

Reducing PN Risk: From Evidence to Clinical Practice Change

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Conflict of Interest

- I have prior and active consulting relationships with Baxter Healthcare Corporation
- No other conflict of interests



Parenteral Nutrition!



مركز السعودية
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Institute for Safe Medication Practices (ISMP)

ISMP List of High-Alert Medications in Acute Care Settings

High-alert medications are drugs that bear a heightened risk of causing significant patient harm when they are used in error. Although mistakes may or may not be more common with these drugs, the consequences of an error are clearly more devastating to patients. We hope you will use this list to determine which medications require special safeguards to reduce the risk of errors. This may include strategies such as standardizing the ordering, storage, preparation, and administration of these products; improving access to information about these drugs; limiting access to high-alert medications; using auxiliary labels and automated alerts; and employing redundancies such as automated or independent double-checks when necessary. (Note: manual independent double-checks are not always the optimal error-reduction strategy and may not be practical for all of the medications on the list.)

Disease/Category of Medication	Specific Medications
adrenergic agents, IV (e.g., EPINEPHrine, phenylephrine, norepinephrine)	EPINEPHrine, subcutaneous
adrenergic antagonists, IV (e.g., propofol, midazolam, fentanyl)	sugammadex (Baxter), IV
anesthetic agents, general, inhaled and IV (e.g., propofol, sevoflurane)	Insulin U-100 (Novo Nordisk)*
antihypertensives, IV (e.g., labetalol, nitroglycerin)	magnesium sulfate injection
antiemetics, oral, intravenous, and rectal (e.g., ondansetron, granisetron, dolasetron)	metoprolol, oral, non-invasive use
anticoagulants (e.g., warfarin, low molecular weight heparins, IV unfractionated heparin)	nitrofurantoin
● Factor Xa inhibitors (e.g., rivaroxaban, apixiban, edoxaban)	nifedipine, IV
● Direct thrombin inhibitors (e.g., argatroban, bivalirudin, dabigatran etexilate)	nifedipine, oral
● Thrombolytics (e.g., alteplase, reteplase, tenecteplase)	potassium chloride for injection concentrate
● glycoprotein IIb/IIIa inhibitors (e.g., abciximab)	potassium phosphate injection
cardiovascular solutions	penciclovir, IV
chemotherapeutic agents, parenteral and oral	propofol, oral or intravenous
chlorides, hypertonic; 30% or greater	
dilute solutions, potassium and benzalkonium	
optical or intrathecal medications	
hypoglycemics, oral	
intracavitary medications, IV (e.g., dexamethasone)	
insulin, subcutaneous and IV	
isoproterenol forms of drugs (IV, topical aerosolized) and conventional counterparts (e.g., epinephrine & desmepressin)	
opioid analgesic agents, IV (e.g., fentanyl, morphine)	
oxytocin solution agents, oral, for children (e.g., citric acid buffer)	
● IV	
● Intradermal	
● Oral (including liquid concentrates, immediate and sustained-release formulations)	
neuromuscular blocking agents (e.g., succinylcholine, rocuronium, vecuronium)	
parenteral saline preparations	
redoxonate agents, IV	
sterile water for injection, infusion, and irrigation (excluding eye bottles) in containers of 30 mL or more	
sodium chloride for injection, hypertonic, greater than 0.9% concentration	

*All forms of insulin, subcutaneous and IV, are considered a class of high-alert medications. Insulin U-100 has been singled out for special emphasis to bring attention to the need for distinct strategies to prevent the types of errors that occur with this concentrated form of insulin.

Background

Based on error reports submitted to the ISMP National Medication Error Reporting Program, reports of harmful events in the literature, studies that identify the drugs most often involved in harmful events, and input from practitioners and safety experts, ISMP created and periodically updates a list of potential high-alert medications. During May and June 2014, practitioners responded to an ISMP survey designed to identify which medications were most frequently considered high-alert drugs by individuals and organizations. Further, to secure relevance and completeness, the clinical staff at ISMP, members of the ISMP Advisory Board, and safety experts throughout the US were asked to review the potential list. This list of drugs and drug categories reflects the collective thinking of all who provided input.

