Published in final edited form as:
J Pediatr. 2020 September ; 224: 57–65.e4. doi:10.1016/j.jpeds.2020.04.044.

The Economic Impact of Donor Milk in the Neonatal Intensive Care Unit

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Abstract

Objective: To assess the cost-effectiveness of mother’s own milk supplemented with donor milk versus MOM supplemented with formula (MOM+F) for very low birth weight (VLBW) infants in the neonatal intensive care unit (NICU).

Study design: A retrospective analysis of 319 VLBW infants born before (January 2011 – December 2012, MOM+F, n=150) and after (April 2013 – March 2015, MOM+DM, n=169) a DM program was implemented in the NICU. Data were retrieved from a prospectively-collected research database, the hospital’s electronic medical record, and the hospital’s cost accounting system. Costs included feedings and other NICU costs incurred by the hospital. A generalized linear regression model was constructed to evaluate the impact of feeding era on NICU total costs, controlling for neonatal and sociodemographic risk factors and morbidities. An incremental cost-effectiveness ratio was calculated for each morbidity that differed significantly between feeding eras.

Results: MOM+DM infants had a lower incidence of necrotizing enterocolitis (NEC) than MOM +F infants (1.8% vs 6.0%, $P = .048$). Total (hospital+feeding) median costs (2016 USD) were $169,555 for MOM+DM and $185,740 for MOM+F (p=0.331), with median feeding costs of

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The authors declare no conflicts of interest.

$1317 and $936 respectively (p<0.001). MOM+DM was associated with $15,555 lower costs per infant (p=0.045) and saved $1812 per percentage point decrease in NEC incidence.

Conclusions: The additional cost of a DM program was small compared with the cost of a NICU hospitalization. After its introduction, the NEC incidence was significantly lower with small cost savings per case. We speculate that NICUs with higher NEC rates may have higher cost savings.

Keywords

very low birth weight; nectrotizing enterocolitis; mother's own milk; cost-effectiveness; healthcare costs; hospital costs; donor milk program

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Very low birth weight infants (VLBW, <1500g) are at increased risk of severe morbidities in the neonatal period. Necrotizing enterocolitis (NEC), one of the most devastating conditions that affects up to 7% of VLBW infants, is associated with prolonged hospitalizations, poor neurodevelopmental outcomes and lifelong health problems.[1–4] Although the pathophysiology of NEC remains poorly understood, the use of mother's own milk is recognized as a standard strategy to reduce the risk of NEC.[5] MOM feeding, compared with formula feeding, is associated with reduced rates of NEC,[6–9] late onset sepsis,[6,7,10–12] bronchopulmonary dysplasia (BPD),[13,14] and retinopathy of prematurity (ROP).[15] Not all VLBW infants are able to receive exclusive MOM and the use of pasteurized donor human milk is recommended as an alternative to formula when MOM pumped volume is insufficient.[16,17]

Although a systematic review of 11 trials demonstrated that DM reduced the risk of NEC in preterm infants,[18] the American Academy of Pediatrics recognizes that the cost of DM is a major limitation to its universal availability for high-risk infants.[17] It has been argued that the higher cost of providing pasteurized DM compared with formula would be offset by the cost savings incurred by improved outcomes and reduced rates of NEC. We have previously shown that a single case of NEC increased hospital costs by an estimated $30,681.[8] Studies have modeled the cost-effectiveness of DM based on costs of obtaining and providing DM with the estimated reductions in NEC and length of hospitalization.[19–23] However, there is a paucity of data to inform how DM directly affects hospital costs in a tertiary neonatal intensive care unit (NICU) in the United States.[24] The study objective was to determine the cost-effectiveness of supplementing MOM with DM rather than with formula for VLBW infants in a single tertiary NICU.

Methods

This study included a total of 319 VLBW infants, 150 of whom were enrolled in the prospective LOVE MOM (**L**ongitudinal **O**utcomes in **V**ery Low Birthweight Infants **E**xposed to **M**other's **O**wn **M**ilk) cohort[25] born before the DM program was implemented in the study NICU (January 2011-December 2012, MOM+Formula (MOM+F) era) and 169 who were admitted after the DM program was implemented (April 2013-March 2015, MOM +DM era). The sample excluded infants with early deaths (death <7 days of life (DOL)) or gestational age ≥ 32 weeks. The institutional review board approved this study and the original LOVE MOM cohort study.

Nutritional Practices

Feeding practices were per the established NICU nutritional guidelines in place during each era. In the MOM+F era, infants were maintained NPO until MOM was available, which may have delayed feeding initiation up to 3–5 days. If MOM was unavailable, preterm formula was used for feedings. MOM and formula caloric density were increased once feedings reached 140 ml/kg/d with the addition of bovine human milk fortifier (Generation 1 Similac) to MOM or by changing to a 24 kcal/oz preterm formula. The DM program was implemented in April 2013 for infants with birth weight <1500g or gestational age (GA) <32 weeks. Pasteurized DM (from The Milk Bank, Indianapolis, IN, USA) was used to supplement insufficient MOM through 34 0/7 weeks corrected GA, at which time DM was transitioned to preterm formula over a one week interval. In the MOM+DM era, feedings were also initiated preferentially with MOM, but if MOM was not available by day 2 or 3 post-birth then DM consent was obtained, and feedings were started with DM. Both MOM and DM were fortified once feedings reached 140 ml/kg/d with the addition of bovine human milk fortifier, using powdered formulation in the MOM+F era and liquid non-acidified formulation during the majority of the MOM+DM era (starting in July 2013). Infants receiving DM also received an additional modular protein (Similac; 0.5–1 g/kg/d). All infants in both eras received parenteral nutrition starting on the day of birth. There were no other changes in NICU lactation or nutritional practices during the study periods.

