Protein: Requirements and Measuring its Impact in the NICU

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Disclosure Statement

- Employee
  - Spouse: Johnson & Johnson
- Consultant
  - Mead Johnson Nutrition- clinical area: Growth and growth assessment of preterm infants
- Speakers Bureau
  - Mead Johnson Nutrition- clinical area: Dietary protein and impact on growth
- I have no conflicts of interest to resolve.
- I will not discuss any unapproved or off-label, experimental or investigational use of a product, drug or device.

Protein: Requirements and Measuring Its Impact in the NICU

Learning Objectives

1. Review evidence for protein requirements of preterm infants
2. Discuss nutrition, growth and health outcomes research in preterm infants
3. Examine growth assessment tools and outcomes used to measure impact in the NICU

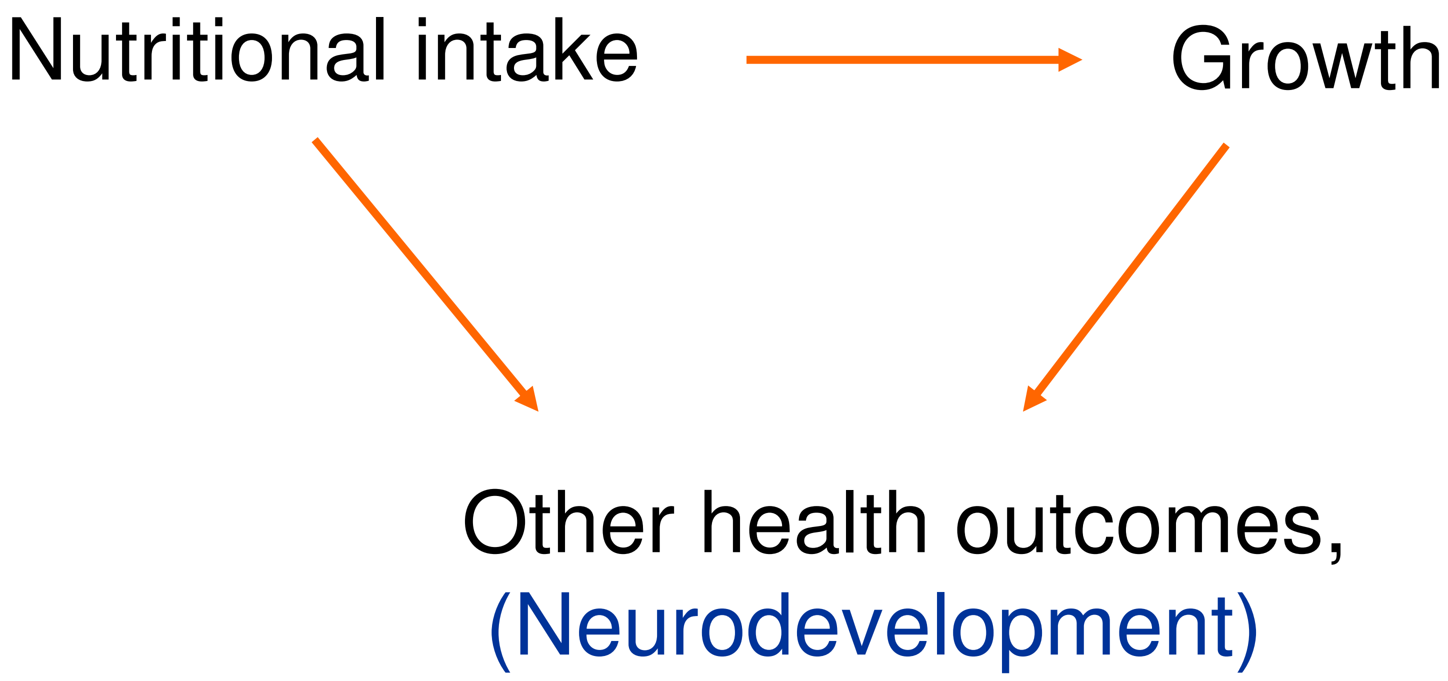
Protein: Requirements and Measuring Its Impact in the NICU

Why is this important?

Impact on health outcomes

Nutritional intake → Growth

Impact on health outcomes



What causes postnatal growth restriction?

"Although it is possible that nonnutritional causes occasionally play a role, for all intents and purposes, growth failure is caused by inadequate nutrition. More specifically, it is most commonly inadequate intake of protein that is responsible, with deficiencies of other nutrients possible but not well documented."

Ziegler EE, Carlson SJ. *Nutrition Today* 2016;51;228

Nutritional intake and growth

- Inadequate nutritional intake leads to poor growth = well documented; e.g.,

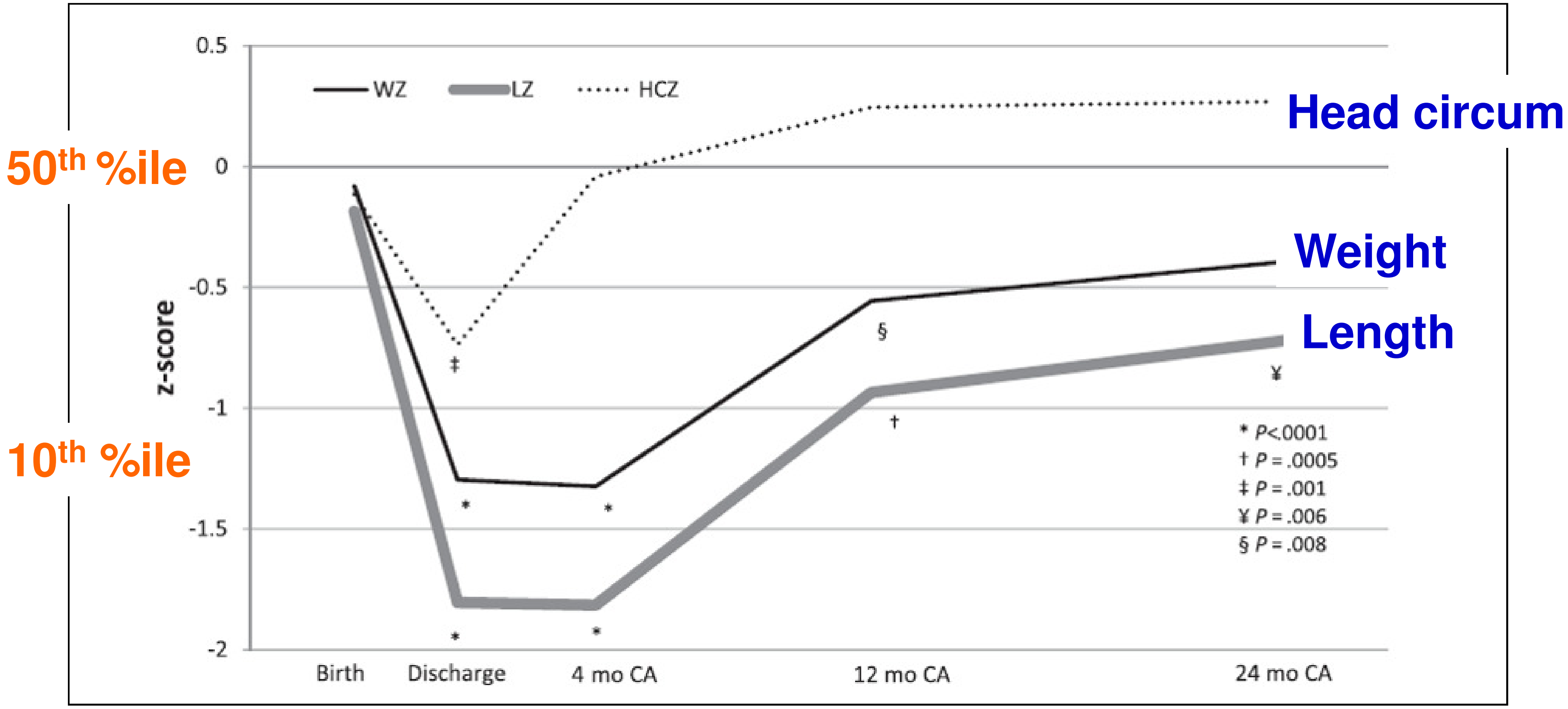
Carlson *JPerinatol* 1998
Embleton *Pediatrics* 2001
Olsen *Pediatrics* 2002
Clark *JPerinatol* 2003
Ziegler *Nutrition Today* 2016
Poindexter *JPediatr* 2006
Ziegler *Ann Nutr Metab* 2011
Senterre *Acta Paediatr* 2012
Iacobelli *BMC Pediatrics* 2015

~ **Bolded articles- Weight only** ~

- "Growth" usually defined as <u>weight growth</u>; head circumference and especially length measurements often not included as growth outcomes

Growth of VLBW preterm infants

Based on retrospective review of n=62 AGA VLBW preterm infants ≤30wks born between 2003 – 2007 with follow up data



Poor postnatal growth: L > WT > HC

Fig. 1. Growth of VLBW preterm infants from birth to 24 months CA. p values refer to statistical significance of the difference between the mean growth Z-score at each time point compared to the mean Z-score at birth.

Adapted from: Ramel SE et al. Neonatology 2012;102:19

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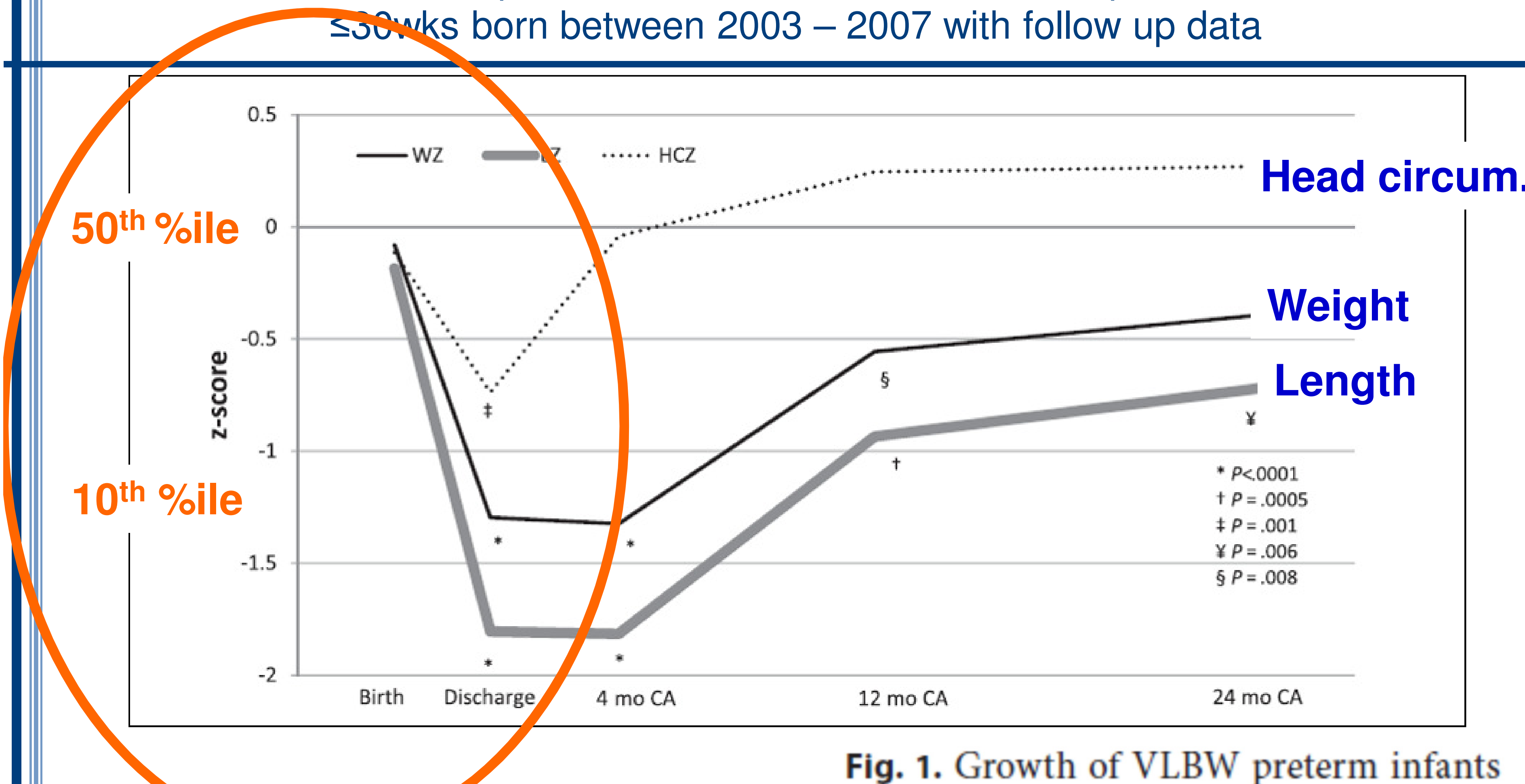

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Nutritional intake and growth

