



# Cost Savings of Mother's Own Milk for Very Low Birth Weight Infants in the Neonatal Intensive Care Unit

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## Abstract

**Objective** The study aim was to determine the relationship between hospitalization costs and mother's own milk (MOM) dose for very low birth weight (VLBW; < 1500 g) infants during the initial neonatal intensive care unit (NICU) stay. Additionally, because MOM intake during the NICU hospitalization is associated with a reduction in the risk of late-onset sepsis, necrotizing enterocolitis (NEC), and bronchopulmonary dysplasia (BPD), we aimed to quantify the incremental cost of these potentially preventable complications of prematurity.

**Methods** The study included 430 VLBW infants enrolled in the Longitudinal Outcomes of Very Low Birthweight Infants Exposed to Mothers' Own Milk prospective cohort study between 2008 and 2012 at Rush University Medical Center in Chicago, IL, USA. NICU hospitalization costs included hospital, feeding, and physician costs. The average marginal effect of MOM dose and prematurity-related complications known to be reduced by MOM intake on NICU hospitalization costs were estimated using generalized linear regression.

**Results** The mean NICU hospitalization cost was \$190,586 (standard deviation \$119,235). The marginal cost of sepsis was \$27,890 (95% confidence interval [CI] \$2934–\$52,646), of NEC was \$46,103 (95% CI \$16,829–\$75,377), and of BPD was \$41,976 (95% CI \$24,660–\$59,292). The cumulative proportion of MOM during the NICU hospitalization was not significantly associated with cost.

**Conclusions** A reduction in the incidence of complications that are potentially preventable with MOM intake has significant cost implications. Hospitals should prioritize investments in initiatives to support MOM feedings in the NICU.

## Key Points for Decision Makers

For very low birth weight (VLBW) infants, the neonatal intensive care unit (NICU) hospitalization cost and cost per day increase significantly with the number of prematurity-related complications, while mother's own milk (MOM) dose decreases significantly with the number of prematurity-related complications.

The marginal or incremental cost of prematurity-related complications in VLBW infants ranges from \$27,890 for late-onset sepsis to \$46,103 for necrotizing enterocolitis (in 2016 US dollars).

A reduction in the incidence of potentially preventable complications has significant cost implications, and hospitals should prioritize investments in MOM feedings for VLBW infants in the NICU.

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## 1 Introduction

In 2019, 51,716 infants were born very low birth weight (VLBW; < 1500 g birth weight) in the US [1]. VLBW infants represent only 1.4% of total births, but account for 36% of dollars spent on newborn care [2], making these infants among the most expensive hospitalized patients. Whereas the lengthy hospitalization (mean 56.5 days) for VLBW infants costs an average of \$219,669 (in 2017 US dollars [US\$]) [2], potentially preventable complications of prematurity, including late-onset sepsis, necrotizing enterocolitis (NEC), and bronchopulmonary dysplasia (BPD), increase these costs significantly by prolonging the NICU hospitalization and increasing the use of expensive pharmaceuticals, surgical interventions, respiratory care, and other therapies. Furthermore, these complications predispose infants to neurodevelopmental problems and other long-term health problems and concomitant costs, presenting significant burden to families, health care programs, and educational systems throughout childhood [3–12]. Thus, a priority in neonatal care is to identify cost-effective interventions to reduce the risk of these potentially preventable complications.

Previous work has shown that mother's own milk (MOM, milk from the infant's own mother and excludes donor human milk) feedings at critical post-birth exposure periods reduce the risk of these neonatal complications in a dose-dependent manner [13–17]. However, the feeding of MOM also has a cost because it necessitates an infrastructure within the individual neonatal intensive care unit (NICU) that is focused on the acquisition and feeding of MOM, including NICU-specific lactation specialists; access to hospital-grade electric breast pumps, collection kits, and other supplies for maternal breastmilk provision; hospital-grade freezers, milk warmers, and other equipment; and professional and peer messaging of evidence-based, actionable information [18]. For many institutions, these start-up costs appear prohibitive and there is reluctance to make the evidence-based investments to acquire MOM for this vulnerable population. As a consequence of insufficient quantities of MOM, donor human milk or formula is substituted, increasing the risk of potentially preventable complications of prematurity.

While prior research has estimated the cost savings associated with reducing the incidence of these prematurity-related complications [13–16], research is lacking on the combined indirect and direct cost savings of MOM received during the NICU stay that includes not only the cost of the NICU hospitalization but also the cost of feeding MOM. The Longitudinal Outcomes of Very Low Birthweight Infants Exposed to Mothers' Own Milk (LOVE MOM) study was a large prospective,

observational study of a racially and ethnically diverse cohort of VLBW infants designed to evaluate the health outcomes and costs associated with MOM dose and exposure period during the NICU hospitalization. To determine the relationship between the NICU hospitalization (hospital, physician, and feeding) costs and NICU dose of MOM for VLBW infants, we analyzed detailed data on neonatal and maternal characteristics, clinical factors, feedings, and costs for LOVE MOM infants. Additionally, because MOM intake during the NICU hospitalization is associated with a reduction in the risk of sepsis, NEC, and BPD, we aimed to quantify the incremental cost of these three prematurity-related complications.