Feeding Outcomes and Feeding Characteristics

Feeding outcomes included the proportion of enteral feedings at NICU discharge that were human milk (MOM or DM) versus formula, any formula feedings during the NICU stay, initiation of MOM feedings during the NICU stay, exclusive MOM feedings through the NICU stay, and any MOM feedings at NICU discharge. Other feeding outcomes for the first 14 DOL included the proportion of enteral feedings that were MOM, DM and formula, any MOM feedings during the first 14 DOL, and any formula feedings during the first 14 DOL. Feeding characteristics included DOL of feeding initiation, DOL at full enteral feedings defined as 140 ml/kg/d, days to full enteral feeding (DOL of full enteral feeding – DOL of feeding initiation), and number of days PN was received.

Neonatal Morbidities and Death during the NICU Hospitalization

Neonatal morbidities included NEC (modified Bell's criteria stage ≥ 2)[26]; culture-proven late onset sepsis; BPD, defined as the receipt of oxygen or positive pressure ventilation at 36 weeks postmenstrual age (PMA)[27]; severe brain injury, defined as grades 3–4 intraventricular hemorrhage, periventricular leukomalacia or post hemorrhagic hydrocephalus[28]; and ROP stage ≥ 3. We evaluated the presence or absence of each morbidity and created a composite variable that indicated whether the infant had any of the 5 morbidities or died during the NICU stay.

NICU Costs

NICU total cost represented the cost incurred by the hospital and included the cost of all hospital and feeding (ie, MOM, DM, formula) resources. Except for feeding-related costs, each resource used during the NICU hospitalization and its associated per-unit cost were collected from the organization's cost accounting system.[11,29] These costs included the following resource categories: NICU room and board (inclusive of nursing care), diagnostic testing, laboratory and pathology, pharmacy, respiratory care, cardiology, surgery, developmental psychology, and therapies. To account for changes in costs over time, all costs were held constant at their 2016 US dollar (USD) values by creating a list of all resources used and their 2016 per-unit costs. For resources that did not have a 2016 cost value, costs were inflated to 2016 USD using the Bureau of Labor Statistics Consumer Price Index for medical care (Series ID: CUSR0000SAM).[30] The resource-level costs in 2016 USD were summed to calculate the hospital cost.

Feeding costs were calculated separately for MOM, DM and formula, and these costs were summed to calculate the total feeding cost. Formula feeding costs were calculated as the total volume of formula consumed in the NICU stay x $0.033 per mL, based on the median formula cost from published studies, inflated to 2016 dollars.[22,31,32]

MOM feeding costs included evidence-based educational materials, hospital-grade electric breast pump rental and supplies needed to support MOM expression, breastfeeding peer counselor support, freezer space, waterless warmers and liners, a creamatocrit to individualize MOM feedings, and infant scales (Table I; available at www.jpeds.com).[33] Because DM is not a billable cost for hospitals in Illinois, DM feeding costs were calculated separately using a bottom-up costing approach and included the cost to purchase DM (direct cost) and cost of resources needed to store and prepare the DM, including personnel, freezer space, waterless warmer and liners (indirect costs) (Table 1).

Neonatal and Sociodemographic Risk Factors

Neonatal risk factors included infant GA, birth weight, sex, Apgar score at 5 minutes, small for gestational age at birth (birth SGA),[34] singleton or multiple birth, mode of delivery (vaginal versus cesarean), and surfactant use. Sociodemographic risk factors included maternal race/ethnicity and primary insurance (Medicaid or commercial).

Statistical Analyses

Continuous variables were expressed as means and standard deviations (SD) or medians and interquartile ranges (IQR), depending on their distribution, and categorical variables were expressed as frequencies and percentages. Independent samples t-tests, Mann-Whitney U tests, chi square tests and Fisher exact tests were used to compare variables between feeding eras, as appropriate. A generalized linear regression model with a log link function and gamma distribution was constructed to determine the relationship between feeding era and NICU costs, adjusting for neonatal (infant GA, infant sex, birth SGA, surfactant use) and sociodemographic risk factors (maternal race/ethnicity, primary insurance) and DOL of first feeding. Another model was constructed with the same covariates that included neonatal morbidities as additional covariates. A modified Park test was used to select the appropriate mean-variance relationship for the regression models.[35] The average marginal effect in 2016 US dollars was computed for feeding era by calculating the adjusted cost for each infant, assuming all infants were in the MOM+F era, holding all other infant characteristics constant, then calculating the adjusted cost for each infant, assuming all infants were in the MOM+DM era, and computing the difference in costs between feeding eras for each infant. The average marginal effect was calculated using a similar approach for all other independent variables. Secondary analyses were conducted for NICU length of stay and NICU total cost per day using a similar approach.

The cost-effectiveness analysis was conducted from the hospital's perspective and evaluated the cost per percentage point reduction in the incidence of NEC. The incremental cost-effectiveness ratio (ICER) was computed as $(\hat{C}_{MOM+DM}-\hat{C}_{MOM+F})/(p_{MOM+DM}-p_{MOM+F})$, where $\hat{C}$ is mean adjusted NICU total cost, p is the proportion of infants with NEC, and subscripts MOM+DM and MOM+F indicate the respective feeding era. To assess uncertainty in costs and effectiveness (i.e., NEC incidence), 1000 bootstrapped replicates were created using random sampling of the full sample size (n = 319) with replacement of the original data set. For each bootstrapped replicate, the ICER was calculated for the MOM +DM era versus MOM+F era and plotted, for a total of 1000 bootstrapped replicate ICERs. The 95% confidence interval for the ICER was computed from the 2.5^{th} and 97.5^{th} percentiles of the 1000 bootstrapped replicates.[36,37] The bootstrapped ICERs were plotted graphically to display the variation in costs versus effectiveness. SAS version 9.3 (Cary, NC) was used for all analyses.

