

Evidence-based discharge nutrition to optimize preterm infant outcomes

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Disclosures:

Role	Sponsors
Consulting	Boehr

Objectives

- Determine the evidence available to direct discharge nutrition for preterm infants.
- I identify the health benefits of discharge nutrition options and how to develop a comprehensive, family-centered plan.

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Consideration 1: Can discharge nutrition be both efficacious and simple?

Preterm infant nutrition at hospital discharge:

Consideration 1: Can it be both efficacious and simple?

Disclosure: I am a part of the problem

Preemie FEED (Facilitating Enteral Education at Discharge) Form

Goals and Recommendations for Infants Born < 32 weeks Gestation
At Discharge, infant is taking _____ ml every _____ hours
At Discharge, mother's 24-hour pumping volume is
<input type="checkbox"/> Adequate (≥ 500 ml) <input type="checkbox"/> Low (<500 ml) <input type="checkbox"/> Mother is no longer pumping

Adapted from University of California San Diego

Preemie FEED (Facilitating Enteral Education at Discharge) Form

Goals and Recommendations for Infants Born < 32 weeks Gestation
At Discharge, infant is taking _____ ml every _____ hours
At Discharge, mother's 24-hour pumping volume is
<input type="checkbox"/> Adequate (≥ 500 ml) <input type="checkbox"/> Low (<500 ml) <input type="checkbox"/> Mother is no longer pumping
Feeding Plan (check applicable plan for this infant):
(Other listed plans are options to consider)
<input type="checkbox"/> Mother's milk with human milk fortifier (HMF) to make 24 kcal/oz. (HMF is available through WIC for first 3 months)
<input type="checkbox"/> Breastfeeding _____ times per day (up to 30 minutes/session) and mother's milk with HMF to make 24 kcal/oz.
<input type="checkbox"/> Mother's milk with postdischarge formula (PDF) powder to make 27 kcal/oz. and 2 PDF 27 bottles per day
<input type="checkbox"/> Breastfeeding _____ times per day (up to 30 minutes/session) and mother's milk with PDF powder to make 27 kcal/oz. and 2 PDF 27 bottles per day
<input type="checkbox"/> Breastfeeding _____ times per day (up to 30 minutes/session) and mother's milk with PDF powder to make 24 kcal/oz. and 2 PDF 24 bottles per day
<input type="checkbox"/> PDF 27 kcal/oz.
<input type="checkbox"/> PDF 24 kcal/oz.
<input type="checkbox"/> Other: _____

84% of US families initiate breastfeeding




Utamaro Gauguin Picasso


Family's Goal for Her Pregnancy Before Interrupted by Preterm Birth: Can We Help Achieve?

Consideration 3: Post-Discharge Nutrition Needs to Optimize


Growth



Health

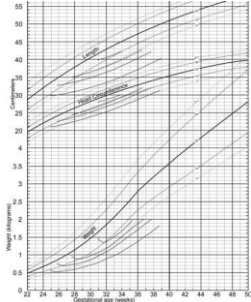


Neurodevelopment

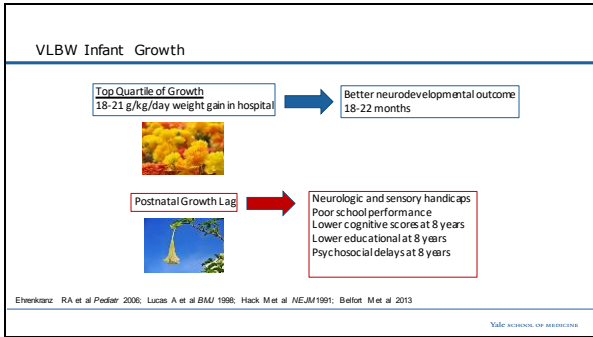


Very Low Birth Weight Preterm Infant Growth Failure

4 cohorts from NICHD NRN 1994-05
 Mean birth weight at:
 -1450 g
 -950 g
 -750 g
 -550 g
 From Ehrenkranz et al *Pediatr* 1999



Fenton et al *BMJ* 2003



Preterm infant in-hospital growth trajectories associated with neurodevelopmental outcome

