


ORIGINAL ARTICLE

Room for improvement in breast milk feeding after very preterm birth in Europe: Results from the EPICE cohort

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Abstract

Breast milk feeding (BMF) is associated with lower neonatal morbidity in the very preterm infant (<32 weeks gestation) and breastfeeding is beneficial for maternal health. Previous studies show large variations in BMF after very preterm birth and recognize the need for targeted breastfeeding support in the neonatal intensive care units (NICU). In a European collaboration project about evidence-based practices after very preterm birth, we examined the association between maternal, obstetric, and infant clinical factors; neonatal and maternal care unit policies; and BMF at discharge from the NICU. In multivariable analyses, covariates associated with feeding at discharge were first investigated as predictors of any BMF and in further analysis as predictors of exclusive or partial BMF. Overall, 58% (3,826/6,592) of the infants received any BMF at discharge, but there were large variations between regions (range 36–80%). Primiparity, administration of antenatal corticosteroids, first enteral feed <24 hr after birth, and mother's own milk at first enteral feed were predictors positively associated with any BMF at discharge. Vaginal delivery, singleton birth, and receiving mother's own milk at first enteral feed were associated with exclusive BMF at discharge. Units with a Baby Friendly Hospital accreditation improved any BMF at discharge; units with protocols for BMF and units using donor milk had higher rates of exclusive BMF at discharge. This study suggests that there is a high potential for improving BMF through policies and support in the NICU.

KEYWORDS

baby friendly hospital, breast milk, breastfeeding, neonatal intensive care unit (NICU), policies, very preterm birth

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1 | INTRODUCTION

Breast milk feeding (BMF) benefits mothers and infants regardless of setting (Victora et al., 2016; WHO, 2011). For the very preterm infant (born <32 weeks of gestation), BMF reduces neonatal morbidity, such as necrotizing enterocolitis (NEC), (Lucas & Cole, 1990; Quigley & McGuire, 2014; Sisk, Lovelady, Dillard, Gruber, & O'Shea, 2007; Sullivan et al., 2010) and is associated with lower rates of late-onset sepsis (Corpeleijn et al., 2016; Underwood, 2013), retinopathy of prematurity (Bharwani et al., 2016; Manzoni et al., 2013), and improved long-term neurocognitive development (Larroque et al., 2008; Lucas, Morley, Cole, Lister, & Leeson-Payne, 1992). In addition, increased duration of breastfeeding is associated with reduced risk of breast and ovarian cancer and cardiovascular disease as well as maternal psychological well-being (Chowdhury et al., 2015; Schwarz et al., 2009; Victora et al., 2016).

After very preterm birth, several factors can hinder establishment of adequate breast milk production. Mothers and infants may be separated during the long hospitalization, and the mother will need to express breast milk for several weeks before the infant can feed sufficient milk volumes from the breast directly (Acuna-Muga et al., 2014; Alves, Magano, Amorim, Nogueira, & Silva, 2016; Alves, Rodrigues, Fraga, Barros, & Silva, 2013; Callen & Pinelli, 2005; Furman, Minich, & Hack, 2002).

The Baby-Friendly Hospital Initiative (BFHI) for Neonatal wards is an adaptation of the WHO "Ten steps to successful breastfeeding" (World Health Organization, 2009) for neonatal wards. It was developed by an expert group, the "Nordic and Quebec Working Group" (Nyqvist et al., 2013), aiming at improving breastfeeding in infants cared for in the neonatal intensive care unit (NICU). This new guideline stresses the importance of early initiation of BMF, skin-to-skin contact, breastfeeding support including antenatal information and continued support throughout the hospital stay, and a follow-up plan (Nyqvist et al., 2015).

The aims of this study were to investigate BMF rates at discharge from neonatal intensive care in a large European cohort of infants born very preterm, and to explore maternal, obstetric and infant factors, as well as maternal and neonatal unit policies that might influence BMF at hospital discharge.

2 | METHODS

2.1 | Context and setting

Data for this study were obtained from the EPICE (Effective Perinatal Intensive Care in Europe) cohort and unit studies. EPICE is a European collaboration project investigating the use of evidence-based practices and their associations with outcomes in a cohort of very preterm infants born below 32 weeks of gestation in 11 countries in 19 European regions during 12 consecutive months in 2011–2012 (6 months in France; Zeitlin et al., 2016).

