Novel strategies to increase use of mother’s own milk in the NICU

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Professor of Pediatrics
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• I have no real or apparent conflicts of interest related to the content of this presentation.

• The following terms are used throughout this presentation for simplicity: mother, woman/women, mother's own milk, breastmilk, and breastfeeding for anatomic clarity and brevity in this lecture.

• All concepts discussed here are applicable to transgender, nonbinary and non-birthing people who lactate and/or chest feed.

• The term "mother's own milk" is intended to distinguish milk provided by a parent from donor human milk, knowing that not all human milk may come from a parent who identifies as a mother.

• We acknowledge that it is important to utilize a patient's preferred pronouns and other preferred terminology when addressing patients directly regarding their lactation experience.
• To articulate the benefits of mother’s own milk feedings for infants and their mothers
• To review the variation in mother’s own milk and in US NICUs
• To identify factors mediating racial/ethnic disparities in mother’s own milk feedings
• To evaluate potential strategies to increase mother’s own milk feedings
AAP recommends maternal human milk as optimal nutrition for VLBW infants

• “AAP supports continued breastfeeding, along with appropriate complementary foods introduced at about 6 months, as long as mutually desired by mother and child for 2 years or beyond.”

• The potent benefits of human milk are such that all preterm infants should receive human milk. Mother’s own milk, fresh or frozen, should be the primary diet, and it should be fortified appropriately for the infant born weighing less than 1.5 kg.”

• “Although a mother’s own milk is always preferred, donor human milk may be used for high-risk infants when the mother’s own milk is not available or the mother cannot provide milk. Priority should be given to providing donor human milk to infants <1500g birth weight.””
Mother's Own Milk (MOM) Components

- **Nutrients:**
  - **Protein:**
    - Whey:Casein 70:30
    - majority α-lactalbumin
  - **Lipids:**
    - milk fat globule
    - fatty acids
    - Bile-salt–stimulated lipase
    - Arachadonic and docosahexaenoic acid
  - **Carbohydrates:**
    - Lactose
    - Oligosaccharides
    - Lower concentrations of Ca and Phos

- **Anti-infective**
  - Secretory IgA
  - Oligosaccharides
  - Lactoferrin
  - Lysozyme
  - Lymphocytes
  - Transforming growth factor-β

- **Impact on intestinal microbiota (synbiotic)**
  - Human milk Oligosaccharides - prebiotic
  - Lactic acid bacteria – probiotic

- **Immunomodulatory**
  - Soluble CD14
  - Soluble Toll like receptor 2
  - Transforming growth factor-β
  - platelet-activating factor acetylhydrolase
  - IL 10

- **Antioxidant**
  - Inositol
  - vitamin E
  - beta carotene
  - Lactoferrin

- **Tissue maturation / development**
  - long-chain polyunsaturated fatty acids
  - Epidermal growth factor
  - Stem cells
  - Milk fat globule membrane

NOURISH
Essential and nonessential fatty acids and amino acids
Micronutrients (minerals and vitamins)

COMMUNICATE
Stem cells
miRNA / exosomes
Flavor compounds

PROTECT
Antibodies
Urea

Some fatty acids
Some amino acids
Enzymes
Proteins/Peptides
Milk fat globule
Some fatty acids
Some amino acids
Microbes
Chemokines/cytokines
Hormones
Growth factors
Immune cells
Oligosaccharides
Glycans

Vitamin A
Vitamin C
Vitamin D
Vitamin E
Vitamin K
Selenium
Zinc
**SPECIFIC & PERSONALIZED:**

- Enteromammary pathway - specific antibodies to pathogens secreted into MOM
- MOM microbiome is highly specific to the breastfeeding dyad - programming function for the infant gut microbiota
- Synergistic anti-infective interactions between MOM and enzymes in the infant’s stomach and saliva

Lemay et al. PLoS One 2013
Demers-Mathieu et al. Nutrients 2018
Patel AL et al. Pediatric Research 2021
Longitudinal Outcomes of Very Low Birthweight Infants Exposed to Mothers’ Own Milk

- 691 VLBW infants born Feb 2008 - Dec 2012
- 459 enrolled
- 29 ineligible after enrollment
  - 21 congenital anomalies
  - 5 transferred before DOL14
  - 3 other
- 232 ineligible or declined
  - 206 ineligible
  - 23 declined by parent
  - 3 declined by physician
- 21 congenital anomalies
- 5 transferred before DOL14
- 3 other

Summary Statistics:

- WIC eligible – low SES: 74%
- Married: 38%
- Completed 4-yr college: 19%
- Non-Hispanic Black: 51%
- Non-Hispanic White/Asian: 22%
- Hispanic: 27%
- Multiple gestation: 15%
- Previously breastfed: 28%
- Initial goal of any MOM: 91%
- Mean daily pumping #: 4.5 times/day
- Infant gestational age: 28 weeks

NR010009; PI: Paula Meier, PhD
691 infants
BW ≤ 1250g
2007-2011

Every increase of 10 mL/kg/day of human milk intake at 4 weeks predicted higher Bayley scores:
Cognitive (0.29)
Language (0.34)
Motor (0.24)
France and Australia: MOM and ND Outcomes

Epipage cohort:
1462 preterm infants 22-32wk
Born 1997
5 yr outcomes

Australian cohort:
180 very preterm infants at age 7 years
BW <1250g
Born 2001-2003

Found positive associations of MOM intake with size of the deep nuclear gray matter and hippocampus at term equivalent age

MOM intake (for every day that MOM>50% intake in first 28 days) associated with neurodevelopmental outcomes:

- Full scale IQ +0.5
- Verbal IQ +0.4
- Performance IQ +0.5
- Math computation +0.5
- Working memory +0.5
- Motor function +0.1

Rozé et al., BMJ Open 2012
Belfort et al. J Peds 2016
Early breast milk exposure modifies brain connectivity in preterm infants


- Neonatal breast milk exposure and brain MRI at term equivalent age
- 47 preterm infants
- mean gestational age 29.43 weeks, range 23.28–33.0
- Fractional anisotropy-weighted connectivity was increased (p=.039) in infants who received >=75% of exclusive breast milk feeds (57 days median) compared to <75% of exclusive breast milk feeds (19 days median)
- The connections involved included intra- and inter- hemispheric fronto-parietal and limbic system structures
- Dose-dependent relationship with breast milk exposure (adjusted for gestational age at birth, chorioamnionitis, and BPD)
Intake of mother’s milk by very-low-birth-weight infants and variation in DNA methylation of genes involved in neurodevelopment at 5.5 years of age

Jingxiong Xu, Jean Shin, Meghan McGee, Sharon Unger, Nicole Bando, Julie Sato, Marlee Vandewouw, Yash Patel, Helen M Branson, Tomas Paus, Zdenka Pausova, and Deborah L O’Connor

EPGENETIC EFFECTS:

• 143 former VLBW infants in DoMINO study studied at 5.5 yr
• Buccal cells and brain MRI scans were obtained at 5.5 yr
• In-NICU MOM intake associated with variations in DNA methylation of genes enriched in neurodevelopmental pathways in early childhood
• These methylation variations associated with brain cortical surface area and IQ
• All these associations were such that higher percentage mother’s milk intake was associated with lower DNAm, and lower DNAm was associated with larger cortical surface area and higher Full-Scale IQ.

Xu et al. Am J Clin Nutr 2022
Breastfeeding is an essential part of women’s reproductive health – recovery of maternal physiological systems to their preconception state

Benefits Associated with Moms Who Breastfeed

- Reduced risk of breast cancer
- Reduced risk of ovarian cancer
- Reduced risk of high blood pressure
- Reduced risk of type 2 diabetes
- Reduced myocardial infarction


Breastfeeding Programs and Policies, Breastfeeding Uptake, and Maternal Health Outcomes in Developed Countries. Comparative Effectiveness Review No. 210. AHRQ Publication No. 18-EHC014-EF. July 2018
Variation in mother’s own milk use in US NICUs
• National Immunization Survey–Child (NIS-Child)
• 167,842 infants
• 2009-2015
Fig. 5  US breastfeeding rates from 1970 to 2015 by maternal race/ethnicity. Based on data from refs. 103–105
The Healthy People 2030 (HP2030) goals to increase

- Exclusively breastfeeding through 6 months from 24% to 42%
- Continue breastfeeding through 12 months from 43% to 54%
Racial/Ethnic Disparities in NICU MOM

B. Any Human Milk at Discharge Among VLBW Infants According to Maternal Race/Ethnicity

Parker MG et al. VON data. JAMA Pediatrics 2019
Quality of Care in US NICUs by Race and Ethnicity

Erika M. Edwards, PhD, MPH, Lucy T. Greenberg, MS, Jochen Profft, MD, MPH, David Draper, PhD, Daniel Helkey, MS, Jeffrey D. Horbar, MD

