PROBLEMI NUTRIZIONALI DEL PRETERMINE

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CORSO DI FORMAZIONE
PROMOZIONE DELL'ALLATTAMENTO AL SENO

Very Low Birth Weight

I Prematuri non sono tutti uguali…

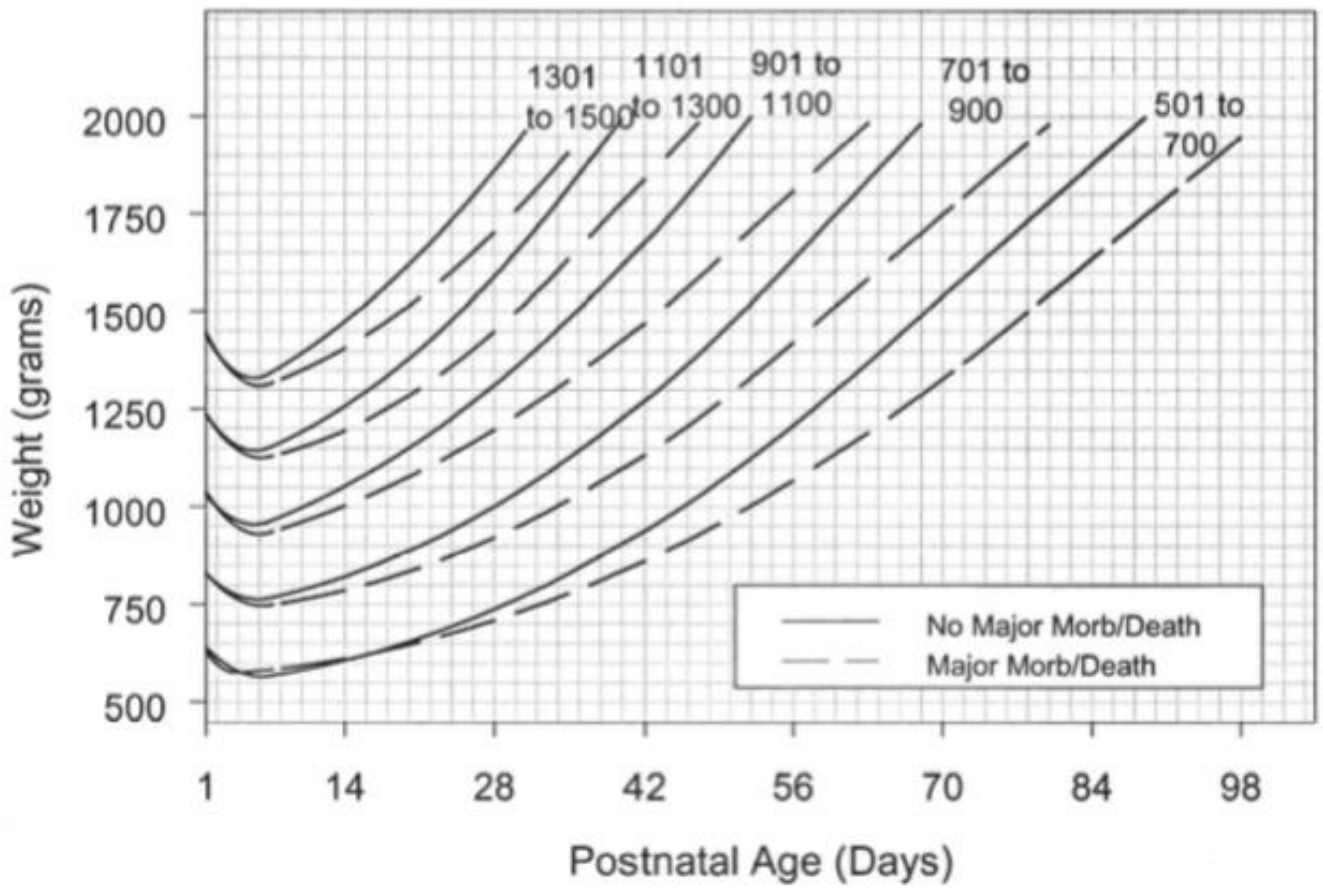
…670 gr

…1820 gr

PRETERMINE LBW

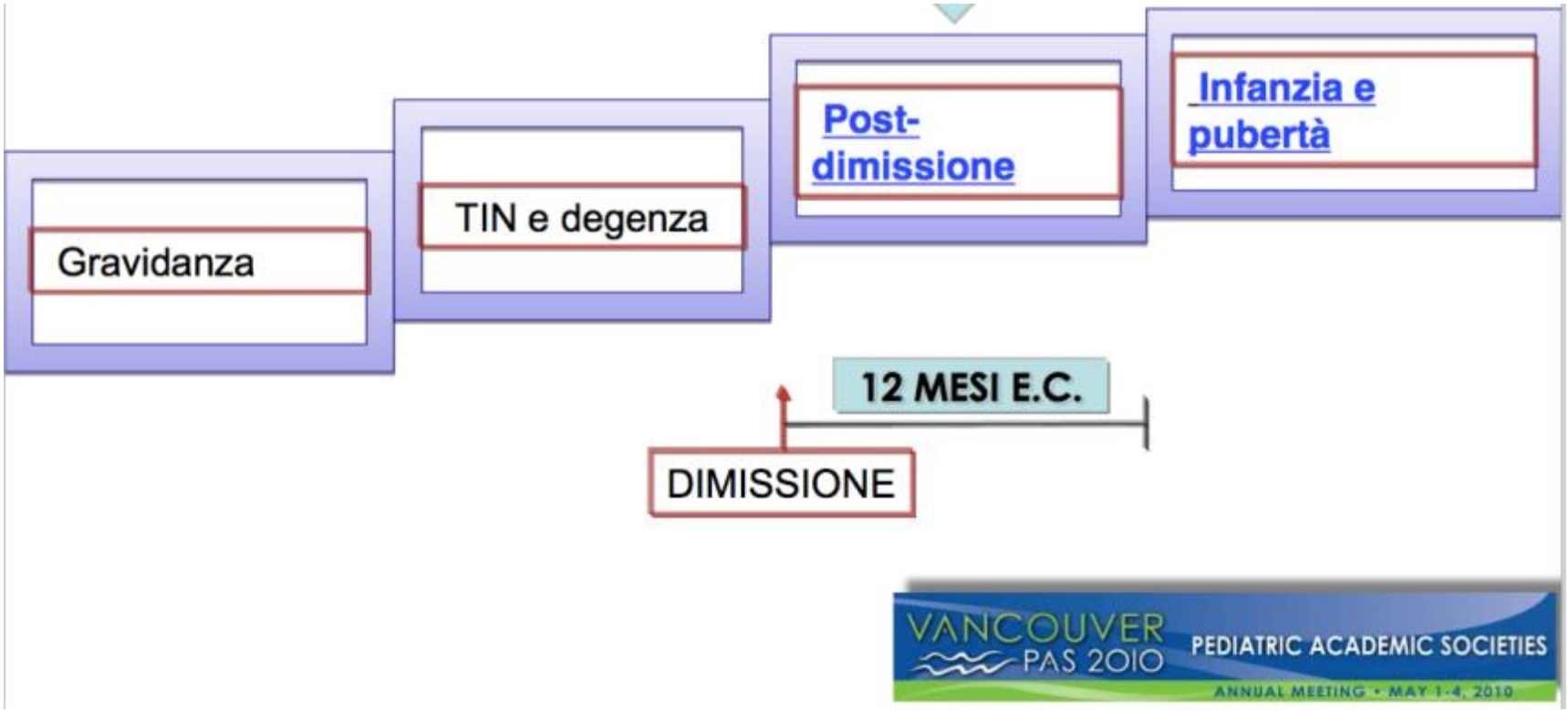
IUGR SGA AGA VLBW ELBW

I Pretermine con co-morbidità crescono meno



Biniwale and Ehrenkranz, Semin Perinatol 30:200-8,2006

...la nutrizione fetale, neonatale e nelle epoche successive puo' condizionare crescita e sviluppo somatico (e neurocognitivo?) nell'eta' evolutiva?



Preterm Birth and Body Composition at Term Equivalent Age: A Systematic Review and Meta-analysis

E' una "malnutrizione" non solo quantitativa ma anche qualitativa

Preterm infant have a different body composition at term corrected age compared with infants born at term:

1. similar fat mass
2. a significant relative deficit in lean tissue

Incremento percentuale e relativo dell'adiposità durante la degenza ospedaliera e dalla dimissione all'età di 12 mesi e.c.