For the cohort study, maternal, obstetric, and infant data were abstracted from medical records using a structured data collection instrument, pretested and jointly revised in the EPICE research group. For the unit study, questionnaires were sent out to the heads of the maternity and neonatal units participating in the EPICE study during

Key messages

- There are still large variations in breast milk feeding at discharge of infants born very preterm despite known benefits of breast milk and breastfeeding.
- A breast milk feeding friendly environment improves breast milk feeding rates at discharge from neonatal care.
- Units where donor milk is used are associated with improved exclusive rates of feeding with maternal milk at discharge from neonatal care.
- There is a high potential for improving breast milk feeding through policies and support in the neonatal intensive care unit.

the spring of 2012 to collect information about policies and practices of medical and care interventions for women at risk of delivering very preterm and for very preterm infants. The questionnaires included questions about the volume of admissions, staffing, perinatal practices, and presence of protocols. The interventions that were studied were based on clinical importance and quality of well-established evidence of their use (or nonuse), and breastfeeding was one of the interventions. The questionnaire could be filled in by several people together in the unit, and if there was an on-going randomized controlled trial, the units were asked to respond about "usual" practices.

2.2 | Ethics

For each region, ethical approval was obtained from regional or hospital ethics committees, as required by national legislation, and parental consent (an active written consent or passive consent i.e., the parents have received information about the study and are assumed to have consented if not stated otherwise) was obtained according to regional and hospital ethics committee requirements.

2.3 | Participants

All infants born alive in hospital between 22 + 0 and 31 + 6 weeks of gestation and admitted to neonatal intensive care were included in the present study ($N = 7,610$). We excluded in hospital deaths, infants with missing data on vital status at discharge, and infants never fed or missing nutritional data at discharge. Infants were followed until final discharge from neonatal intensive care. The final study population consisted of 6,592 infants. Inclusions and exclusions are shown in Figure S1.

The unit study included neonatal units with at least 10 very preterm admissions during the study period, as well as the maternity unit associated with each neonatal unit. Only infants admitted and discharged from the same unit were linked to units with answers from both maternal and neonatal unit questionnaires to be able to assign the

infant to the correct unit exposure, regardless if the infant was transferred or not during hospital stay.

Data for this analysis were collected from 82 units who cared for 3,765 infants in the sample.

2.4 | Exposure

The unit questionnaire covered availability of dedicated lactation personnel, advice given about when to start milk expression, if the unit was accredited a Baby Friendly Hospital or national equivalent, provision of donor milk, and maternity and neonatal policies as shown in Table 1. Investigated unit policies were associated with interventions that could potentially influence establishment of lactation (Kramer et al., 2001; Maastrup, Bojesen, Kronborg, & Hallstrom, 2012; Merewood, Philipp, Chawla, & Cimo, 2003; L. A. Parker, Sullivan, Krueger, & Mueller, 2015; M. G. Parker, Burnham, Mao, Philipp, & Merewood, 2016; World Health Organization, 2009). If there were incomplete answers, reminders were sent to the units, and in some cases, telephone interviews were performed for completion of the questionnaire.

2.5 | Outcome measures

BMF status at discharge was investigated as receiving maternal breast milk, without differentiating between mother's own milk and donor milk, and defined as receiving only maternal breast milk (*exclusive BMF*); or a combination of maternal breast milk and formula (*partial BMF*); or only formula (*no BMF*). Feeding at discharge was considered regardless of route (feeding at breast, tube, cup or bottle). In the

analyses, BMF exclusively or partially at discharge were also combined into one category, and defined as *any BMF*. Breastfeeding from the breast at discharge is described in the group of infants receiving any BMF.

2.6 | Individual-level covariates

We investigated the following maternal and obstetric covariates: maternal age, country of birth dichotomized as native (born in country where data were collected) or nonnative (born outside country where data were collected), except in the UK where data were available only on ethnicity; data on ethnicity were not available in the other European regions (most of the foreign-born (nonnative) women in our sample came from north and Sub-Saharan Africa, Eastern Europe, Asia, and South America), parity, preeclampsia (hypertension with proteinuria)/eclampsia (hypertension associated with one or more convulsions (seizures) or coma)/HELLP (Haemolysis Elevated Liver enzymes Low Platelet count-syndrome based on laboratory abnormalities) as a composite (yes vs. no), administration of antenatal corticosteroids (any vs. no), type of delivery (vaginal or caesarean), and type of birth (single or multiple). Infant covariates were gestational age (GA), small for GA (SGA; categorized as birth weight < 3rd or between 3rd and 10th percentiles for GA and sex, adapted to national population values for term birth weight; Mikolajczyk et al., 2011; Zeitlin et al., 2017), Apgar score < 7 at 5 min, time of first enteral feed; <1 day, 1–6 days, or >6 days, mother's own milk at first enteral feed, any major congenital anomaly, any major neonatal morbidity, such as intraventricular haemorrhage grade ≥ 3 according to Papile's classification (Papile, Burstein, Burstein, & Koffler, 1978), cystic

TABLE 1 Questions and results from unit policy questionnaires administered to head of the maternal and neonatal units.