Growth or body composition parameter at or prior to term age/hospital discharge	Positively associated outcomes
Weight gain	
Change in z score of BS from birth to 36 weeks	Predicted PDI but not MDI at 18 months
Change in z score of BS from birth to discharge	Predicted MDI but not PDI at 2 years
Change in z score of BS from birth to discharge	Predicted normal standard neurologic evaluation at 5 years
Weight gain from birth to hospital discharge	Predicted mental processing speed outcome at 5 years
Linear slope of weight gain from 1 week to term age	Predicted speed of processing at 4 years
Weight growth velocity	Predicted BSID at 18 months
Length at a specific time point	
Length at hospital discharge	Predicted speech measured by BSIDII at 2 years
Length gain	
A smaller difference from expected length z score from birth to hospital discharge	Predicted optimal neurodevelopmental outcome at 2 years
Length gain from birth to hospital discharge	Predicted speed of processing at 4 years
Linear z slope of length gain from 1 week to term age	Did not predict symbolic ability at 4 years
Head circumference gain	Predicted PDI but not MDI at 18 months
Change in z score of BS from birth to discharge	Predicted composite motor and cognitive scores but not language scores at 18 months
Head circumference gain from birth to discharge	Predicted neuromotor and psychomotor assessment at 2 years
Head circumference gain from birth to discharge	Predicted normal standard neurologic evaluation at 5 years
Linear slope of head circumference gain from 1 week to term age	Predicted less risk of impaired mobility at 5 years
Body Mass Index (BMI) gain	Did not predict faster speed of processing at 4 years
Fat free mass gain	Predicted PDI but not MDI at 18 months
Fat free mass gain from birth to hospital discharge	Predicted faster speed of processing at 4 years

Shah 2006; Zoya 2018; Ranz 2009; Pfister 2018; Belfort 2011; Ehrenkranz 2005; Ramel 2012; Simon 2014; Scad 2017; Raghuram 2017

Is Human Milk Intake Associated with Preterm Infant Neurodevelopment?

Optimal Preterm Infant Balance for Neurodevelopment?

Human Milk

Growth

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Significant risk adjustments for infants in the United States

<p><u>Ever Breastfeeding</u></p> <ul style="list-style-type: none"> 11% ↓ Leukemia 12% ↓ Asthma 5-18 years 33% ↓ Otitis media 29% ↓ Crohn's disease 22% ↓ Ulcerative colitis 22% ↓ Childhood & adult obesity 33% ↓ Type 2 diabetes mellitus 64% ↓ Gastrointestinal infections 72% ↓ Lower respiratory infections 19% ↓ infant mortality (U.S.) 51% ↓ Neonatal mortality 21% ↓ Postneonatal mortality (to 38% ↓ if >3 months) 	<p><u>>6 months exclusive breastfeeding compared to <4 months exclusive</u></p> <ul style="list-style-type: none"> 19% ↓ Lower respiratory tract infection 30% ↓ Severe or persistent diarrhea
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AFanti figure

AHRQ, 2007 & AAP 2022

Significant Risk Adjustment for Mother

<p><u>Any or Ever</u></p> <ul style="list-style-type: none"> 22% ↓ Breast cancer 30% ↓ Ovarian cancer 11% ↓ Endometrial cancer 9% ↓ Thyroid Cancer <p><u>Longer vs Shorter</u></p> <ul style="list-style-type: none"> 32% ↓ Type 2 diabetes mellitus 78% ↓ GDM and Type 2 diabetes <p><u>Hypertension</u></p> <ul style="list-style-type: none"> < 6 months, 8% ↓ 6-12 months, 11% ↓ >12 months, 13% ↓ 	<p>Cezanne</p>
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AAP 2022