- "Aggressive nutrition" practices, including earlier and higher protein, improves growth (randomized clinical trials)
  - Arslanoglu S et al. *J Perinatol* 2006;26:614
  - Costa-Orvay JA et al. *Nutrition Journal* 2011;10:140
  - Moya F et al. *Pediatrics* 2012;130:e928
  - Morgan C et al. Pediatrics 2014;133:e120 **(Head only)**
  - Lapointe M et al. Acta Paediatrica 2016;105:e54 (historical cohort)
- Implementation of "optimized" or "best" nutrition practices improves growth
  - **Bloom BT et al. *Pediatrics* 2003:112:8 (WT only)**
  - Senterre T, Rigo J. *J Pediatr Gastroenterol Nutr* 2011;53:536
  - Hanson C et al. *Nutr Clin Pract* 2011;26:614
  - Roggero P et al. *PLOS ONE* 2012;7:e51166

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Nutritional intake and growth

- **Protein** not kilocalories is the rate-limiting nutrient to **growth** in preterm infants

Kashyap *AJCN* 1990

Carlson *JPerinatol* 1998

Olsen *Pediatrics* 2001

Arslanoglu *JPerinatol* 2006

Senterre *Acta Paediatarica* 2012

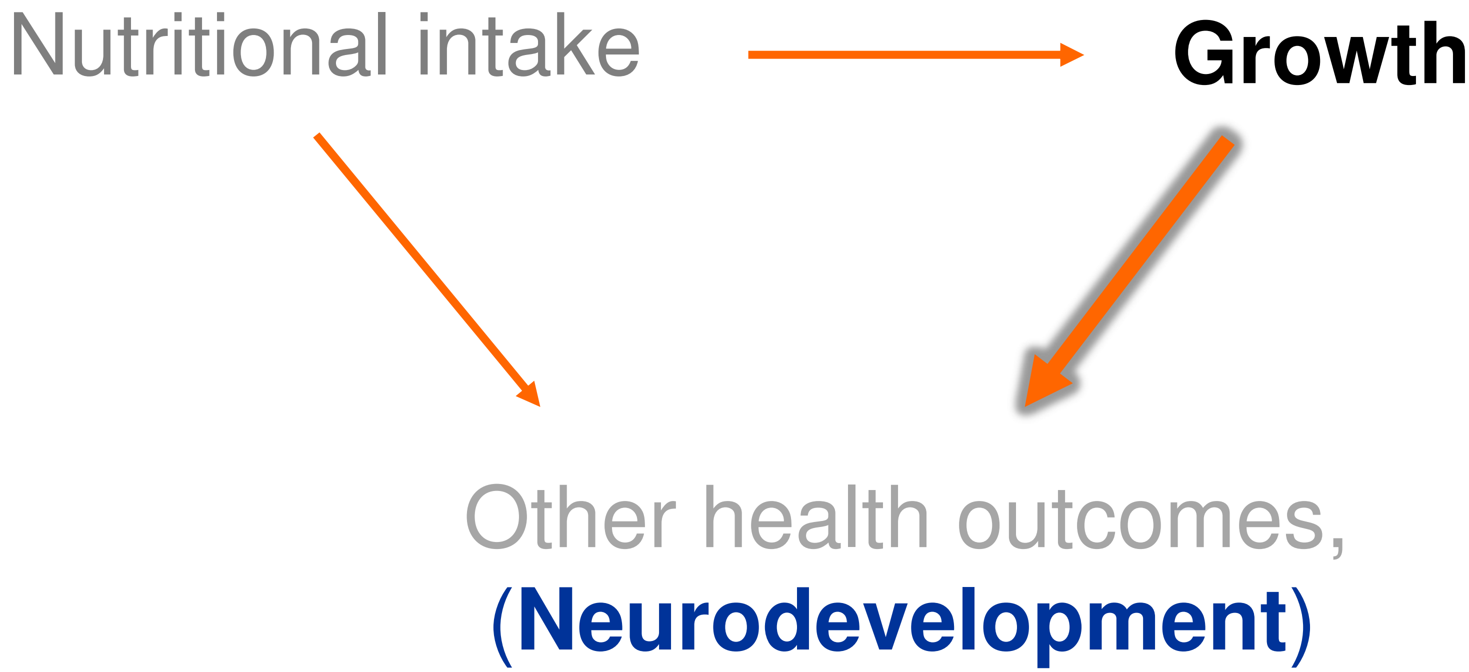
Iacobelli BMC *Pediatrics* 2015

van Goudoever et al Amino Acids and Proteins. In: Koletzko B, Poindexter B, Uauy R, eds. *Nutritional Care of Preterm Infants*. Basel, Karger;2014;49-63.

~ **Bolded articles reported weight growth only** ~

- Our understanding of optimal nutrition, optimal growth (in all growth measures) and the impact on other outcomes in preterm infants continues to evolve…

Growth and neurodevelopment

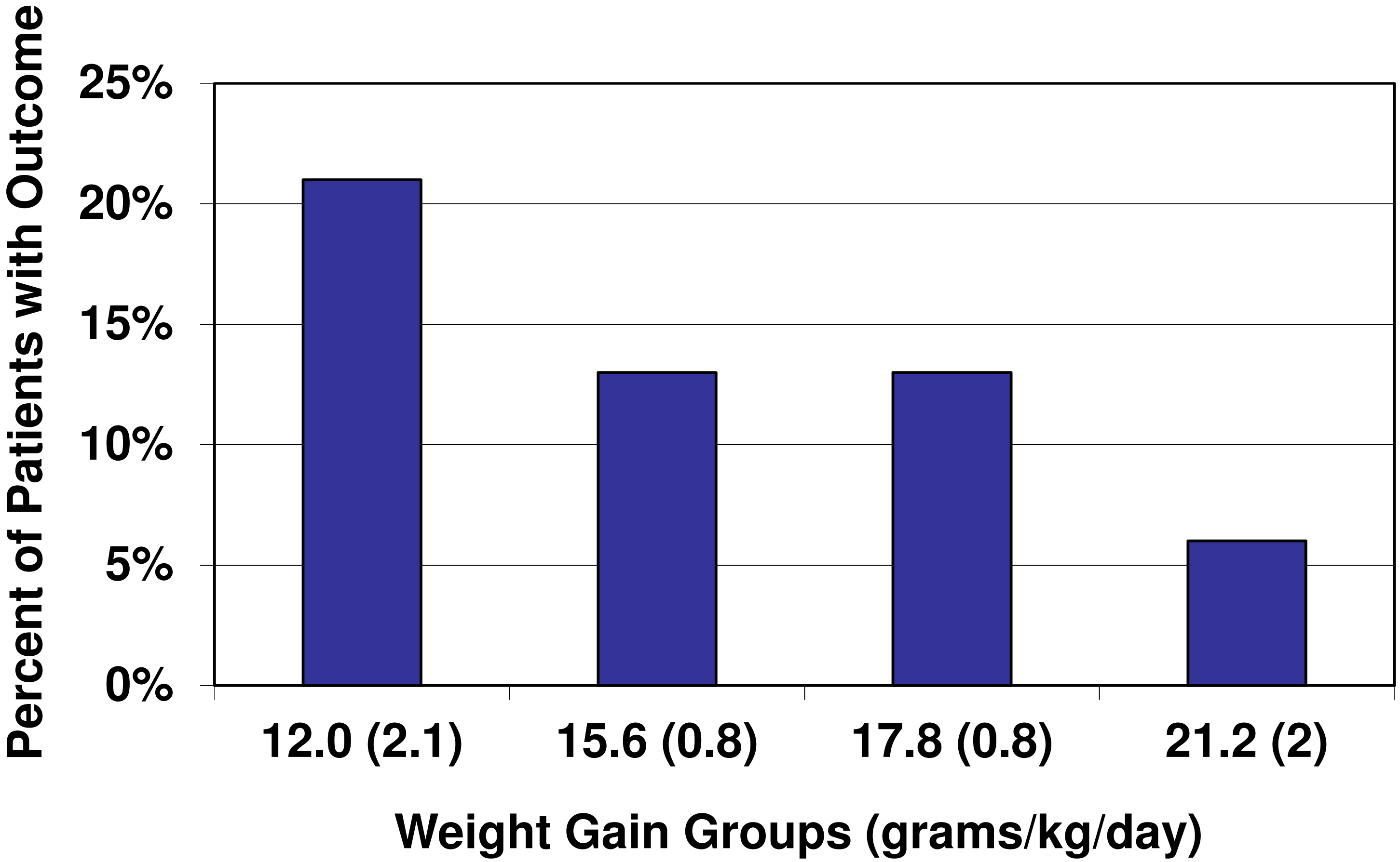


Growth and neurodevelopment

Postnatal growth restriction has negative impact on health outcomes

- **Evidence of impact of weight and head growth on neurodevelopment**
  - Ehrenkranz RA et al. *Pediatrics* 2006;117:1253
  - Poindexter B et al. *PAS Abstract # [1395.2]* 2013
  - Franz AR et al. *Pediatrics* 2009;123:e101
  - Ong KK et al. (review) *Acta Paediatrica* 2015;104:974
  - Belfort MB et al. *Pediatrics* 2011;128:e899

Cerebral palsy by in-hospital weight gain quartile



Modified from: Ehrenkranz RA et al. Pediatrics 2006:117:1253-61

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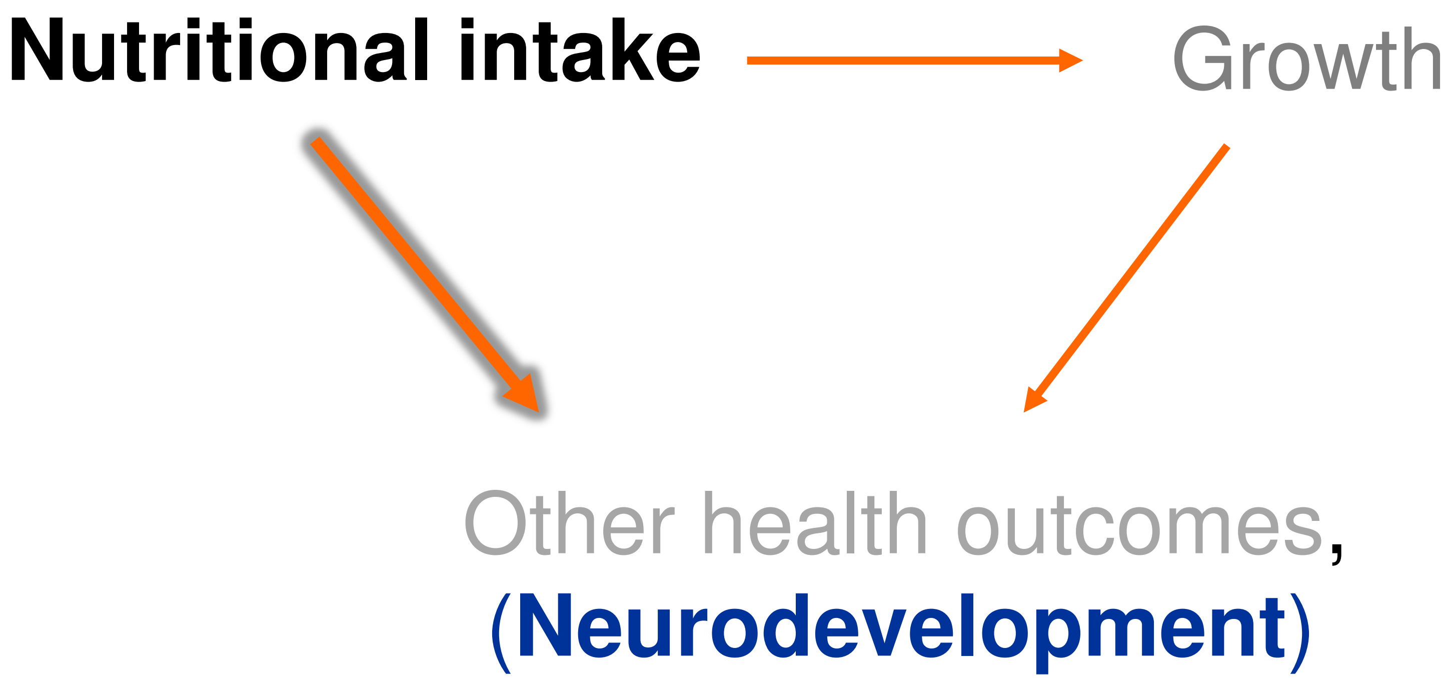
Growth and neurodevelopment

Postnatal growth restriction has negative impact on health outcomes

- **Now evidence of impact of BMI and length growth on neurodevelopment**
  - Belfort MB et al. *Pediatrics* 2011;128:e899
  - Ramel SE et al. *Neonatology* 2012;103:19

Nutritional intake and neurodevelopment



Nutritional intake and neurodevelopment

Suboptimal postnatal nutritional intake has negative impact on neurodevelopment.