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INSTITUTE FOR SAFE MEDICATION PRACTICES
www.ismp.org

Frequency and Severity of Harm of Medication Errors Related to the Parenteral Nutrition Process in a Large University Teaching Hospital. **Pharmacotherapy 2009, 29, 966-974**

[Gordon S Sacks](#)¹, [Steve Rough](#), [Kenneth A Kudsk](#)

- **Study objective:** To determine the frequency of medication errors, as well as the severity of harm resulting from these errors, related to the prescription, transcription, preparation, and administration of parenteral nutrition formulations.
- **Design:** Prospective, observational study.
- **Setting:** 471-bed, academic teaching hospital.
- **Patients:** All adult and pediatric inpatients receiving parenteral nutrition between November 1, 2002 and May 31, 2004.

4730 prescriptions of parenteral nutrition

74 errors = 1,56% error rate

1 calculation error

29 copy errors

18 production errors

26 application errors

6 errors were dangerous ones

66% concerning electrolytes

Observational Study of Accuracy in Compounding i.v. Admixtures at Five Hospitals. **Am J Health-Syt. Pharm** 1997, 54,904-912 [E A Flynn¹](#), [R E Pearson](#), [K N Barker](#)

- 1679 preparations – 179 TPN
- Most common failures – additions of components
- Automatic production – 22% error Rate
- Manual production – 37% error rate

Frequency and Severity of Parenteral Nutrition Medication Errors at a Large Children's Hospital After Implementation of Electronic Ordering and Compounding **J Nutr Clin Prac 2016**

Mark MacKay¹, Collin Anderson², Sabrina Boehme², Jared Cash², Jeffery Zobel³

- Error rate before Implementation 1,56%
- Error rate after implementation 0,27%

Evaluation of Microbial Contamination Associated With Different Preparation Methods for Neonatal Intravenous Fat Emulsion Infusion **Am J Health-Syst Pharm 2010**

Catherine M Crill¹, Emily B Hak, Lawrence A Robinson, Richard A Helms

Sterility test of Intralipid

- In original package – n=60 – no contamination
- In syringe – n=90 - 3 contaminations
- 3,3% contamination rate!

Sterility of Pediatric Lipid Emulsions Repackaged by an Automated Compounding Device **JEPN 2010**

Joseph V Ybarra¹, Warren E Rose, Caitlin S Curtis, Gordon S Sacks

Sterility test of Intalipid

- In original package – n=40 – no contamination
- In syringe – n=152 - 12 contaminations
- 7,9% contamination rate!

Association of Intravenous Lipid Emulsion and Coagulase-Negative Staphylococcal Bacteremia in Neonatal Intensive Care Units **NEJM 1990**

[J Freeman¹](#), [D A Goldmann](#), [N E Smith](#), [D G Sidebottom](#), [M F Epstein](#), [R Platt](#)

- 882 neonates
- IV Lipid and risk of coag-negative sepsis – **580% !**

How frequently do you change your Lipid IV delivery system?

- Every 72 hours – 2,43% contamination rate
 - Every 24 hours – 0,86% contamination rate
-
- Matlow A et al Infect Contr Hosp Epid 1999

Instability and Compatability

- Do you know what you mix?
- Is it safe to mix?



versus



Some points to think about....