www.pediatrics.org/cgi/doi/10.1542/peds.2011-3379

Carenze Nutrizionali

QUANTITATIVO

QUALITATIVO

DANNI NEUROLOGICI

SQUILIBRI METABOLICI

CRESCITA CELLULARE LIMITATA

DECORSO CLINICO

FOLLOW UP A DISTANZA

Modificata da Corpeleijn WE, Vermeulen MJ, van den Akker CH, van Goudoever JB. Feeding very-low-birth-weight infants: our aspirations versus the reality in practice. Ann Nutr Metab. 2011;58 Suppl 1:20-9

Nutrition and the Developing Brain: Nutrient Priorities and Measurement

- Periodo caratterizzato da una serie di rapide trasformazioni di processi neurologici (formazione di sinapsi, la mielinizzazione, aumento cellule gliali)

- I possibili deficit proteico-energetici riducono il contenuto neuronale di DNA e RNA → riduzione di cellule neuronali, una ridotta sintesi proteica e una ipomielinizzazione → le dimensioni cerebrali si riducono →anomalie di sviluppo cognitive/motorie, attività verbali e visive particolarmente a rischio

Georgieff MK, Am J Clin Nutr, 2

Postnatal Growth in VLBW Infants: Significant Association with Neurodevelopmental Outcome