- **Evidence of impact of nutritional intake, in particular protein, on neurodevelopment**
  - Lucas A et al. *BMJ* 1998;317:1481
  - Stephens BE et al. *Pediatrics* 2009;123:1337
  - Isaacs EB et al. *JPediatr* 2009;155:229
  - Franz AR et al. Pediatrics 2009;123:e101

Stephens BE et al. *Pediatrics* 2009;123:1337

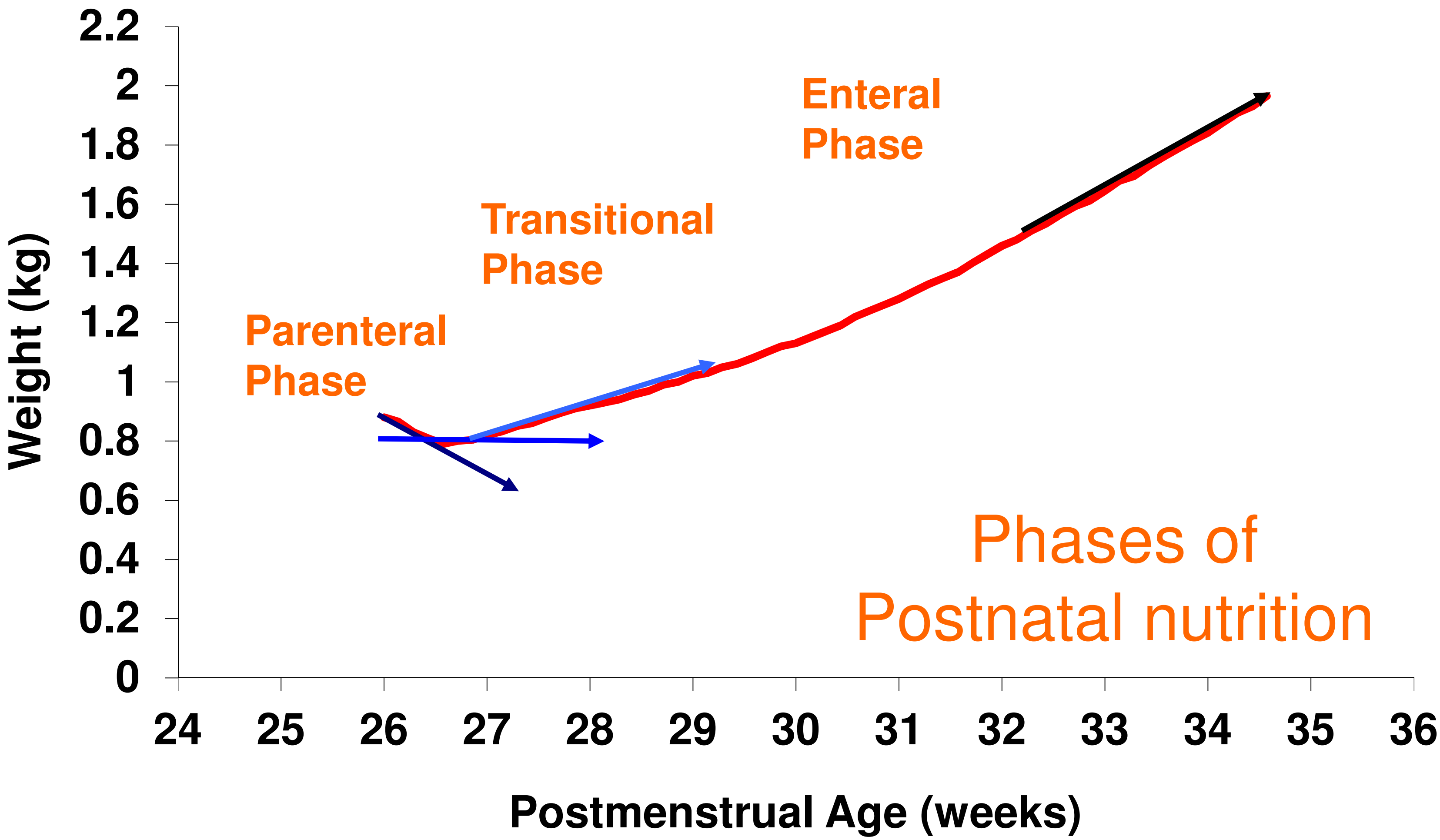
- Retrospective study of 1^{st} 4 weeks of life
- 148 ELBW survivors in a single NICU
- Collected total daily EN and PN kcalorie and protein intake, for weekly comparisons to outcomes
- 18 mo. corrected age outcomes
  - Neurodevelopment (Bayley MDI and PDI scores)
  - Growth (weight, length, head circumference)
- Results:
  - Week 1 energy and protein intake independently related to improved neurodevelopment scores at 18mo.
  - Higher protein associated with lower rates of LN $<10^{th}$%ile
  - Energy and protein intake unrelated to WT and HC

Protein: Requirements and Measuring Its Impact in the NICU

Protein requirements

Postnatal growth pattern: Not constant

Inborn Infants Who Survived, 26 weeks EGA (n=1000)
Based On Data in the Pediatrix Clinical Data Warehouse 2009-2010



Modified from: Clark et al. *Clin Perinatol* 2014;41:295

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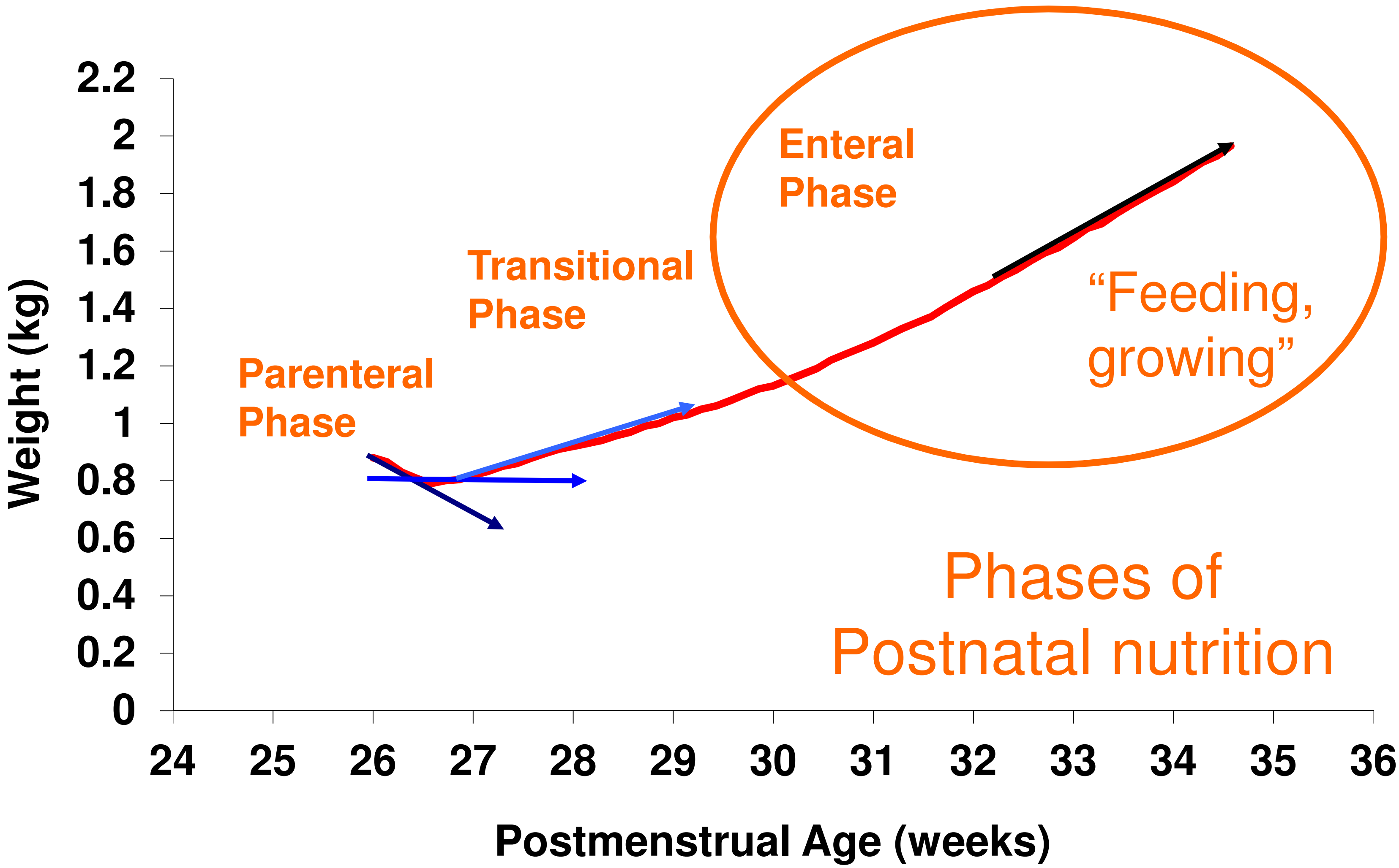


Modified from: Clark et al. *Clin Perinatol* 2014;41:295

Protein requirements

Recommended Enteral Intakes for VLBW infants (unless weight indicated)		
	Koletzko et al. 2014*	**ESPGHAN 2010****
Energy, kcal/kg/d	110-130	110-135
Protein, g/kg/d	3.5-4.5	3.5-4.5 (1-1.8kg) 4.0-4.5 (<1.0kg)

*Koletzko B, Poindexter B, Uauy R (eds): Nutritional Care of Preterm Infants: Scientific Basis and Practical Guidelines. World Rev Nutr Diet. Basel, Karger, 2014, vol 110, pp 297-299.

**Agostoni C et al; ESPGHAN Committee on Nutrition: Enteral nutrient supply for preterm infants- Commentary from the European Society of Paediatric Gastroenterology, Hepatology and Nutrition Committee on Nutrition. *J Pediatr Gastroenterol Nutr* 2010;50:85-91.

In the NICU, are recommendations met?

- Suboptimal nutritional intake (kcalorie and protein) leads to **deficits.** eg.,
  - Carlson *JPerinatol* 1998
  - **Embleton *Pediatrics* 2001 (figure)**
  - Clark *JPerinatol* 2003
  - Ziegler *Ann Nutr Metab* 2011
  - Senterre *Acta Paediatr* 2012
  - Iacobelli *BMC Pediatrics* 2015

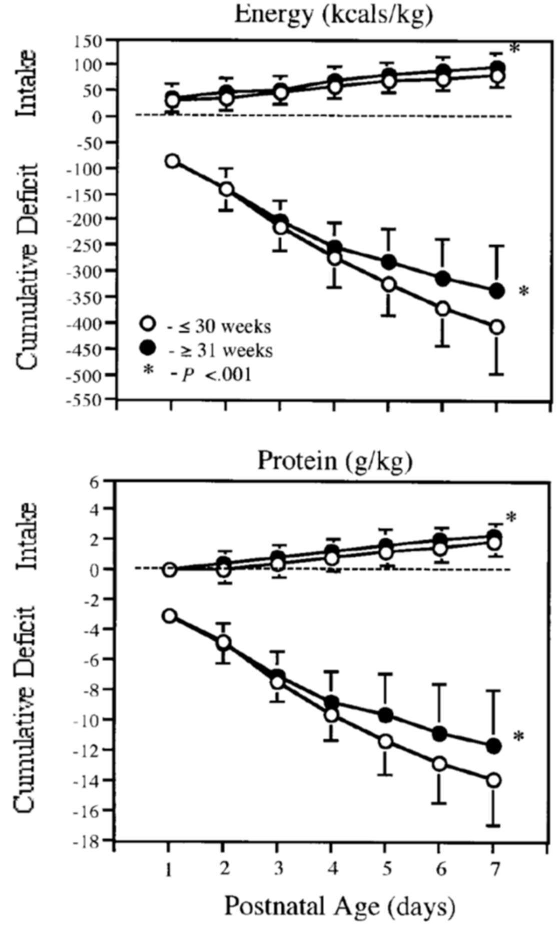


Fig 1. Nutrient intake and cumulative nutrient deficit during the first weeks of life. Data were analyzed using ANOVA. The asterisk indicates overall level of significant difference between infants at ≤30 weeks and ≥31 weeks as determined using ANOVA.

Individualized nutritional plans

Individualized fortification of human milk:

- Based on analysis of human milk
  - Creamatocrit, mid-infrared and near infrared spectrophotometry (Kim *Early Human Dev* 2013)

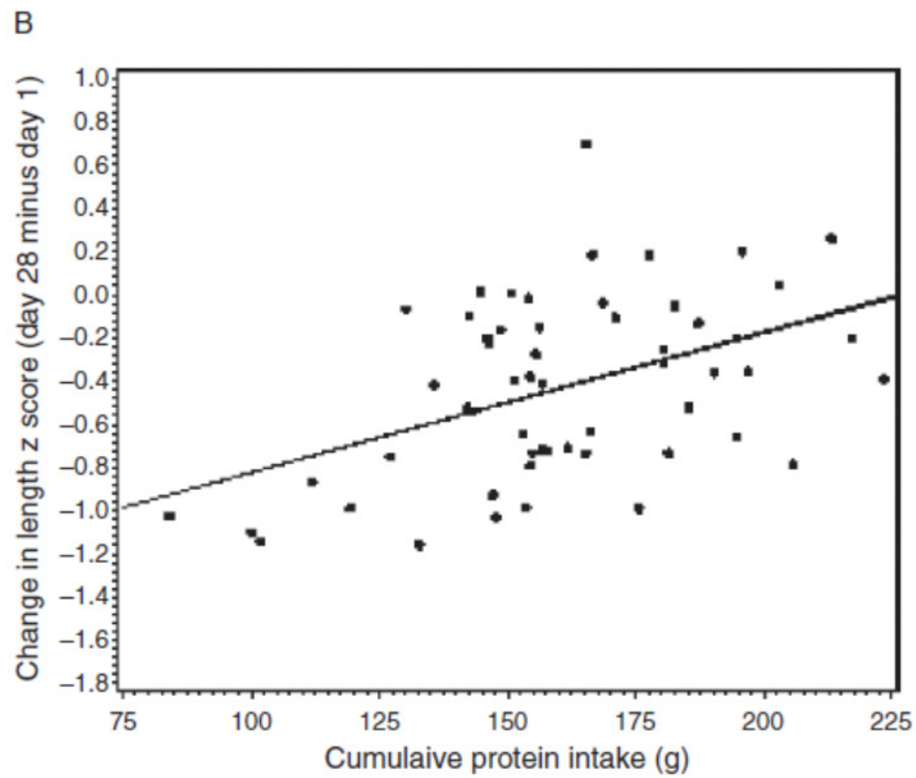
- Adjusted based on blood urea nitrogen (BUN)
  - Human milk fortifier and protein supplement added based on infant's metabolic response (BUN 2x/wk)
    - Moro GE et al. *JPGN* 1995;20:162
    - **Arslanoglu S et al. *JPerinatol* 2006;26:614 (RCT)**
    - Arslanoglu S et al. *JPGN* 2015;61:s4

Enough protein to support growth?