Upper respiratory infection symptom days in 39 infants born <2 kg

Table 4 Days of Upper Respiratory Infections

Time period	Human milk		Formula		p
	mean ± SD (range), median	mean ± SD (range), median	mean ± SD (range), median	mean ± SD (range), median	
Discharge-1 mo	0.6 ± 1.7 (0-7), 0	0.6 ± 1.7 (0-7), 0	3.5 ± 5 (0-20), 2	3.5 ± 5 (0-20), 2	<0.025
Discharge-3 mo	6.6 ± 7 (0-23), 5	6.6 ± 7 (0-23), 5	14.6 ± 15 (0-46), 9	14.6 ± 15 (0-46), 9	0.06
Discharge-7 mo	17.6 ± 15 (0-53)	17.6 ± 15 (0-53)	38.4 ± 36 (9-96)	38.4 ± 36 (9-96)	<0.025
Discharge-12 mo	42.7 ± 28 (15-96)	42.7 ± 28 (15-96)	54.8 ± 36 (9-121)	54.8 ± 36 (9-121)	ns

Blaymore-Bier et al 2002

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Consideration 4: What is the likelihood of sustaining maternal milk supply?

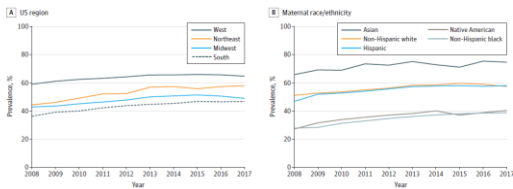
Year	Ever breastfed	At 6 months	At 12 months	Exclusively at 3 months	Exclusively at 6 months
2008	72	44	18	24	12
2020	83	53	34	40	19



Georgia state flower Cherokee Rose

CDC Breastfeeding Report 2020 & 2008

VLBW Infants Receiving Human Milk at Hospital Discharge



Parker M et al 2019

Consideration 5: Options for feeding type



25

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Enriched Formula Studies



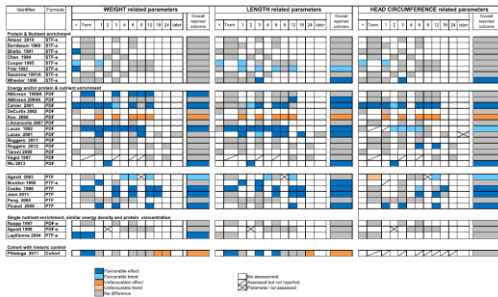
- Post-discharge formula (enriched formula, transitional formula) versus standard term formula
- Preterm formula versus standard term formula

TABLE 1. Macromineral composition of standard, postdischarge and preterm formula.

	Standard formula	Postdischarge formula	Preterm formula
Protein (g/100 mL)	1.4–1.5	1.8–1.9	2.2–2.3
Energy (kcal/100 mL)	67	72–74	80–90
Calcium (mg/100 mL)	35–54	70–80	100–108
Phosphorus (mg/100 kcal)	1.2.2	1.2.5	1.2.8

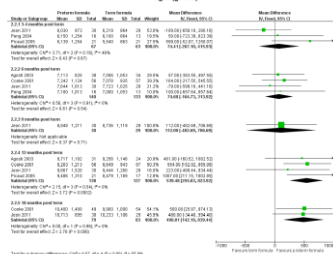
Aggett P et al 2006

Enriched formula not consistently associated with improved growth parameters



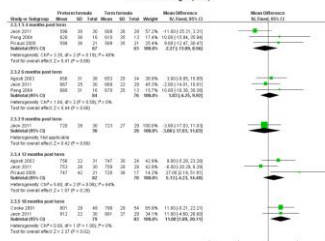
Teller et al 2016

Figure 6. Forest plot of comparison: 2 Preterm formula versus standard term formula, outcome: 2.3 Weight (grams).



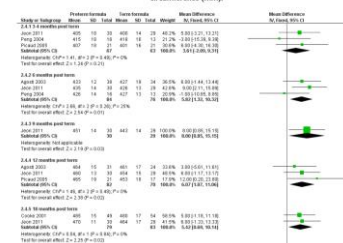
Young et al 2016

Figure 7. Forest plot of comparison: 2 Preterm formula versus standard term formula, outcome: 2.3 Crown-head length (mm).



Young et al 2016

Figure 8. Forest plot of comparison: 2 Preterm formula versus standard term formula, outcome: 2.4 Head circumference (mm).



