

Evidence based lactation practices in the NICU: What, when, and why?


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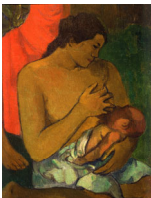
Disclosures

Relationships	Commercial Interests
Serve as site principal investigator for industry-sponsored research at Yale University	Ferring Pharmaceuticals Pfizer Prolacta Bioscience

Lactation in the NICU



Maternal milk for infant



Achieve family's feeding goal

To determine the lactation practices to best initiate and sustain maternal milk, to optimize infant outcomes, and to support the transition to breastfeeding.

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Disease related to preterm birth

**Necrotizing enterocolitis**

- Devastating gastrointestinal inflammatory disease
- 5-10% VLBW infants

**Late-onset sepsis**

- 20% VLBW infants

**Retinopathy of prematurity**

- 50% of VLBW infants
- Severe ROP in 5-6% VLBW infants
- May lead to blindness

**Bronchopulmonary dysplasia**

- Lung disease of prematurity
- 25-30% VLBW infants

ALL REDUCED WITH VLBW INFANT INTAKE of MATERNAL MILK

**Necrotizing enterocolitis**

**Late-onset sepsis**

**Retinopathy of prematurity**

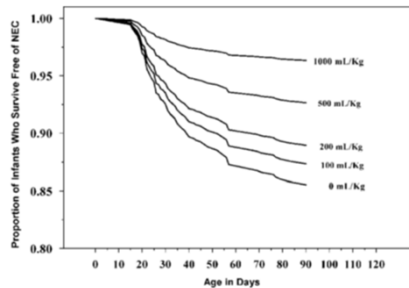
- Severe ROP

**Bronchopulmonary dysplasia**

ALL REDUCED WITH VLBW INFANT INTAKE of MATERNAL MILK

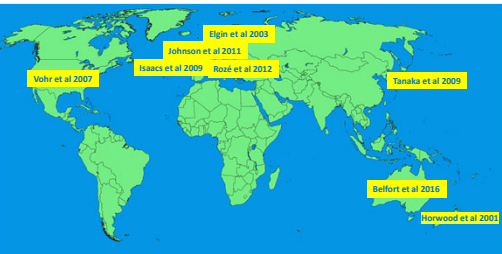
*I respect that not all parents who feed at the chest identify as mother or as breastfeeding. Through this talk, I will use the term maternal milk which should also be considered parent milk. The term breastfeeding is used in the description of some studies presented.*

Extremely Preterm Infant NEC and Survival Improve Proportional to Maternal Milk Intake



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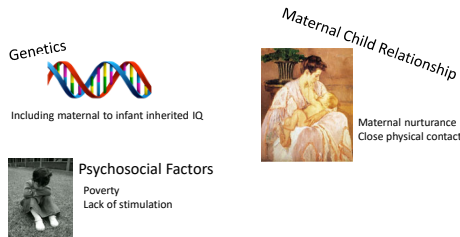
Maternal milk studies with neurodevelopmental outcomes measured at > 2 years of age