- Studies have tested protein intake at or slightly above protein recommendations with improved **weight** growth and adequate tolerance
  (Cooke *Pediatr Res* 2006; Arslanoglu *JPerinatol* 2006; Fanaro *Early Hum Dev* 2010; Miller *AJCN* 2012)
- Moya et al. (*Pediatrics* 2012) safety and efficacy trial of a high protein, liquid HMF vs older powder HMF - showed improved weight, length and head circumference growth with adequate tolerance

Enough protein to support growth?

- Olsen et al. **secondary analysis** of Moya data showed improved LN growth with higher cumulative protein intake over 28d study period
- Warrants further research



Modified from: Olsen IE et al. *JPGN* 2014;58:409

“Protein ceiling effect”?

- Randomized clinical trial, single center (2012-14)
- 60 Preterm infants (<32wk, <1500g at birth)
- Intervention (intent-to-treat analysis), n=30 per group
    1. Lower protein group - +1g bovine pro/100ml HM via HMF
    2. Higher protein group, n=15 per group
        a. Standardized high protein w/ study fortifier (+1.8g bovine pro/100ml HM)
        b. Individualized high protein “based on pro and fat content of HM”
- Primary outcome: weight gain (g/kg/d) (birth to study end)
- Results: WT gain similar (16.3 vs 16.0g/kg/d, p=0.7); also HC and lower leg LN growth similar
- “Actual” pro intake: 3.7 vs 4.3g/kg/d by group (dif. 0.6g/kg/d)

Maas C et al. *JAMA Pediatrics* 2017;171:16

“Protein ceiling effect”?

Questions?

- “Actual” protein intake: 3.7 vs 4.3g/kg/d by group
  - Unfortified HM analyzed 2x/wk (mean of 3 measurements, 1 sample; mid-infrared spectroscopy)
  - Accurate assessment of “actual” protein intake?
- Primary outcome: Weight growth velocity (g/kg/d)
  - Ideal measures of growth outcome? (LN, HC, BMI, body comp)
- Is this a “protein ceiling effect” or suboptimal protein to support growth, in particular linear growth? Warrants further research.

Maas C et al. *JAMA Pediatrics* 2017;171:16

Growth assessment tools and Outcomes

How do we measure the impact of nutrition and growth in the NICU?

Nutrition and growth: Data and outcomes

What are ideal measures for preemies?

- Nutritional intake:
  - Actual vs assumed (estimated)
- Growth
  - Available, accurate growth measurements (WT, LN, HC; body composition, as possible)
  - Growth assessment tools
    - Growth velocity
    - Growth curves
    - Growth status (%iles, z-scores)
    - Body proportionality ratios (BMI)

Nutritional intake: Actual vs assumed

- 3-week study compared actual vs assumed (estimated) kcalorie and protein intake for each week
- Actual intake from HM analysis with feeding volumes, fortification, % Mom's or donor milk (2/7days, pooled)
- Assumed intake based on published data (HM, HMF, protein supplement content); recorded volumes
- Results-
  - Protein: Actual < Assumed – significant and consistent during each study week (dif range 0.5-0.8g/kg/d)
  - Kcalories: Small differences between study groups
- *Is "actual" intake always feasible? Should it be our standard?*

Arslanoglu et al. *JPerinatol* 2009;29:489

Nutrition and growth: Data and outcomes

What are ideal measures for preemies?

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Growth measurements: Available, accurate

- Weight
  - Electronic scale; to nearest 10gm
  - Daily
- Length
  - Length board; to nearest 0.1cm
  - Weekly
- Head circumference
  - Non-stretch measuring tape; to nearest 0.1cm
  - Essential to move the measuring tape to find largest circumference
  - Weekly

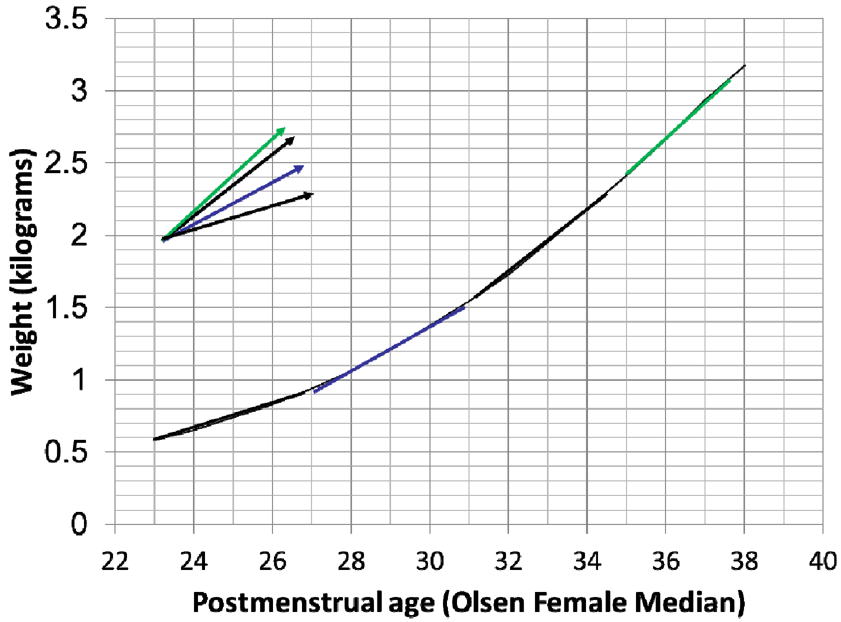
Assessment tools: Growth velocity

- Common measure of growth in preterm infants
- Lacks generally accepted standard for calculation
  - Variation in calculation methods produce different estimates (vary by interval, formula)
  - In comparisons to published growth velocity estimates
- Single estimates **oversimplify** growth because growth rate is **not constant** before or after birth
  - Appropriate rate of growth varies (gender, gestational age, postnatal age)
- Important to use in conjunction with growth curves

Pre and postnatal growth: Not constant

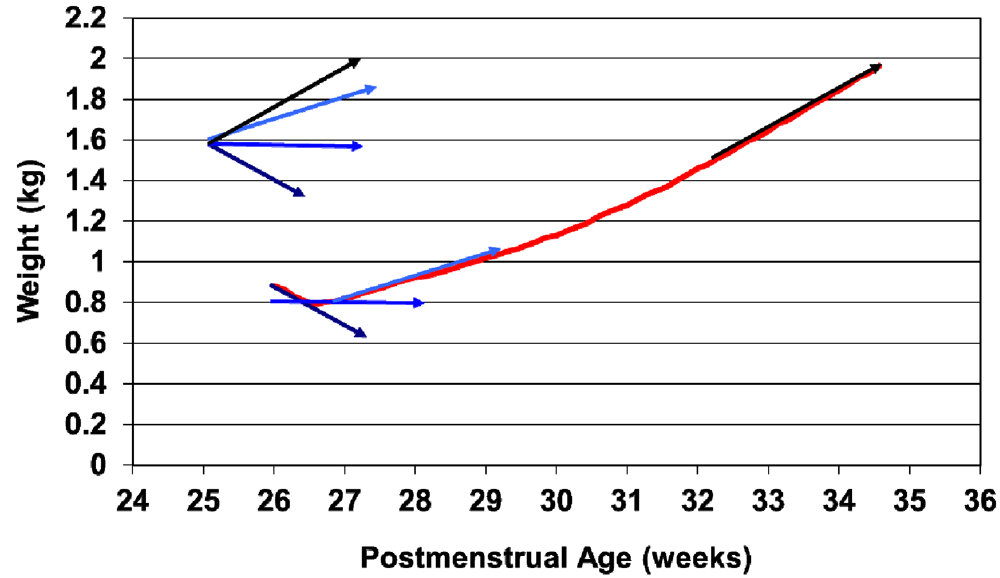
Prenatal growth: Not constant

Based on Olsen female growth curves



Postnatal growth: Not constant

Inborn infants who survived, 26wk EGA (n=1000)
Based on data in the Pediatrix Clinical Data Warehouse 2009-10



Clark et al. *Clin Perinatol* 2014; 41:295

Example: Growth velocity estimates

Olsen intrauterine curves (Olsen et al. *Pediatrics* 2010;125:e214)

(Weekly intervals based on medians, 23-36wk GA, genders combined)

– Weight mean ~18gm/kg/d (15-20gm/kg/d)

» Using "Beginning WT" as end point

– Length mean ~1.4cm/wk (1.2-1.5cm/wk)

– Head circum. mean ~0.9cm/wk (0.8-1cm/wk)

Based on Clark et al. *Clin Perinatol* 2014;41:295

Growth velocity estimates: Not constant

- Weight GV estimate based on:
  Weekly intervals, median weights, 23-36wk GA, "Beginning WT" as end point
  - Mean ~18gm/kg/d (15-20gm/kg/d) for females and males

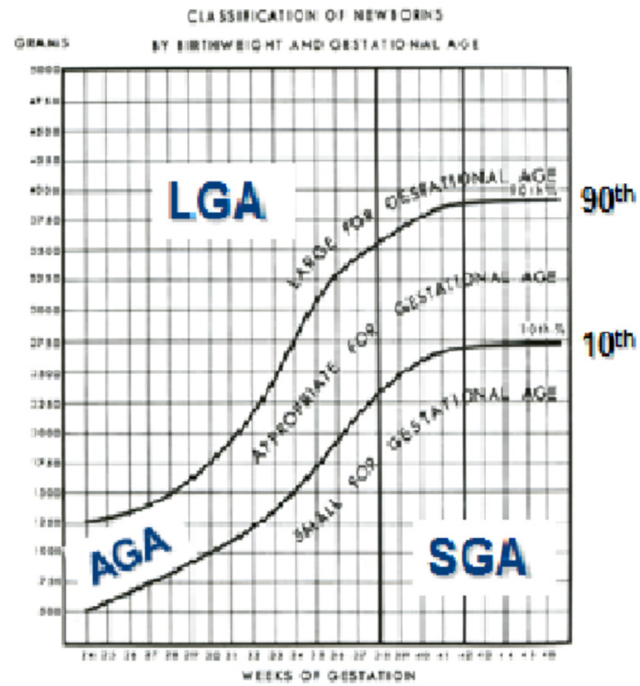
Table 1
Estimated intrauterine weight gain velocity by EGA based on Olsen charts

	Female			Male		
	Median Weight (g)	Change (g/d)	Change (g/kg/d)	Median Weight (g)	Change (g/d)	Change (g/kg/d)
23	584			622		
24	651	9.6	16	689	9.6	15
25	737	12.3	19	777	12.6	18
26	827	12.9	18	888	15.9	20
27	936	15.6	19	1001	16.1	18
28	1061	17.9	19	1138	19.6	20
29	1204	20.4	19	1277	19.9	17
30	1373	24.1	20	1435	22.6	18
31	1546	24.7	18	1633	28.3	20
32	1731	26.4	17	1823	27.1	17
33	1956	32.1	19	2058	33.6	18
34	2187	33	17	2288	32.9	16
35	2413	32.3	15	2529	34.4	15
36	2664	35.9	15	2798	38.4	15

Clark RH, Olsen IE, Spitzer AR. Assessment of neonatal growth in prematurely born infants. *Clin Perinatol*. 2014;41:295-307