Results

Neonatal and sociodemographic risk factors, feeding characteristics, incidence of morbidities and unadjusted costs for the 150 infants in the MOM+F era and 169 in the MOM+DM era are reported in Table 2. Infants in the MOM+DM era had shorter times to first feeding, achieved full feeds sooner, and had fewer days with PN. Additionally, the proportion of infants in the MOM+DM era with any formula use by DOL14 was significantly lower than for infants in the MOM+F era, although the proportion of infants with exclusive MOM at DOL14 was lower for infants in the MOM+DM era. The cumulative proportion of total enteral feedings that consisted of formula for the NICU stay was significantly lower for infants in the MOM+DM era, whereas the proportion of infants with any MOM at NICU discharge was not significantly different between the 2 groups.

NEC incidence was significantly lower in the MOM+DM era compared with the MOM+F era (1.8% versus 6.0%, p=0.048; difference, 4.2% (95% CI, −0.7% to 8.5%)), with fewer infants receiving surgical treatment for NEC in the MOM+DM era (Table 2). The occurrence of other neonatal morbidities was not significantly different between feeding eras, and half of infants in each feeding era had at least one major morbidity or died during their NICU hospitalization.

Median NICU length of stay, total cost and cost per day were not significantly different between groups (Table 2 and Figure 1). Median feeding costs were significantly higher in the MOM+DM era ($1317 versus $936, p<0.001). The median cost per 100 mL was $3.30

for formula and $12.35 for MOM (Table 1). The median DM cost was $21.18 per 100 mL, with the direct cost to purchase DM from a milk bank representing 68% ($14.37) of the cost and the indirect cost (e.g., supplies, staff time) representing the remaining cost ($6.81). Mean costs for each component were similar between feeding eras (Table 3; available at www.jpeds.com), with the exception of feeding, laboratory/pathology and pharmacy costs. The difference in pharmacy costs was primarily driven by differences in PN costs (median cost, $4323 (IQR: $2797, $6612) in the MOM+F era versus $2798 (IQR: $2289, $4578) in the MOM+DM era).

After adjusting for neonatal and sociodemographic risk factors and feeding characteristics, infants in the MOM+DM era had 7% lower NICU total costs, translating into −$15,555 in NICU costs per infant relative to the MOM+F era (p=0.045) (Table 4 and full results reported in Table 5 [available at www.jpeds.com]). Model 2 also adjusted for neonatal morbidities, and the MOM+DM era remained significant, with -$14,599 in NICU costs per infant relative to the MOM+F era. Additionally, NEC was associated with $66,015 higher costs per infant (p<0.001), and BPD was associated with $74,084 higher costs per infant (p<0.001).

The ICER for NEC was $1812 (95% confidence interval (CI): −$7010, $14,542) or a cost savings of $1812 per percentage point reduction in NEC (Table 6). In the 1000 bootstrapped replicates, 80.3% of the replicates had mean adjusted costs that were lower in the MOM +DM era, 97.6% of the replicates had a lower incidence of NEC in the MOM+DM era and 78.6% had ICERs where both the mean adjusted cost and incidence of NEC were lower in the MOM+DM era (Figure 2, quadrant A).

In the secondary analysis of the relationship between feeding era and NICU length of stay, MOM+DM era was associated with a mean reduction of 5.8 (SD=2.4) days after controlling for neonatal morbidities and other risk factors (p=0.031) (Table 7; available at www.jpeds.com). Feeding era was not significantly associated with NICU total cost per day.

Discussion

In this retrospective analysis of NICU outcomes and costs for VLBW infants, both the incidence of NEC and NICU costs were significantly lower after implementation of a DM program. Contrary to concerns regarding the cost of DM, we found that NICU costs were not significantly higher after implementing the DM program, even after accounting for both the direct cost of DM and the associated indirect costs. The incidence of NEC was 4.2 percentage points lower and adjusted NICU costs were $15,555 lower in the MOM+DM era compared with the MOM+F era. In the cost-effectiveness analysis, DM was associated with a cost savings of $1812 per percentage point reduction in the incidence of NEC, with 98% probability that the NEC incidence would be lower with the DM program and 79% probability that both the incidence of NEC and NICU costs would be lower with the DM program.

This study comprehensively calculated the cost of DM in the NICU for DM acquired through an independent milk bank, including both direct and indirect costs of DM. Although the direct cost or "purchase price" of DM ($14.37 / 100 mL) was similar to the cost of acquiring MOM feedings ($12.37 / 100 mL) in our study, the purchase price represents only 68% of the cost of DM feedings in the NICU. Thus, the cost estimates for DM that do not include the staff time and resources required to manage and prepare DM will under-estimate its true cost in the NICU setting. However, even after comprehensively accounting for these costs, the additional feeding costs were miniscule relative to the cost of the NICU hospitalization. We found that the median feeding cost in the MOM+DM era was only $381 higher than the feeding cost in the MOM+F era. In a study of 64 preterm infants in an Australian NICU, Carroll and Herrmann estimated that the mean DM cost per infant was $237 (in 2011 US dollars), taking into account only the purchase price of DM.[38] In a systematic review of the cost and cost-effectiveness of DM, Buckle and Taylor found that the cost per infant of DM as an adjunct to MOM ranged from $224 to $319, also based exclusively on the DM purchase price.[24] These estimates based on the DM purchase price are remarkably consistent with our direct cost calculations for DM (median = $259 or 68% of $381). Although these prior studies under-estimate the actual cost of DM due to the omission of indirect costs associated with DM, all of these estimates are quite low in comparison with the NICU hospitalization. This is likely due to the relatively small volumes and short time frame during which VLBW infants receive DM at most institutions, namely when enteral feedings are being advanced and although total volumes of intake are low during the first 2–8 weeks that DM is commonly utilized.[39,40]