<table>
<thead>
<tr>
<th>Measure and Race and Ethnicity</th>
<th>No. Infants</th>
<th>Baby-MONITOR Score (99% CI)</th>
<th>Race/Ethnicity Within NICU Compared With White Infants in the Same NICU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any human milk at discharge</td>
<td></td>
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</tr>
<tr>
<td>African American</td>
<td>48801</td>
<td>$-2.4$ ($-2.5$ to $-2.3$)</td>
<td>707</td>
</tr>
<tr>
<td>Hispanic</td>
<td>29760</td>
<td>$-0.6$ ($-0.7$ to $-0.5$)</td>
<td>711</td>
</tr>
<tr>
<td>Asian American</td>
<td>8434</td>
<td>$-0.1$ ($-0.2$ to $0.0$)</td>
<td>642</td>
</tr>
<tr>
<td>American Indian</td>
<td>1326</td>
<td>$-1.2$ ($-1.3$ to $-1.1$)</td>
<td>233</td>
</tr>
</tbody>
</table>

MOM after NICU Discharge

- Retrospective cohort
- Preterm infants (GA <37 weeks) born in 2018-2019
- Followed with a pediatrician at our academic medical center after NICU discharge
- Feeding history collected at routine visits (newborn, and 2, 4, 6, 9 and 12 months)
- 120 infants completed all visits through 12 months

Breastmilk feeding rates by Race/Ethnicity

Unpublished Data
Larsen N et al, under review
Factors mediating racial/ethnic disparities in mother’s own milk feedings
Breastfeeding: crucially important, but increasingly challenged in a market-driven world

Figure 1: The 2023 Lancet Breastfeeding Series framework

Pérez-Escamilla R et al. Lancet 2023
Barriers Faced by Mothers in the NICU

**Delayed Lactogenesis**
- Premature delivery
- Cesarean delivery
- Maternal blood loss
- High BMI
- Diabetes mellitus
- Maternal hypertension
- Prolonged bedrest
- Duration and stress of labor

**Other Barriers**
- Mother-infant separation
- Stress associated with NICU
- Lack of skin to skin (STS)
- Breast pump dependence
- Cost or lack of equipment
- Lack of training/ availability of hospital providers
- Maternal health issues
- Limited maternity leave
- Transportation issues
- Competing responsibilities
- Lack of knowledge
- Lack of family support
- Embarrassment

Nommsen-Rivers et al. *Am J Clin Nutr* 2010
Hurst. *J Midwifery and Women’s Health* 2007
Hernandez et al., *PLoS ONE* 2012
Parker and Patel. *Sem Perinatol* 2017
LOVE MOM Cohort:
Large disparity in MOM at NICU discharge

Figure 2 Proportion of VLBW Infants Receiving Any HM as NICU Discharge Approaches

- White (n 90)
- Black (n 212)
- Hispanic (n 113)

Percentage of Infants

- MOM initiation
- MOM feeding at NICU discharge

Bigger et al. J Perinatol 2014
**MOM at NICU Discharge**

**White vs. Black mothers**
- maternal age
- low SES
- daily pumping frequency

**Hispanic vs. Black mothers**
- maternal age
- daily pumping frequency

**Odds Ratio (95% CI):**
- OR = 0.36 (95% CI: 0.16, 0.91)
Impact of DM on MOM

The Effect of a Donor Milk Policy on the Diet of Very Low Birth Weight Infants

Kathleen A. Marinelli, MD, IBCLC; Mary M. Lussier, BSN, IBCLC; Elizabeth Brownell, PhD, MA; Victor C. Herson, MD; and James I. Hagadorn, MD

Impact of Donor Milk Availability on Breast Milk Use and Necrotizing Enterocolitis Rates

Didier Tshuma,*, Aneta Pelecanos* and Mark W Davies*  

Donated human milk use and subsequent feeding pattern in neonatal units

Impact of DM on MOM

- Retrospective study of 313 VLBW infants (2011-2015)
- 57% non-Hispanic Black, 22% Hispanic, 21% non-Hispanic White

<table>
<thead>
<tr>
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<th>Pre-DHM</th>
<th>DHM</th>
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<tbody>
<tr>
<td>First feeding type = MOM*</td>
<td>89%</td>
<td>75%</td>
</tr>
<tr>
<td>Exclusive MOM DOL 1-14*</td>
<td>68%</td>
<td>55%</td>
</tr>
<tr>
<td>Feedings initiated ≤ 3 d*</td>
<td>55%</td>
<td>72%</td>
</tr>
<tr>
<td>Any Formula*</td>
<td>82%</td>
<td>69%</td>
</tr>
<tr>
<td>Any MOM at Discharge</td>
<td>41%</td>
<td>44%</td>
</tr>
<tr>
<td>Last day MOM</td>
<td>43</td>
<td>42.5</td>
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Potential strategies to increase mother’s own milk feedings
NICU Lactation Strategies