Mother's Milk and Preterm Infant Neurodevelopment				
Study	Population	Human Milk Dose	Age at evaluation	Outcome
Vohr et al 2007 (n=773)	ELBW	Breast milk for hospitalization	30 months	For every 10 ml/kg/day increase in breast milk, MDI increased by 0.58, PDI by 0.56, and total behavior percentile score by 0.99 by BSID-II
Tanaka et al 2008 (n=18)	VLBW	More than 80% breast milk feeds in first month	5 years	Breastfed group had significantly higher sequential processing on KABC, Day-Night Test, KRISP, Motor Planning Test scores
Røed et al 2012 (n=1462)	Born 22-32 weeks PMA, EPAPAGE Cohort	Breastfeeding at time of discharge	5 years	Breastfeeding at discharge associated with a 35% lower risk for suboptimal neurodevelopment by KABC
Delfort et al 2016 (n=180)	Born < 30 weeks/ <1250 g	First 28 days with >50% breast milk	7 years	Predominant breast milk feeding in first 28 days significantly associated with better IQ by WASI, mathematics by WRAT, working memory, and motor function tests by MABC
Horwood et al 2001 (n=260)	VLBW	Duration of breast milk feeding	7-8 years	Increasing duration of breast milk feeding significantly associated with increased verbal & performance IQ by WISC-R. Breastfed for > 8 months adjusted mean verbal IQ 6 points higher than those with no breast milk.
Igin et al 2003 (n=130)	LBW	>30% breast milk in neonatal ward	11 years	Lack of breast milk associated with a significant mean reduction in IQ by WISC-R but this was no longer significant when adjusted for parental education
Johnson et al 2011 (n=307)	Born <26 weeks PMA	Received breast milk in NICU	11 years	Breast milk in NICU significantly associated with higher reading scores
Isaacs et al 2010 (n=59)	Born <30 weeks, PMA	% maternal milk received for hospitalization	Adolescence	Milk dose significantly positively associated with Verbal IQ (specifically in boys) and performance IQ (specifically in girls) in 2009. In 2009, mean verbal IQ was 100.0 (SD 14.0) and mean performance IQ was 99.0 (SD 14.0).

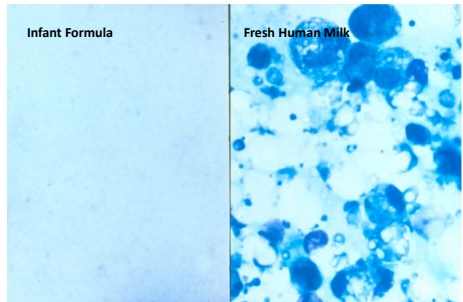
ISI: Wechsler Adult Intelligence Scale Third Edition; WASI: Wechsler Abbreviated Scale of Intelligence; WRAT: Wide Range Achievement Test; MABC: Movement Assessment Battery for Children

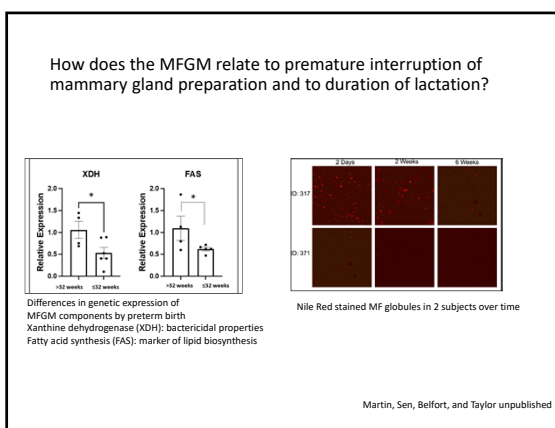
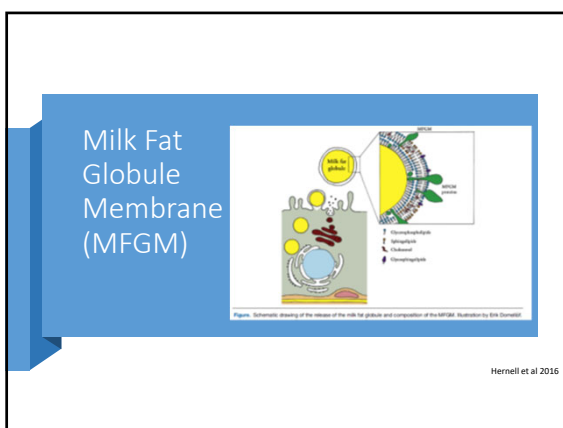
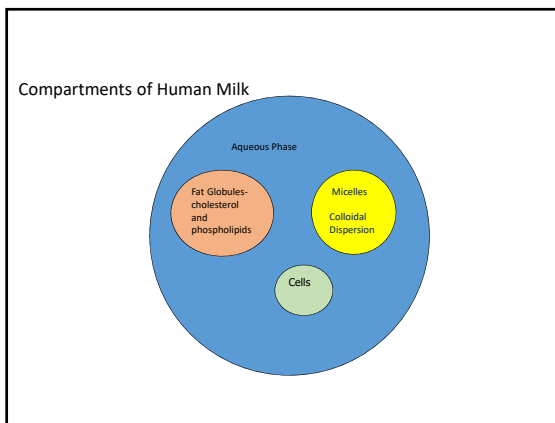
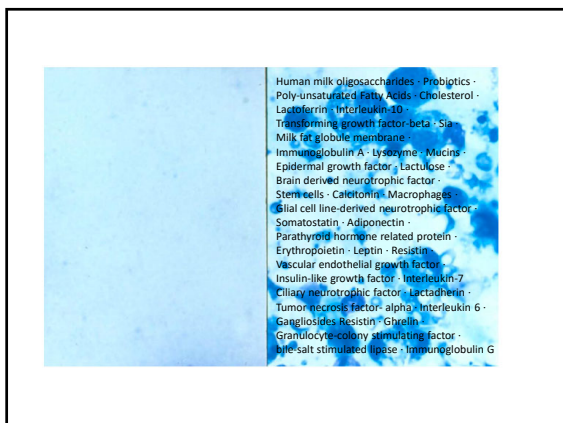
Mother's Milk and Neurodevelopment have a complex relationship with contributions from