219 VLBW
94 SGA
125 AGA

Table II. Postnatal growth pattern and neurodevelopmental outcome at age 2

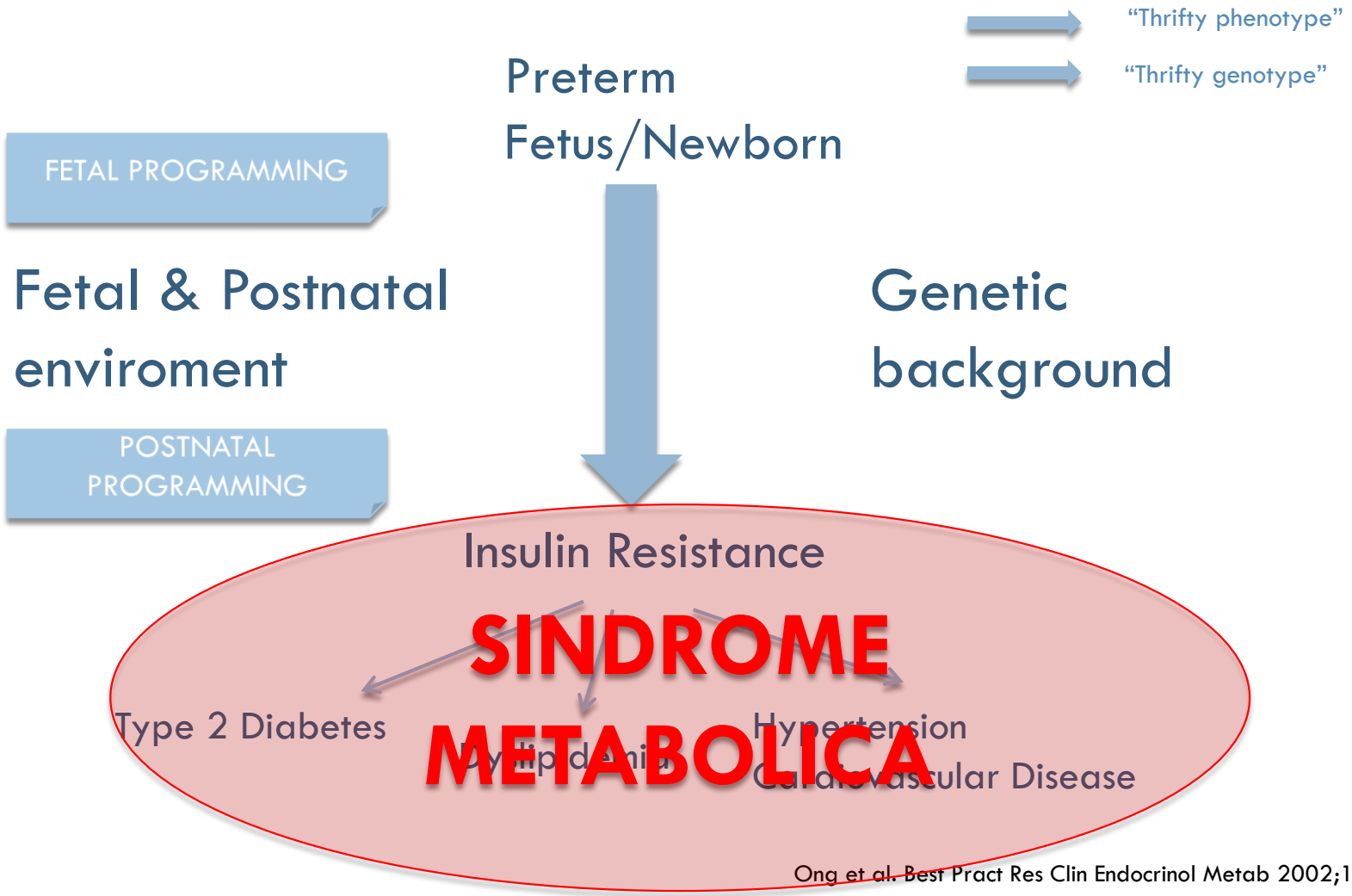
Weight at birth / Weight at age 2 / Group		Weight <10th P / <10th P / 1 N = 52	Weight <10th P / >10th P / 2 N = 41	Weight >10th P / <10th P / 3 N = 35	Weight >10th P / >10th P / 4 N = 86	P value*
MDI	Mean (SD)	94.7 (16.6)	98.2 (15.1)	94.9 (22.9)	101.7 (14.7)	3-4[a]
<84	n (%)	12 (23.1)	7 (18.9)	10 (28.6)	9 (10.5)	NS
<68	n (%)	2 (3.9)	0 (0)	6 (17.1)	0 (0)	3-4[c†]
PDI	Mean (SD)	89.9 (17.4)	101.8 (14.5)	81.9 (25.3)	95.1 (15.6)	1-2[c], 1-3[a], 2-3[c], 3-4[c]
<84	n (%)	14 (26.9)	4 (9.8)	16 (45.7)	12 (14.5)	1-2[a], 1-3[a], 2-3[c], 3-4[c]
<68	n (%)	5 (9.8)	1 (2.8)	12 (34.3)	3 (3.6)	1-3[a], 2-3[c], 3-4[c]
CP						
Mild/moderate	n (%)	13 (25.0)	5 (12.5)	6 (17.1)	12 (14.1)	NS
Severe	n (%)	2 (3.8)	1 (2.5)	7 (20.0)	1 (1.2)	1-3[b], 2-3[b], 3-4[b]

*Significance, adjusted for covariables (gestational age, socioeconomic status, sex, cohort, multiple birth status, PDA, BPD, IVH grade III or IV), is expressed as follows $^{a}P \leq .05$, $^{b}P \leq .01$, $^{c}P \leq .001$. The numbers indicate the groups for which level of significance is given. Adjustment performed for continuous outcome variable (MDI, PDI) using ANCOVA, for dichotomous outcome variables logistic regression. Results of ANCOVA include also adjustment for moderate or severe CP.
†P value χ^2 without adjustment due to small number of outcome variable.

...diventare SGA, anche nel corso dei primi 2 anni di vita peggiora significativamente l'outcome neurologico...