	Units N = 82 (%)	Infants N = 3765 (%)
Unit policies		
Is there a designated staff to support mothers who are expressing or breastfeeding while they are hospitalized in the unit?		
Yes	62 (75.6)	2928 (77.8)
No	19 (23.2)	837 (22.2)
Missing	1 (1.2)	52 (1.4)
Are mothers at risk of delivering before 32 weeks of gestation advised to start expressing within 6 hr?		
Yes	54 (65.9)	2468 (65.6)
No	27 (32.9)	1177 (31.3)
Missing	1 (1.2)	120 (3.2)
Does the neonatal unit use human bank milk/donor milk to feed very preterm infants whose mothers do not express their milk?		
Yes	38 (46.3)	1604 (42.6)
No	44 (53.7)	2161 (57.4)
Are the units accredited a baby friendly hospital or national equivalent?		
Yes	23 (28.1)	1237 (32.9)
In process	12 (14.6)	412 (10.9)
No	45 (54.9)	2013 (54.5)
Missing	2 (2.4)	103 (2.7)
Does the unit have a written protocol for breast milk feeding and human milk use?		
Yes	74 (90.2)	3358 (89.2)
No	8 (9.8)	394 (10.1)

periventricular leukomalacia, NEC defined as surgery or peritoneal drainage for NEC; retinopathy of prematurity stage ≥ 3 , diagnosis of bronchopulmonary dysplasia defined as receiving oxygen or positive pressure ventilation at 36 weeks postmenstrual age (PMA), between hospital transfers any time during neonatal care (to investigate if any transfer might influence breastfeeding at discharge), and PMA at discharge.

2.7 | Missing data

The proportion of missing data was 0.3% for maternal age, 9.9% for maternal country of birth, 1.8% for preeclampsia/eclampsia/HELLP, 0.8% for type of delivery, 2.8% for time of first enteral feed, 7.8% for mother's own milk at first enteral feed, 3.5% for any major morbidity, 2.0% for bronchopulmonary dysplasia, and 4.6% for Apgar score. In the regression analysis, missing data for preeclampsia/eclampsia/HELLP and any major morbidity was treated as "no"; otherwise, we carried out a complete case analysis.

2.8 | Statistical analysis

2.8.1 | BMF at discharge

Descriptive statistics are presented as numbers and proportions for categorical data and medians and interquartile ranges for continuous data. Differences between the feeding categories at discharge (any BMF vs. no BMF and exclusive BMF vs. partial BMF) and individual level characteristics were tested using Wilcoxon rank sum for continuous variables, and chi-squared test for categorical variables.

2.8.2 | Maternal, obstetric and infant characteristics, and BMF at discharge

BMF at discharge was analysed as a dichotomous variable in two different regression analyses. First, we investigated BMF at discharge as *any BMF* versus *no BMF*, and in the second analysis, we excluded infants receiving only formula at discharge and investigated *exclusive BMF* versus *partial BMF*.

Covariate associations with any versus no BMF and exclusive versus partial BMF at discharge were analysed in two models. Model one adjusted for GA in days (continuous variable). Model two additionally adjusted for other potential confounders of the association between preterm birth and BMF; maternal age, country of birth, parity, preeclampsia/eclampsia/HELLP, administration of antenatal corticosteroids, type of delivery, multiple birth, Apgar score at 5 min, SGA, congenital anomalies, and time of first enteral feed, mother's own milk at first feed, infant morbidity, and between hospital transfers.

We used a mixed-effects modified Poisson model with robust standard errors to estimate risk ratios with 95% confidence intervals (Zou & Donner, 2013) for the associations between maternal, infant and neonatal unit characteristics, and BMF outcome at discharge. This model accounted for the clustering of infants within mothers and NICUs. NICU corresponds to the unit where the infant spent the first 48 hr after birth (as early establishment of milk production is most likely to be influenced by first unit).