Luby et al 2016

Why?





### Multifunctional Milk Components

**Lactoferrin**

- Chelates free iron potentially for iron absorption
- Removes unbound iron which bacteria need
- Stimulates macrophage phagocytosis
- Inhibits HIV, CMV, and herpes virus
- Partial digestion
  - Lactoferricin B
    - Broad antibacterial activity

Gomez HF et al 2002 & 2003; Ochoa T et al 2003; Lima MF & Kierszenbaum F 1987; Hartmann MC et al 1995; Hasagawa K et al 1994

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### Human Milk and Immune Cells

- Initially, 1 billion leukocytes/ Liter
  - Polymorphonuclear cells, macrophages
  - Hypofunctional activity
- By 6 months, epithelial cells predominate

Ruescher ES 2001

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## Maturation of the intestinal wall

- Decreased intestinal permeability
  - Human milk dose-dependent
- Stem cells in human milk
- Epithelial cell maturation and differentiation
  - Numerous growth factors
- Apoptosis
  - Lactalbumin and HAMLET

Taylor SN et al 2009; Cregan M et al 2008; Koldovsky O 1995; Gustafsson L et al 2005

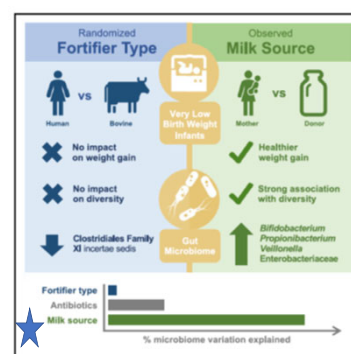
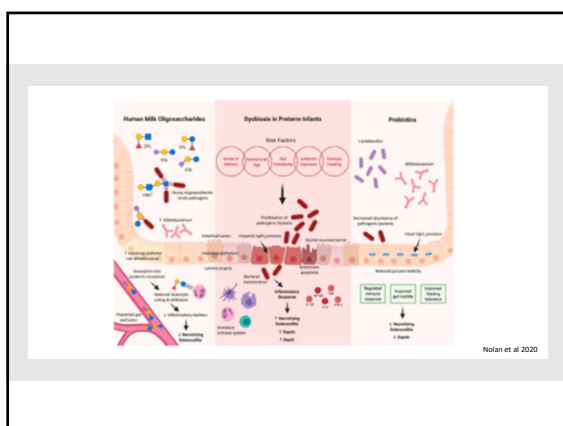
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## Human Milk Oligosaccharides

- Do you remember bifidus factor? (Gyorgy et al 1954)
- 3<sup>rd</sup> most abundant component (only lactose and lipids are greater)
- Non-digestible
- 3 primary roles
  - Establish infant microbiome
  - Protect against infection
  - Protect against inflammation

Taylor 2020

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## Pasteurized donor human milk decreases NEC

Risk	Risk with formula	Number of participants (studies)	Certainty of the evidence (GRADE)
	Relative effect (95% Confidence Interval)		
Formula instead of PDHM increases risk of NEC	1.87 (1.23 to 2.85)	1675 (9 studies)	moderate

