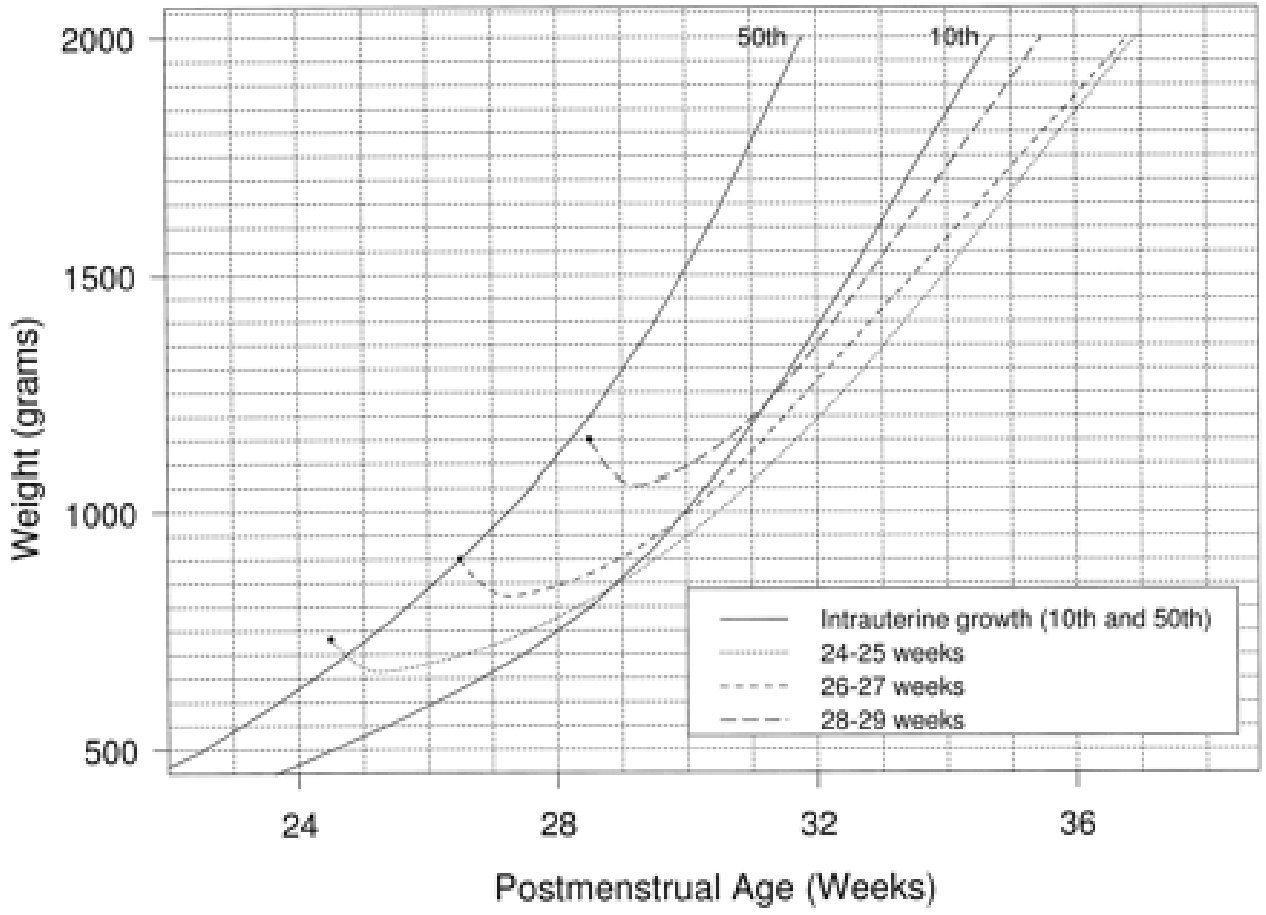
Nutrition and the Premature Infant

- Interrupted flow of placenta-provided nutrients
- Partial replacement
  - Dextrose only
  - Delay in total parenteral nutrition
  - Inability to provide adequate amounts of the same
- Impaired growth

Time to Return To Birthweight

- Critical factor
- As time to regain birthweight increases, overall rate of weight gain decreases and extrauterine growth restriction occurs
- Aggressiveness and success of early nutrition can decrease the time
  - Early parenteral nutrition
  - Early enteral nutrition

Extremely Low Birth Weight Infants Grow Poorly



Average body weight compared to intrauterine growth

Ehrenkranz, Pediatrics, 1999

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Available Stores, Ziegler et al., 1976

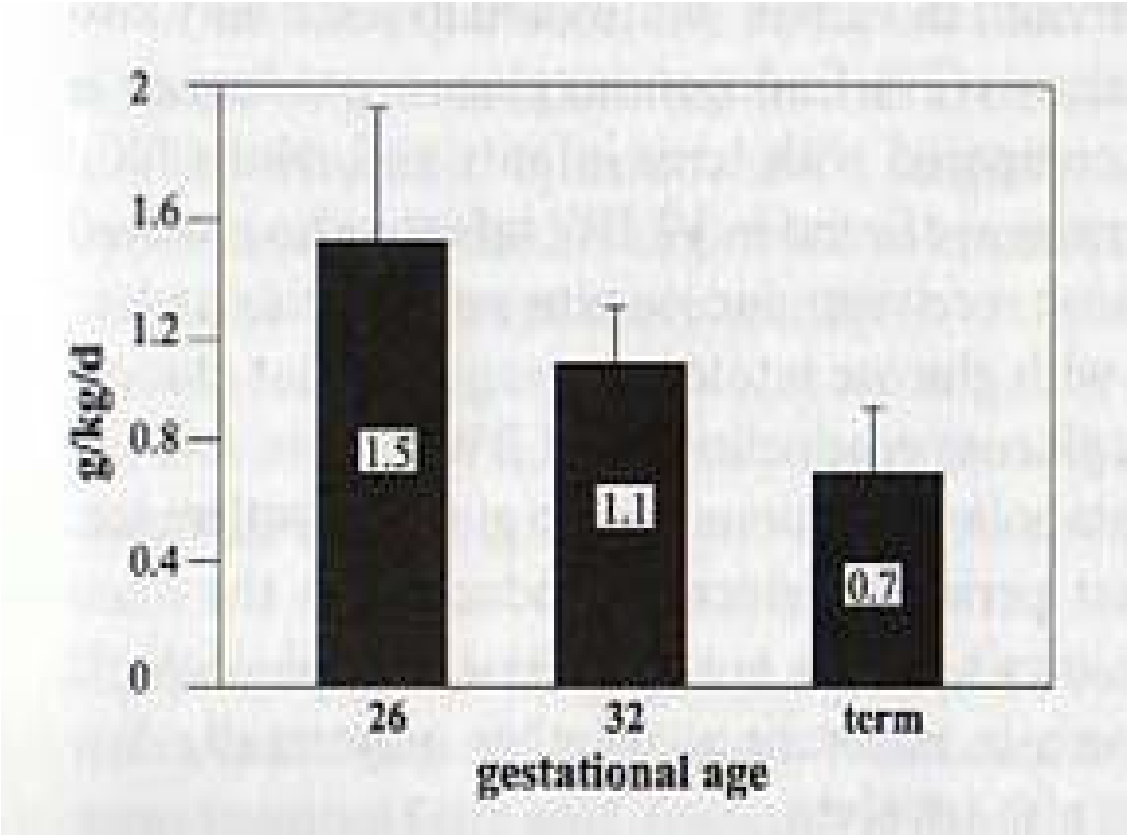
Weeks	Weight,g	Protein%	Lipid%	Energy, kcal
24	690	8.8	0.1	19.5
26	880	9.2	1.5	123.6
28	1160	9.6	3.3	326.2
40	3450	12	11.2	3152.4
2 mo	5450	11.4	22.4	9866