2.8.3 | Unit policies and BMF at discharge

Descriptive statistics of unit policies are presented as numbers and proportions, and differences between BMF groups at discharge were tested using chi-squared test.

In regression analyses of the association between unit policies and BMF outcome at discharge, risk ratios were calculated using the same methodology described above with the following exceptions: first, the multivariable model did not adjust for time of first enteral feeding and own mother's milk at first enteral feed, as these can be intermediate variables in the causal pathway between the exposure, unit policy, and BMF at discharge; second, region, instead of unit, was used as the random variable.

2.8.4 | Breastfeeding at breast at discharge

Descriptive statistics of breastfeeding at breast are presented as numbers and proportions.

Analyses were computed using STATA IC 14.0 (www.stata.com).

3 | RESULTS

In this cohort of 6592 infants, 58.0% (3826) received any breast milk at discharge from the neonatal unit. Distributions of exclusive, partial and no BMF across the 19 included regions are shown in Figure 1. Rates of any BMF varied between the regions and within countries, with the highest rates, 80.1% in Denmark, Eastern region, to the lowest in the UK Northern region, 35.7%. The East-central region in the Netherlands had the highest rate of exclusive BMF at discharge 51.5% (Figure 1).

3.1 | Any versus no BMF at discharge

Characteristics differed between the infants receiving any versus no BMF at discharge (Table 2). After adjustment, obstetric and infant covariates that were positively associated with the likelihood of receiving any BMF at discharge were: primiparity, administration of antenatal corticosteroids, first enteral feed at less than 24 hr after birth, and

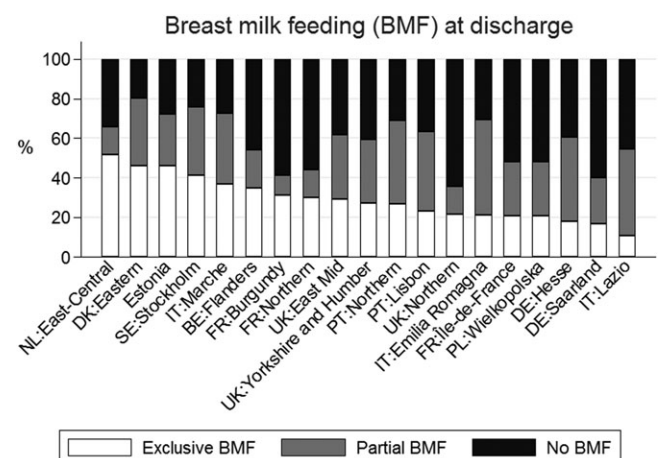


FIGURE 1 Breast milk feeding at discharge from neonatal care after very preterm birth across included regions

TABLE 2 Regression analysis of breast milk feeding at discharge. Risk ratios and 95% confidence interval of any versus no breast milk feeding, N = 6592