But is not equivalent to maternal milk  
Need further research

Quigley et al 2019

## Maternal milk to NICU patients



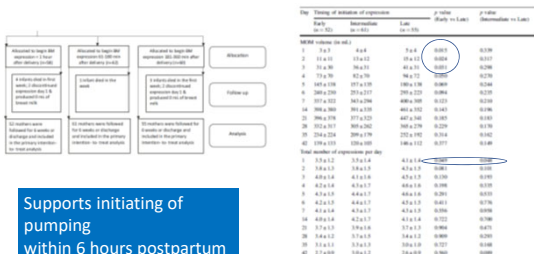
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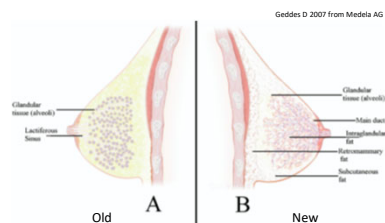
### Timing of milk expression following delivery in mothers delivering preterm very low birth weight infants: a randomized trial

Leslie A. Parker<sup>1</sup> · Sandra Sullivan<sup>1</sup> · Charlene Kruger<sup>1</sup> · Martina Mueller<sup>2</sup>

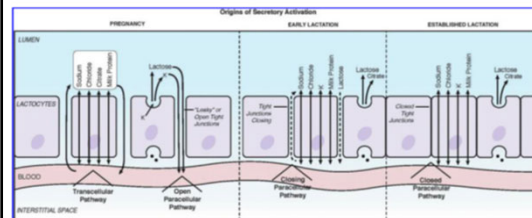
2020



## New Age of Breast Anatomy



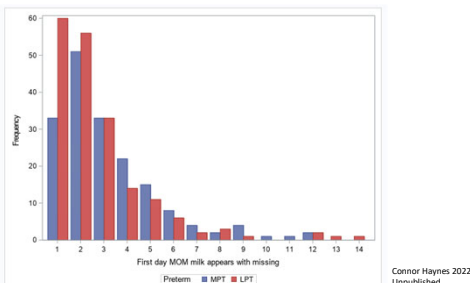
## Secretory Activation (Formerly Lactogenesis II)



Medina Poeliniz et al 2020

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## First day of maternal milk feeds in late and moderate preterm infants

Connor Haynes 2022  
Unpublished

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## The Physiology of Lactation: Minimal Knowledge

## Delayed or inhibited secretory activation

- Preterm delivery
- Antenatal steroids 3-9 days prior to delivery
- Post-cesarean section
- Insulin-dependent diabetes mellitus (potentially not in GDM)
- Maternal obesity
- Polycystic ovary syndrome

Henderson JJ et al. 2008; Hartmann P &amp; Cogan M 2001; Rasmussen KM et al. 2004

How prevalent is no secretory activation?

## The Physiology of Lactation: Minimal Knowledge

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Perceived insufficient milk supply versus  
Actual insufficient milk supply

Chronic Lactation Insufficiency Is a Public Health Issue:  
Commentary on "We Need Patient-Centered Research  
in Breastfeeding Medicine" by Stuebe.  
Breastfeed Med 2021;16:349-350.

Helen Sherris<sup>1,2</sup>, Laurel Wilson<sup>1,3</sup>, Haniy Dabbous<sup>1,4</sup>, L. Elizabeth Moore<sup>1</sup>,  
Susanne Finckh Scott<sup>5</sup> and Helen Baker<sup>1,2</sup>

## To Establish Maternal Milk Supply

- Pump early and often
  - By 6 hours
  - 6-8 times per day (at least 5 times)
- Skin-to-skin time
- Ensure secretory activation occurs
- Problem solving with lactation specialists
  - Comfort
    - Including proper phalange fit
  - Hospital grade pump

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### First, Establish and Sustain Mother's Milk Supply

- To sustain to >40 weeks gestation
  - Express by 6-hours post-delivery
  - Perform kangaroo care
  - Express milk  $\geq 5$  times per day
- To have adequate supply at discharge
  - Double pumping
  - 500 ml/day by day 10
  - Higher score for breast pump comfort
  - NICU environment
    - Staffing, nurse level of education, nurse support of breastfeeding