Young et al 2016

Enriched post-discharge formula not associated with better preterm infant neurodevelopment

Outcomes	Anticipated effects* (95% CI)	absolute	Number of participants (studies)	Quality of the evidence (GRADE)
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Postdischarge formula compared with standard term formula after hospital discharge

Development - Bayley Scales of Infant Development II: Mental Development Index	MD 0.9 higher (3.24 lower to 5.04 higher)		184 (1 RCT)	⊕⊕⊕⊕ High
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Preterm formula compared with standard term formula after hospital discharge

Development - Bayley Scales of Infant Development II: Mental Development Index	MD 1.44 lower (6.22 lower to 3.35 higher)		143 (2 RCTs)	⊕⊕⊕⊕ High
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Young et al 2016



What about mother's milk?

Nutrient-Enrichment vs. No Enrichment of Mother's Milk Post-Hospital Discharge

Study	Population	Intervention	Outcomes reaching statistical significance
O'Connor et al 2008	39 ≥80% mother's milk and 750-1800 g at birth infants	Protein 0.8g/kg Calories 10-15/kg Fortified with HMF 5% of feeds for 12 weeks	Intervention infants at 4-6 months: • Greater visual development Intervention infants at 12 months: • Heavier by 1.2 kg • Longer • Greater bone mineral content Infants born <1250 g at 12 months: • Greater head circumference Intervention infants at 18 months: • No difference in Bayley II scale
Zachariassen et al 2011	320 infants born 24-32 weeks PMA receiving breastmilk at discharge	Protein 1.37 g/day Calories 17/day For 4 months	At 12 months: • No difference in growth
De Cunha et al 2016	53 exclusively breastfed VLBW infants	Protein 0.5g/day Calories 20/day For 4-6 months	At 12 months: • No difference in Bayley II scale • No difference in developmental delay

Nutrient concentrations from Arslanoglu et al 2019

ESPGHAN 2006 "Feeding Preterm Infants After Hospital Discharge"

- Monitor closely
- Measure weight, length, head circumference to identify infants with poor growth
- AGA infants should be breast-fed when possible
- When formula-fed, feed regular infant formula
- If SGA at discharge, supplement with human milk fortifier or enriched formula
 - Until at least 40 weeks'
 - Potentially until 52 weeks'

Focus on growth: To maintain growth velocity 25-35 g/day (term age to 3 months)

- To maintain growth at a specific z-score or percentile
- To achieve growth at a specific z-score (catch-up growth)

By 40-52 weeks postmenstrual age

- Preterm infants without significant brain, lung, cardiac disease develop the ability to "feed" to grow (at least calories).
- Titrates volume to obtain calories required to gain weight

Likely plays a role in the mixed results from post-discharge nutrition RCTs

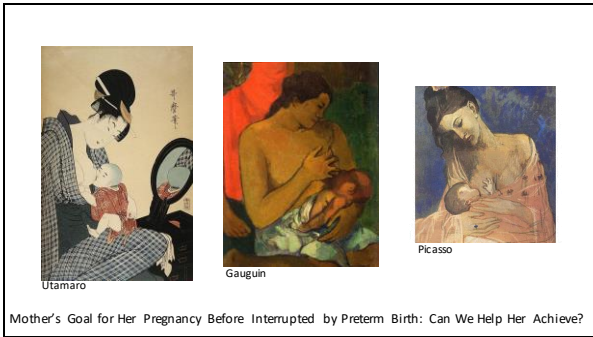
Still do not know how to have just the right amount of "baby fat"

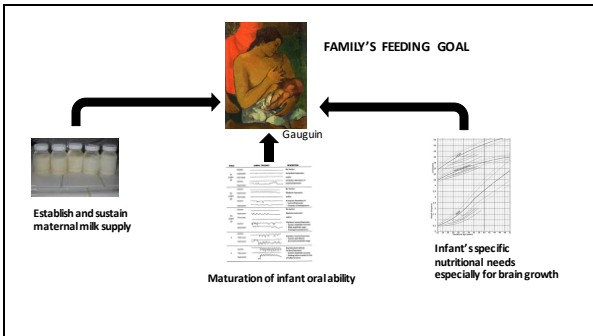
POGO Study
Patterns of Growth and Outcomes
PIs: Sarah Taylor and Cami Martin