- Lipid – emulsion stability
- Lipid peroxidation – free radicals
- Vitamins stability – light? Temperature? time?
- Electrolytes stability – Calcium and Phosphate?
- Trace elements stability
- Amino acids stability – AA 1-1,5% - unstable

Malnutrition

- Iatrogenic Malnutrition in Neonatal Intensive Care Units: Urgent Need to Modify Practice **JPEN 2008** [Anuj Grover¹](#), [Minesh Khashu](#), [Anindyalal Mukherjee](#), [Venkatesh Kairamkonda](#)
- Parenteral Nutrition Objectives for Very Low Birth Weight Infants: Results of a National Survey **JPGN 2009** [Alexandre Lapillonne¹](#), [Laure Fellous](#), [M Mokthari](#), [Elsa Kermorvant-Duchemin](#)

- **Conclusions:** In comparison with recent guidelines for parenteral nutrition for VLBW infants, the results indicate that the majority of the departments are familiar with target macronutrient and energy intakes, but the time of introduction and the rate of progression of macronutrients, particularly proteins and lipids, are frequently lower than those defined by the guidelines. The large-scale publication of new nutritional guidelines for the parenteral nutrition of neonates and preterm infants as well as regular, specific training in the parenteral nutrition of preterm infants are needed.

Objectives

1. The need for parenteral nutrition on the NICU is essential
2. The way from individualised parenteral nutrition to the industrialised 3 chamber bag
3. The daily work and practice with the 3-chamber-bag (3CB)



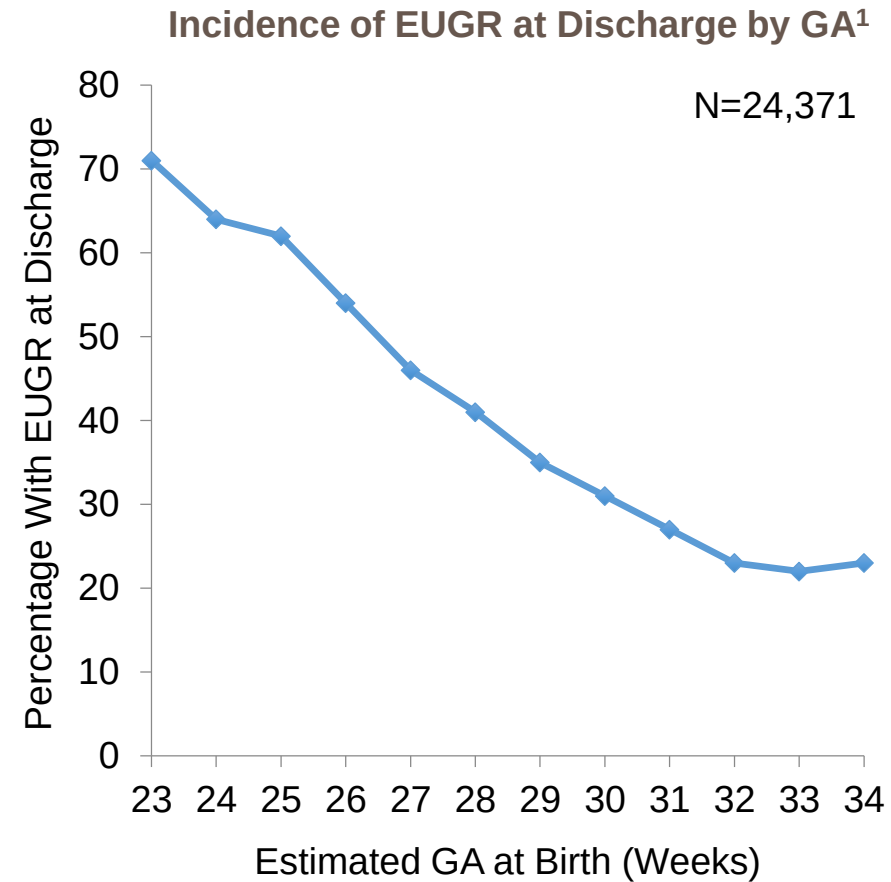
Objective 1

- It is essential to provide parenteral nutrition on the NICU



Extrauterine Growth Restriction is Common in Preterm Infants

- Extrauterine growth restriction (EUGR) has been observed in 28%¹ to 75%² of preterm infants
- EUGR was associated with gestational age (GA) and weight at birth¹