Weight loss

- Proportion of initial weight loss through extracellular fluid vs endogenous stores not known
- Endogenous protein losses ~1g/kg/d
- Intracellular water ~4g/kg/d
- Assuming low energy intake, glycogen and lipid losses ~2-5g/kg/d

Protein Losses During Glucose Infusion

Semin Neonatal 6:377, 2001



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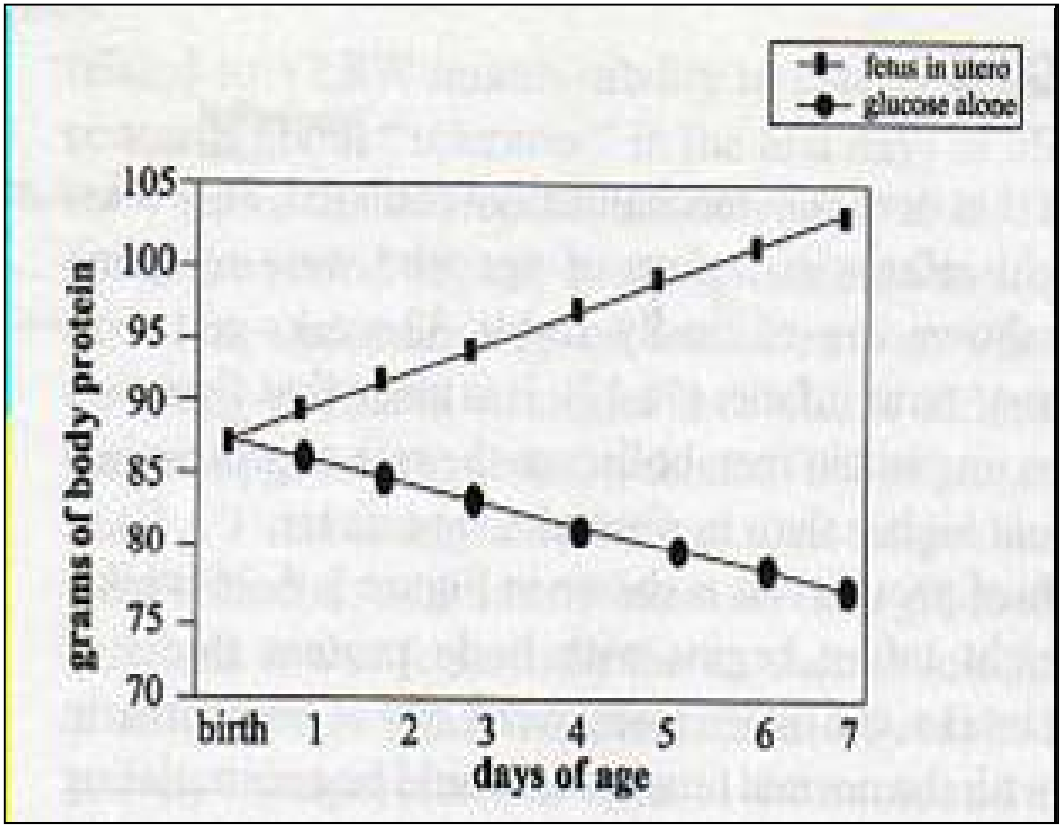
Changes in Protein Stores [Denne 2001]



Early Postnatal Nutrition

- Predominantly parenteral
  - Disease states precluding enteral nutrition
  - Even if enteral nutrition is started, inability to reach full volumes quickly in ELBW infants
  - However, usual IV feeds are glucose
  - Reasons for delaying amino acids and lipids not clear

Initial More Aggressive approach

Thureen et al., 2003

- N=28, ELBW infants
- Randomized to 3.0 or 1.0g AA/kg/day at ~24h of life
- More positive nitrogen balance without differences in most amino acids, metabolic acidosis or BUN
- Impact: realization that BUN increased regardless of intake!!

Aggressive Parenteral Nutrition

Ibrahim et al., J Perinatol 24:482-86,2004

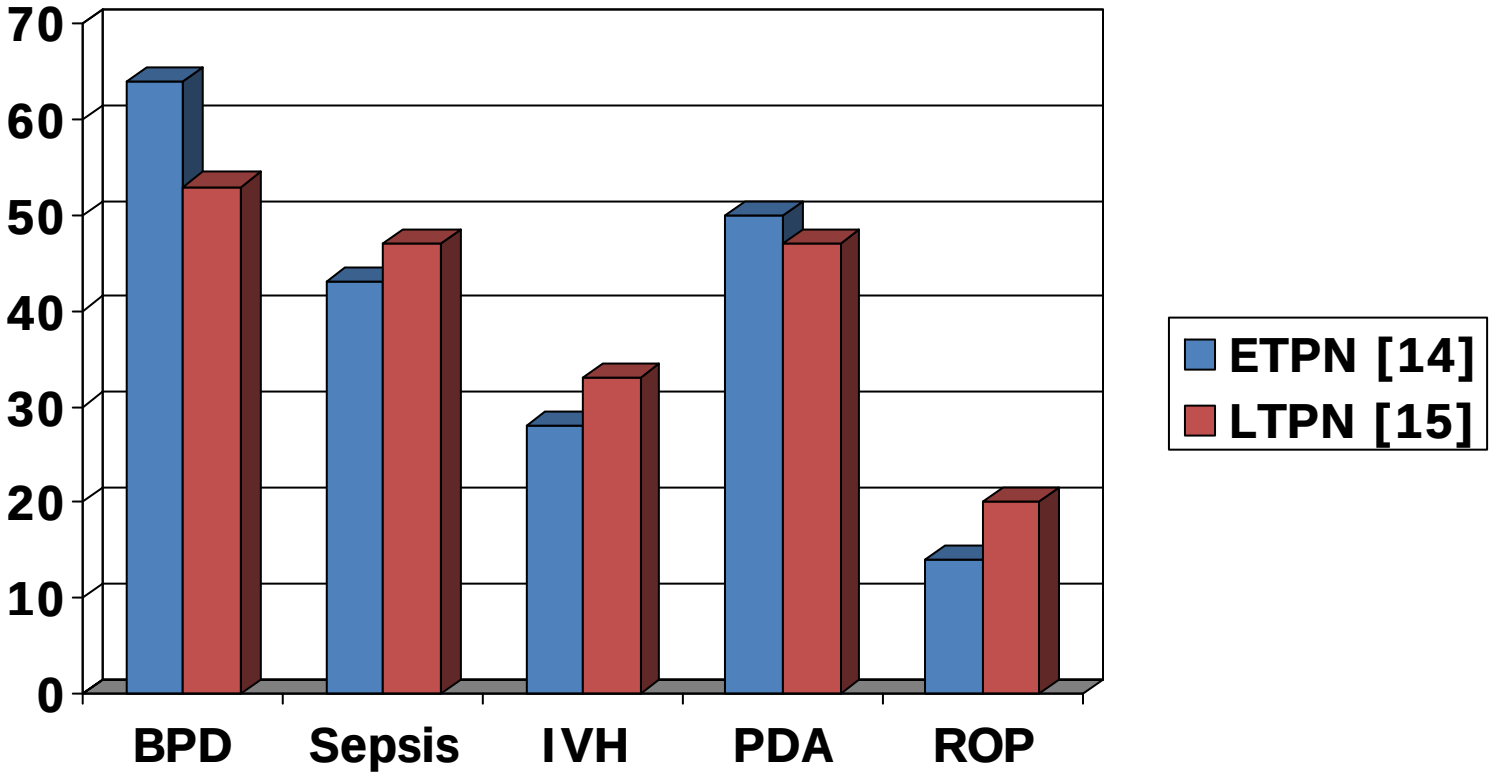
- 500-1250g
- 3.5g AA/kg/d, 3g lipids/kg/d within 2h of life [n=16]
- 2g AA/kg/d, 0.5g lipids/kg/d @dol2 and then advanced in 0.5g increments to same levels as above [n=16]