	Numbers and column percentages			Any vs. no breast milk feeding risk ratios (95% confidence interval)	
	Total cohort N = 6,592	Any breast milk feeding N = 3,826	No breast milk feeding N = 2,766	Gestational age adjusted	Multivariable adjusted ^a
Maternal, obstetric, and infant characteristics					
Maternal age (years)					
<25	1,093 (16.6)	451 (11.8)	642 (23.2)	0.68 (0.62–0.74)	0.68 (0.62–0.75)
25–34	3,724 (56.7)	2,304 (60.2)	1,420 (51.3)	1.00 (reference)	1.00 (reference)
≥35	1,753 (26.7)	1,062 (27.8)	691 (25.0)	0.96 (0.91–1.02)	1.00 (0.95–1.06)
Country of mother's birth ^b					
Native	4,618 (77.8)	2,748 (71.8)	1,870 (67.6)	1.00 (reference)	1.00 (reference)
Other	1,321 (22.2)	783 (20.5)	538 (19.5)	1.00 (0.93–1.07)	1.05 (0.99–1.12)
Parity					
1	3,718 (57.0)	2,286 (59.7)	1,432 (51.8)	1.00 (reference)	1.00 (reference)
2	1,601 (24.5)	916 (23.9)	685 (24.8)	0.94 (0.89–0.99)	0.89 (0.84–0.95)
3	706 (10.8)	363 (9.5)	343 (12.4)	0.85 (0.78–0.93)	0.80 (0.73–0.89)
≥4	503 (7.7)	230 (6.0)	273 (9.9)	0.76 (0.68–0.84)	0.71 (0.64–0.79)
Preeclampsia/eclampsia/HELLP, yes	1,028 (15.6)	618 (16.2)	410 (14.8)	1.02 (0.95–1.09)	1.02 (0.95–1.08)
Any antenatal corticosteroids, yes	5,860 (88.9)	3,473 (90.8)	2,387 (86.3)	1.19 (1.09–1.30)	1.21 (1.11–1.33)
Type of delivery					
Vaginal	2,049 (31.3)	1,184 (30.9)	865 (31.3)	1.00 (reference)	1.00 (reference)
Caesarean	4,492 (68.7)	2,623 (68.6)	1,869 (67.6)	0.97 (0.93–1.02)	1.00 (0.96–1.05)
Type of pregnancy					
Singleton birth	4,498 (68.2)	2,556 (66.8)	1,942 (70.2)	1.00 (reference)	1.00 (reference)
Multiple birth	2,094 (31.8)	1,270 (33.2)	8,25 (29.9)	1.05 (0.99–1.10)	0.99 (0.93–1.04)
Gestational age (weeks)					
≤25	521 (7.9)	245 (6.4)	276 (10.0)	0.74 (0.66–0.83)	0.88 (0.78–0.99)
26–27	1,090 (16.5)	569 (14.9)	521 (18.8)	0.83 (0.77–0.90)	0.90 (0.84–0.98)
28–29	1,779 (27.0)	1,025 (26.8)	754 (27.3)	0.93 (0.88–0.98)	0.94 (0.89–1.00)*
30–31	3,202 (48.6)	1,987 (51.9)	1,215 (43.9)	1.00 (reference)	1.00 (reference)
Small for gestational age at birth ^c					
<3 percentile	1,351 (20.5)	741 (19.4)	610 (22.1)	0.91 (0.86–0.96)	0.93 (0.87–0.99)
3rd–10th	786 (11.9)	460 (12.0)	326 (11.8)	0.98 (0.92–1.04)	0.97 (0.91–1.04)
>10th	4,454 (67.6)	2,624 (68.6)	1,830 (66.2)	1.00 (reference)	1.00 (reference)
Apgar score < 7 at 5 min, yes	941 (15.0)	476 (12.4)	465 (16.8)	0.89 (0.83–0.95)	0.97 (0.91–1.05)
Time of first enteral feed					
<1 day	1,744 (27.2)	1,177 (30.8)	567 (20.5)	1.00 (reference)	1.00 (reference)
1–6 days	4,282 (66.8)	2,388 (62.4)	1,894 (68.5)	0.87 (0.82–0.93)	0.83 (0.77–0.89)
≥7 days	380 (5.9)	170 (4.4)	210 (7.6)	0.72 (0.58–0.94)	0.72 (0.58–0.89)
Mother's own milk at first enteral feed, yes	2,276 (37.5)	1,530 (40.0)	746 (30.0)	1.39 (1.28–1.50)	1.42 (1.32–1.53)
Major congenital anomalies, yes	539 (8.2)	255 (6.7)	284 (10.3)	0.81 (0.74–0.89)	0.87 (0.79–0.95)
Any major morbidity ^d , yes	675 (10.6)	312 (8.2)	363 (13.1)	0.84 (0.76–0.92)	0.87 (0.80–0.95)
Bronchopulmonary dysplasia, yes	922 (14.3)	394 (10.3)	528 (19.1)	0.74 (0.66–0.83)	0.78 (0.69–0.88)
Between hospital transfers					
No transfer	3,838 (58.2)	2,247 (58.7)	1,591 (57.5)	1.00 (reference)	1.00 (reference)
Transferred at least once	2,754 (41.8)	1,579 (41.3)	1,175 (42.5)	0.99 (0.90–1.08)	1.06 (0.97–1.17)
PMA at discharge, median IQR	37.4 (36.1–39.1)	37.1 (35.9–38.6)	37.9 (36.4–40.0)	0.95 (0.94–0.97)	0.95 (0.93–0.97)

^aModel 2 was adjusted for maternal age, country of birth, parity, preeclampsia/eclampsia/HELLP, administration of antenatal corticosteroids, type of delivery, multiple birth, gestational age, Apgar at 5 min, SGA, congenital anomalies, time of first enteral feed, mother's own milk as first feeding, infant morbidity, and any between hospital transfer.

^bEthnic group in the UK regions.

^cBirth weight less than 10th percentile of intrauterine references.