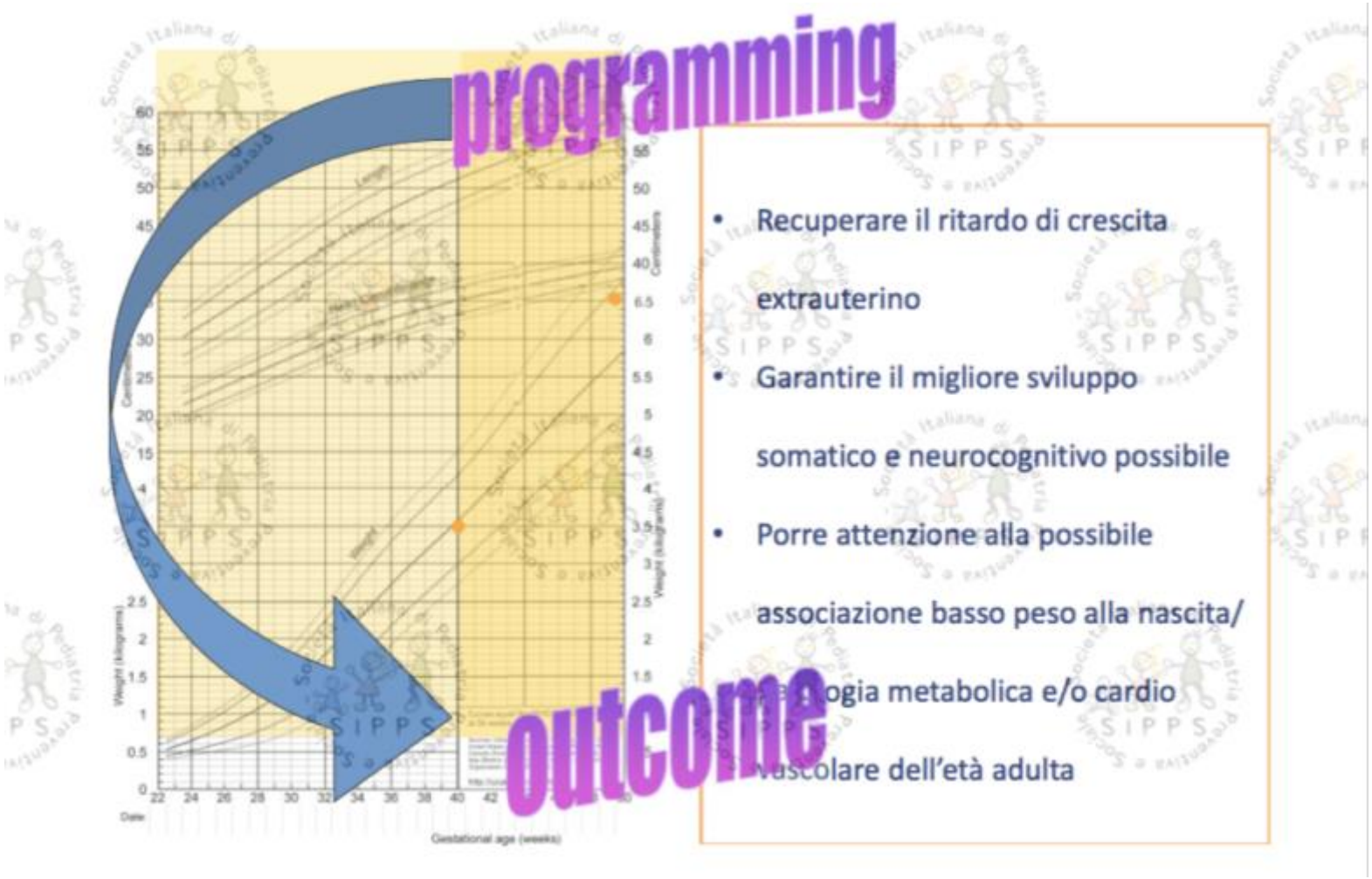
J Pediatr 2003;143:163-70

Hypotheses linking low birthweight to adulthood disease



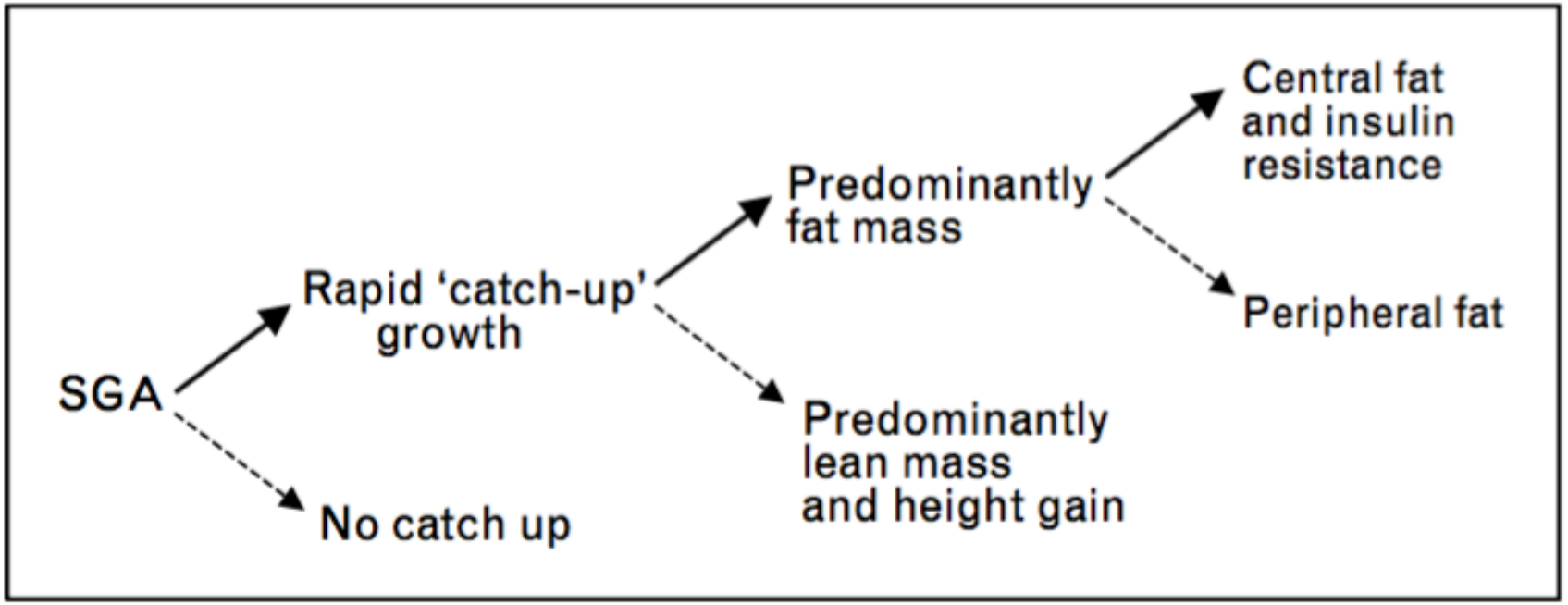
Ong et al. Best Pract Res Clin Endocrinol Metab 2002;16:191

Obiettivi nutrizionali nel primo anno di vita



Massimo Agosti, L'alimentazione del neonato pretermine e del neonato SGA
Congresso Nazionale Società italiana di Pediatria Preventiva e Sociale

Catch-up growth in small for gestational age babies: good or bad?



… not too slow, not too fast …

Ong et al. Curr Opinion Endocrinol Diabetes Obesity, 2007

…anche se

- …la resistenza insulinica è stata dimostrata anche nei pretermine che non mostrano un catch-up growth

- …l'ipotesi quindi di limitare il catch-up growth nella fase post-natale non solo puo' compromettere lo sviluppo neurologico a distanza di questi bambini, ma probabilmente non li preserva dallo sviluppo della sindrome metabolica

Remains serious problems in prematurely born neonates

…verso casa con

SCARSE RISERVE DI NUTRIENTI

MINERALIZZAZIONE OSSEA INSUFFICIENTE

DEFICIT ENERGETICO IMPORTANTE

Protein/Energy Intake

Table 1. Nutritional needs by weeks of gestation

	Nutritional needs per kg/day GA, weeks					
	<28	28–31	32–33	34–36	37–38	39–41
Fetal growth						
Weight gain, g	20	17.5	15	13	11	10
Lean body mass gain, g	17.8	14.4	12.1	10.5	7.2	6.6
Protein gain, g	2.1	2	1.9	1.6	1.3	1.2
Requirements						
Energy, kcal/kg	125	125	130	127	115	110
Proteins, g/kg	4	3.9	3.5	3.1	2.5	1.5
Protein/energy ratio, g/100 kcal	3.2	3.1	2.7	2.4	2.2	1.4
Calcium, mg/kg	120–140	120–140	120–140	120–140	70–120	55–120
Phosphorus, mg/kg	60–90	60–90	60–90	60–90	35–75	30–75

Nutritional Status at Hospital Discharge