In our detailed analysis of the direct and indirect cost of DM feedings, we found that the average cost per 100 mL of DM was $21.18. In a similar study of the hospital costs of infant feedings in the NICU, Fengler et al calculated the cost of DM feedings in a German hospital with an internal milk bank, including the acquisition and preparation of DM.[41] They calculated a total cost of 8.29 EUR (approximately $9.20 USD) per 100 mL of DM, which is substantially lower than the cost in our study. A portion of the cost difference is likely due to the acquisition costs of DM in the two studies (through an in-hospital milk bank versus independent milk bank). The "purchase price" of DM in our study was $14.39, more than the entire cost of DM feedings in the study by Fengler et al. Future work should evaluate differences in the processeses and associated costs for acquiring and feeding DM in the NICU.

Our findings differ from those of Trang et al in the direction of the cost-effectiveness of DM feedings.[22] Trang et al evaluated the cost-effectiveness of DM for VLBW infants enrolled in a randomized controlled trial of DM versus formula as supplements to MOM in four Canadian NICUs.[42] In this RCT, costs of enteral feeding (direct cost or "purchase price" of DM, fortifier and formula) were significantly higher for infants with DM supplementation ($41 CAD for infants with formula supplementation versus $921 CAD for infants with DM supplementation), with both groups receiving similar proportions of enteral intake as MOM. Although not the primary outcome, infants randomized to the supplemental DM arm had significantly lower incidence of stage ≥ 2 NEC than infants in the supplemental formula arm (1.7% versus 6.6%), similar to the three-fold difference in the incidence of NEC that we report. Analyzing the reported data from Trang et al in a similar manner to our analytic plan by only including NEC stage ≥ 2 and costs through NICU discharge (excluding caregiver and physician expenses), we can better compare the results from these 2 studies. Their reduction of 4.9 percentage points in the incidence of NEC stage ≥ 2 would translate into \$1691 (CAD) in *additional* costs per percentage point reduction in NEC stage ≥ 2 (difference in costs = \$8287 CAD, difference in proportion of infants with NEC = −4.9%).[22] In contrast, we found MOM+DM *saved* \$1812 USD per percentage point reduction in NEC stage ≥ 2. This difference in direction is due to the substantially higher costs through discharge for infants in the supplemental DM arm in the Trang et al study. Infants in their supplemental DM arm had higher enteral feeding costs and higher hospital case costs, likely due in part to a substantially longer hospital length of stay, while we had lower overall hospital costs through discharge for infants in the MOM+DM feeding era.

Another potential difference may relate to differences in the timing of the first feeding between the two studies. Alhtough the Canadian RCT did not report a difference in median day of first feedings between study groups,[42] we found a significant difference, with earlier first feedings in the MOM+DM era. Although no formal feeding initiation guideline changes were made, the availability of DM likely resulted in clinicians' comfort in starting feeds earlier, thus resulting in the shortened duration to full feeds and decreased PN days observed in the DM era in our NICU. Correspondingly, pharmacy costs, specifically related to PN, were significantly lower in the DM era and may confer some of the cost savings observed in the DM era as a whole.

This study also differs from a prior study that compared the costs and benefits of DM for infants who received exclusive formula versus exclusive human milk diets that demonstrated greater costs with exclusive formula,[19] in that we did not compare the subset of infants in our cohort who received exclusive formula versus a combination of MOM and DM. Given that the majority of NICUs have reported stable or increased rates of MOM feedings after instituting DM programs, indicating DM is primarily being used as a supplement to MOM,[43–45] our goal was to conduct a cost-effectiveness analysis that was representative of current DM practice.

Several factors will impact the cost-effectiveness of DM in other settings. For example, the use of DM as exclusive nutrition or for a longer duration would clearly increase acquisition cost and impact cost-effectiveness. Similarly, cost-effectiveness would be affected by an individual NICU's incidence of NEC. Institutions with higher NEC rates may garner a greater cost savings if the absolute reduction in NEC is greater than in our study. Finally, the relative costs of resources used during the NICU stay may differ across countries, and application of our findings to other settings should take these potential differences into account.

The current study has several limitations, including the fact that it was retrospective, with with a pre-post intervention design spanning several years in a single tertiary NICU. The design precluded our controlling for all factors that might be associated with NICU total costs, including clinical practice changes between eras. For example, surfactant usage was significantly lower in the post-DM era coinciding with an effort to decrease invasive ventilation and to give less prophylactic surfactant in VLBW infants. However, it is important to note that the rates of BPD were similar between groups, and the costs associated with respiratory care were not significantly different between the feeding eras.

Another clinical practice change was the conversion from powdered to liquid bovine fortifier, which occurred almost simultaneously with DM introduction. Although we were unable to adjust for this confounding, a randomized trial of these same two fortifiers did not reveal any difference in feeding outcomes.[46] Additionally, we did not account for costs due to fortification of MOM or DM. Given that the formula usage was nearly halved in the DM era, the additional fortification may have resulted in increased enteral feeding costs. Baseline characteristics and clinical outcomes outside of NEC were similar between eras suggesting a comparative pre-post population; however, we cannot exclude the possibility of other unaccounted confounding factors that could impact NICU costs.