## 2 Methods

### 2.1 Study Design and Sample

LOVE MOM was a National Institutes of Health (NIH)-funded prospective, observational cohort study of 430 VLBW infants admitted to the Rush University Medical Center NICU located in Chicago, IL, USA, and followed from admission to discharge between February 2008 and June 2012. Infants who met the following inclusion criteria were eligible for the study: birth weight < 1500 g, gestational age < 35 weeks, enteral feedings initiated by day of life (DOL) 14, no major congenital anomalies or chromosomal disorders, and a negative maternal drug screen. This study was limited to infants who were not transferred to a referral hospital prior to NICU discharge [13]. The cost analysis was conducted from the healthcare system perspective that included inpatient and physician resources used and their associated costs for the initial NICU hospitalization. The study was approved by the Rush University Medical Center Institutional Review Board.

### 2.2 Mother's Own Milk

MOM feedings were measured as dose (mL/kg/day) and as a proportion of total enteral intake (milliliters MOM ÷ [milliliters MOM + milliliters formula]) [19]. Donor human milk was not used in the study NICU during this time period, and therefore, was not included in the analysis. The primary MOM feeding variable was the cumulative proportion of MOM received by the infant during the NICU hospitalization. Additionally, we examined mean daily dose of MOM feedings received for DOL 1–14, DOL 1–28, and DOL 1 through discharge. For DOL 1–28, MOM was also categorized as exclusive or non-exclusive.

### 2.3 Prematurity-Related Complications

Prematurity-related complications included late-onset sepsis, NEC, and BPD. Infants were classified as having late-onset sepsis (sepsis) if they had a positive blood culture after DOL 3 and received antibiotic treatment for 5 or more days [13]. NEC was defined by having both clinical and radiologic criteria, based on the modified Bell's criteria  $\geq 2$  [16, 20]. NEC did not include spontaneous intestinal perforation, isolated bowel perforation by DOL 7 with no pneumatosis intestinalis or portal venous gas. NEC with surgical treatment was defined by receipt of a peritoneal drain or undergoing laparotomy, otherwise cases were classified as medically managed. BPD was defined as requiring either  $> 21\%$  oxygen or receiving continuous positive airway pressure or mechanical ventilation at 36 weeks postmenstrual age [21]. In addition to the presence or absence of each complication, the total number of complications (sepsis, NEC, BPD) was calculated (0, 1, 2, 3) and a categorical variable representing the eight unique combinations of the three complications was created (none, NEC only, sepsis only, BPD only, NEC and sepsis, NEC and BPD, sepsis and BPD, all three complications). Because of its impact on cost, severe brain injury, defined as intraventricular hemorrhage, periventricular leukomalacia, or acquired hydrocephalus [17], was included in the analysis. We did not include severe brain injury in either the number or combination of complications because it is not associated with MOM feedings.

### 2.4 Neonatal and Sociodemographic Risk Factors

Neonatal risk factors included gestational age (completed weeks), birth weight (g), sex, small for gestational age at birth [22], and singleton or multiple birth. Sociodemographic characteristics included maternal age at birth, maternal race and ethnicity (Hispanic, non-Hispanic Black, non-Hispanic White, and other, including American Indian or Alaskan Native, Asian, and more than one race), and primary payer (Medicaid [including two infants who were uninsured] and commercial payer), based on maternal insurance coverage. DOL of first feeding and surfactant therapy were included as measures of early neonatal severity of illness, and death ( $n = 9$ ) prior to hospital discharge was included as a covariate as an overall measure of severity. Because of the small number of infants who died during the NICU hospitalization and high variability in the timing of death, ranging from 18 to 27 days of life, and all with at least one of the potentially preventable complications of prematurity, we included death as a covariate. Additionally, transfer to an outside hospital at the time of NICU discharge was included as a covariate.

### 2.5 Length of Stay and Cost Calculations

Length of stay was calculated as the difference between hospital discharge and admission (birth) dates, including any hospital days outside of the NICU (a small number of infants were transferred from the NICU to the pediatric unit prior to hospital discharge). Cost data for the NICU hospitalization were obtained from the institution's cost accounting system and reflected the cost to the hospital or clinician to provide care from birth to hospital discharge. Hospital and clinician costs were determined based on the number and type of resources used, as detailed in our previous publications [13, 23]. Hospital costs were classified into the following categories: NICU room and board (including nursing care), cardiology, developmental psychology testing and assessment, diagnostic testing, laboratory and pathology, pharmacy, respiratory care, surgery, therapies, and feeding, while clinician costs were classified into the following specialties: neonatology, pediatric cardiology, pediatric surgery, pediatric non-surgical specialties, other pediatric surgical specialties, and other inpatient pediatrics.