- Approccio individualizzato alla nutrizione

It is clear that the nutritional status of preterm infants at the time of discharge is heterogeneous and that it varies according to gestational age, postnatal age, in utero growth, nutritional management during hospitalization, associated morbidities and likely genetic factors. Therefore, it is unlikely that a standardized nutritional practice may covert the need of all preterm infants after hospital discharge and an individualized approach would best meet this goal. However, common features might be identified and should be known by physicians in order to adapt their prescription and guidelines given to parents.

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 264–277

Nutritional Status at Hospital Discharge

- Follow up

In its recent position statement, the ESPGHAN Committee on Nutrition concluded that infants discharged home with a normal weight for post-conceptional age are not at increased risk of long-term growth failure and could be fed similarly to term infants of similar gestational age. By contrast, those with a subnormal weight for post-conceptional age are at increased risk of long-term growth failure and require particular attention and follow-up [23].

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 264–277

Current Practices for Feeding after Hospital Discharge

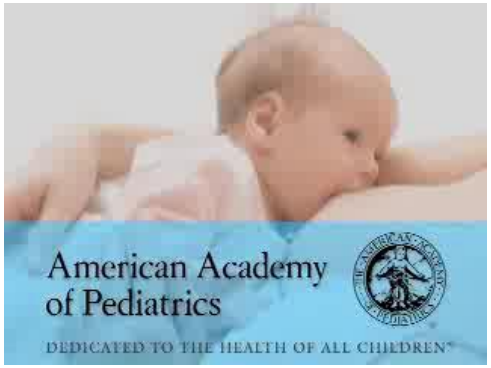
- Latte materno (*)
- Formule postdischarge

Feeding Preterm Infants After Hospital Disharge: ESPGHAN Committee on Nutrition, JPGN 2006. 42:596-503

Il latte Materno: " the perfect nutrient" anche nel pretermine

IQ, Brain Size, White Matter Development

positive correlation



8 studi su ex pretermine
Follow-up fino all'adolescenza (13-19 a.)