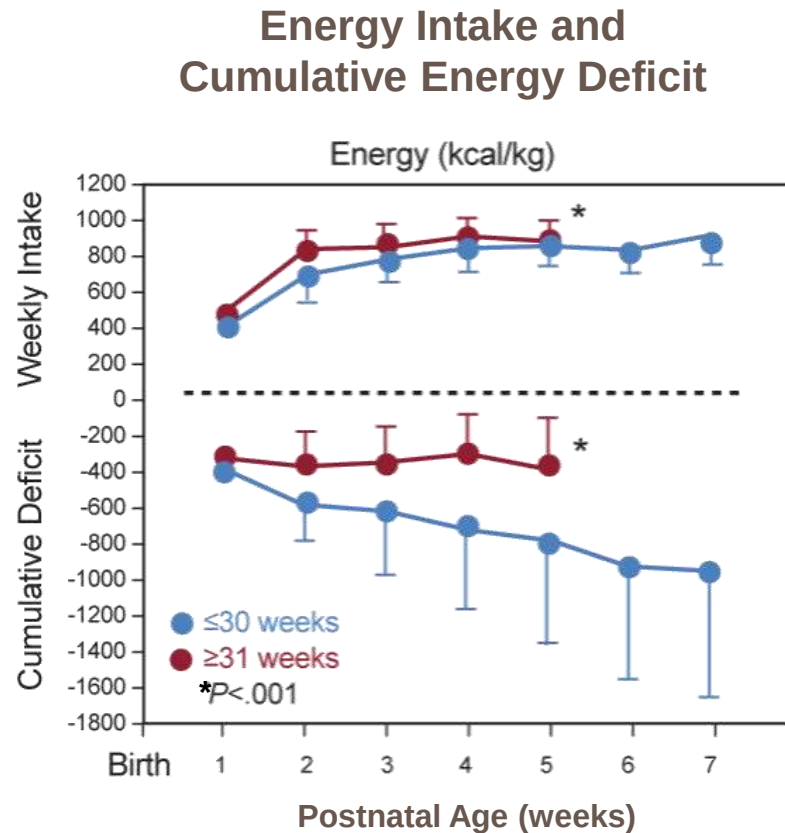


Adapted from Clark RH, et al. *Pediatrics*. 2003;111:986-990.

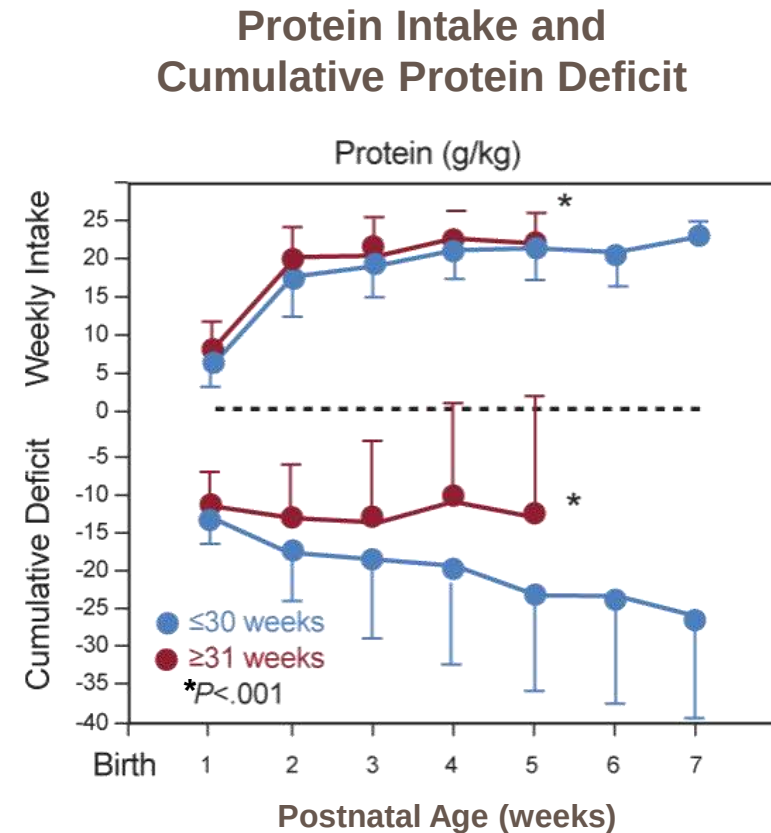
¹Clark RH, et al. *Pediatrics*. 2003;111:986-990.