Another limitation of this study is that costs only included those incurred directly in the NICU. Our calculations did not account for medical costs incurred after the initial hospitalization or for the opportunity costs incurred by the family and society. Trang et al found that caregiver expenses, including productivity losses due to foregone labor market earnings, did not differ for infants in the supplemental DM versus formula arms during the infant's initial NICU stay, but caregiver productivity losses were 20% lower for infants in the supplemental DM arm in the 18 months post-discharge.[22] Additionally, the mother's time (i.e., opportunity cost) spent pumping is a cost currently incurred by the mother rather than the NICU and should be considered in future cost-effectiveness analyses. Based on prior work on the maternal cost of providing MOM for infants in the NICU, the maternal opportunity cost could add $2.44 per 100 mL of MOM, based on a federal minimum wage of $7.25 per hour.[47] Future research should examine the cost-effectiveness from a societal perspective, taking into account maternal opportunity cost due to time spent pumping and other costs incurred by the mother.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Supported by the National Institutes of Health (NR010009 [to P.M.]).

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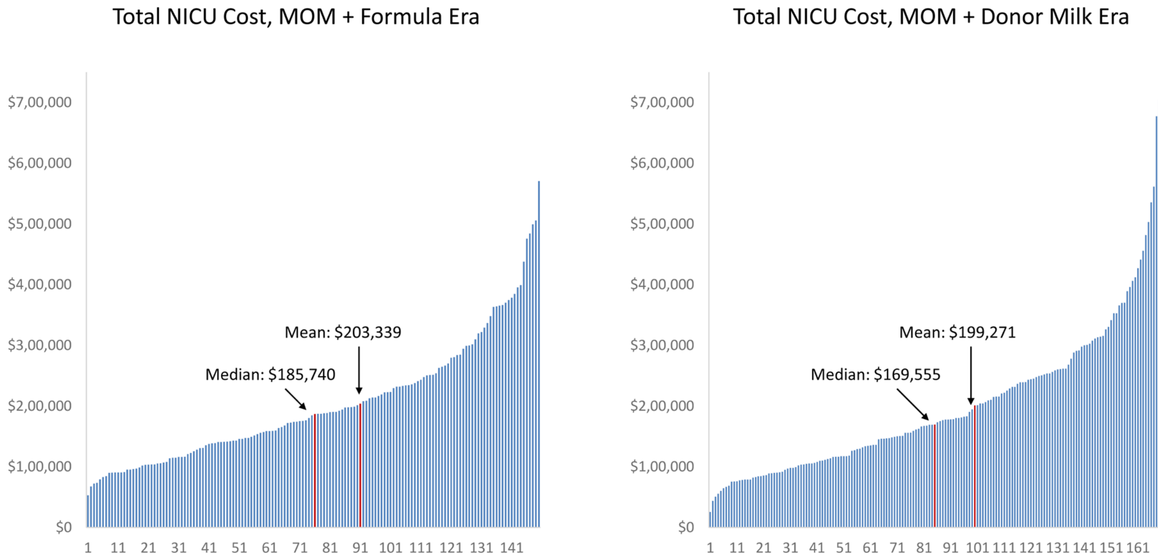

Figure 1. Distribution of NICU Costs by Feeding Era

Histogram of total NICU costs, with each bar representing one NICU discharge.

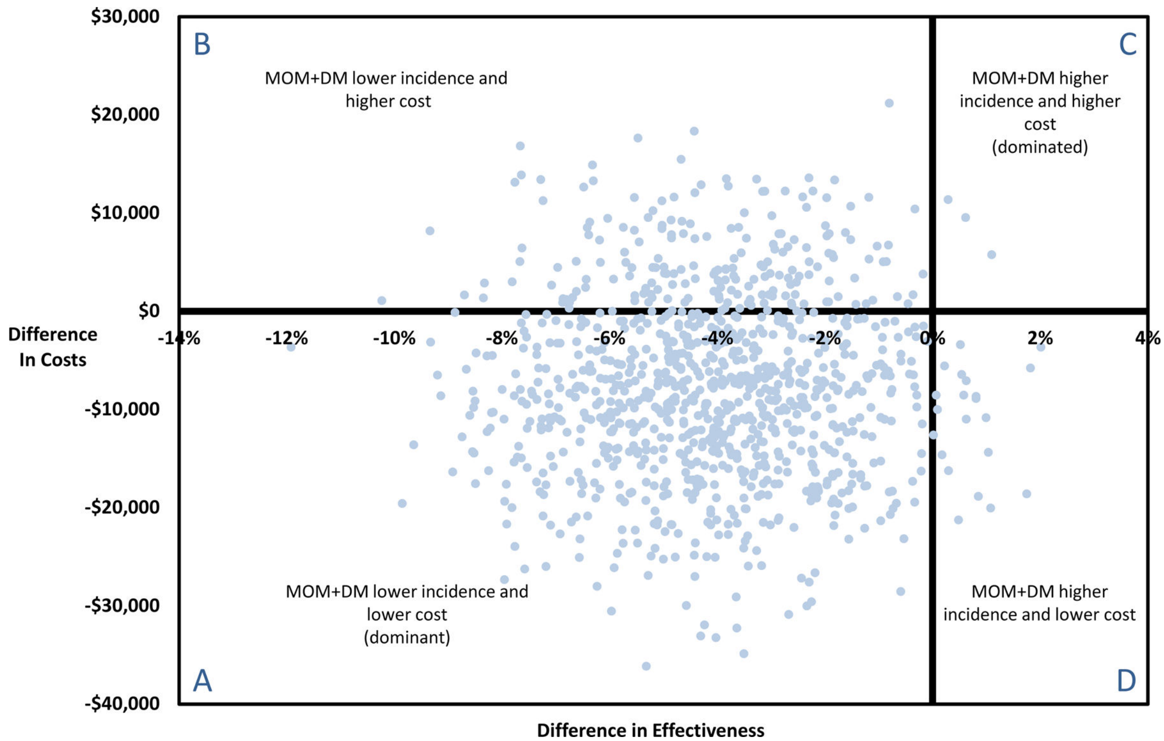

Figure 2. Incremental Cost Effectiveness Ratio for Incidence of Necrotizing Enterocolitis