Isaacs, Pediatr Res 67: 357-362, 2010

Fortified Breast Milk?

(*) Secondo una meta analisi del 2013 l'utilizzo di latte materno fortificato dopo la dimissione non si associa ad una migliore crescita ponderale o ad un miglior outcome cognitivo rispetto al latte materno non fortificato

Multinutrient fortification of human breast milk for preterm infants following hospital discharge. Co- chrane Database Syst Rev

Formule PDF

Caratteristiche generali simili alla starting formula ma “rinforzata” in proteine (1.9-2.1/100 ml), calcio-fosforo, ferro, LCPUFA, minerali, vit A ecc... per ottemperare alle maggiori richieste del pretermine

Feeding Preterm Infants After Hospital Disharge: ESPGHAN Committee on Nutrition, JPGN 2006. 42:596-503

Post Discharge Formula: Razionale

- Miglior accrescimento staturo-ponderale
- Aumento di peso e lunghezza > nei maschi
- Vantaggiosa in particolari pazienti (BPD, SGA, ...)
- Aumento contenuto minerale osseo e massa magra
- Miglior sviluppo neurologico ?

rispetto alle starting e follow on formule per neonati e lattanti a termine

Post Discharge Formula: quando impiegarle

- Mancanza latte materno
- Dimissione molto prima rispetto alla data presunta del parto
- Caduta sotto il 3° o il 5° percentile della curva di crescita di riferimento
- Comorbidità che richiedono elevati apporti nutrizionali

Feeding Preterm Infants After Hospital Disharge: ESPGHAN Committee on Nutrition, JPGN 2006. 42:596-503

Post Discharge Formula: fino a quando

Non conoscendo il reale potenziale di crescita di questi neonati, sembra opportuno continuare con una formula "post-discharge" fino a quando non si raggiunga una dieta bilanciata nei suoi nutrienti piu' importanti e/o non venga recuperato il deficit auxologico postnatale

long-chain fatty acids than standard term formula should be provided until the preterm infant reaches 40 weeks' post-conceptional age but possibly until 52 weeks' post-conceptional age [23, 24].

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 264–277

Post Discharge Formula: quali benefici

- Lapillone 2014

provide evidence that nutrient-dense formula after discharge does not promote central adiposity in preterm infants [27] and may be beneficial in increasing immediate weight gain and mineralization.

Results with regard to outcomes other than growth or body composition showed no significant effect of feeding either a post-discharge formula or a preterm formula after discharge on development (tables 1, 2). Furthermore, there is no data allowing studying the effect of feeding an enriched formula after discharge on later blood pressure or insulin resistance [25].

Post Discharge Formula: quali benefici

- Cochrane Dicembre 2016:

Main results

We included 16 eligible trials with a total of 1251 infant participants. Trials were of variable methodological quality, with lack of allocation concealment and incomplete follow-up identified as major potential sources of bias. Trials (N = 11) that compared feeding infants with 'postdischarge formula' (energy density about 74 kcal/100 mL) versus standard term formula (about 67 kcal/100 mL) did not find consistent evidence of effects on growth parameters up to 12 to 18 months post term. GRADE assessments indicated that evidence was of moderate quality, and that inconsistency within pooled estimates was the main quality issue.

Trials (N = 5) that compared feeding with 'preterm formula' (about 80 kcal/100 mL) versus term formula found evidence of higher rates of growth throughout infancy (weighted mean differences at 12 to 18 months post term: about 500 g in weight, 5 to 10 mm in length, 5 mm in head circumference). GRADE assessments indicated that evidence was of moderate quality, and that imprecision of estimates was the main quality issue.

Few trials assessed neurodevelopmental outcomes, and these trials did not detect differences in developmental indices at 18 months post term. Data on growth or development through later childhood have not been provided.

Authors' conclusions

Recommendations to prescribe 'postdischarge formula' for preterm infants after hospital discharge are not supported by available evidence. Limited evidence suggests that feeding 'preterm formula' (which is generally available only for in-hospital use) to preterm infants after hospital discharge may increase growth rates up to 18 months post term.

DHA e Pretermine

Funzione strutturale: costituzione delle membrane cellulari

Funzione metabolica: immunita'/infiammazione, aggregazione piastrinica, pressione arteriosa, attivita' cardiaca

Reference	DHA, mg/kg/day	Effects on DHA status
Current DHA intake, see [14]	14–30	Decline in DHA status
[19]	32	Decline in DHA status (PPL)
[21]	45[a]	RBC DHA at expected term <6%[d]
[21]	54[b]	RBC DHA at expected term = 6.5–9%[d]
[19]	59[c]	Increase in DHA status by 12% (PPL)

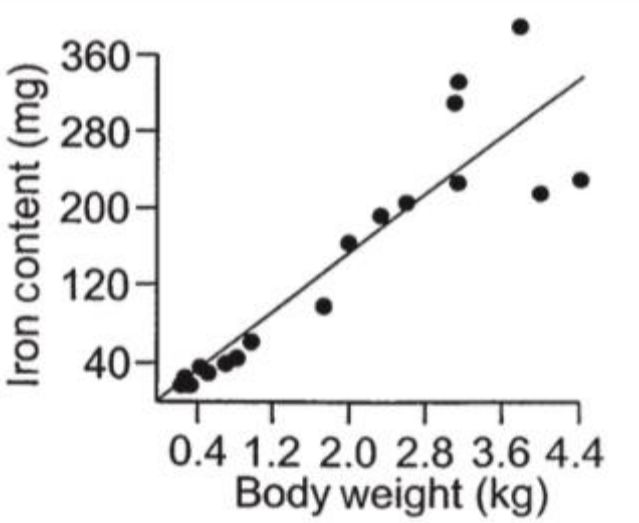
[a] Human milk from Danish mothers likely consuming fish.
[b] Human milk supplemented with a DHA supplement.
[c] Mother's milk of women receiving 3 g of tuna oil per day.
[d] Values observed for RBC DHA in term infants at birth is ~8%.