²Martin CR, et al. *Pediatrics*. 2009;124:649-657.

Failure to Achieve Nutritional Goals Produces Nutritional Deficits



Energy goal = 120 kcal/kg/d



Protein goal = 3 g/kg/d

N=105 preterm infants ≤34 weeks GA and a birth weight ≤1750 g

Increasing Nutrition During the First Week of Life Improves Outcomes

- Every 10 kcal/kg/d increase in energy was associated with a 4.6-point increase in MDI at 18 months

Energy Intake and 18-Month MDI Scores

Variable	b (SE)	P-Value
Birth weight	0.03 (0.01)	.0244
Energy (1 kcal/kg/d)	0.46 (0.18)	.0134

- Every 1 g/kg/d increase in protein was associated with an 8.21-point increase in MDI at 18 months

Protein Intake and 18-Month MDI Scores

Variable	b (SE)	P-Value
Birth weight	0.03 (0.01)	.0227
Protein (1 g/kg/d)	8.21 (3.67)	.0274

N=124 ELBW infants

MDI=mental developmental index; b (SE)=effect size (standard error)

Considerations for Choosing Individual or Standard PN Solutions in the NICU

Why Choose Individualized PN?	• Specific needs for each birth weight group¹ • Nutritional needs vary every day – Adaptation to extrauterine life² – Postnatal maturation and rapid growth velocity² • Unstable metabolic control¹
Why Choose Standardized PN?	• Suitable for most preterm infants¹ • Reduces chances for errors and contamination¹ • Is immediately available¹ • Can be adjusted according to individual needs¹ • Advantages in efficiency, economy, and clinical appropriateness in selected patient populations³

¹Riskin A, et al. *IMAJ*. 2006;8:641-645.

²Fusch C, et al. *German Med Sci*. 2009;7:Chapter 13.

³Kochevar M, et al. *JPEN*. 2007;31:441-448.

Industrially Prepared Standardized PN

- Convenient TPN treatment for most adult patients¹
- Improved patient safety compared with PN compounded in pharmacy or in ward²
- Multichamber bags for adults have an excellent safety profile and are ergonomic¹
- Industrially prepared multichamber bags
 - Good Manufacturing Practice standards³
 - Sterility³
 - Long-term storage without Maillard reactions³

Could industrially prepared multichamber bags also be useful in the NICU?

¹Genton L, et al. *Curr Opin Clin Nutr Metab Care*. 2006;9:149-154.

²Miller SJ. *Nutr Clin Pract*. 2009;24:459-469.

³Muhlebach S, et al. *German Med Sci*. 2009;7:Chapter 10.

Use of Individualized and Standardized PN in the NICU

- Standardized PN found to result in similar biochemical responses and to be more cost-effective than individualized PN¹
- Standardized PN provided more optimized levels of protein^{2,3} and energy³
- Proportion of individualized and standardized solutions in surveyed NICUs depends on level of care⁴

	Individualized PN (%)	Standardized PN (%)
Type III* (n=37)	75.7	24.3
Type II (n=53)	31.7	68.3
All (N=90)	54.6	45.4

*Highest acuity

¹Yeung MY, et al. *J Paediatr Child Health*. 2003;39:613-617.