^dcPVL = cystic periventricular leukomalacia; IVH = intraventricular haemorrhage; NEC = necrotizing enterocolitis; ROP = retinopathy of prematurity

PMA = postmenstrual age.

*p value is .04.

maternal breast milk at first enteral feed. Low GA, higher PMA at discharge, and neonatal morbidity were negatively associated with the chance of receiving any breast milk at discharge.

3.2 | Exclusive versus partial BMF at discharge

Among infants receiving BMF, maternal and infant covariates that were positively associated with exclusive BMF at discharge in multivariable models were vaginal delivery, singleton birth, and receiving maternal breast milk at first enteral feed (Table 3). Having a nonnative mother was associated with a lower chance of exclusive BMF at discharge, as was increasing PMA at discharge. Parity, preeclampsia/eclampsia/HELLP, administration of antenatal corticosteroids, GA, SGA, time of first enteral feed, infant morbidity, between hospital transfers, and infant morbidity were not associated with exclusive BMF at discharge.

3.3 | Unit policies and BMF at discharge

A majority of the included units had written BMF policies, and 66% (54/82) had policies to support mothers to start expressing within 6 hr

after birth. More than half of the units did not use donor milk, 28% (23/82) had a Baby Friendly Hospital (BFH) accreditation and 15% (12/82) were in the process of applying for a BFH accreditation (Table 1). Adjusted analysis showed a higher chance of the infant receiving any BMF in units with a BFH accreditation, but other investigated unit policies were not associated with any BMF at discharge (Table 4).

In analyses of exclusive BMF, being admitted to a hospital with BMF protocols and donor milk provision was positively associated with the infants' likelihood of exclusive BMF at discharge. Individual support and BFH accreditation were not associated with exclusive BMF (Table 4).

3.4 | Breastfeeding at breast at discharge

Among 3,826 infants receiving any BMF at discharge, 67.8% (2593) were breastfeeding at breast. There were large variations between the regions with the highest at breast feeding rates in the Stockholm region—Sweden, 92.5%—and Eastern region—Denmark, 84.9%. The lowest rates were seen in Marche—Italy, 15.5%—and Saarland—Germany, 21.7% (Figure S2).

TABLE 3 Regression analysis of exclusive versus partial breast milk feeding at discharge. Risk ratios and 95% confidence interval of exclusive versus partial breast milk feeding, $N = 3826$

	Numbers and column percentages		Exclusive vs. partial breast milk feeding risk ratios (95% confidence interval)	
	Exclusive breast milk feeding $N = 1,812$	Partial breast milk feeding $N = 2,014$	Gestational age adjusted	Multivariable adjusted ^a
Maternal, obstetric and infant characteristics				
Maternal age (years)				
<25	187 (10.3)	264 (13.1)	0.85 (0.75–0.96)	0.82 (0.72–0.95)
25–34	1,124 (62.0)	1,180 (58.6)	1.00 (reference)	1.00 (reference)
≥35	496 (27.4)	556 (27.6)	0.99 (0.92–1.07)	0.97 (0.89–1.05)
Country of mother's birth ^b				
Native	1,371 (75.7)	1,377 (68.4)	1.00 (reference)	1.00 (reference)
Other	294 (16.2)	489 (24.3)	0.77 (0.70–0.85)	0.81 (0.73–0.90)
Parity				
1	1,075 (59.3)	1,211 (60.1)	1.00 (reference)	1.00 (reference)
2	462 (25.5)	454 (22.5)	1.07 (0.98–1.16)	1.05 (0.96–1.15)
3	164 (9.1)	199 (9.9)	0.95 (0.83–1.08)	0.92 (0.79–1.06)
≥4	90 (5.0)	140 (7.0)	0.86 (0.72–1.03)	0.82 (0.66–1.01)
Preeclampsia/eclampsia/HELLP, yes	305 (16.8)	313 (15.5)	1.02 (0.93–1.12)	1.05 (0.94–1.17)
Any antenatal corticosteroids, yes	1,635 (90.2)	1,838 (91.3)	0.92 (0.81–1.04)	0.94 (0.82–1.08)
Type of delivery				
Vaginal	643 (35.5)	541 (26.9)	1.00 (reference)	1.00 (reference)
Caesarean	1,156 (63.8)	1,467 (72.8)	0.83 (0.76–0.89)	0.88 (0.80–0.96)
Type of pregnancy				
Singleton birth	1,320 (72.8)	1,236 (61.4)	1.00 (reference)	1.00 (reference)
Multiple birth	492 (27.2)	778 (38.6)	0.74 (0.67–0.82)	0.71 (0.64–0.80)
Gestational age, weeks				
≤25	105 (5.8)	140 (7.0)	0.91 (0.78–1.05)	0.95 (0.80–1.13)
26–27	279 (15.4)	290 (14.4)	1.00 (0.91–1.11)	1.01 (0.91–1.14)
28–29	489 (27.0)	536 (26.6)	1.00 (0.92–1.09)	0.99 (0.90–1.08)