• Parent education – prenatally and postnatally
• Staff education
• Access to NICU-specific and culturally adapted lactation expertise
• Early milk expression
• Frequent pumping +/- hand expression
• Monitoring milk volumes during the first 14 days postpartum to achieve at least 500ml/day (coming to volume)
• Skin-to-skin (STS)
• Successful transition to direct breastfeeding

Think about the perspective: who bears the costs?
Who bears the cost of feedings?

Mother’s Own Milk

Mother
$12.35 / 100 mL

Donor Milk

NICU
$21.18 / 100 mL

Johnson et al, J Peds 2020
**Breastfeeding is not free!**

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Costs</th>
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<tbody>
<tr>
<td>1. Reduced incidence of neonatal morbidity</td>
<td>1. Access to evidence-based lactation care</td>
</tr>
<tr>
<td>2. Reduced incidence of childhood health conditions</td>
<td>2. “Opportunity costs” of breastfeeding in terms of mother’s own time</td>
</tr>
<tr>
<td>3. Reduced incidence of maternal diseases</td>
<td>3. Breastfeeding supplies</td>
</tr>
<tr>
<td>4. Improvement in neurodevelopment</td>
<td>4. Employer and government policies to support breastfeeding</td>
</tr>
<tr>
<td>5. Reduction in infant mortality</td>
<td></td>
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<tr>
<td>6. Avoidance of costly healthcare services</td>
<td></td>
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<tr>
<td>7. Reduction in healthcare costs</td>
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Are cash transfers one approach for mitigating economic barriers?

<table>
<thead>
<tr>
<th>Unconditional Cash Transfers</th>
<th>Conditional Cash Transfers</th>
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<tbody>
<tr>
<td>Payments or financial transfers made without any expectation beyond eligibility</td>
<td>Payments or financial transfers made in return for fulfilling specific behavioral conditions</td>
</tr>
<tr>
<td>Temporary Assistance for Needy Families (TANF), Medicaid</td>
<td>Have been used to increase children's school attendance, childhood vaccinations and adherence to prenatal visits</td>
</tr>
</tbody>
</table>

World Health Organization, 2008
Are conditional cash transfers one approach for mitigating economic barriers?

Conditional cash transfers are being used across the world to increase preventive health, including breastfeeding rates.

Research on incentives to increase breastfeeding in term infants suggests:
- Mothers value cash or cash equivalents more than other financial incentives such as grocery vouchers or baby supplies.
- Healthcare providers are generally positive but caution about choosing the proper incentive and monitoring that its use did not impact other family or provider relationships.

World Health Organization, 2008
Financial incentives for breastfeeding: Nourishing Start for Health (NOSH)

Goal: increase breastfeeding prevalence and duration in wards with low breastfeeding rates in the UK

Financial incentive: shopping vouchers of £40 over 6 months: 2 days, 10 days, 6 weeks, 3 months, 6 months

Comparison: Usual care following Baby Friendly standards

Conditionality: baby receiving breast milk

Evidence: woman’s signed claim form

April 2015 – March 2016

N = 10,010 mother-infant dyads

Mean Ward Level 6 to 8 Week Breastfeeding Prevalence

Control: 31.7%

Intervention: 37.9%

Breastfeeding Prevalence Over Time

5.7 percentage point different in breastfeeding prevalence after adjusting for baseline rates and ward

Relton C et al, BMJ Open 2016;
Relton C et al, JAMA Pediatr 2018
Financial incentives for breastfeeding: Pilot study of low-income Puerto Rican mothers

**Goal:** increase breastfeeding prevalence among Puerto Rican mothers receiving WIC in Philadelphia

**Financial incentive:** monthly payment that increased by $10 each month ($20, $30,... $70) for a maximum of $270

**Comparison:** WIC only versus WIC plus financial incentive

**Conditionality:** continued breastfeeding

**Evidence:** demonstrated breastfeeding at visit Feb 2015 – Feb 2016

N = 36 mothers
Goal: assess monthly financial incentives contingent on observed breastfeeding for 6 months postpartum among WIC-enrolled mothers on breastfeeding rates over 12 months in two cities (Philadelphia, Newark)