Scatterplot of 1000 bootstrap samples of cost-effectiveness (i.e., NEC incidence) pairs. Quadrant A indicates samples with mean differences in cost and effectiveness favoring MOM+DM era; Quadrant B indicates samples with mean difference in cost favoring MOM +F era and mean difference in effectiveness favoring MOM+DM era; Quadrant C indicates samples with mean differences in costs and effectiveness favoring MOM+F era; Quadrant D indicates samples with mean differences in costs favoring MOM+DM era and differences in effectiveness favoring MOM+F era.

Table 1.

Feeding Components, per Unit Costs and Median and Mean Feeding Costs per Infant by Type of Feeding

Feeding Component	Description	Source	Type of Cost[1]	Cost per Unit	Median Cost		Mean Cost	
					per 100 mL in 2016 USD	per Infant	per 100 mL in 2016 USD	per Infant
Formula Feeding	Cost per Infant with *any* Formula Feeding (n = 278)							
Formula product cost	Hospital cost to purchase formula	Median cost per published studies[21,30,31]	Variable	$0.033 per mL	$3.30	$321.70	$3.30	$477.34
Total formula feeding cost					**$3.30**	**$321.70**	**$3.30**	**$477.34**
Mother's Own Milk (MOM) Feeding	Costs per Infant with Any MOM Feeding (n = 313)							
Evidence-based materials	Evidence-based materials targeting importance of MOM for preterm infants + monitoring of MOM volume and MOM feeding goals	Meier et al.[32]	Fixed	$15.80	$0.35	$15.80	$6.06	$15.80
Hospital-grade electric breast pump rental	Pump rental for number of months infant received any MOM (days infant received any MOM, rounded up to next month)	Meier et al.[32]	Variable	$40.51/month	$1.56	$81.02	$16.12	$84.00
Provision of pump kit	1 kit per infant	Meier et al.[32]	Fixed	$33.33	$0.74	$33.33	$12.78	$33.33
Custom-fitted breast shields	1 set per infant	Meier et al.[32]	Fixed	$7.09	$0.16	$7.09	$2.72	$7.09
Hospital-grade storage containers for pumped MOM	Containers in sets of 3 per day; (mL MOM per day * 1.2) / 120 = number of containers rounded up to multiple of 3	Meier et al.[32]	Variable, cost per average mL MOM/day	$0.21 per container	$0.56	$23.61	$1.48	$30.24
Breastfeeding peer counselors	Provision of NICU-specific lactation support from NICU-based certified breastfeeding peer counselors; 2 hrs/day for DOL1–2 (and DOL3, if C-section) + 3 hrs for first 2 weeks; 1 hr/wk until last 2 weeks of NICU stay; for infants discharged on MOM, 2.5 hrs/wk for last 2 weeks	Meier et al.[32]	Variable, cost per day infant received any MOM	$18.23 per hour	$5.63	$244.79	$64.11	$270.31
NICU freezers for safe storage of pumped MOM	Cost of $7.01 per infant per 71-day NICU stay or $0.10 per day	Meier et al.[32]	Variable, cost per day infant received any MOM	$0.10 per day	$0.09	$3.65	$0.23	$4.48
Waterless warmers for MOM	$783 per warmer; 1 warmer per infant per 71-day NICU stay or $0.43 per day	Meier et al.[32]	Variable, cost per day infant received any MOM	$0.43 per day	$0.38	$15.87	$0.99	$19.46

Feeding Component	Description	Source	Type of Cost[1]	Cost per Unit	Median Cost		Mean Cost	
					per 100 mL in 2016 USD	per Infant	per 100 mL in 2016 USD	per Infant
Liners for waterless warmer	$3.29 per liner; 1 liner per day	Meier et al.[32]	Variable, cost per day infant received any MOM	$3.29 per day	$2.91	$121.78	$7.60	$149.34
Creamatocrit	Basic creamatocrit to individualize MOM feedings and MOM collection strategies; $1519 per creamatocrit and 1 per NICU for 5 year lifespan; $0.38 per infant	Meier et al.[32]	Fixed	$0.38	$0.01	$0.38	$0.15	$0.38
Infant scale	Measurement of MOM intake during breastfeeding; 1 scale per 15 infants; $3.94 per infant	Meier et al.[32]	Variable, cost per day infant received any MOM	$3.94	$0.09	$3.94	$1.51	$3.94
Total MOM feeding cost					**$12.35**	**$555.67**	**$113.74**	**$618.38**
DM Feeding	Costs per Infant with Any DM Feeding (n = 122)							
DM product cost	Hospital cost to purchase DHM from milk bank	Actual 2016 cost	Variable	$0.14 per mL	$14.37	$361.62	$14.37	$516.77
DM peer counselors	Provision of NICU-specific DHM support and management of DHM supply in NICU; 2.5 hours per day for preparation of all DHM, assuming 10 infants with DHM per day	Actual 2016 cost	Variable, cost per day infant received any DHM	$4.56 per day	$3.70	$97.40	$20.26	$115.07
NICU freezers for safe storage of donor human milk	Cost of $7.01 per infant per 71-day NICU stay or $0.10 per day	Meier et al.[32]	Variable, cost per day infant received any DHM	$0.10 per day	$0.08	$2.11	$0.44	$2.49
Waterless warmers for DM	$783 per warmer; 1 warmer per infant per 71-day NICU stay or $0.43 per day	Meier et al.[32]	Variable, cost per day infant received any DHM	$0.43 per day	$0.35	$9.17	$1.91	$10.83
Liners for waterless warmer	$3.29 per liner; 1 liner per day	Meier et al.[32]	Variable, cost per day infant received any DHM	$3.29 per day	$2.67	$70.34	$14.63	$83.11
Total DM feeding cost					**$21.18**	**$561.31**	**$51.60**	**$728.28**

[1] The cost per 100 mL for feeding components that have a fixed cost is calculated by dividing the fixed cost by the total mL of nutrition (MOM, DM) for each infant.