Assessment tools: Growth curves

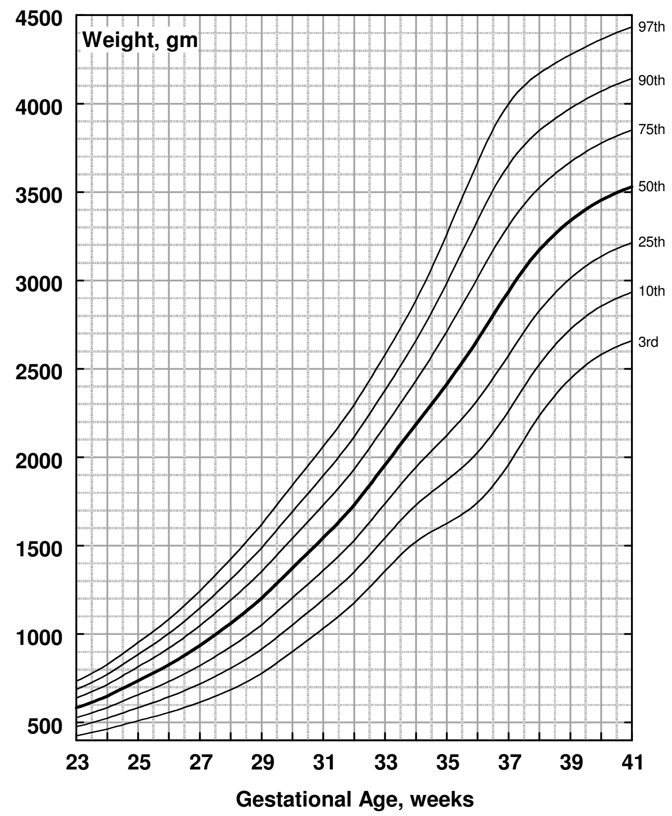
- **Why are growth curves important?**
  - Visualize and track growth over time (plotted weekly)
  - Identify high-risk infants
    - Small-for-gestational age (SGA) - <10th percentile
    - Large-for-gestational age (LGA) - >90th percentile



- **Growth curve choice matters**
  - High-risk categories vary based on the curve
  - Misclassification of infants to high risk
    - Neubauer V et al. *ActaPaediatrica.* 2016;105:268
    - Sankilampi U. (editorial) *ActaPaediatrica.* 2016;105:228

Intrauterine growth curves

- Based on cross-sectional data; fetal growth; comparison to “ideal” growth
- Examples of WT, L and HC-for-age curves:
  - Fenton (2003; 2013)
  - Olsen (2010)
  - Bertino (2010)
  - Niklasson (2008)
  - Babson/Benda (1976)
  - Lubchenco (1963, 1966)



Olsen IE et al. *Pediatrics* 2010;125:e214

Selection of growth curves

- For which parameters? (WT, L, HC and BMI?)
- Sample size, data source and how recent?
- Sample selection
  - "population" vs "reference" sample selected for "healthy" infants
- Gender (combined or gender-specific)
- Race/ethnicity (combined or separate)
- Gestational age
- "Smoothing" curves
- Validation

Selection of growth curves:
Data in 2013 Fenton curves - preterm only

Data sources	Kramer 2001	Voight 2010	Roberts 1999	Bonnelie 2008	Bertino 2010	Olsen 2010
Preterm infants?	Yes	Yes	Yes	Yes	Yes	Yes
Data origin	Canada	Germany	Australia	Scotland	Italy	U.S.
Para-meters	Weight only	Weight only	Weight only	Weight only	WT, L, HC	WT, L, HC

Adapted from: Fenton and Kim. *BMC Pediatrics* 2013 13:59

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Fenton WT-for-Age curves

Fenton L-for-Age and HC-for-Age

m: F

Olsen curves: How did we do?

Sample:

- Dataset from Pediatrix Clinical Data Warehouse
- n= 391,861 infants
- 22 to 42 wk gestation at birth (1998-2006)
- 248 U.S. NICUs from 33 U.S. states

Birth data:

- Weight, length, head circum, gestational age, gender

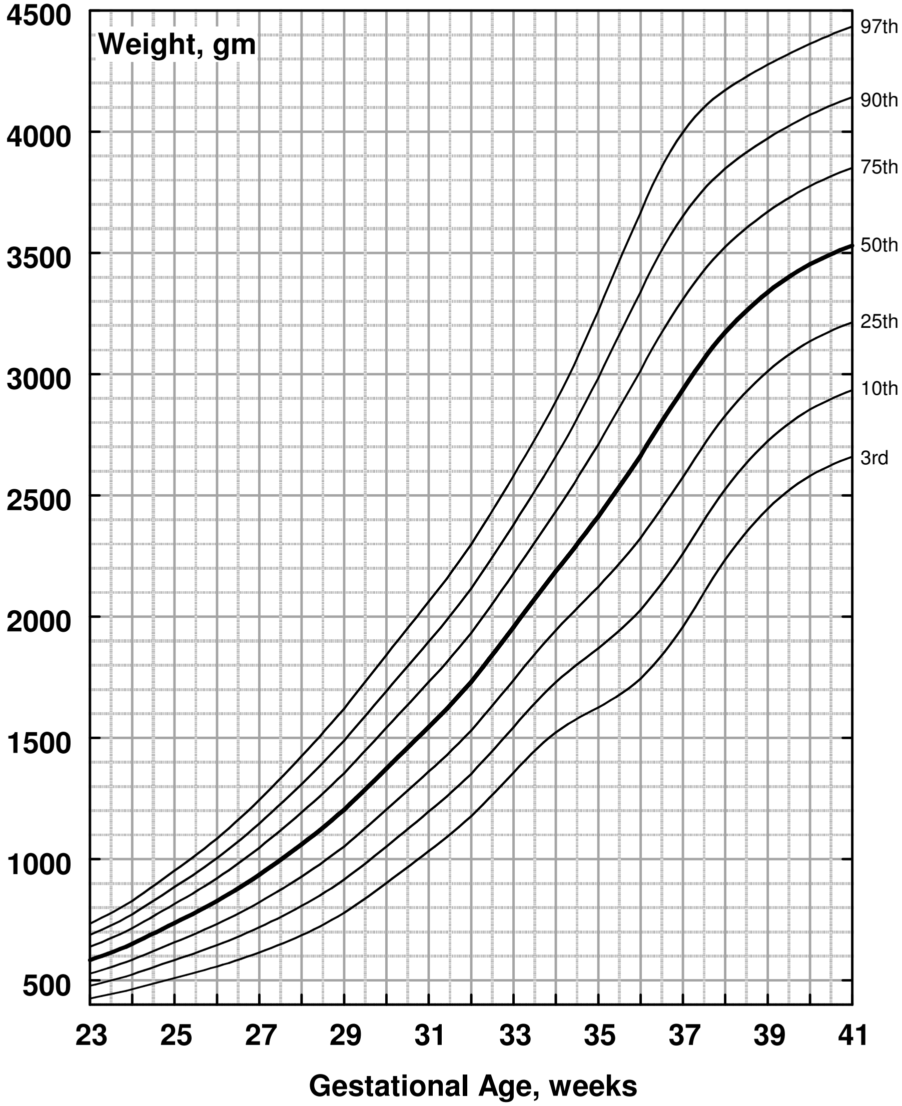
Exclusions

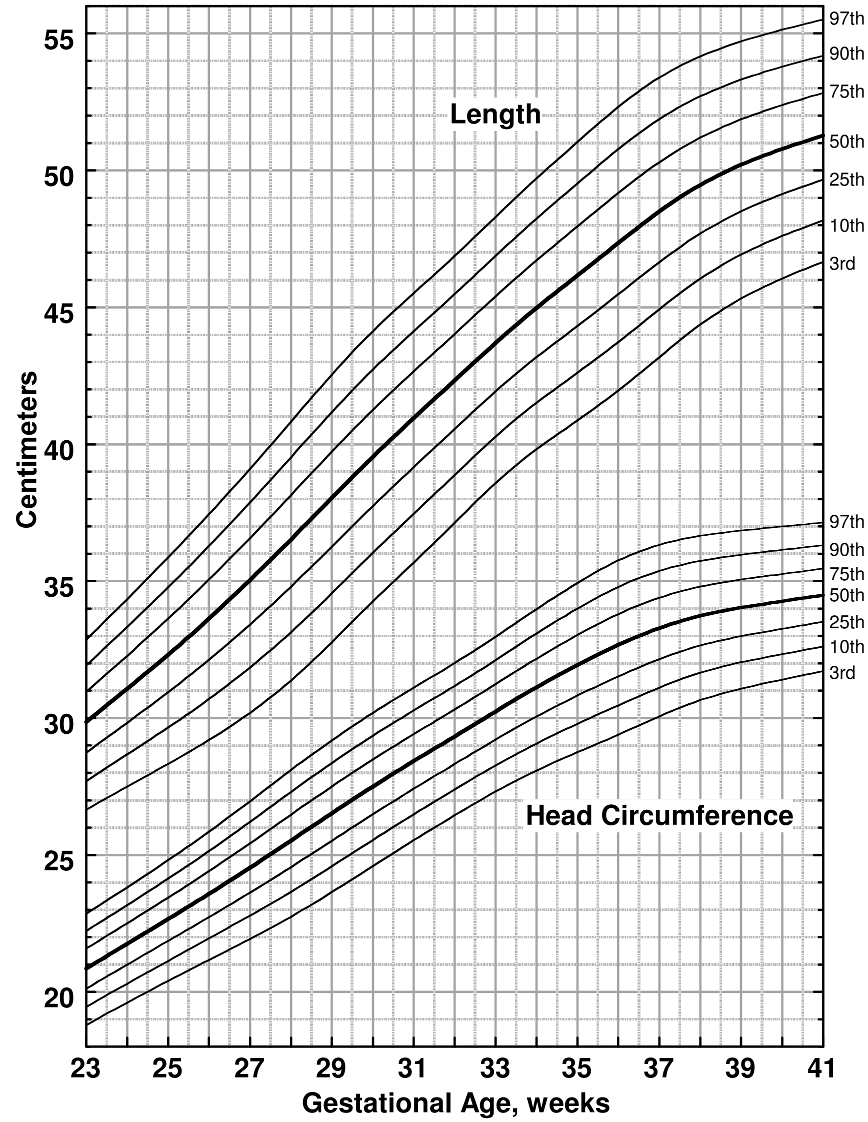
- Missing growth measurements or gender
- Factors with negative impact on growth
- Physiologically improbable growth measurements
  (“extreme outliers” Tukey *Exploratory Data Analysis* 1977)

Validation

- Internally and externally (De Jesus *J Pediatr* 2013) validated

Female Intrauterine Growth Curves





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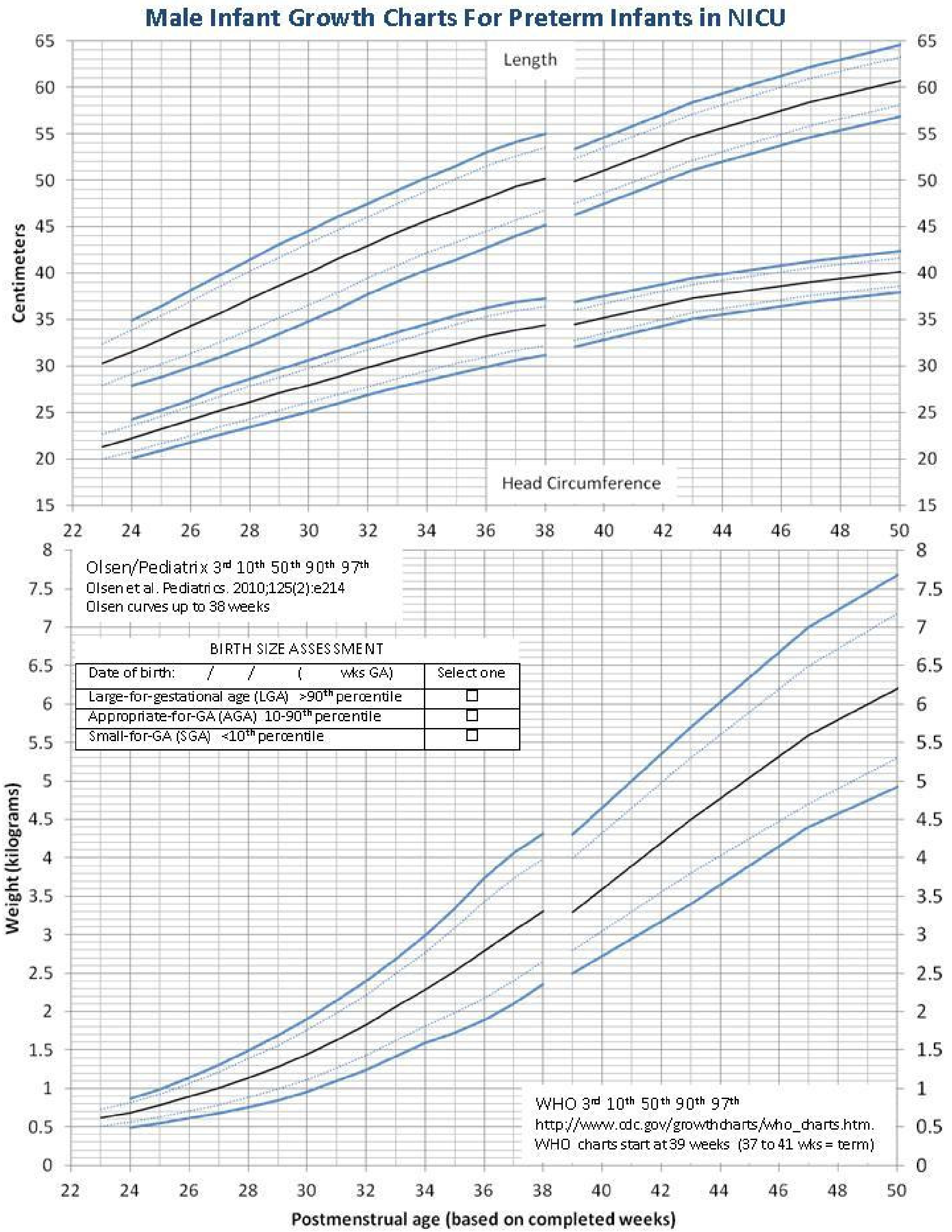