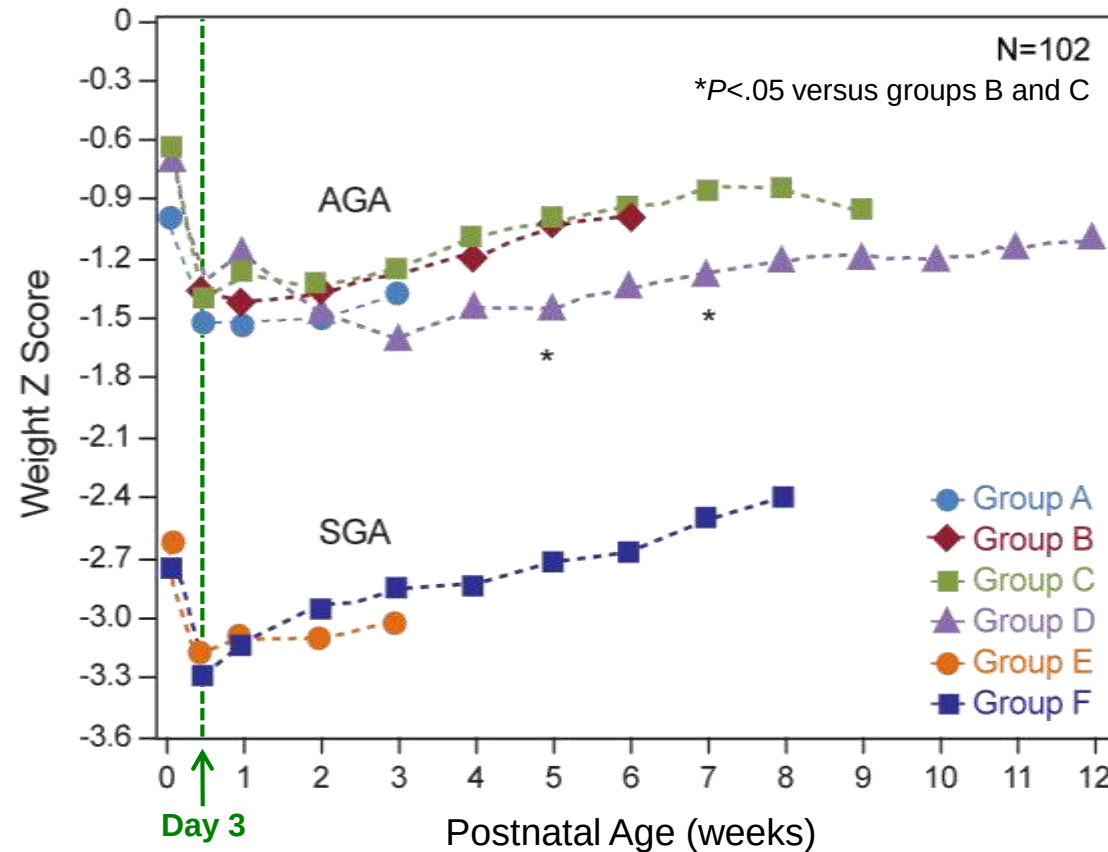
²Lenclen R, et al. *Eur J Pediatr*. 2006;165:512-518.

³Iacobelli S, et al. *Neonatology*. 2010;98:84-90.

⁴Lapillonne A, et al. *Arch Pediatr*. 2009;16:1329-1336.