Furman L et al 2002; Hallowell SG et al 2016; Casavant SG et al 2015; Fewtrell MS et al 2016

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### Kangaroo Mother Care

Table 2: Association Between Minutes of Skin-to-Skin/Day and Breastfeeding (Exclusive and Partial) in Very Preterm (VPT, n = 103) and Preterm (PT, n = 197) Dyads

Post-term	1 Month		2 Months		3 Months		4 Months		5 Months		6 Months	
	n	Mean $\pm$ SD	n	Mean $\pm$ SD	n	Mean $\pm$ SD	n	Mean $\pm$ SD	n	Mean $\pm$ SD	n	Mean $\pm$ SD
<32 weeks												
VPT not bf	72	139 $\pm$ 84*	69	143 $\pm$ 84*	61	141 $\pm$ 87	54	144 $\pm$ 85	47	151 $\pm$ 89*	42	148 $\pm$ 89*
VPT not bf	26	108 $\pm$ 59	30	109 $\pm$ 62	37	114 $\pm$ 91	45	116 $\pm$ 88	52	112 $\pm$ 88	55	116 $\pm$ 75
PT not bf	169	126 $\pm$ 104	157	127 $\pm$ 105	146	125 $\pm$ 102	137	126 $\pm$ 103	122	128 $\pm$ 98	112	124 $\pm$ 98
PT not bf	26	127 $\pm$ 98	38	123 $\pm$ 95	46	133 $\pm$ 108	56	131 $\pm$ 109	72	129 $\pm$ 110	62	131 $\pm$ 110

Note: VPT = very preterm; PT = preterm; bf = breastfeeding; SD = standard deviation.

\*A statistical difference between groups, p-value < .05.

Flack et al 2011

### RCT of later preterm (32-36) weeks, intervention group (unlimited kangaroo care)

- Longer duration of breastfeeding (5 versus 2 months)
- Longer exclusive breastfeeding

Hale-Brooks & Anderson 2008

### NICU Environment Supportive of Maternal Milk Volume

- Staffing
  - Adequately staffed so that RNs/lactation consultants can provide lactation care
- Nurse level of education
  - At least basic skills in pumping techniques
- Nurse support of breastfeeding
  - Culture

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### Every Drop Counts!

brought to you by the Lactation QI team and TrackMyMilk

**In the first days, volume counts a lot.** Every drop counts, and every drop of expressed milk should be labeled, timed, and brought to the bedside for feeding or oral care. Check for an OII order!

With regular pumping (at least 6 times every 24 hours, with no interval > than 5 hours) milk volume should increase slowly over time, from 100 mL on day 4 to 500 mL on day 10, and more!

Keep track of expressed milk using a pumping log. The Lactation feature in MyChart app puts expressed milk data into the hospital computer system!

Aim for 500 mL a day by day 10. Maintaining this volume >500 mL/day will ensure the supply is maintained during the hospitalization and as the infant grows.

By 2-3 weeks, expect about an ounce an hour. **Keep about 100 mL a full milk supply for one week.** Until the baby grows into this much milk, it is a risk to stop pumping. Milk can be safely frozen for 6 months to a year, depending on the freezer.

### Why does cessation occur?

- Return to work
- Maternal wellbeing/mental health
- Other obligations
- Biology?