Ferro e Pretermine

term infant receive a supplement of iron after discharge from hospital [36, 37]. The AAP recommends that all preterm infants should have an iron intake of at least 2 mg/kg/day through 12 months of age, which is the amount of iron supplied by iron-fortified formulas. Preterm infants fed human milk should receive an iron supplement of 2 mg/kg/day by 1 month of age, and this should be continued until the infant is weaned to iron-fortified formula or begins eating complementary foods that supply the 2 mg/kg of iron. An exception to this practice would include infants who have re-

Cio' determina un'anemia a 4-8 settimane di eta' piu' evidente quanto minori sono l'eta' gestazionale ed il peso alla nascita

...iron requirements for fetal growth rise steadily in proportion to the weight of the fetus...



Apporto Calcio/ Fosforo e Vit D

- Feeding post-discharge preterm infants formulas or breast milk with higher concentrations of calcium and phosphorus than those found in formulas for term infants results in improved bone mineralization

- Regard to vitamin D intake, there is no evidence that the preterm infant after discharge should receive higher doses that term infants

Raccomandazioni nutrizione pretermine I

- **Close monitoring of growth** (weight-, length- and head circumference-for-age, indexes of body proportionality) and feed intake (i.e. at expected term and every 2–4 weeks after discharge) using appropriate growth curves
- **Selective biological indexes** (e.g. BUN, ferritin, 25(OH) vitamin D) may be useful in order to assess selective nutrient deficiencies but should be determined on an individual basis.

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Indicatori di crescita e stato nutrizionale del neonato pretermine dopo la dimissione

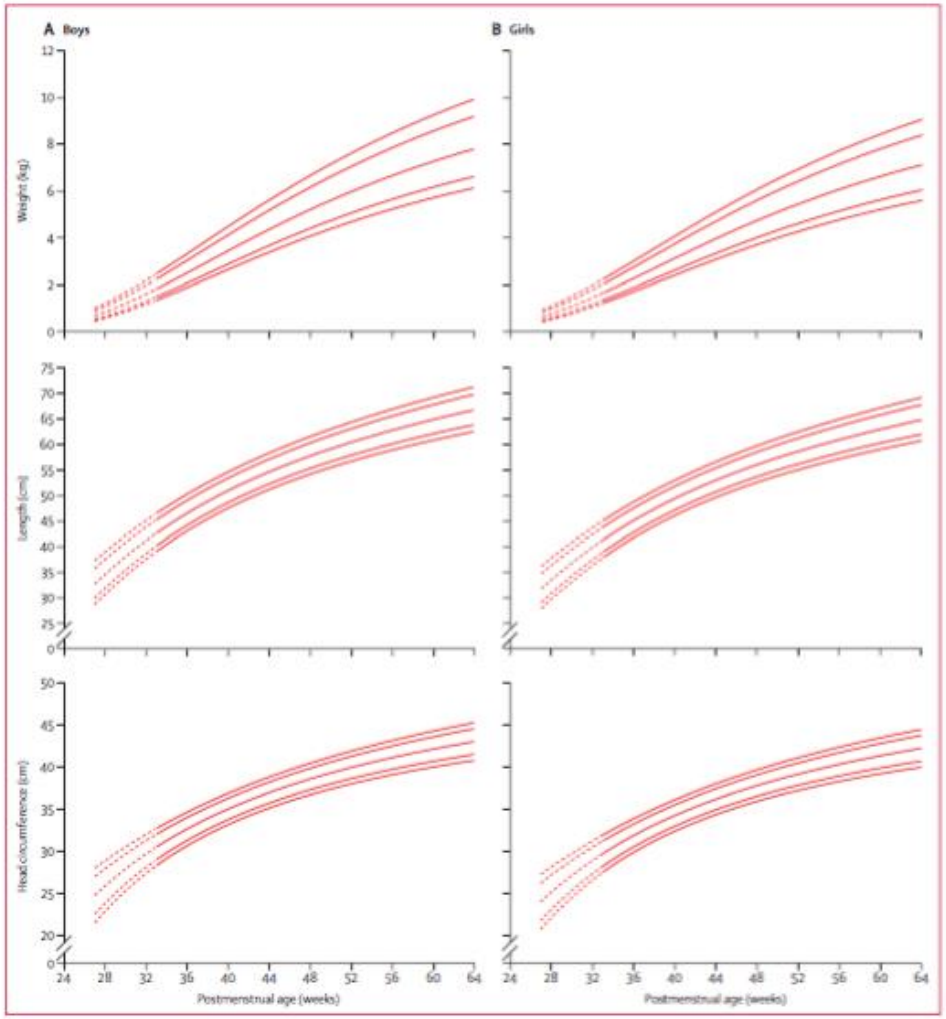
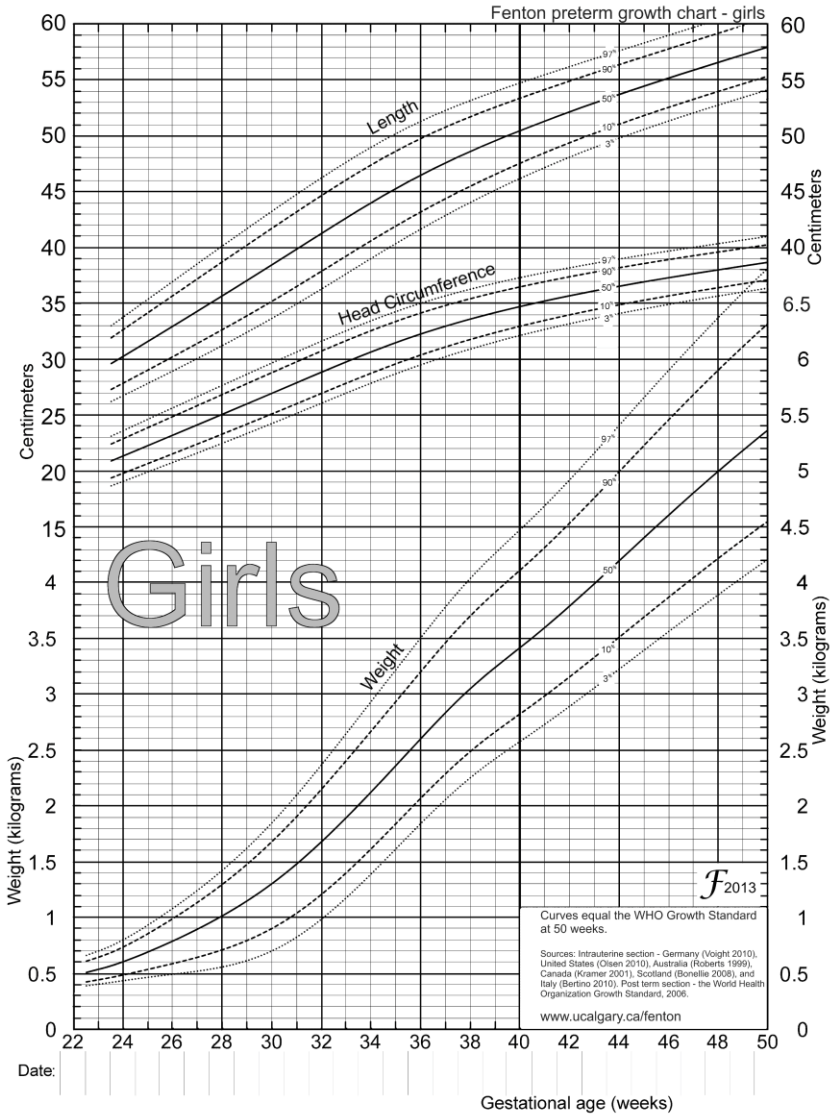