Olsen intrauterine growth charts

(23 to 38 wk)

presented with

WHO growth charts

(39 to 50 wk)

- Curves not joined because independent sets of data
- WHO “fullterm”: 37-41wk

Weblink to PDF:
http://www.pediatrix.com/workfiles/NICUGrowthCurves7.30.pdf

Adapted from:
Olsen IE et al. *Pediatrics* 2010;125:e214-224
and
http://www.who.int/childgrowth/standards/en/

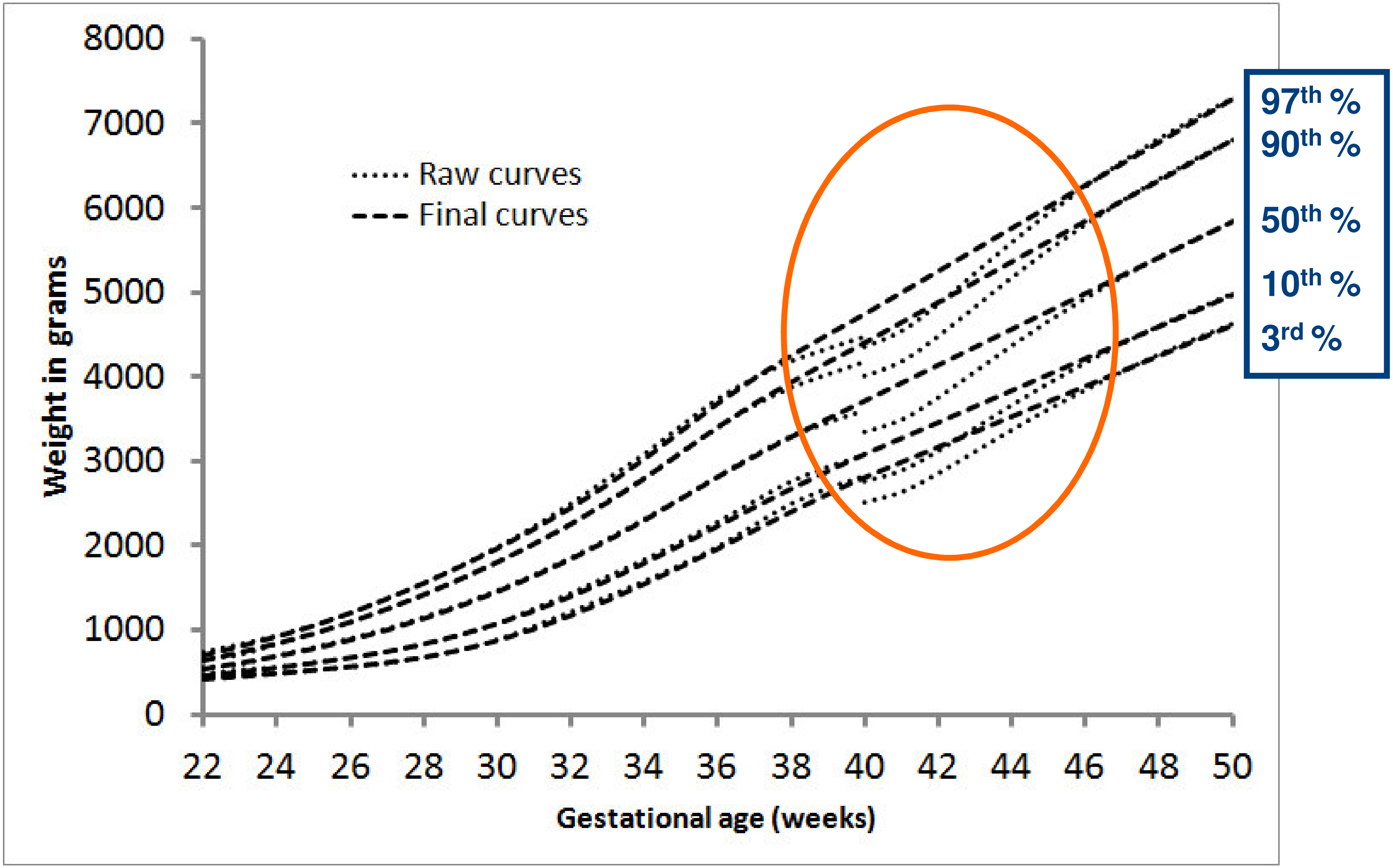
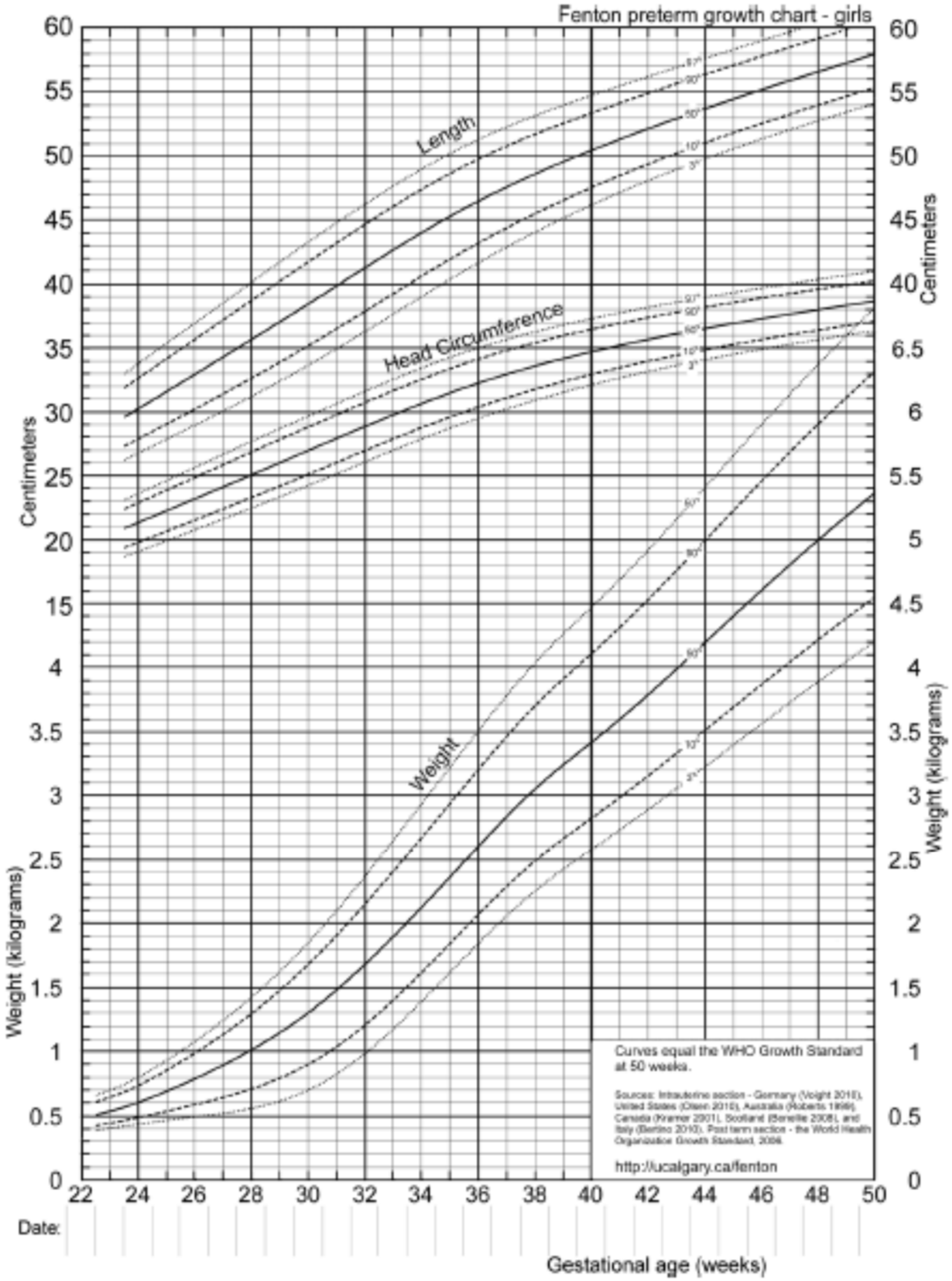


Figure 5

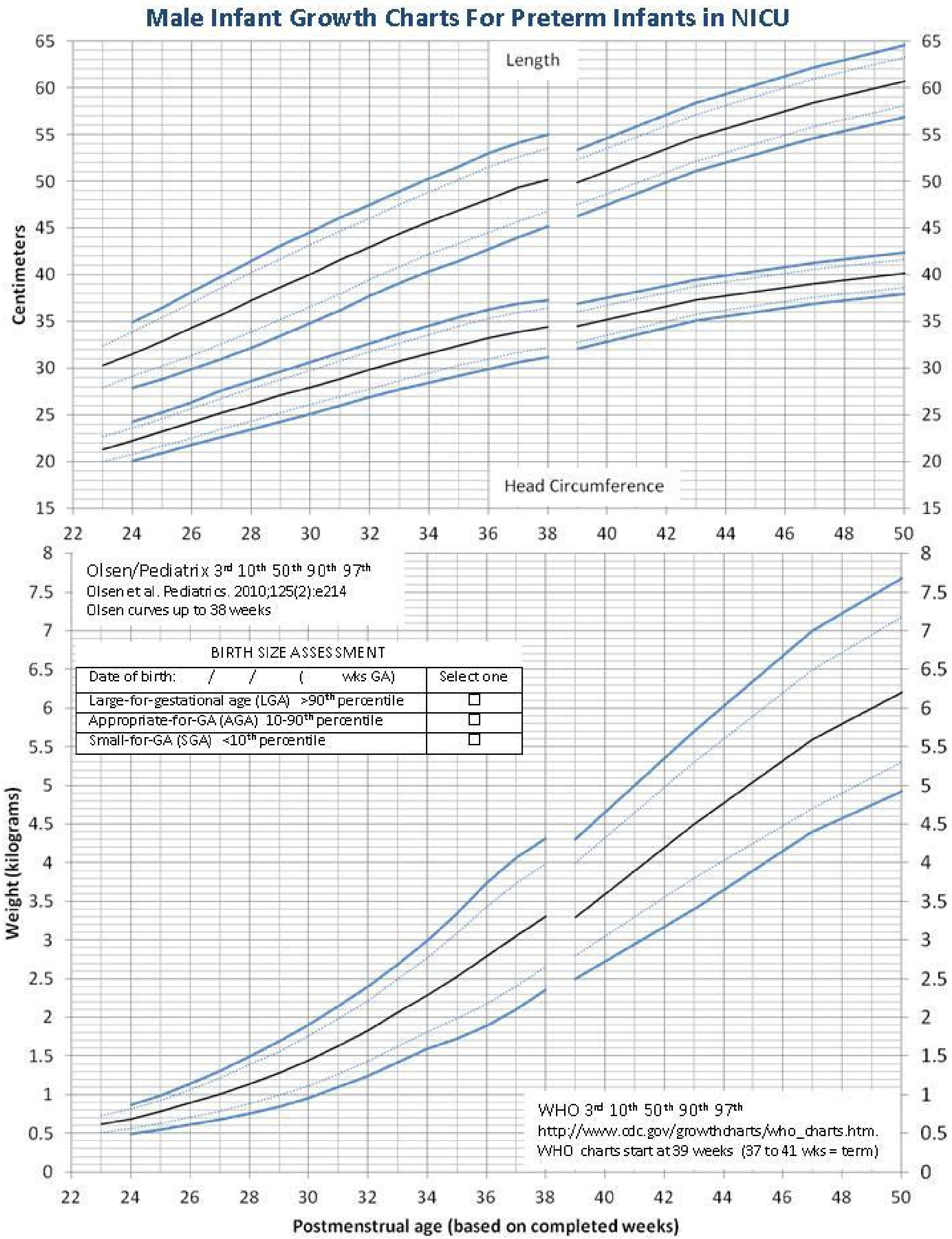
Boys meta-analysis weight curves (dotted) with the final smoothed growth chart curves (dashed).