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Table 2.

Description of the Sample, N = 319

	MOM+formula† N = 150 (47%)	MOM+DM†† N = 169 (53%)	p value
Gestational age (wks), Mean ± SD	27.3 ± 2.1	27.1 ± 2.3	0.299
Birth weight, (g), Mean ± SD	986 ± 246	989 ± 268	0.923
Race/ethnicity, n (%)			0.881
Black/African American	84 (56.0)	90 (53.3)	
Non-Hispanic White	34 (22.7)	40 (23.7)	
Hispanic	32 (21.3)	39 (23.1)	
Female, n (%)	66 (44.0)	81 (47.9)	0.482
5 minute Apgar, Median [IQR]	8 [7, 8]	8 [7, 9]	0.642
Birth SGA, n (%)	27 (18.0)	21 (12.4)	0.165
Multiple gestation, n (%)	24 (16.0)	47 (27.8)	0.011
Cesarean delivery, n (%)	100 (66.7)	126 (74.6)	0.122
Primary payer			0.917
Medicaid/self-pay	102 (68.0)	114 (67.5)	
Commercial	48 (32.0)	55 (32.5)	
DOL first feeding, Median [IQR]	3.5 [3, 5]	3 [2, 3]	<0.001
DOL full feeding, Median [IQR]	21 [15, 29]	15 (12, 24)	<0.001
Days to full feeding, Median [IQR]	16 [11, 23]	11.5 [9, 20]	<0.001
Days with PN, Median [IQR]	17 [11, 26]	11 [9, 18]	<0.001
MOM initiation during NICU stay, n (%)	145 (96.7)	168 (99.4)	0.072
DOL14, percent MOM, Median [IQR]	100.0 [92.9, 100.0]	100.0 [62.0, 100.0]	0.010
DOL14, any formula, n (%)	44 (29.3)	6 (3.6)	<0.001
DOL14 exclusive MOM, n (%)	106 (70.7)	90 (53.6)	0.002
Cumulative % of formula for NICU stay, Median [IQR]	82.6 [7.8, 96.3]	40.4 [0.3, 70.9]	<0.001
Any MOM at discharge, n (%)	53 (35.3)	74 (43.8)	0.124
Surfactant, n (%)	120 (80.0)	100 (59.2)	<0.001
Any neonatal morbidities or death, n (%)	75 (50.0)	84 (49.7)	0.958
NEC, n (%)*	9 (6.0)	3 (1.8)	0.048
NEC, with surgical treatment, n (%)*	5 (3.3)	1 (0.6)	0.103
ROP, stage 3 or higher, n (%)	0 (0)	0 (0)	
Late onset sepsis, n (%)	15 (10.0)	16 (9.5)	0.873
Bronchopulmonary dysplasia, n (%)	64 (42.7)	75 (44.4)	0.758
Severe brain injury, n (%)	7 (4.7)	9 (5.3)	0.788
In-NICU death, n (%)	5 (3.3)	3 (1.8)	0.374
NICU length of stay, Median [IQR]	79 [59, 107]	78 [51, 110]	0.851
NICU total cost, hospital + feeding, Median [IQR]	185,740 [130626, 250469]	169,555 [110186, 254472]	0.331

	MOM+formula† N = 150 (47%)	MOM+DM†† N = 169 (53%)	p value
Hospital cost, Median [IQR]	184,784 [129833, 249666]	168,184 [109541, 251356]	0.309
Feeding cost, Median [IQR]	936 [721, 1199]	1317 [875, 2123]	<0.001
NICU cost per day, Median [IQR]	2254 [2183, 2394]	2232 [2159, 2368]	0.077
PN cost, Median [IQR]	4323 [2797, 6612]	2798 [2289, 4578]	<0.001

† n = 149 for DOL of full feeding and days to full feeding

†† n = 167 for 5 minute Apgar; n = 164 for DOL of full feeding; n = 168 for DOL14, percent MOM, and DOL14, exclusive MOM.

Independent samples t-tests were performed for continuous variables when normally distributed; otherwise, Mann Whitney U tests were performed for continuous variables. Differences between groups of categorical variables were compared with Fisher's exact test when noted with *; otherwise χ^2 tests were used.

Table 3.