Figure 5: Third, tenth, 50th, 90th, and 97th centiles for weight, length, and head circumference over time in preterm babies
Data were calculated with fractional polynomial powers in a multilevel framework to account for repeated measures. Adjustment for gestational age at birth (27–32 weeks' gestation vs 33–36 weeks' gestation) and interaction between sex and age did not modify the overall fit. Dashed lines represent periods with a small sample size for boys and extrapolated values for girls.



Raccomandazioni nutrizione pretermine II

- The **individualized approach** should be based on growth, quality of growth, personal history and selective nutrient deficiencies. As a rule of thumb, however, infants that are born small (i.e. <1,000 g) and/or that are discharge small (<2,000 g) most certainly will require some kind of post-discharge nutritional intervention.
- To avoid creating nutritional deficits after discharge, preterm infants should at least receive the **nutrient intake of their respective corrected age** until their reach full term (i.e. 39–41 weeks)

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Raccomandazioni nutrizione pretermine III

- The use of a human milk fortifier or formula powder or concentrate in the case of the human milk-fed infant or enriched formulas (i.e. preterm formula, post- discharge formulas) in case of formula feeding may be an effective strategy in addressing early discharge nutrient deficits and poor growth.
- **A post-discharge nutritional intervention is more effective in promoting growth if performed early** (i.e. before expected term). As a rule of thumb, it should be undertaken until indexes of growth are >–2 SD. However, the strategy should be limited to the period of poor feeding or poor growth and should be discontinued as soon as possible after expected term to avoid overfeeding.

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Raccomandazioni nutrizione pretermine IV

- **The recommendations for** DHA, AA and EPA supply for preterm infants should be continued until they reach full term. Thereafter, recommendations for term infants should be applied.
- **Screening for iron deficiency** is warranted. Iron supplementation should be continued after discharge for hospital, at least until 6–12 months of age depending on diet.
- Further studies are needed before routine supplementation with other vitamins or micronutrients is implemented.

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 264–277

Key Points Nutrizionali

- Promuovere allattamento al seno
- Arginare il Postnatal Growth Failure"
- Ottimizzare gli apporti e correggere prontamente eventuali deficit nutrizionali quando vengono identificati
- Evitare una sovra-alimentazione
- Valutare le ricadute sullo sviluppo somatico e neuro-comportamentale

Grazie per l'attenzione