We calculated feeding costs using a previously developed algorithm [18, 24] reflecting hospital costs. Formula and MOM feeding costs were calculated separately and were summed to determine the total feeding cost. The cost for formula was estimated at \$0.033 per milliliter in 2016 US\$ [25–27]. The cost for MOM feedings included both equipment and supply costs (evidence-based education materials, hospital-grade electric breast pump rental, pumping supplies, freezer space, waterless warmers and liners, creamatocrit and infant scales) and NICU-specific lactation specialists (breastfeeding peer counselor support) [18, 26, 27].

To account for changes in costs over time that may have varied by resource, all costs were held constant at their 2016 US\$ values using the 2016 per-unit cost to the hospital. Because per-unit clinician costs were not available, average provider payment per encounter was used as a proxy for cost. In cases where a resource did not have a 2016 per-unit cost, cost was inflated to 2016 US\$ using the Consumer Price Index for Medical Care from the US Bureau of Labor Statistics (Series ID: CUSR0000SAM) [28]. The resource-level costs in 2016 US\$ were summed to calculate the total NICU cost per infant. NICU hospitalization cost per day was calculated by dividing the total NICU cost by length of stay.

### 2.6 Statistical Analysis

Descriptive analyses included medians (interquartile range [IQR]), means (standard deviation [SD]), and number (percentage). Because maternal and infant characteristics may be associated with both MOM provision and costs, leading to different distributions of covariates by MOM provision, we constructed a propensity score for exclusive MOM

feeding for DOL 1–28 (coded as 1/0) using a binary logistic regression model, including neonatal risk factors, sociodemographic characteristics, neonatal severity of illness, and neonatal complications as covariates. The predicted probability of receiving exclusive MOM through 28 DOL was estimated, and the inverse probability of treatment weight (IPTW) was computed, such that each subject with exclusive MOM through DOL 28 was assigned a weight of  $1/\text{propensity score}$  and each subject with non-exclusive MOM through DOL 28 was assigned a weight of  $1/(1-\text{propensity score})$ . Observations with non-overlapping propensity scores were trimmed at both the lower and upper ends ( $n = 3$ ) [29]. A comparison of the mean propensity score by quintile bin for infants with exclusive and non-exclusive MOM through DOL 28 was performed to ensure an adequately balanced distribution. We assessed overlap in the distribution of the estimated propensity score across DOL 28 MOM feeding groups and the balance of individual covariates by calculating the standardized mean differences [30, 31]. A maximum standardized difference  $<20\%$  was assumed to be sufficiently balanced for the propensity score [32, 33].

A generalized linear regression model with a gamma distribution and log-link function was constructed for NICU hospitalization costs that included the cumulative proportion of MOM received during the NICU hospitalization, individual prematurity-related complications (late-onset sepsis, NEC, BPD, severe brain injury), infant gestational age, sex, small for gestational age at birth, and multiple versus singleton birth; maternal age and race/ethnicity; primary payer; and neonatal severity of illness (DOL of first feeding, surfactant therapy, death, or transfer to an outside hospital). A modified Park test was used to select the appropriate mean–variance relationship for the regression model [34], and model goodness of fit was assessed via a modified Hosmer–Lemeshow Test and Pregibon link test. The average marginal effect and 95% confidence intervals (CIs) were computed for a one percentage point increase in the cumulative proportion of MOM received during the NICU hospitalization using the method of recycled predictions, by calculating the adjusted cost for each infant, holding all other infant characteristics constant, then calculating the adjusted cost for each infant after adding one percentage point to the cumulative proportion of MOM received [35–37]. The average marginal effect was calculated as the difference in adjusted costs for one additional percentage point of MOM during the NICU hospitalization. For individual prematurity-related complications, the average marginal effect and 95% CIs were computed using recycled predictions by turning on and off the complication for all infants in the sample and calculating the difference in costs. Similar procedures were used to construct the regression model and estimate average marginal effects for NICU hospitalization cost per day. All statistical analyses were performed using SAS version 9.4

(SAS Institute Inc., Cary, NC, USA) and Stata version 17.0 (StataCorp LLC, College Station, TX, USA).

### 3 Results

The sample included 430 VLBW infants with a median gestational age of 28 weeks (IQR 26–30) and birth weight of 1053 g (IQR 840–1245) [Table 1; Online Resource 1]. The sample was 27% Hispanic and 52% non-Hispanic Black. Overall, 12% had sepsis, 10% had NEC, and 32% had BPD. Additionally, 2% ( $n = 9$ ) of infants died during the NICU hospitalization, all having developed at least one of the above-mentioned complications. The median NICU hospitalization length of stay was 65 days (IQR 46–94).

Table 2 details the breakdown of hospital and clinician costs per infant. The mean NICU hospitalization cost was \$190,586 (SD \$119,235) and the mean cost per day was \$2548 (SD \$340). Hospital costs represented 91% of the NICU hospitalization costs. The category with the highest hospital costs was NICU room and board, including nursing care, followed by pharmacy costs. Neonatology represented 93% of the clinician costs.