Aggressive Parenteral Nutrition

[J Perinatol 2004, 482-6]

	ETPN	LTPN	P
Bilirubin [mg/dL]	7.7 [0.4]	6.2 [0.4]	0.02
TG [mg/dL]	70.0 [9.8]	84.9[10.1]	NS
Bicarb [mEq/dL]	23.1[0.5]	23.9[0.7]	NS
Glucose [mg/dL]	83.2[5.2]	101.1[5.4]	0.03

Secondary Outcomes [%]



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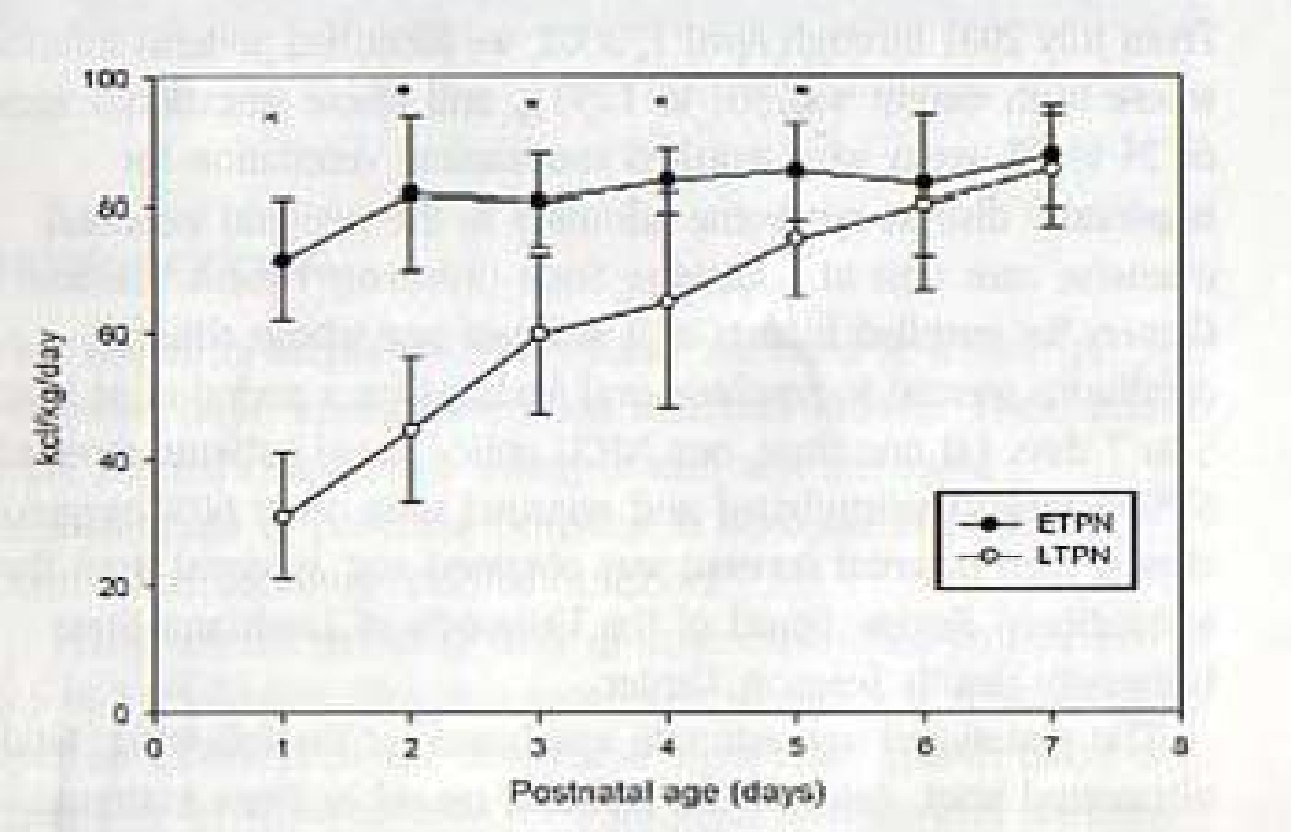
Energy Intake