Adapted from: Fenton and Kim. *BMC Pediatrics* 2013 13:59



Fenton Preterm Growth Chart, 2013 for girls

Fenton and Kim. *BMC Pediatrics* 2013 13:59



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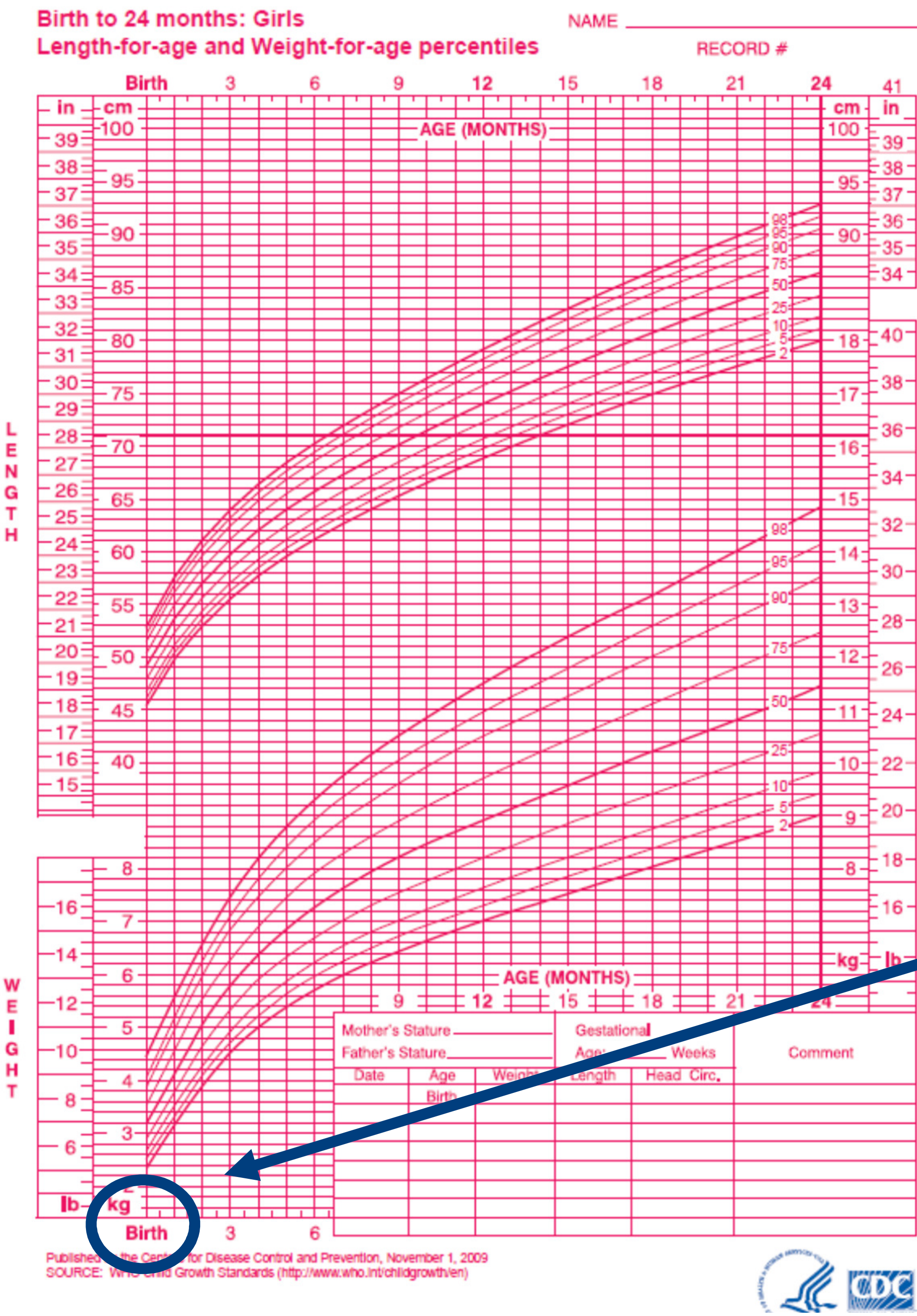
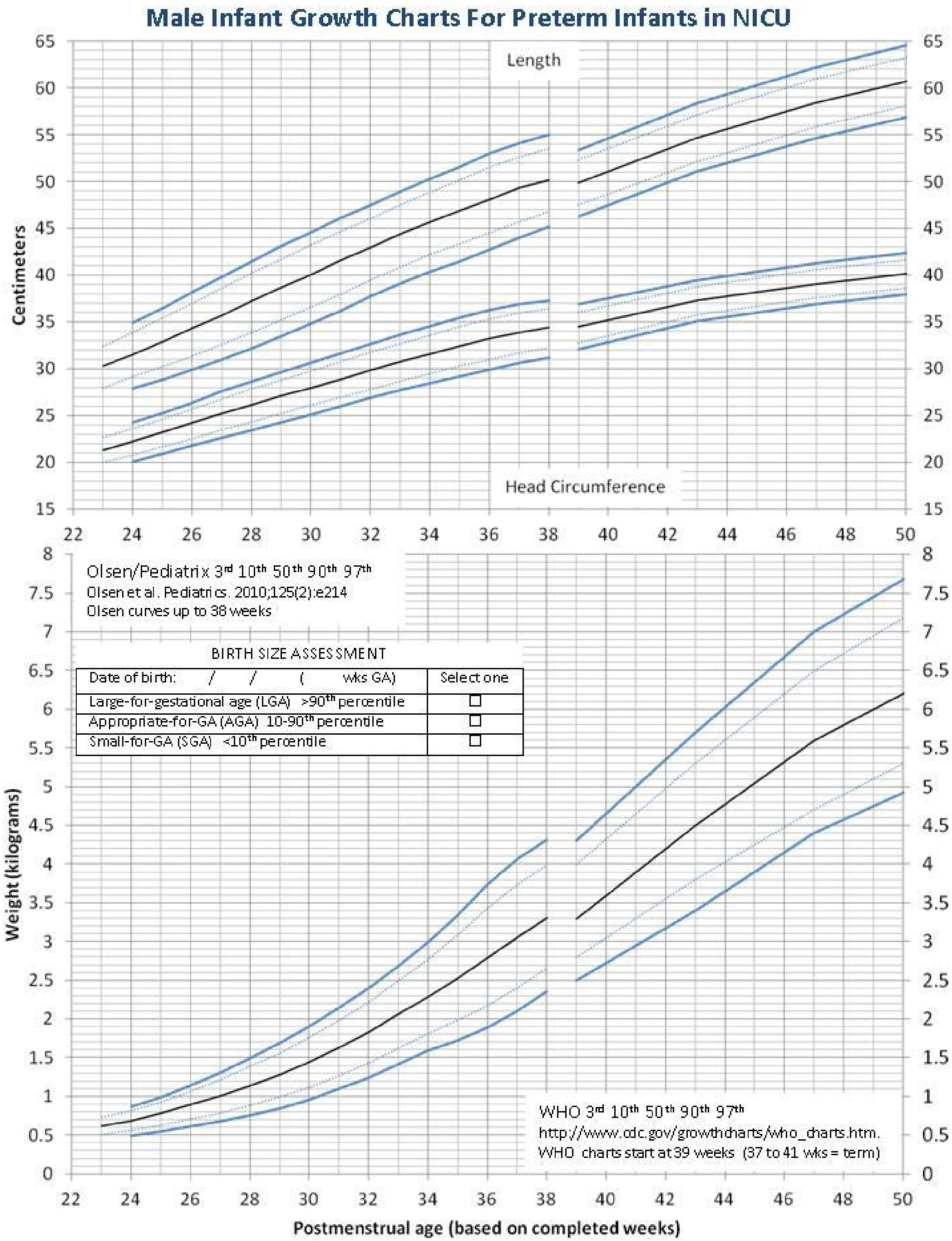


WHO Child Growth Standards Growth Chart **for girls**

WHO "fullterm":

37 – 41 wk

http://www.who.int/childgrowth/standards/en/



Olsen intrauterine growth charts

(23 to 38 wk)

presented with

WHO growth charts

(39 to 50 wk)

- Curves not joined because independent sets of data
- WHO “fullterm”: 37-41wk

Weblink to PDF:
http://www.pediatrix.com/workfiles/NICUGrowthCurves7.30.pdf

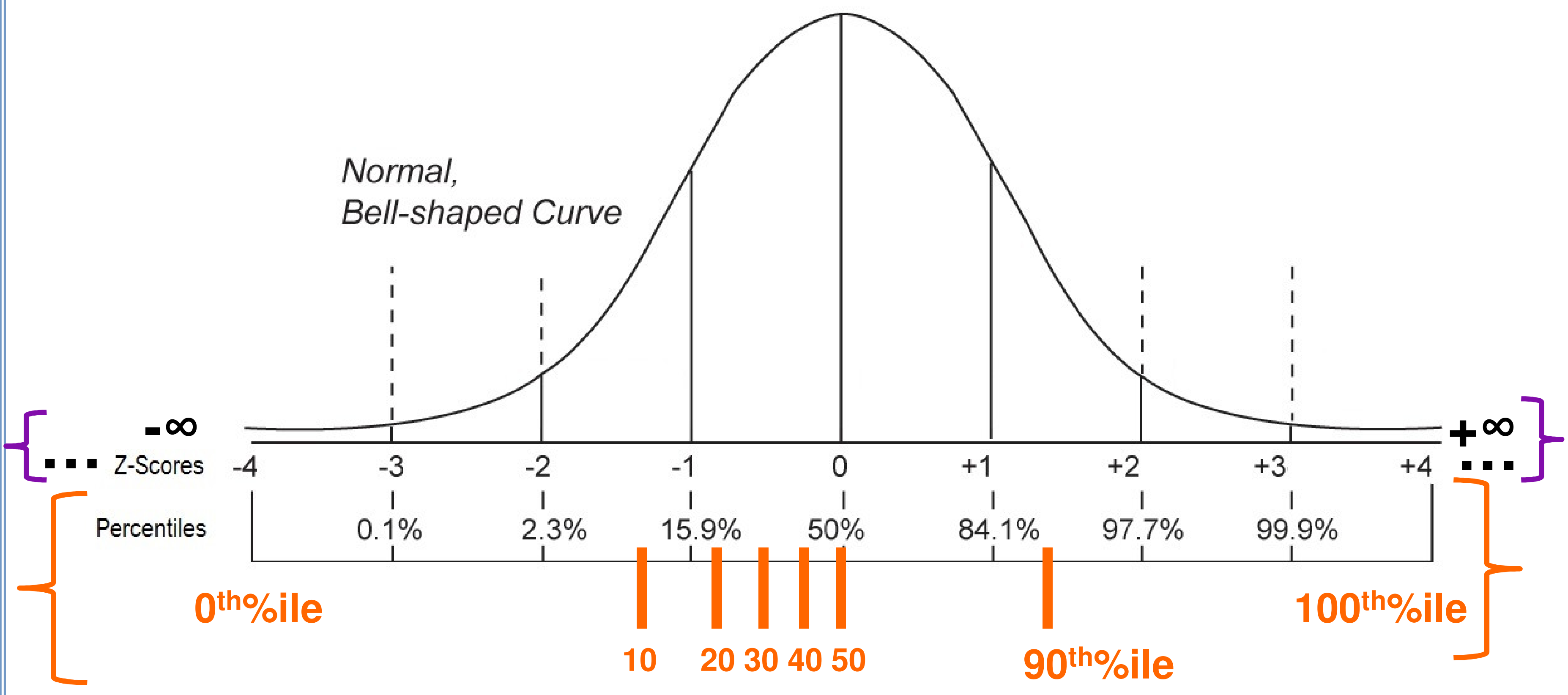
Adapted from:
Olsen IE et al. *Pediatrics* 2010;125:e214-224
and
http://www.who.int/childgrowth/standards/en/

Nutrition and growth: Data and outcomes

What are ideal measures for preemies?

- Nutritional intake:
  - Actual vs estimated
- Growth
  - Available, accurate growth measurements (WT, LN, HC; body composition, as possible)
  - Growth assessment tools
    - Growth velocity
    - Growth curves
    - **Growth status (percentiles, z-scores)**
    - Body proportionality ratios (BMI)

Growth status: Z-score vs Percentile



Modified from: https://lexile.com/about-lexile/grade-equivalent/performance-standards/
By Derek Cox of Project Grow Baby Grow, Kennesaw State University – Statistics Dept.