Overall, 256 (60%) of the infants had no complications, 124 (29%) had one complication, 40 (9%) had two complications, and 10 (2%) had all three complications (Table 3). There were significant differences in infant characteristics by the number of complications, including MOM feedings, NICU length of stay, and NICU hospitalization costs. Online Resource 2 describes the feeding characteristics, NICU length of stay, and costs by combination of complications.

Each complication was associated with significantly higher unadjusted NICU hospitalization costs (Table 4). The largest difference in cost was for BPD, with an unadjusted cost difference of \$152,447 (95% CI \$128,158–\$176,736).

Online Resource 3 summarizes the variables included in the binary logistic regression model used to construct the propensity score for exclusive MOM at DOL 28. Infants who received exclusive MOM at DOL 28 differed modestly from those who received non-exclusive MOM at 28 DOL, including younger gestational age (27 vs. 28 weeks), older maternal age (28 vs. 26 years), more infants of White and Hispanic race/ethnicity, fewer with Medicaid (51% vs. 74%), and longer durations of parenteral nutrition (18 vs. 15 days). The IPTW weighting decreased the standardized mean difference between groups for all but two covariates (infant sex and death before discharge), and the standardized mean difference was  $<0.1$  for all variables after IPTW weighting (Online Resources 4 and 5). Additionally, the propensity score was well-balanced within each quintile bin, demonstrating that the covariates were balanced between DOL 28 MOM feeding groups (exclusive/non-exclusive) [Online Resource 6]. Trimming observations with non-overlapping

**Table 1** Sample description  
(*N* = 430)

| Variable  |                    |
|---|--------------------|
| Gestational age, weeks [median (IQR)]                     | 28 (26–30)         |
| Birth weight, g [median (IQR)]                            | 1053 (840–1245)    |
| Female [n (%)]  | 201 (46.7)         |
| Small for gestational age at birth                        | 86 (20.0)          |
| Multiple gestation [n (%)]                                | 64 (14.9)          |
| Maternal age, years [median (IQR)]                        | 27 (22–32)         |
| Surfactant therapy [n (%)]                                | 309 (71.9)         |
| Race and ethnicity [ <i>n</i> = 429]                      |                    |
| Hispanic  | 114 (26.6)         |
| Non-Hispanic Black  | 223 (51.0)         |
| Non-Hispanic White/Other                                  | 92 (21.4)          |
| Primary payer [n (%)]                                     |                    |
| Medicaid  | 275 (64.3)         |
| Commercial  | 153 (35.8)         |
| DOL first feeding [median (IQR)]                          | 4 (3–5)            |
| Days with parenteral nutrition [median (IQR)]             | 16 (11–27)         |
| DOL 1–14 feeding  |                    |
| MOM daily dose, mL/kg/day [median (IQR)]                  | 21.0 (6.2–49.3)    |
| Percentage MOM [median (IQR)]                             | 100.0 (85.4–100.0) |
| DOL 1–28 feeding (or through discharge if before DOL 28)  |                    |
| MOM daily dose, mL/kg/day [median (IQR)]                  | 46.1 (14.6–85.9)   |
| Percentage MOM [median (IQR)]                             | 96.3 (38.0–100.0)  |
| Exclusive MOM [n (%)]                                     | 185 (43.0)         |
| DOL 1—discharge feeding (NICU stay)                       |                    |
| MOM daily dose, mL/kg/day [median (IQR)]                  | 54.2 (11.5–106.5)  |
| Cumulative percentage of MOM for NICU stay [median (IQR)] | 42.5 (7.5–98.3)    |
| Any neonatal complications [n (%)]                        | 190 (44.2)         |
| Late-onset sepsis [n (%)]                                 | 52 (12.1)          |
| Necrotizing enterocolitis [n (%)]                         | 43 (10.0)          |
| Necrotizing enterocolitis with surgical treatment [n (%)] | 13 (3.0)           |
| Bronchopulmonary dysplasia [n (%)]                        | 139 (32.3)         |
| Severe brain injury                                       | 24 (5.6)           |
| In-NICU death <sup>a</sup> [n (%)]                        | 9 (2.1)            |
| Transfer to outside hospital [n (%)]                      | 43 (10.0)          |
| NICU length of stay [median (IQR)]                        | 65 (46–94)         |

Data are expressed as *n* (%) unless otherwise specified

<sup>a</sup>All deaths had at least one complication

*IQR* interquartile range, *DOL* day of life, *MOM* mother’s own milk, *NICU* neonatal intensive care unit

propensity scores modestly improved the balance in the highest and lowest quintile bins.