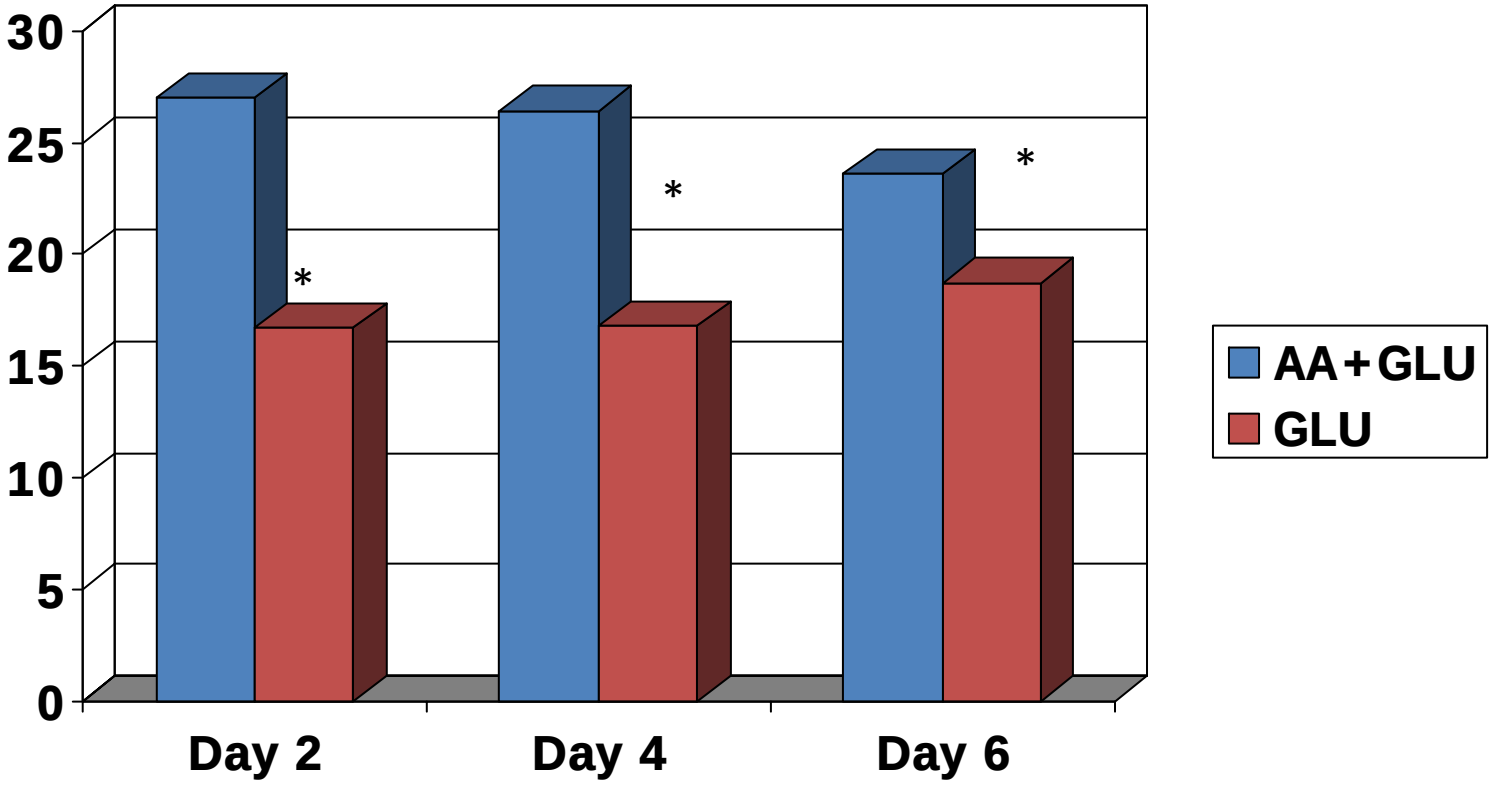


Early TPN

te Braake et al., J Pediatr, 147, 2005

- Randomized clinical trial
- <1500g
- Glucose and 2.4g AA/kg/d from birth [n=66] OR glucose with 1.2g AA/kg/d on day 2 and 2.4g/kg/d from day 3[n=69]
- Both groups received 1.4g lipids/kg/d on d2 and 2.8g/kg/d from d3
- Minimal enteral feeds by d2-3

Early TPN: BUN [mg/dL]



Minimal Parenteral Nutrition and Catabolism

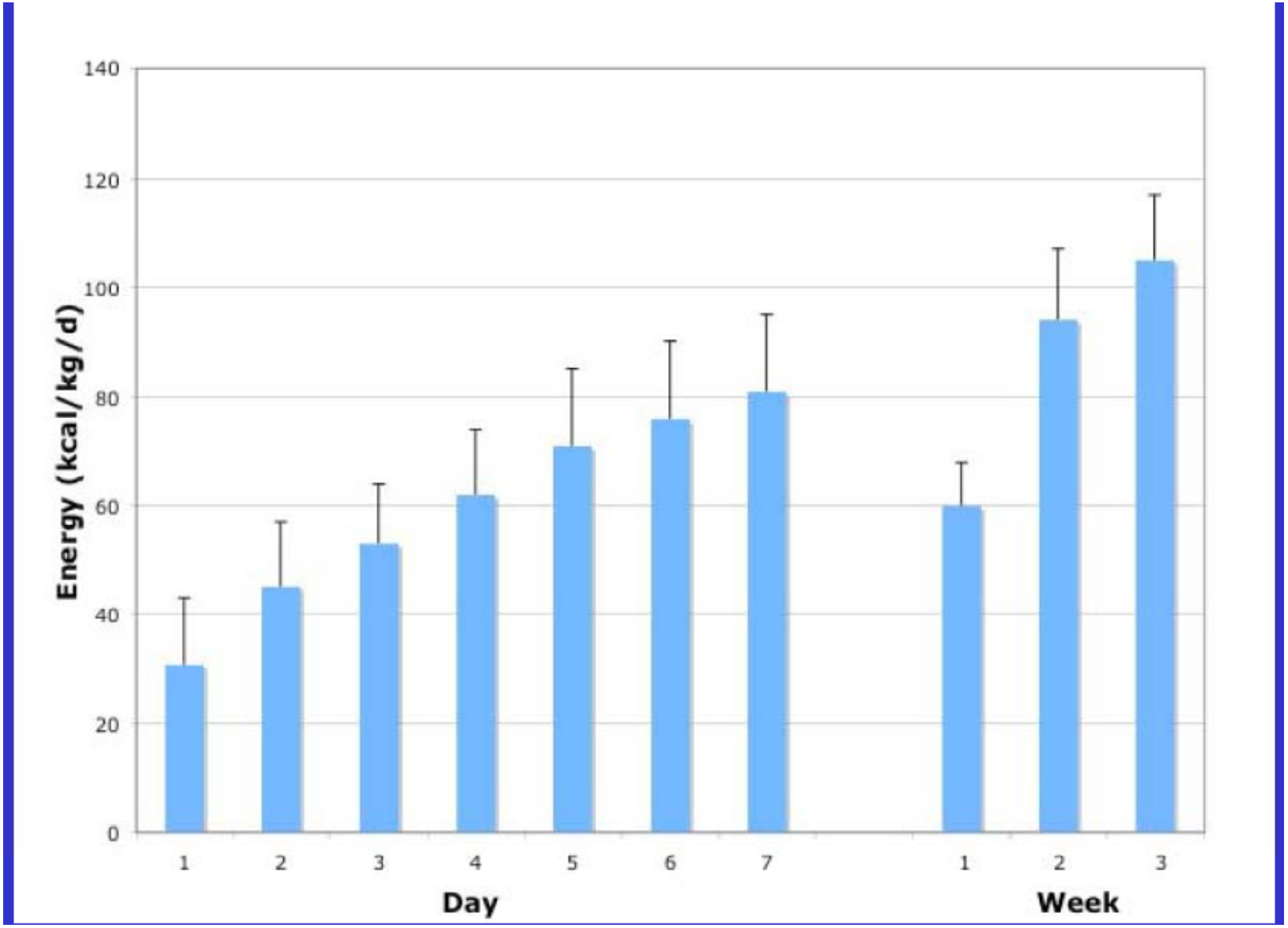
Protein, g/kg/d	N balance mg/kg/d	Decrease in early weight loss
1	0	5g/kg/d
2	160	10g/kg/d
3	320	15g/kg/d