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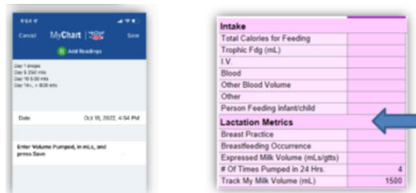
	Maternal Mental Health History			
	Depression and anxiety	Depression only	Anxiety only	Neither
Number of infants (% of total n=156)	n=14 (9%)	n=11 (7%)	n=22 (14%)	n=109 (70%)
GA at birth, median (IQR)	29.3 weeks (26.6 - 30.7wks)	28.7 weeks (25.7 - 28.9wks)	30.1 weeks (28.1 - 31.7wks)	28.7 weeks (26.3 - 30.7wks)
Birthweight, median (IQR)	1145g (760 - 1430g)	1030g (680 - 1230g)	1245g (1010 - 1600g)	1110g (860 - 1470g)
Length of NICU stay, median (IQR)	80 days (48 - 108 days)	85 days (30 - 162 days)	65 days (42 - 69 days)	61 days (42 - 98 days)
Singleton, n (%)	9 (64%)	9 (82%)	20 (91%)	93 (76%)
Receiving any mother's milk at discharge, n (%)	1 (7%)	3 (27%)	10 (45%)	40 (37%)
Number of ED visits in 1 <sup>st</sup> year post-discharge, mean (range)	0.4 (0-2)	2.1 (0-15)	0.8 (0-4)	0.7 (0-7)
Number of rehospitalizations in 1 <sup>st</sup> year post-discharge, mean (range)	0.1 (0-1)	2.2 (0-10)	0.5 (0-7)	0.4 (0-5)
Percent of completed subspecialty appointments completed in 1 <sup>st</sup> year post-discharge, median (IQR)	47% (36 - 68%)	33% (20 - 53%)	43% (35 - 50%)	60% (43 - 69%)

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Dioneda et al 2023 unpublished

## Milk Volume Tracking

Mother's 24 Hour Pumped Milk Volume is a Vital Sign!



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## Oral Immune Therapy

TABLE 1 Recommended Colostrum as Oral Immune Therapy Protocol	
Procedure	Key Points
1. Obtain fresh or refrigerated colostrum from mother	1. Give mother small breast milk collection containers and teach mothers hand expression to increase volumes of colostrum.
2. Verify the colostrum identifier matches infant's identifier	2. Label colostrum in the order it was pumped.
3. Wash hands and don gloves	3. Use fresh colostrum whenever possible.
4. Separate a sterile cotton swab with colostrum (approximately 0.2 mL)	4. HMBANA recommends to refrigerate only for 48-66 h for hospitalized infants***
5. Gently press the tongue, gums, and inner cheek with colostrum	5. If < 0.2 mL colostrum is available, can mix with small amount of sterile water
6. Repeat every 3-6 h until when enteral feeding is begun via gavage tube***	6. Document colostrum as oral immune therapy when administered.
	7. Recommend that parents do this when possible.

Abbreviation: HMBANA, Human Milk Banking Association of North America.  
 Synthesized from recommendations of Meier et al, 2010<sup>10</sup> and Spatz and Edwards, 2008.<sup>10</sup>

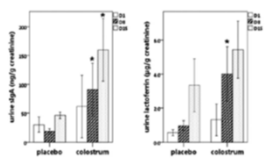
From Gephart S & Weller M *Advances Neon Care* 2014

From Lee J et al *Pediatrics* 2015

## Oral Immune Therapy Evidence

- Full enteral feeds sooner & decreased PN days
- Days to full enteral feeds were reduced with MD of -2.58 days (95% CI -4.01 to -1.14; six studies, 335 infants;  $P = 0.0004$ ;  $I^2 = 28\%$ ; very low-quality evidence).
- Safe

Nasir Ali et al 2018 Cochrane Review



Lee J et al *Pediatrics* 2015

## Take home points

- Maternal milk is full of bioactives that are important for preterm infant outcomes
- To initiate milk production
  - Pump by 6 hours
  - Pump often (every 6-8 hours and at least every 5)
  - Optimize pump efficiency and pumping comfort
  - Skin-to-skin
  - Unsure if certain maternal diseases relate to lactation insufficiency
- To sustain
  - 500 mL 24-hour volume by day 10
  - Skin-to-skin
  - Pump at least 5 times per day and at least every 7 hours
- NICU culture, staff knowledge, and staffing model impact sustaining maternal milk volume
- Need to learn more about biologic lactation insufficiency, role of maternal mental health wellbeing, and how to improve efficiency of milk production → empower families

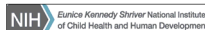
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**The Yale Neonatal NOURISH Team**  
**Nutrition Outcomes Research In Sustaining Mother and Infant Health**

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