Table 5 shows the adjusted average marginal effect for the cumulative proportion of MOM feedings during the NICU hospitalization and for each prematurity-related complication (the full set of regression coefficients is provided in Online Resource 7). The cumulative proportion of feedings that were MOM during the NICU hospitalization was not significantly associated with cost, after adjusting for the presence of the prematurity-related complications and other maternal and infant factors. In absolute dollar terms, the

NICU hospitalization cost attributed to NEC was \$46,103 (95% CI \$16,829–\$75,377), higher than the cost attributed to either BPD or sepsis. Figure 1a–d show the average marginal effect for the cumulative proportion of MOM and for each prematurity-related complication by gestational age. The NICU hospitalization cost attributed to each complication was largest for the youngest gestational age, decreasing as gestational age increased.

The adjusted average marginal effects of MOM provision and neonatal complications on NICU hospitalization costs *per day* are shown in Online Resource 8. The NICU



**Table 2** Mean costs in 2016 US dollars ( $N = 430$ )

| Cost category                         | Mean (SD)         |
|---------------------------------------|-------------------|
| Total NICU hospitalization cost       | 190,583 (119,235) |
| Hospital cost                         | 173,048 (103,335) |
| NICU room and board                   | 141,872 (79,174)  |
| Cardiology                            | 1421 (1792)       |
| Developmental psychology              | 684 (352)         |
| Diagnostic testing                    | 2579 (2532)       |
| Laboratory/pathology                  | 6544 (5541)       |
| Pharmacy                              | 10,856 (13,305)   |
| Parenteral nutrition                  | 5613 (7417)       |
| Other pharmacy                        | 5242 (6272)       |
| Respiratory care                      | 7354 (10,347)     |
| Surgery                               | 1081 (2310)       |
| Therapies                             | 659 (700)         |
| Feeding                               | 839 (378)         |
| Mother's own milk                     | 538 (268)         |
| Formula                               | 302 (348)         |
| Physician cost                        | 16,698 (11,375)   |
| Neonatology                           | 15,511 (10,196)   |
| Pediatric cardiology                  | 183 (356)         |
| Pediatric surgery                     | 474 (938)         |
| Pediatric non-surgical subspecialties | 108 (288)         |
| Other pediatric surgical specialties  | 391 (601)         |
| Other inpatient pediatrics            | 31 (474)          |
| Total cost per day                    | 2548 (340)        |

NICU neonatal intensive care unit, SD standard deviation

Note: 161 (37.4%) had surgery costs; 166 (38.6%) had pediatric subspecialty physician costs

hospitalization cost per day attributed to NEC was \$223 (95% CI \$100–\$346), and \$99 (95% CI \$49–\$148) for BPD. Cumulative proportion of feedings that were MOM and sepsis were not significantly associated with NICU hospitalization costs per day.

## 4 Discussion

To our knowledge, this is the first study to investigate the relationship among MOM feedings during the NICU hospitalization, incidence of prematurity-related complications, and NICU hospitalization costs for VLBW infants. The results of this study shed light on the 'return on investment' associated with the costs of a NICU infrastructure that supports the acquisition and feeding of MOM via a reduction in the incidence of prematurity-associated complications. Unique to this study is the inclusion of the cost of supporting the provision of MOM in the feeding costs, which are more difficult to calculate than costs of donor milk or formula. While the costs associated with MOM provision have often

been overlooked [38], we calculated the per milliliter cost [27] to determine the exact costs of MOM in this economic evaluation. Prior research has shown that higher doses and durations of MOM during the NICU hospitalization are associated with a reduction in the risks of sepsis, NEC, and BPD [13, 14, 16], and our findings add to this research by demonstrating substantial cost savings with institutional investments in MOM feedings. After controlling for neonatal and maternal risk factors, sociodemographic characteristics, and infant severity of illness, we found the NICU hospitalization costs attributable to these prematurity-related complications are significant, ranging from \$27,890 (in 2016 US\$) for sepsis to \$46,103 for NEC. These costly complications not only increase NICU hospitalization costs via longer lengths of stay but also increase the NICU hospitalization costs per day due to the use of costly pharmacy products, therapies, surgical treatments, and other services.

Overall, our unadjusted NICU hospitalization cost per VLBW infant was similar to costs reported by Phibbs et al. [2]. (\$222,031 in 2017 US\$ by Phibbs et al. vs. \$190,583 in 2016 US\$); however, the mean NICU length of stay for VLBW infants reported by Phibbs et al. was considerably shorter (57 days vs. 73 days [results not shown]) and cost per day higher (\$3756 vs. \$2548) than in our study. Their study included 13,017 VLBW infants born in non-federal hospitals in California between 2009 and 2011, but did not include the prevalence of prematurity-related complications; therefore, the underlying distribution of these complications and other infant characteristics may have differed from our cohort.