Early AA Intake and Nitrogen Balance

	AA g/kg/d	Study day	N balance mg/kg/d
Thureen et al	0.9/2.7	2	-42/+186
Ibrahim et al	0/3.5	1	-203/+384
Te Braake et al	0.4/2.4	2	-84/+145

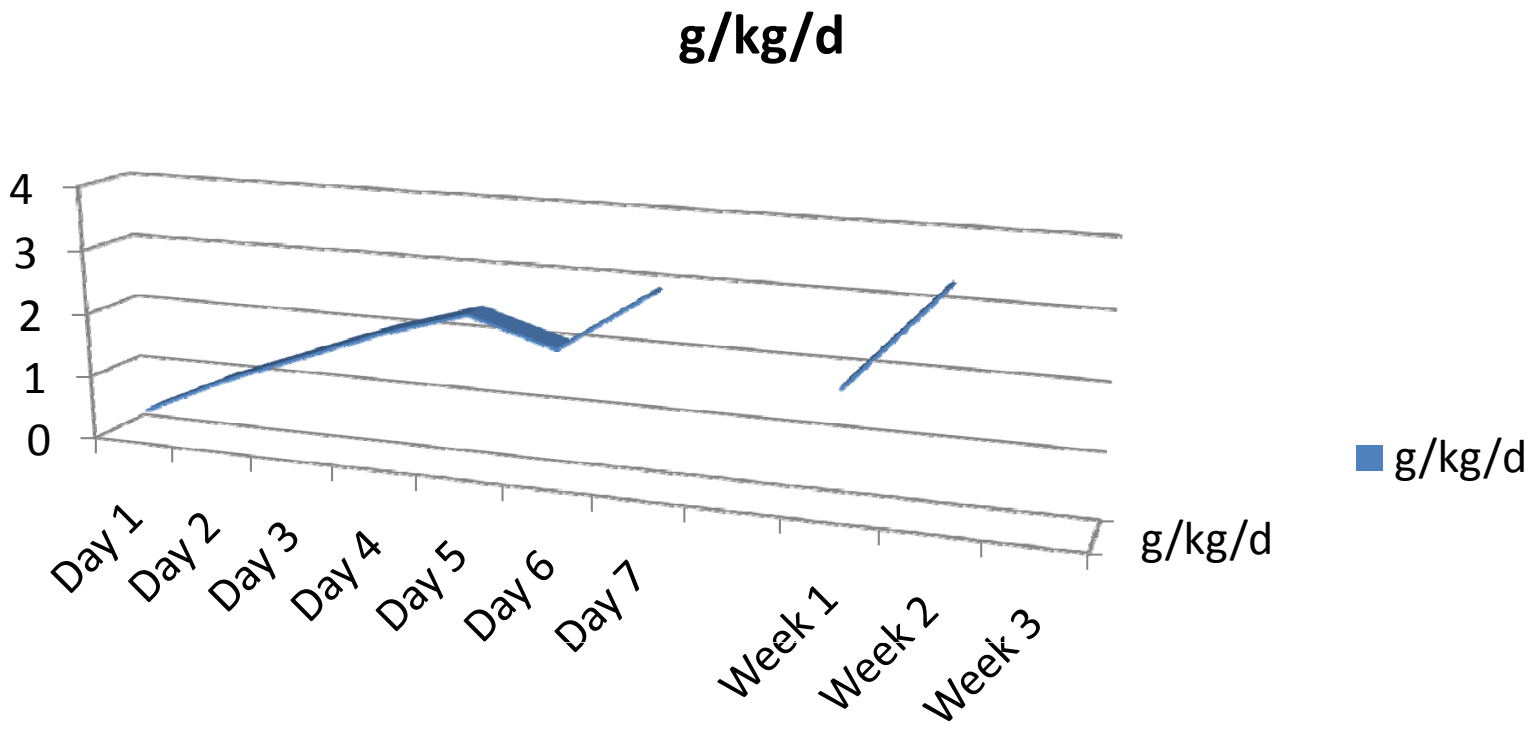
Early Nutrition and Cognitive Outcome, Stephens et al., Pediatrics 2009

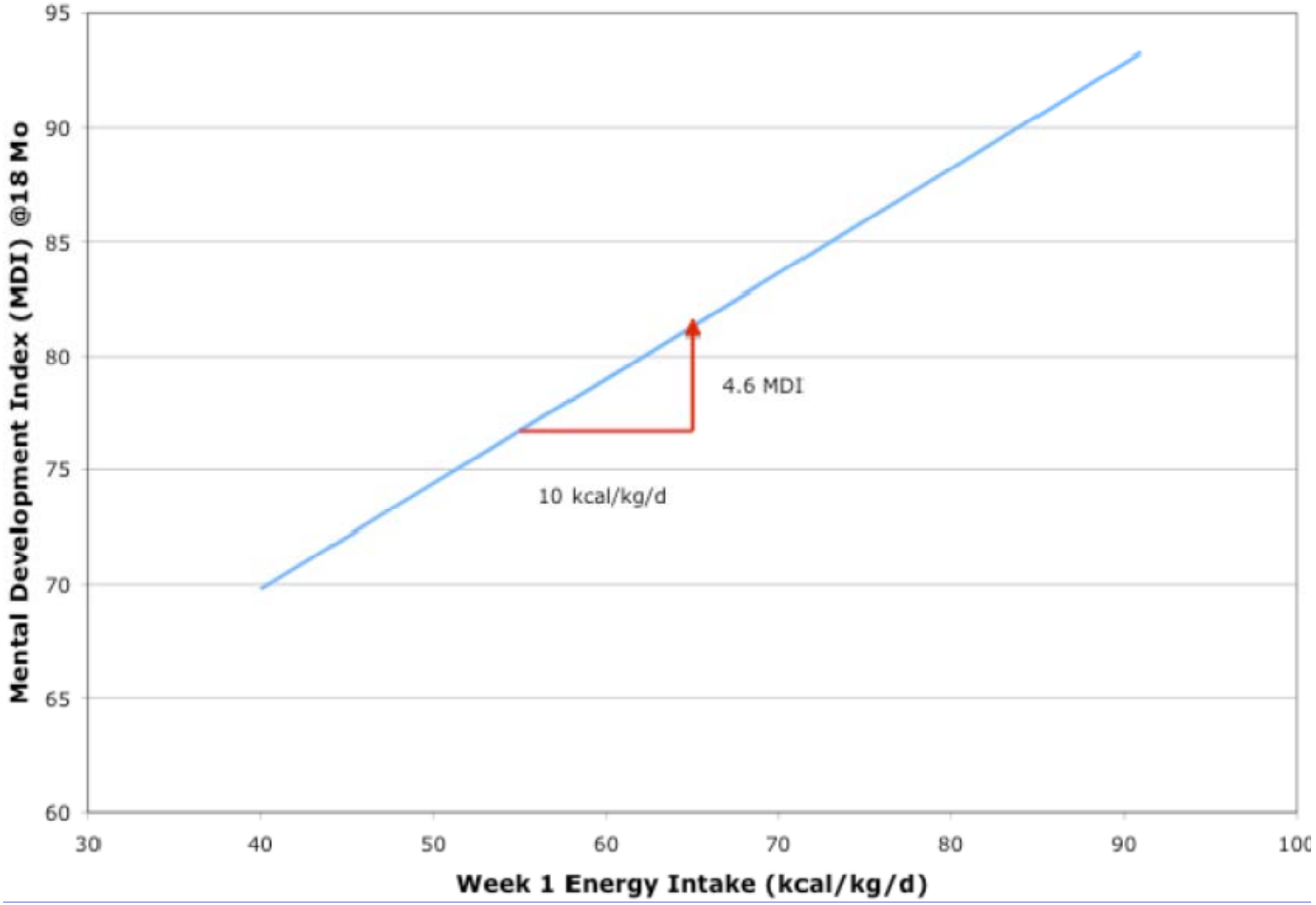
- 124 ELBW infants
- Protein and energy intakes in first 7 days of life
- Mental Developmental Index at 18 months