Mean Costs, N = 319

	MOM+formula N = 150 (47%) Mean ± SD	MOM+DM N = 169 (53%) Mean ± SD	p value	Difference in Means (95% Confidence Interval)
Hospital cost	202,340 ± 100,916	197,701 ± 117,960	0.708	4,638 (−19,701 – 28,977)
NICU room and board	165,273 ± 71,218	164,805 ± 87,678	0.958	468 (−17,269 – 18,204)
Cardiology	1922 ± 1954	1819 ± 1874	0.632	103 (−319 – 525)
Diagnostic testing	3151 ± 2941	2786 ± 2755	0.254	365 (−263 – 993)
Laboratory/pathology	7939 ± 6490	6356 ± 5008	0.016	1583 (293 – 2872)
Pharmacy	12,266 ± 11,080	9201 ± 7949	0.005	3065 (915 – 5215)
PN	6039 ± 5667	3966 ± 3244	<0.001	2073 (1037 – 3109)
Non-PN pharmacy	6227 ± 5914	5235 ± 5461	0.120	992 (−261 – 2245)
Psychology	687 ± 332	735 ± 287	0.169	−48 (−116 – 20)
Respiratory care	9254 ± 12,778	9919 ± 15,921	0.680	−664 (−3830 – 2501)
Surgery	1054 ± 1928	1098 ± 2385	0.855	−44 (−520 – 431)
Therapies	794 ± 734	982 ± 1065	0.064	−189 (−388 – 11)
Feeding costs	1000 ± 414	1570 ± 907	<0.001	−571 (−724 – −418)
MOM	574 ± 297	637 ± 334	0.069	−63 (−133 – 7)
Formula	425 ± 415	408 ± 591	0.755	18 (−94 – 129)
DM	0	526 ± 628	<0.001	−526 (−621 – −43-)
Total NICU cost	203,339 ± 101,235	199,271 ± 118,571	0.741	4,068 (−20,150 – 28,286)
Total cost per day	2329 ± 259	2288 ± 183	0.106	41 (−8 – 91)

Note: PN = parenteral nutrition

Table 4.

Generalized Linear Regression Model Results for NICU Total Cost, N = 319

	Model 1			Model 2		
	RR (95% CI)	**Average Marginal Effect**	**p-value**	**RR (95% CI)**	**Average Marginal Effect**	**p-value**
DM feeding era	0.93 (0.86 – 1.00)	−15,555 ± 6654	0.045	0.93 (0.87 – 0.99)	−14,599 ± 6886	0.027
NEC				1.33 (1.13 – 1.57)	66,015 ± 30259	<0.001
Late onset sepsis				1.08 (0.97 – 1.20)	15,921 ± 7313	0.148
Bronchopulmonary dysplasia				1.46 (1.35 – 1.56)	74,084 ± 24975	<0.001
Severe brain injury				1.11 (0.97 – 1.27)	21,744 ± 10160	0.132

Models adjust for gestational age, maternal race/ethnicity, infant sex, birth SGA, primary payer, DOL of feeding initiation and surfactant use.

Table 5.

Generalized Linear Regression Model Results for NICU Total Cost, N = 319

	Model 1			Model 2		
	RR (95% CI)	**Average Marginal Effect**	**p-value**	**RR (95% CI)**	**Average Marginal Effect**	**p-value**
Gestational age	0.83 (0.81 – 0.84)	−35,179 ± 15000	<0.001	0.86 (0.85 – 0.88)	−27,440 ± 12844	<0.001
Female	1.09 (1.02 – 1.17)	17,673 ± 7457	0.015	1.09 (1.03 – 1.16)	17,664 ± 8233	0.004
Birth SGA	1.19 (1.08 – 1.32)	37,509 ± 16305	<0.001	1.16 (1.07 – 1.26)	31,692 ± 15050	<0.001
Surfactant	1.08 (1.00 – 1.18)	16075 ± 6615	0.061	1.02 (0.94 – 1.09)	2984 ± 1388	0.688
Black	0.97 (0.89 – 1.07)	−5665 ± 2398	0.554	0.96 (0.89 – 1.03)	−8984 ± 4178	0.260
Hispanic	0.92 (0.83 – 1.03)	−16,344 ± 6920	0.141	0.93 (0.85 – 1.02)	−14,986 ± 6969	0.109
Medicaid	0.97 (0.90 – 1.05)	−5688 ± 2420	0.494	0.96 (0.90 – 1.03)	−7381 ± 3451	0.286
DOL of first feeding	1.00 (0.99 – 1.02)	442 ± 188	0.804	1.00 (0.98 – 1.01)	−562 ± 263	0.708
DM feeding era	0.93 (0.86 – 1.00)	−15,555 ± 6654	0.045	0.93 (0.87 – 0.99)	−14,599 ± 6886	0.027
NEC				1.33 (1.13 – 1.57)	66,015 ± 30259	<0.001
Late onset sepsis				1.08 (0.97 – 1.20)	15,921 ± 7313	0.148
Bronchopulmonary dysplasia				1.46 (1.35 – 1.56)	74,084 ± 24975	<0.001
Severe brain injury				1.11 (0.97 – 1.27)	21,744 ± 10160	0.132

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Table 6.

Incremental Cost Effectiveness Ratio for MOM+DM Relative to MOM+F

Feeding Era	N	Mean Adjusted Cost	Δ Cost	Proportion of Infants with NEC	Δ NEC	ICER
MOM+F	150	$205,899 ± 83,700		6.000%		
MOM+DM	169	$198,244 ± 88,169	−7,655	1.775%	−4.225%	1812 (−7,010 – 14,542)

Table 7.

Generalized Linear Regression Model Results for Other NICU Outcomes, N = 319

	Model 1			Model 2		
	RR (95% CI)	**Average Marginal Effect***	**p-value**	**RR (95% CI)**	**Average Marginal Effect***	**p-value**
Outcome: NICU Length of Stay						
DM feeding era	0.95 (0.88 – 1.01)	−4.8 ± 1.9	0.110	0.93 (0.88 – 0.99)	−5.8 ± 2.4	0.031
Outcome: Cost per Day						
DM feeding era	0.99 (0.97 – 1.00)	−24±1	0.274	1.00 (0.98 – 1.01)	−4.9 ± 0.3	0.800

*Model 1 adjusts for neonatal risk factors (GA, birth SGA, surfactant), sociodemographic risk factors (race/ethnicity, sex, payer) and DOL of the first feeding. Model 2 also adjusts for the presence of morbidities.