Our adjusted cost multipliers for sepsis, BPD, and NEC are considerably lower than those reported by Beam et al. [39] in a study of commercially insured, low birth weight (LBW; <2500 g) and preterm (gestational age < 37 weeks) infants born between 2008 and 2016 in the US. Beam et al. reported adjusted cost multipliers (i.e., exponentiated coefficients from their generalized linear regression model) of 1.29 for sepsis, 1.91 for NEC, and 2.15 for BPD for the first 6 months of life, while we reported equivalent cost multipliers (computed by adding 1 to the percentage change reported in Online Resource 7) of 1.15 for sepsis, 1.25 for NEC, and 1.24 for BPD for the initial NICU hospitalization. While differences in inclusion criteria, including predominantly Medicaid-insured VLBW infants in our study versus commercially insured LBW infants in the study by Beam et al., and differences in covariate adjustment may explain some of the differences, the fact that our adjusted cost ratios are similar for sepsis suggest that the post NICU discharge healthcare costs attributed to NEC and BPD through the first 6 months of life may be substantial and warrant future study [40, 41].

In our investigation, unadjusted NICU hospitalization costs for infants with and without BPD were very similar to the unadjusted cost estimates reported by Lapcharoensap

**Table 3** Description of sample by number of complications (*N* = 430)

| Characteristic                                       | No complications<br>[ <i>n</i> = 256 (59.5%)] | 1 complication <sup>a</sup><br>[ <i>n</i> = 124 (28.8%)] | 2 complications<br>[ <i>n</i> = 40 (9.3%)] | 3 complications<br>[ <i>n</i> = 10 (2.3%)] | <i>p</i> -Value |
|--|---|--|--|--|-----------------|
| Gestational age, weeks [median (IQR)]                | 29 (27–30)                                    | 26 (25–28)   | 27 (26–28)                                 | 25 (24–26)                                 | < 0.001         |
| Birth weight, g [median (IQR)]                       | 1183 (1000–1340)                              | 858 (720–1045)   | 859 (675–1065)                             | 920 (660–1040)                             | < 0.001         |
| DOL first feeding [median (IQR)]                     | 3 (3–5)                                       | 5 (3–8)  | 4 (3–8)                                    | 4 (4–5)                                    | < 0.001         |
| DOL 14 feeding                                       |   |  |  |  |                 |
| MOM daily dose, mL/kg/day [median (IQR)]             | 30.6 (12.5–66.0)                              | 10.9 (3.1–23.7)  | 13.1 (3.9–27.9)                            | 10.8 (1.6–24.9)                            | < 0.001         |
| Percentage MOM [median (IQR)]                        | 100 (72–100)                                  | 100 (100–100)  | 100 (91–100)                               | 100 (100–100)                              | 0.001           |
| DOL 28 feeding (or discharge)                        |   |  |  |  |                 |
| MOM daily dose, mL/kg/day [median (IQR)]             | 71.0 (22.5–98.5)                              | 31.4 (11.7–63.2)   | 23.6 (6.4–69.7)                            | 9.9 (5.2–30.6)                             | < 0.001         |
| Percentage MOM [median (IQR)]                        | 91 (30–100)                                   | 100 (51–100)   | 100 (42–100)                               | 92 (62–100)                                | 0.109           |
| Discharge feeding                                    |   |  |  |  |                 |
| MOM daily dose, mL/kg/day [median (IQR)]             | 75.2 (15.4–117.6)                             | 37.2 (8.8–94.1)  | 17.5 (3.2–48.2)                            | 11.7 (6.8–21.5)                            | < 0.001         |
| Cumulative percentage MOM [median (IQR)]             | 56 (10–100)                                   | 23 (5–88)  | 17 (2–86)                                  | 13 (62–100)                                | 0.003           |
| Exclusive MOM [ <i>n</i> (%)]                        | 56 (21.9)                                     | 13 (10.5)  | 7 (17.5)                                   | 1 (10.0)                                   | 0.050           |
| NICU length of stay, med (25th, 75th) [median (IQR)] | 52 (40–67)                                    | 95 (74–120)  | 101 (68–126)                               | 135 (109–174)                              | < 0.001         |
| NICU hospitalization cost, in 000s [mean (SD)]       | 133 (57)                                      | 256 (99)   | 283 (136)                                  | 476 (305)                                  | < 0.001         |
| NICU cost per day [mean (SD)]                        | 2429 (149)                                    | 2621 (190)   | 2882 (452)                                 | 3354 (1343)                                | < 0.001         |

*IQR* interquartile range, *DOL* day of life, *MOM* mother’s own milk, *NICU* neonatal intensive care unit, *SD* standard deviation

<sup>a</sup>Three infants also had retinopathy of prematurity

**Table 4** Mean total NICU hospitalization cost by presence/absence of each prematurity-related complication (*N* = 426)

| Complication               | Present<br>[mean (SD)] | Absent<br>[mean (SD)] | Difference (95% CI)         |
|----------------------------|------------------------|-----------------------|-----------------------------|
| Late-onset sepsis          | \$297,182 (185,378)    | \$175,273 (96,927)    | \$121,909 (70,648–173,169)  |
| Necrotizing enterocolitis  | \$283,026 (211,759)    | \$179,727 (97,609)    | \$103,299 (40,515–166,083)  |
| Bronchopulmonary dysplasia | \$293,574 (138,760)    | \$141,127 (63,377)    | \$152,447 (128,158–176,736) |