Data of B E Stephen et al., Pediatrics 2009; 123:1357 124 ELBW infants born in 2000 and 2001

Protein Intake, g/kg/d





Data of B E Stephen et al., Pediatrics 2009; 123:1357 124 ELBW infants born in 2000 and 2001

Early Nutrition and Cognitive Outcome

Stephens et al., Pediatrics 2009

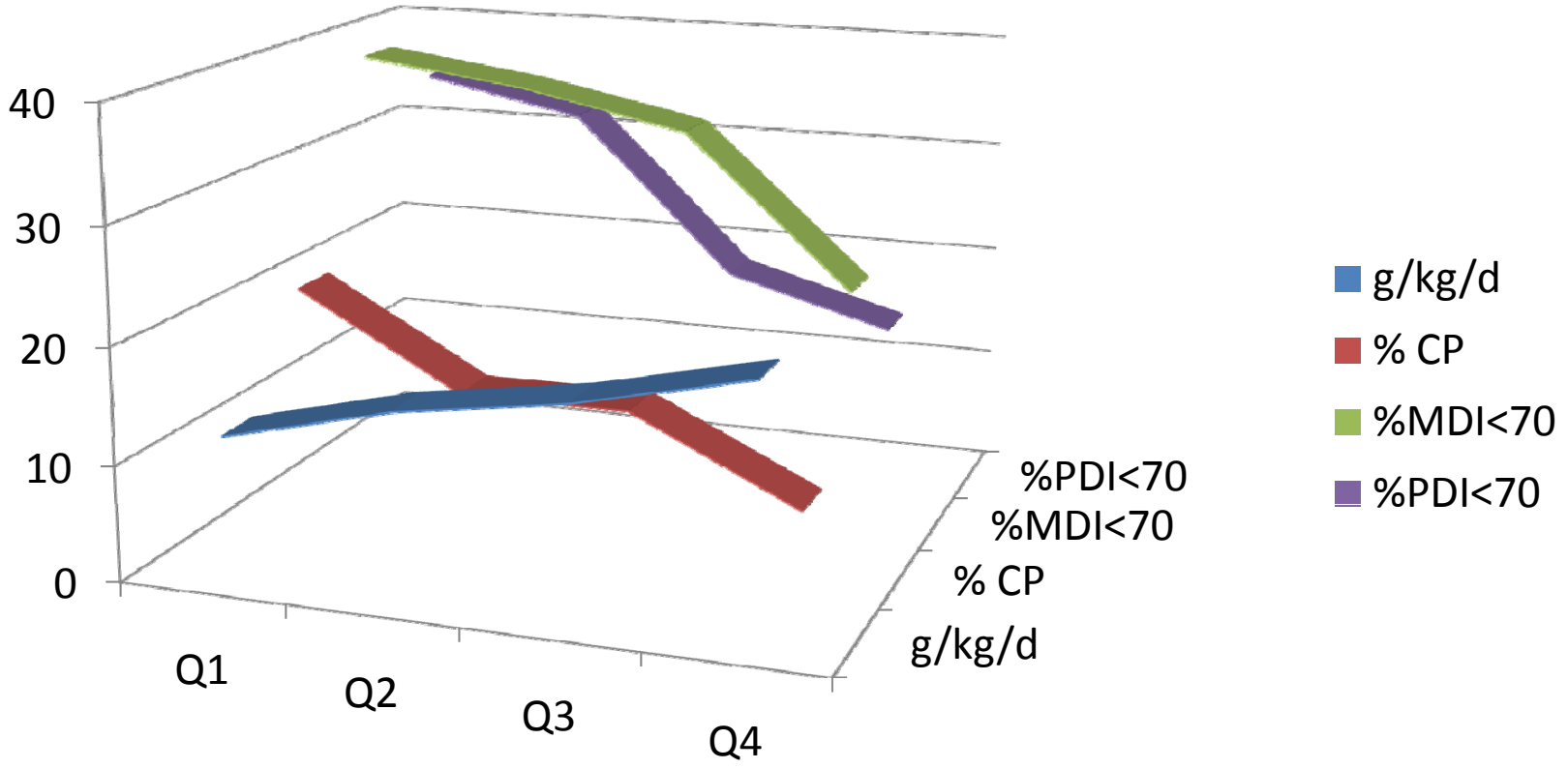
- For every **10 kcal/kg increase** in energy intake in the first week of life, *4.6 point increase in MDI at 18 months*
- For each **1g/kg increase** in protein intake in the first week of life, *8.2 point increase in MDI at 18 months*

Extrauterine Growth Restriction and Outcome

Ehrenkranz et al., Pediatrics 2006

- NICHD Neonatal network
- 1994-1995, 600 infants, 500-1000g
- Weight gain from regained birthweight to discharge
- 4 quartiles reported
- Follow up at 18-22 months [n=495]