(Continues)

TABLE 3 (Continued)

	Numbers and column percentages		Exclusive vs. partial breast milk feeding risk ratios (95% confidence interval)	
	Exclusive breast milk feeding N = 1,812	Partial breast milk feeding N = 2,014	Gestational age adjusted	Multivariable adjusted ^a
30–31	939 (51.8)	1,048 (52.0)	1.00 (reference)	1.00 (reference)
Small for gestational age at birth ^c				
<3rd percentile	344 (19.0)	397 (19.7)	0.93 (0.85–1.02)	0.99 (0.88–1.10)
3rd–10th	203 (11.2)	257 (12.8)	0.90 (0.82–0.99)	0.96 (0.87–1.07)
>10th	1,265 (69.8)	1,359 (67.5)	1.00 (reference)	1.00 (reference)
Apgar < 7 at 5 minutes, yes	221 (12.2)	255 (12.7)	0.98 (0.88–1.09)	0.99 (0.89–1.11)
Time of first enteral feed				
<1 day	592 (32.7)	585 (29.0)	1.00 (reference)	1.00 (reference)
1–6 days	1,103 (60.9)	1,285 (63.8)	0.97 (0.87–1.07)	0.93 (0.83–1.03)
≥7 days	70 (3.9)	100 (5.0)	0.92 (0.75–1.13)	0.84 (0.68–1.05)
Mother's own milk at first enteral feed, yes	784 (43.3)	746 (37.0)	1.27 (1.14–1.42)	1.25 (1.11–1.41)
Major congenital anomalies, yes	120 (6.6)	135 (6.7)	1.03 (0.90–1.17)	1.08 (0.92–1.26)
Any major morbidity ^d , yes	130 (7.2)	182 (9.0)	0.91 (0.80–1.04)	0.94 (0.83–1.06)
Bronchopulmonary dysplasia, yes	182 (10.0)	212 (10.5)	0.95 (0.81–1.12)	0.86 (0.71–1.05)
Between hospital transfers				
No transfer	1,048 (57.8)	1,199 (59.5)	1.00 (reference)	1.00 (reference)
Transferred at least once	764 (42.2)	815 (40.5)	0.89 (0.79–1.00)	0.90 (0.79–1.02)
PMA at discharge, median IQR	37.0 (35.9–38.6)	37.1 (35.9–38.7)	0.97 (0.95–0.99)	0.97 (0.95–1.00)*

^aModel 2 was adjusted for maternal age, country of birth, parity, preeclampsia/eclampsia/HELLP, administration of antenatal corticosteroids, type of delivery, multiple birth, gestational age, Apgar at 5 min, SGA, congenital anomalies, time of first enteral feed, mother's own milk as first feeding, infant morbidity, and any between hospital transfer.

^bEthnic group in the UK regions.

^cBirth weight less than 10th percentile of intrauterine references.

^dcPVL = cystic periventricular leukomalacia; IVH = intraventricular haemorrhage; NEC = necrotizing enterocolitis; ROP = retinopathy of prematurity.

PMA = postmenstrual age.

*p value is 0.02.

TABLE 4 Unit study variables in relation to breast milk feeding at discharge. Risk ratios (95% confidence interval)

	Any vs. no breast milk feeding N = 3,765			Exclusive vs. partial breast milk feeding N = 2,226		
	Risk ratios (95% CI)		p value	Risk ratios (95% CI)		p value
	Unadjusted	Adjusted ^a		Unadjusted	Adjusted ^b	
Unit questionnaire variables						
Is there a designated staff member whose role is to support mothers who are expressing or breastfeeding while they are hospitalized in the unit?						
Yes vs. No	1.09 (0.94–1.27)	1.12 (0.97–1.29)	.12	1.12 (0.78–1.61)	1.17 (0.84–1.65)	.35
Are mothers at risk of delivering before 32 weeks of gestation advised to start expressing within 6 hr?						
Yes vs. No	1.01 (0.86–1.19)	1.01 (0.87–1.16)	.93	0.93 (0.65–1.33)	0.96 (0.67–1.37)	.82
Does the neonatal unit use human bank milk/donor milk to feed very preterm infants whose mothers do not express their milk?						
Yes vs. No	1.12 (0.99–1.27)	1.09 (0.98–1.21)	.12	1.28 (1.05–1.55)	1.25 (1.00–1.57)	.048
Is the unit accredited a baby friendly hospital or national equivalent?						