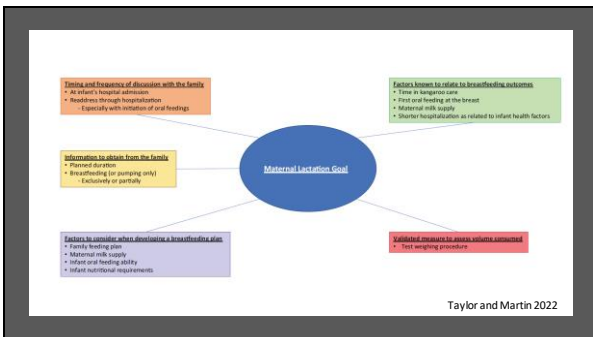
Body composition patterns
Neurodevelopment at 2 years corrected age

Growth pattern phenotypes
Very preterm infant

- From birth to term age
- From birth to 1-year corrected age







Preterm infant follow-up of growth and nutrition

Clinic support

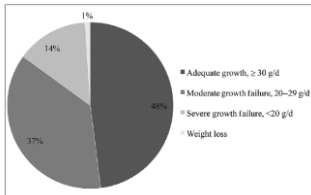
Developed Nutrition NICU Graduate Clinic

Table 1. Patient Demographics.

Characteristic	n (mean or range)
Number of patients	227
Mean gestational age (range)	30.12 wk (23-40)
Male, n (%)	103 (45.4)
Racial group, n (%)	
African American	120 (52.9)
Caucasian	89 (39.2)
Hispanic	12 (5.3)
Mean BW (range)	1.31 kg (0.45-3.75)
BW classification, n (%)	
LBW < 2.5 kg	215 (94.7)
Very LBW < 1.5 kg	167 (73.6)
Extremely LBW < 1 kg	75 (33)
Mean discharge gestational age	40.75 wk (33.4-45.1)

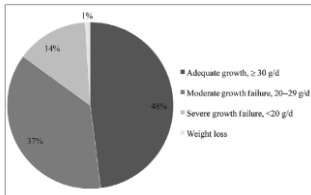
Zhang et al 2020

Growth trajectory from hospital discharge to first clinic visit



Zhang et al 2020

Growth trajectory from hospital discharge to first clinic visit



Interventions at first visit
In 92% of infants


- 61% required nutrition regimen change
- Increase calories in 26%
- Decrease calories in 26%

18.5% of families were mixing improperly

Zhang et al 2020

Clinical Application of Preterm Infant Discharge Nutrition Evidence

- Know family's feeding goal
- Protect maternal milk intake
- Monitor growth
- Target positive growth trajectory "Feed to Grow"
- Consider the infant's other needs based on disease, growth pattern, and previous nutrition
- Simplify when able (for parents and pediatricians)



<https://www.feedtoGrow.org>
af@usa.gov

Yale School of Medicine



The Yale Neonatal NOURISH Team
Nutrition Outcomes Research In Sustaining Mother and Infant Health

Investigators: Caty Buck, Veronika Shabanova, Angela Montgomery
 Team: Ruthfirst Ayandé, Christine Henry, Tessa Kehoe, Terri Motraghi, Taryn Donovan, Dina Pasareba, James Lawrence, Ellery Neiderer, Ambika Bhatnager, Justyna Breuley, Gabi Wiggill, Inumidun Oyebode

Collaborators:
 Lisa Koonikova and Bummy Olatoye (Yale)
 Kimberly Doughty (Fairfield)
 Camilla Morin (Cornell), Kristin Santos (BIDMC)
 Cynthia Bianco (UTHCT), Kara Calkins (UGA), Daniel Robinson (Northwestern)
 Sharon Donovan (Illinois) and Robert Chaplin (Texas A&M)
 Carl Wagner, Bruce Hollis, Jimmy Roberts (MUSC)
 Jennifer Cavassese, Amy Hale, Joe Kim (PASC Society)
 Career development mentees: Ariel Salas (UAB) and Kate Orsini (Children's National)




5th Annual Richard A Ehrenkrantz Symposium
 June 4, 2024
 Yale University
 New Haven, CT

Yale Pediatrics 100 Years in 2022!
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