Growth outcomes: Z-score

For data that is not normally distributed

$$\text{Z-score} = \frac{[(X/M)^{L} - 1]}{LS}$$

* *Where*

X: Measured value (Weight, kg; Length, cm; Head circum, cm)

M: Median

L: Box-Cox power transformation of skewness

S: Coefficient of variation

*Gender and GA-specific values from Olsen et al. growth curves data (*Pediatrics* 2010)

Growth outcomes: Z-score

$$\text{Z-score} = \frac{\left[(X/M)^{L} - 1\right]}{LS}$$

X: Measured value (WT, kg; LN, cm; HC; cm)

M: Median

L: Box-Cox power transformation of skewness

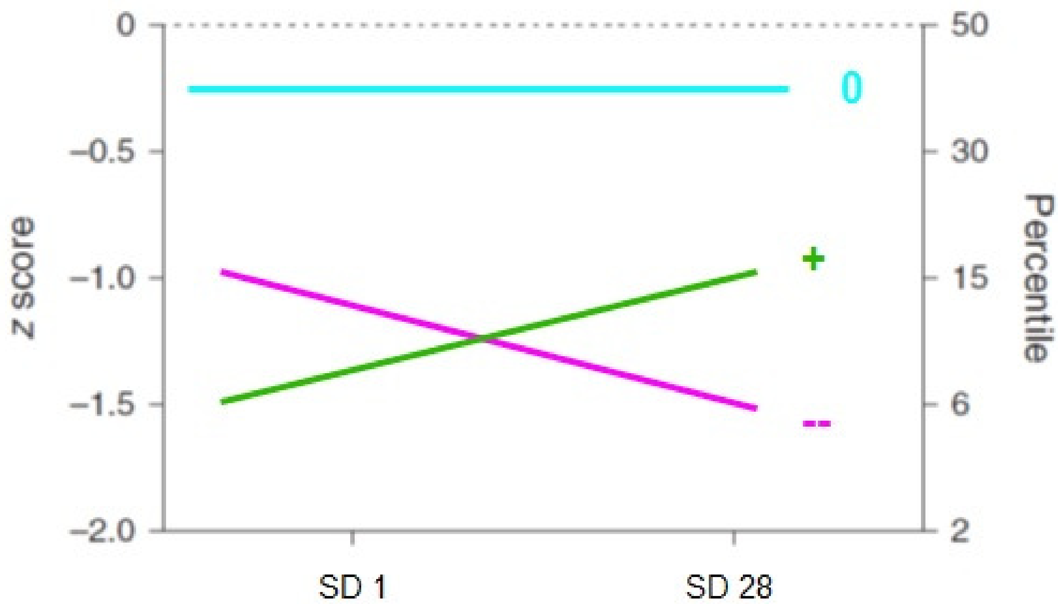
S: Coefficient of variation

TABLE 3 Gender-Specific Weight-, Length-, and HC-for-Age Growth Curves L, M, and S Parameters

GA, wk	Weight-for-Age Curve			Length-for-Age Curve			HC-for-Age Curve		
	L Curve Value	M Curve Value	S Curve Value	L Curve Value	M Curve Value	S Curve Value	L Curve Value	M Curve Value	S Curve Value
Female growth curves									
23	1.195	0.584	0.140	1.613	29.861	0.055	1.338	20.863	0.052
24	1.180	0.651	0.149	1.799	31.074	0.058	1.412	21.759	0.051
25	1.161	0.737	0.159	2.005	32.323	0.062	1.500	22.667	0.052
26	1.140	0.827	0.169	2.234	33.638	0.065	1.599	23.584	0.053
27	1.116	0.936	0.178	2.395	35.047	0.067	1.685	24.541	0.054
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

Change in Z-score

- Accounts for initial size in addition to gender and GA specific
- Changes:
  - Positive (+) change in z-score
    - Improvement in growth status
  - Negative (-) change in z-score
    - Decline in growth status
  - No (0) change in z-score
    - Growth status stable or unchanged



Modified from: Olsen IE et al.
JPGN 2014;58:409

Change in Z-score

- Changes:
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Nutrition and growth: Data and outcomes

What are ideal measures for preemies?

- Nutritional intake:
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- Growth
  - Available, accurate growth measurements (WT, LN, HC; body composition, as possible)
  - Growth assessment tools
    - Growth velocity
    - Growth curves
    - Growth status (%iles, z-scores)
    - **Body proportionality ratios (BMI)**

Assessment tools: Body proportionality

- Preterm infants have higher postnatal fat accretion than term infants (Reichman *NEJM* 1981; Bhatia *Acta Paediatr Scand* 1988; Kashyap *J Pediatr* 1986; 1988; Schulze *J Pediatr* 1987)
- Preterm infants at corrected term have higher percent body fat than term infants (Johnson *Pediatrics* 2012; 130:e640; Gianni *Pediatric Research* 2016;79:710)
- Small term infants at birth with rapid postnatal growth at risk (Oken *Obes Res* 2003; Baird *BMJ* 2005; Singhal *Lancet* 2003; Baird *BMJ* 2005; Stettler *Circulation* 2005; Gillman *AJCN* 2008; Taveras *Pediatrics* 2009)
- Impact of rapid postnatal weight gain on later metabolic outcomes in preterm infants less clear (Embleton et al. *Arch Dis Child* 2016; Ong et al. (review) *Acta Paediatrica* 2015)

What is the “ideal” measure of **body proportionality** for preterm infants?

- We used gender-specific samples from our WT, L and HC-for-age curves (Males n= 74,375; Females n= 55,708) (Olsen et al. *Pediatrics* 2010;125:e214)
- “Ideal” ratio is most highly correlated with weight and uncorrelated with length (Benn *Br J Prev Soc Med* 1971;25:42. Cole TJ et al. *Annals of Hum Bio* 1997;24:289)
- We tested several Weight/Length ratios
- BMI (WT/L^2): Best candidate overall across gender and GAs
- Curves created and validated (methods paper pending)

Olsen IE et al. *Pediatrics* 2015

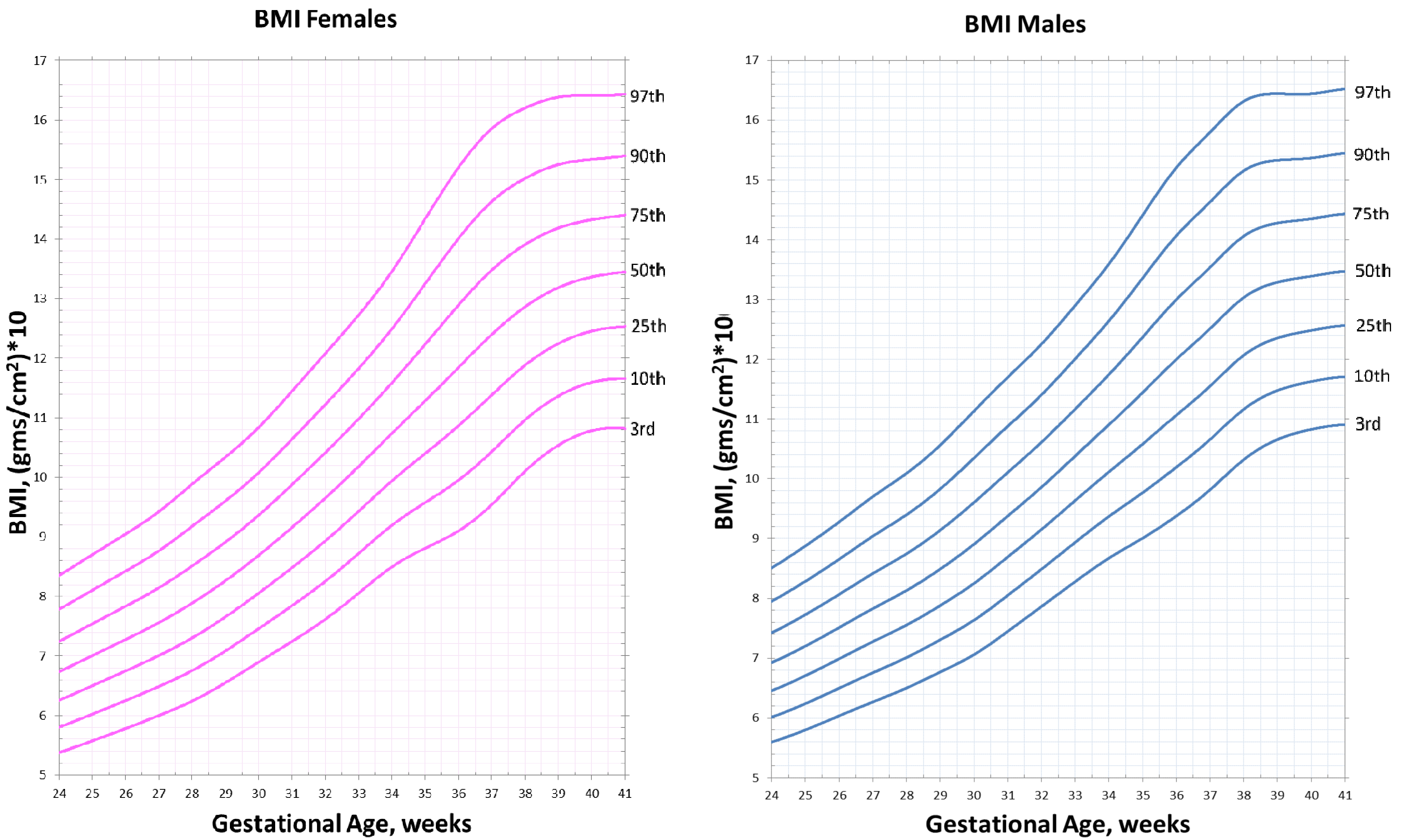


Figure 2 from: Olsen IE et al. *Pediatrics* 2015;135:e572.

BMI limitations

- BMI does not distinguish between body fat mass and fat-free mass
  - Need to evaluate with body comp data as available
- Since BMI quantifies asymmetry between weight and length growth, symmetric growth stunting, excess or appropriate growth will not be identified
- Thus, BMI-for-age curves to be used along with size-for-age curves (WT, L, HC-for-age) not in place of them

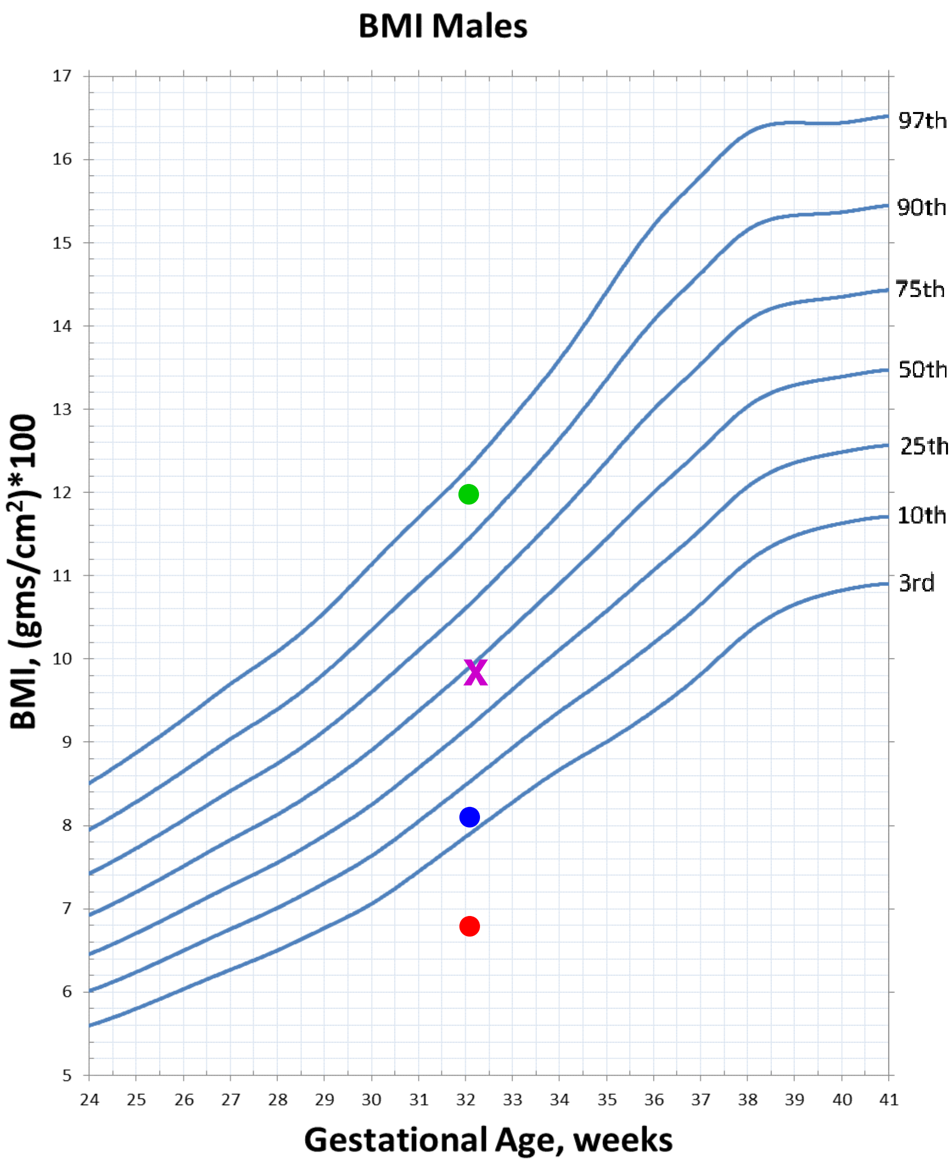
Asymmetrical or Disproportionate growth status

WFA: WT-for-Age
LFA: L-for-Age

75th WFA
25th LFA

25th WFA
75th LFA

10th WFA
90th LFA



Symmetrical or Proportionate growth status

WFA: WT-for-Age
LFA: L-for-Age

9th WFA
9th LFA

Adapted from: Olsen IE et al. *Pediatrics* 2015;135:e572.

Body proportionality: BMI-for-age curves

- Recommend BMI curves as adjunct to WT, LN, HC-for-age intrauterine curves
- Provides more individualized growth assessment to inform nutrition and clinical decisions
- Balance between adequate and excess growth?
  - Belfort MB et al. *JPediatr* 2013
  - Brown and Hay. (edit.) *JPediatr* 2013
  - Singhal A. "Optimizing Early Protein Intake for Long-Term Health of Preterm Infants". In *Nestle Nutr Inst Workshop Ser*, vol 86, pp 129-137, 2016

Overall Summary and Conclusions

- Still more work to be done in determining (or confirming) optimal protein recommendations to support optimal outcomes in preterm infants
- Standardization of nutrition and growth data and outcomes used in clinical and research settings would help comparisons and making clinical decisions and policies (Cormack et al. Pedi Res 2015)
- Growth outcomes (at minimum): Weight, length, head circumference and BMI z-scores and change in z-scores; body composition, as possible

Thanks and Questions?