Growth Quartiles and Outcomes



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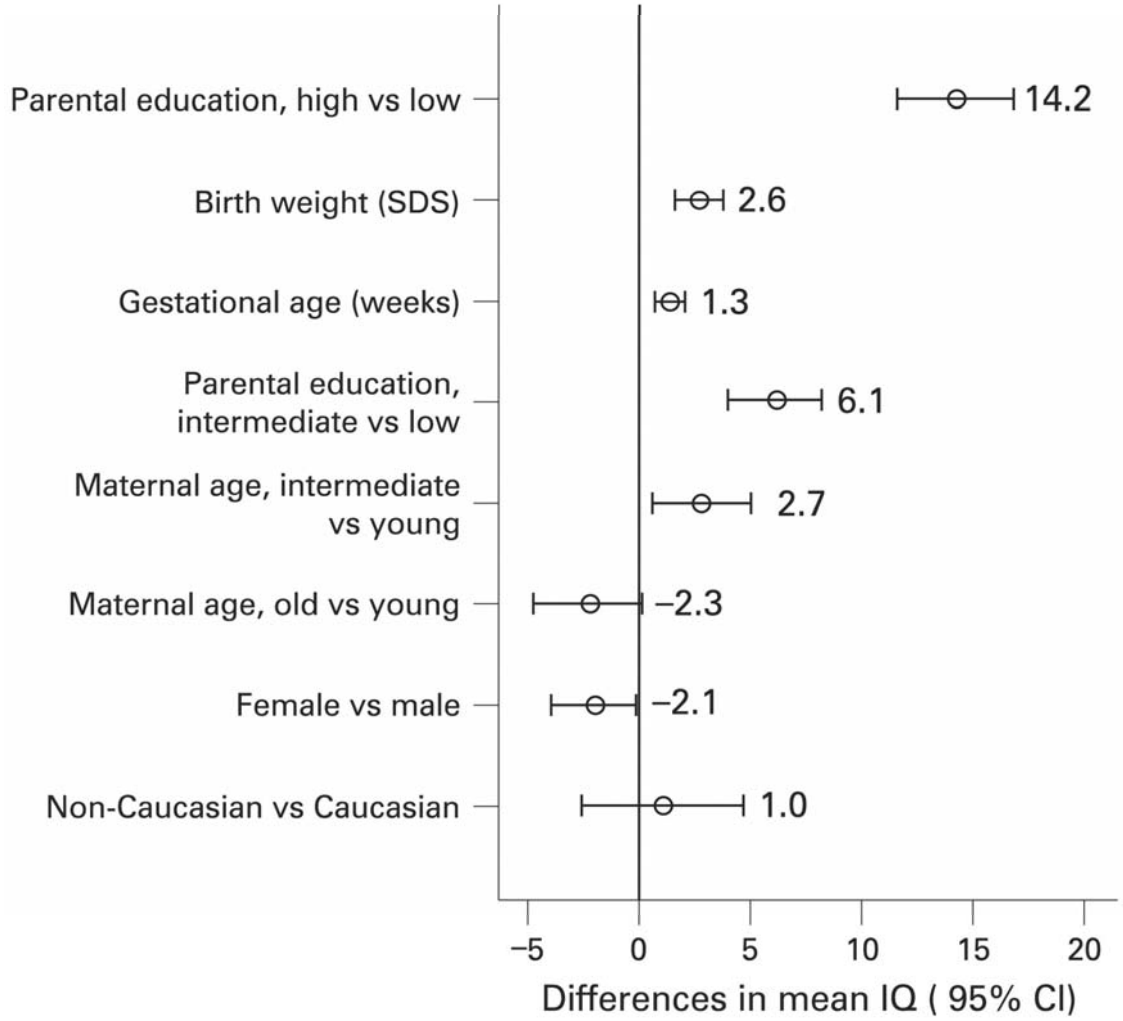
Differences in mean IQ for gestational age and birth weight SDS and environmental and personal factors in multiple regression analyses.



Weisglas-Kuperus N et al. Arch Dis Child Fetal Neonatal Ed 2009;94:F196-F200

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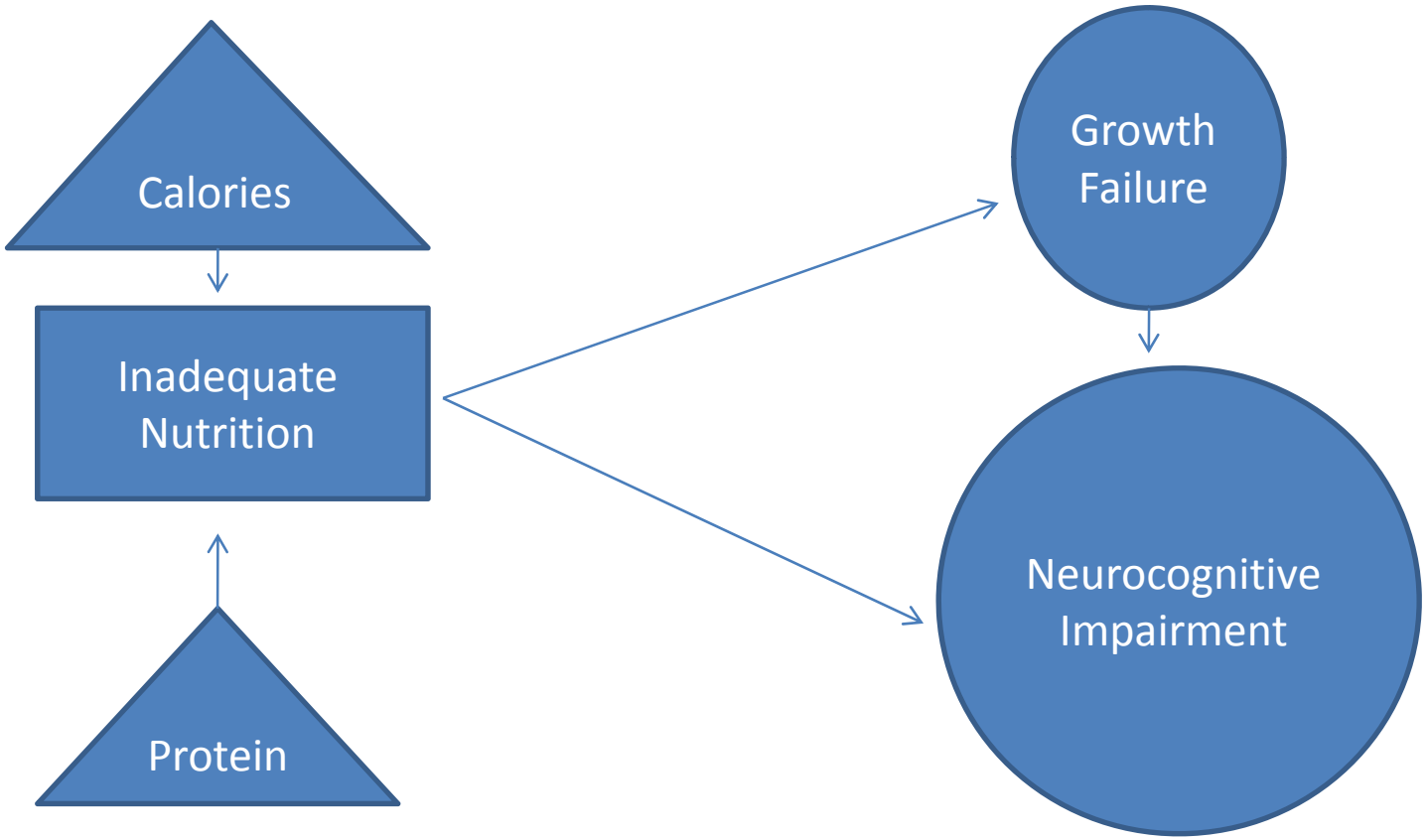
Outcomes of early amino acid administration

- Suboptimal nutrient intake: impaired growth, under- or mal-nutrition, increases vulnerability to infections and more lung injury, impaired tissue repair

- High vs low amino acid intake
  - At 36 weeks, weight, L and HC greater in high group
  - At 18 months, HC<10%ile more likely in males on low AA intake
  - For every extra gram of AA or extra 10 kcal/kg/d increased MDI by 8.2 and 4.6 points!