Financial incentive: monthly payment plus bonus incentive

Comparison:
standard care control (WIC + home-based intervention support)
versus
standard care + financial incentive

Conditionality: continued breastfeeding

Evidence: demonstrated breastfeeding at each home visit

June 2019 – April 2023

N = 168 mothers

Financial incentive

- $20 at month 1, with payments escalating by $10 through month 6 ($20, $30, ... $70)
- Bonus incentive of $50 at baseline, 3 and 6 months contingent on selecting full WIC breastfeeding food package

Control group receives lump-sum payment at end of 6 months based on number of completed home visits
• Randomized controlled trial to test an intervention designed to remove economic barriers to breastfeeding provision during the infant’s NICU stay
• Mothers and their preterm infants (<32 weeks gestational age) randomized to one of two arms:

1. **Mother Provides MOM**
   - Standard NICU Lactation Care

2. **NICU Acquires MOM**

**ReDiMOM Trial**

Johnson et al, *BMC Pediatrics* 2022
Aim 1: Compare infant and maternal MOM outcomes for **NICU acquires MOM** versus **mother provides MOM**
- Receipt of MOM at NICU discharge

Aim 2: Describe and compare the cost of NICU acquires MOM versus NICU acquires donor human milk as supplemental feedings

Aim 3: Compare the cost-effectiveness of **NICU acquires MOM** versus **mother provides MOM** for the infant and maternal outcomes

**SUB-STUDIES**
- Maternal Matriarchs Qualitative Sub-Study (Dr. Devane-Johnson)
- Family structure (Dr. Leslie Harris)
- Pumping patterns (Amelia Tan - student volunteer)
- Family out of pocket costs

Johnson TJ et al, *BMC Pediatrics* 2022
Design of conditional cash transfer

1. Near real-time opportunity cost payment via HIPAA compliant debit card

2. Opportunity cost payment tied to the Illinois minimum wage rate ($14 in 2024; increasing annually by $1 to max of $15 in 2025)

3. Opportunity cost payment tied to the average time spent pumping by mothers of preterm infants (2 hours/day)

4. Validation of pumping collected via SMART breast pump

Up to $96 per week
- For average 73-day NICU stay, maximum of $2044
- Maximum transfer amount/week equivalent to 35% increase in monthly income for family of 3 at the federal poverty level
Data Collection

Maternal
• Health and lactation history
• Work and economic history
• Pump log
• Visitation
• Lactation practices
• COVID-19 experiences
• Stress
• Work, opportunity and out-of-pocket costs
• Serial milk samples

Infant
• Medical information/outcomes
• Cost of care

Intervention
• Smart pump electronic data
• Opportunity cost payments
• Intervention perceptions

Electronic Medical Record
REDCap Questionnaires
Smart Pump
Laboratory Analysis
Financial Records
Qualitative interviews
Prospective cohort study that leverages the ReDiMOM RCT to assess outcomes through 20 months’ corrected age (CA) in the Neonatal High Risk Follow-Up Clinic

**Aim 1:** Determine the effect of RCT treatment group on early childhood outcomes:
- Neurodevelopment
- Adiposity
- Duration of MOM feedings over the first year of life
- Total cost of care and cost-effectiveness

**Aim 2:** Determine the association between the total number of days MOM is received in the first year of life and early childhood outcomes
Aim 1: Determine the effect of ReDiMOM on childhood (6 yr) outcomes:
• Neurodevelopment
• Behavior
• Health (growth, adiposity, BP, hospitalizations)
• Quality of life
• Costs

Aim 2: Determine the association between the dose of MOM received and childhood outcomes
Childhood Education: Mammals and Milk

Objective: To provide breastfeeding education to potentially help future generations realize breastfeeding is the norm for all mammals, including humans, and help reduce racial and ethnic disparities in breastfeeding provision.
Conclusions

• The breastfeeding gap between Black and White infants in the US may be increasing
• The majority of NICUs still encounter racial/ethnic disparities in maintenance of lactation with fewer Black infants receiving MOM at NICU discharge
• Breastfeeding is not free
  • The cost is borne by the parent providing milk
  • Magnified for parents of infants in the NICU and/or low-income parents
• Conditional cash transfers are being tested worldwide, in term and preterm infants, in community and in hospital settings
• Qualitative studies are necessary to better understand mothers’ experiences in providing MOM
• Our efforts should focus on supporting MOM and breastfeeding broadly, without which DHM will not be available as a second option
• We need innovative strategies that address structural and socioeconomic barriers
• We need cost-effectiveness analyses (short- and long-term) to facilitate translation into policy and practice
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