Standardized PN in the NICU Can Meet Guidelines and Reduce EUGR

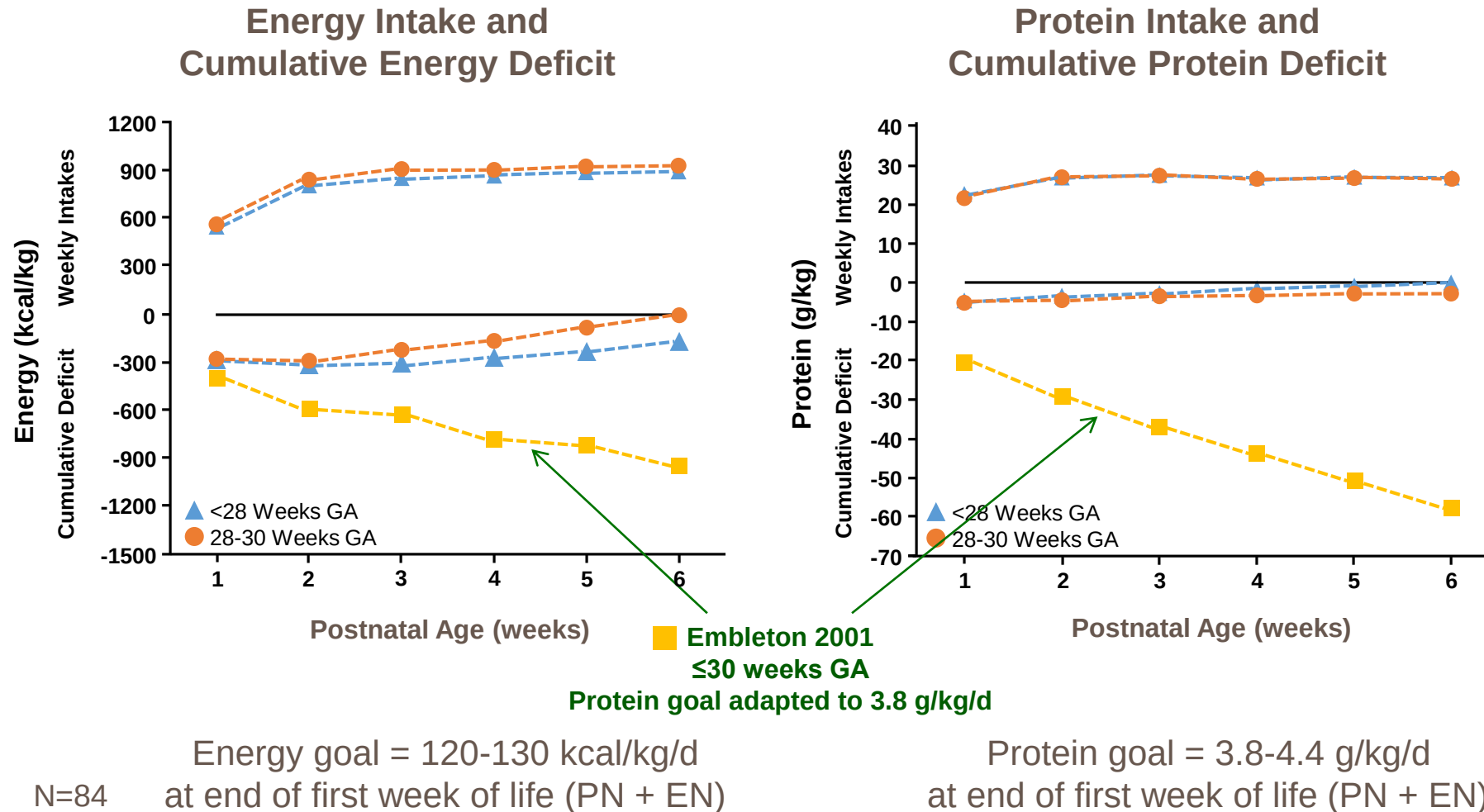
- Mean intakes at 1 week of age in SGA group
 - 3.8 g/kg/d protein, 118 kcal/kg/d
- Mean intakes at 1 week of age in AGA group
 - 3.8 g/kg/d protein, 113 kcal/kg/d
- Little cumulative nutritional deficit compared with earlier studies



$P < .05$ between AGA and SGA infants during the entire study

AGA=appropriate for gestational age; SGA=small for gestational age

Standardized PN in the NICU Can Meet Guidelines and Reduce Nutrition Deficits



Objective 2

- The way from individualised parenteral nutrition to the industrialised 3 chamber bag



+



Questions ???