Inadequate Nutrition



Strategies to Improve Outcome

- Early aggressive parenteral nutrition
  - 2.5-3g/kg AA per day
  - 0-0.5g/kg lipids per day
  - Dextrose based on clinical needs
  - Begin as soon as vascular access is achieved
  - Calcium gluconate in infants <1800g

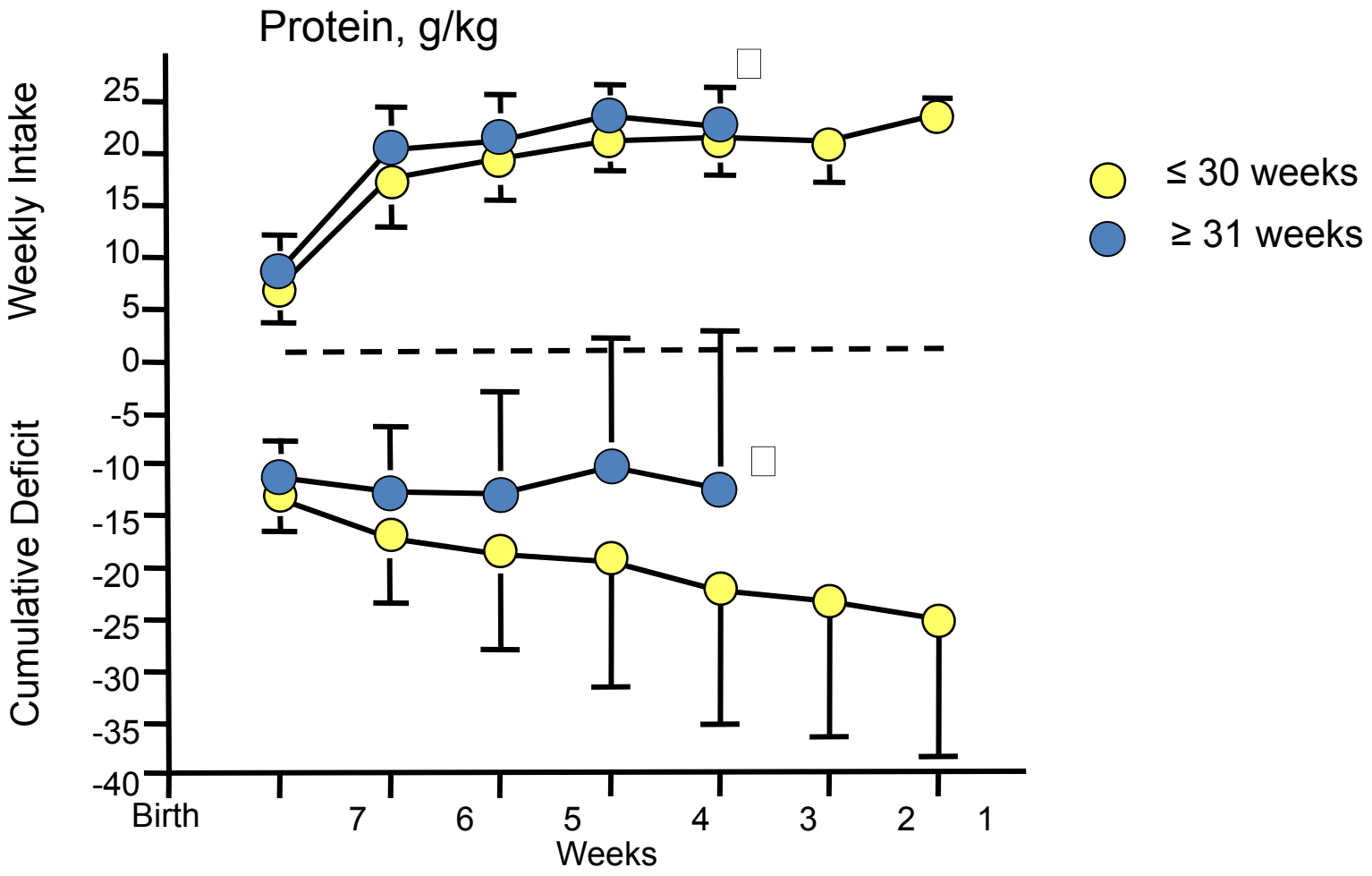
Strategies to Improve Outcome

- Early enteral nutrition
  - *If the gut works use it!*
  - Trophic feeds
  - 20 mL/kg/d of human milk or premature infant formula
  - 30 mL/kg/d in larger infants
  - Advance per clinical tolerance
  - Fortify human milk at 2/3 intake

Protein and Energy Requirements

- <1000g: 3.6g protein
  - 1000-1599g: 2.7
  - High rates of energy expenditure, 85 kcal/kg/d *Pediatr Res 47:284, 2000*
  - Therefore, ~130 kcal/kg/d or higher may be needed
- Protein Content
  - Human milk ~ 2.2 g/100 kcal [decreases as lactation progresses]
  - Energy content of donor milk 10-30 kcal/30 mL
  - Premature Infant Formulas: >3g/100 kcal
  - Therefore, protein and energy deficit

Weekly Protein Intake and Cumulative Deficit



*P<0.01 for overall intakes and deficits vs infants ≤30 weeks.

Embleton NE, et al. Pediatrics 2001;107:270-3.

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Human Milk

- Mother's own milk preferred
- Donor's milk has multiple components that are altered and effects not known
  - Lactoferrin
  - IgA
  - Other
  - Both need fortification
  - Close monitoring of growth

Trophic effects of human milk

- Stimulates cell proliferation
- Decreases permeability
- Enhances maturation of motility
- Early feeds
  - Reduced rate of sepsis
  - No increase in necrotizing enterocolitis
  - Fidel-Rimon et al., 2004; Ronnestad et al., 2005; Hartel et al., 2009; Terrin et al., 2009

Summary

- Very premature infants exhaust their energy stores without exogenous energy
- Early amino acid [protein] intake provides metabolic, growth and neurocognitive benefits
- Early enteral feeds have multiple beneficial effects
- Maximal gain without adverse effects!