*NICU* neonatal intensive care unit, *SD* standard deviation, *CI* confidence interval

**Table 5** Adjusted average marginal effects for NICU hospitalization costs in 2016 US\$ (*N* = 426)

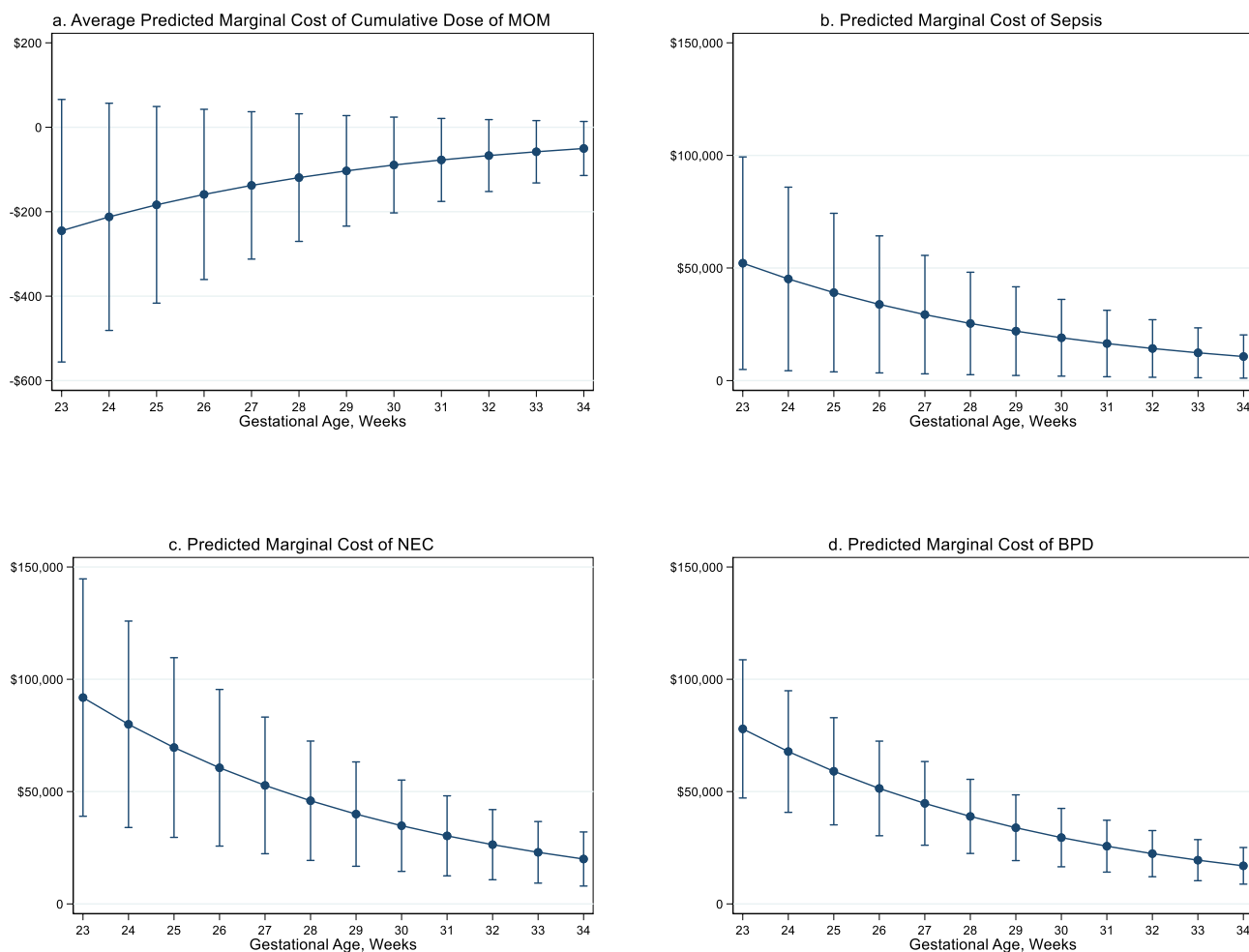
|   | Average marginal effect | 95% CI           |
|---|-------------------------|------------------|
| Cumulative percentage of MOM at discharge | – \$131                 | – 297 to 35      |
| Late-onset sepsis                         | \$27,890                | 2934 to 52,646   |
| Necrotizing enterocolitis                 | \$46,103                | 16,829 to 75,377 |
| Bronchopulmonary dysplasia                | \$41,976                | 24,660 to 59,292 |

*NICU* neonatal intensive care unit, *CI* confidence interval, *MOM* mother’s own milk

Note: Model controls for gestational age, small for gestational age at birth, race and ethnicity, sex, primary payer, maternal age, surfactant therapy, day of life of first feeding, multiple or single gestation, severe brain injury, death, and transfer to an outside hospital. Model weighted by inverse probability of treatment weight

et al. (unadjusted cost ratio of 2.07 vs. 2.05) [42]; however, we found a much smaller adjusted difference in costs for BPD. After adjusting for infant clinical factors,

Lapcharoensap et al. found an adjusted cost multiplier of 1.55 (i.e., infants with BPD had 1.55 times higher costs than infants without BPD), while adjusted costs for infants with BPD in our sample were only 1.24 times higher than those without BPD. Although our study time periods and statistical methods were similar, the difference in our findings may be explained by underlying differences in the characteristics of the samples, including differences in the severity of BPD and the prevalence of other complications. The California cohort of infants included in the study by Lapcharoensap et al. [23] had much higher and disproportionate rates of retinopathy of prematurity (ROP) and intraventricular hemorrhage for infants with BPD compared with infants in our study, and the combination of BPD and these complications may have increased costs in their study. Additionally, given the impact of MOM dose on the reduction of BPD, it is important to understand diet and MOM intake when interpreting the prevalence and NICU hospitalization costs of BPD.



**Fig. 1 a–d** Predicted marginal effects by gestational age, in weeks. *Sepsis* late-onset sepsis, *NEC* necrotizing enterocolitis, *BPD* bronchopulmonary dysplasia

One important limitation to note is that many NICUs in the US use donor human milk, rather than formula, for the first few weeks of life, and as such, the comparative outcomes may differ from the results of this study; however, donor milk programs are not yet universal in the US and worldwide. Within US NICUs, an estimated 12% of level 3 and 4 NICUs and 28% of level 2 NICUs reported that they did not have a donor milk program in 2017. Furthermore, with the COVID-19 pandemic, some NICUs began to ration donor human milk in anticipation of shortages to ensure availability for the sickest infants [43]. Research has demonstrated a reduction in the incidence and severity of NEC with donor human milk rather than formula supplementation, but no impact on the incidence or severity of sepsis or BPD [44]. While feeding costs are a relatively small proportion of the overall NICU hospitalization costs, donor human milk costs 15 times more than formula per milliliter [24]. Additionally, this study followed infants through to NICU discharge, and therefore, we did not have information

about post-discharge healthcare utilization, quality-adjusted life-years, or years-of-life lost associated with these morbidities over the lifespan and could not evaluate the long-term cost effectiveness of MOM. Future work should model the long-term cost-effectiveness of MOM in this population of vulnerable infants. Additionally, while we found cumulative dose of MOM was not significantly associated with NICU hospitalization costs after accounting for the three prematurity-related complications, other research suggests a longer-term impact of MOM dose on neurodevelopment that is only seen after NICU discharge [11, 45]. Therefore, cost savings due to reductions in the incidence of these three prematurity-related complications are likely to be a lower bound of the longer-term economic implications of MOM through childhood.

This study examined the relationship between three prematurity-related complications with strong evidence to suggest a causal relationship with MOM feedings; however, it is important to note the exclusion of ROP. While



there is moderate evidence that ROP is associated with MOM feedings [46, 47], there were only two cases of ROP in our sample, making NICU hospitalization costs unanalyzable.

## 5 Conclusion

We examined the association between MOM intake, prematurity-related complications, and NICU hospitalization costs for VLBW infants and found that NICU hospitalization costs attributed to complications that are potentially preventable via MOM intake in VLBW infants are high, each increasing hospitalization costs by 15–30%. There is substantial clinical and biological evidence of an association between high-dose MOM and a reduction in the risk of prematurity-related complications, including sepsis, NEC and BPD, and cost savings attributed to reducing the incidence of these complications ranges from \$27,790 to \$46,103. Because VLBW infants are among the most expensive patients in the hospital, these study findings can inform policymakers, payers, and healthcare providers that investments in the infrastructure to optimize MOM feedings in the NICU is a low cost and effective strategy for improving infant health and reducing costs in an extremely vulnerable patient population.

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## Declarations

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**Conflicts of interest** Tricia Johnson has received speaker honorarium and consulting fees from Medela, a company that provides products to support breastfeeding. Aloka Patel, Michael Schoeny, and Paula Meier have no conflicts of interest or competing interests to declare.

**Availability of data and material** Anonymized data sets created and/or analyzed for this study are available upon reasonable request from the corresponding author.

**Code availability** SAS syntax is available upon request from the corresponding author.

**Author contributions** All authors conceptualized and designed the study. PPM obtained funding for the study. TJJ, ALP, and PPM were responsible for data acquisition. TJJ and MES were responsible for the statistical and economic analysis. The manuscript was drafted by TJJ and PPM, and all authors were responsible for making critical comments and editing the manuscript. All authors reviewed the final version of the manuscript for submission and approved of its submission.

**Ethical approval** The study protocol was reviewed and approved by the Rush University Medical Center Institutional Review Board.

**Consent to participate** Informed consent was obtained from all individual participants (maternal data) included in the study, and informed consent was obtained from mothers for infant data included in the study. Anonymity and confidentiality were maintained in this publication.

**Consent for publication** Not applicable.

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