(Continues)

TABLE 4 (Continued)

	Any vs. no breast milk feeding N = 3,765			Exclusive vs. partial breast milk feeding N = 2,226		
	Risk ratios (95% CI)		p value	Risk ratios (95% CI)		p value
	Unadjusted	Adjusted ^a		Unadjusted	Adjusted ^b	
Yes vs. No	1.13 (1.02–1.25)	1.15 (1.05–1.26)	.02	1.25 (0.88–1.80)	1.27 (0.87–1.87)	.22
In process vs. No	1.15 (0.98–1.35)	1.10 (0.97–1.26)	.13	0.82 (0.50–1.32)	0.85 (0.52–1.39)	.52
Does the unit have a written protocol for breast milk feeding and human milk use?						
Yes vs. No	1.17 (0.99–1.40)	1.19 (1.00–1.42)	.06	1.51 (1.08–2.12)	1.49 (1.07–2.10)	.02

^aAdjusted for maternal age, country of mother's birth, parity, preeclampsia/eclampsia/HELLP, administration of antenatal corticosteroids, type of delivery, multiple birth, gestational age, Apgar at 5 min, SGA (birth weight less than 10th percentile of intrauterine references), congenital anomalies, infant morbidity, and any between hospital transfers.

4 | DISCUSSION

In this cohort of very preterm infants born in 19 regions in Europe, we found that it is possible to achieve high rates of any BMF at discharge after very preterm birth, but there were large variations between regions (36–80%), both across and within countries. Infants who received their mother's milk at first enteral feed were more likely to receive breast milk at discharge. Units that used donor milk had higher rates of exclusive BMF at discharge. Breastfeeding at the breast also varied widely between the regions (16–93%).

Some of the differences between the regions might be explained by national variations in breastfeeding culture and in the possibilities for paid maternity leave or for parents to spend time in the hospital with their baby. The length and level of payment of maternity leave influences breastfeeding rates, higher payment results in higher leave, and duration, which is positive for breastfeeding (Strang & Broeks, 2016). Maternity leave varies across the European regions across multiple dimensions: duration, whether it is mandatory, percent compensation, the agency that provides it, and flexibility in uptake (Strang & Broeks, 2016); how these differences affect breastfeeding rates for very preterm infants should be investigated further.

An important factor of BMF establishment during neonatal care is the possibility to spend time in the NICU, shown to vary largely between countries in Europe (Greisen et al., 2009). Further, skin-to-skin is the first step to breastfeeding at breast and kangaroo mother care contributes to increased breastfeeding at breast (Hurst, Valentine, Renfro, Burns, & Ferlic, 1997; K. H. Nyqvist et al., 2010; Sharma, Farahbakhsh, Sharma, Sharma, & Sharma, 2017).

Previous studies have indicated variations in BMF among very preterm infants (Bonet, Blondel, & Khoshnood, 2010; Bonet et al., 2011) and recognized the need to explore the associations between unit practices and BMF rates after very preterm birth. In a cross-sectional study on lactation support and breastfeeding in three European regions, Bonet et al. (2015) identified different attitudes between regions towards the mother's decision to breastfeed, as well as about the benefits of mother's own milk and of donor milk.

Results from a systematic review about barriers of BMF in the NICU from a parent perspective revealed that knowledge about breastfeeding, strengthening mothers' motivation and concordance between the needs of the parents and NICU routines were factors associated with successful BMF in the NICU (Alves et al., 2013).

Early breast milk expression after very preterm birth is essential for increased milk production (Furman et al., 2002), and a recent study has indicated that expression should preferably start during the first hour after birth (Hill, Aldag, Chatterton, & Zinaman, 2005; L. A. Parker et al., 2015). High intake of mother's own milk during the first postnatal week has also been associated with exclusive BMF at 36 weeks PMA in infants born between 23 and 31 weeks of gestation (Wilson, Christensson, Brandt, Altman, & Bonamy, 2015).

Our study showed that receiving mother's own milk at first enteral feeding was associated with a higher chance of BMF at discharge. This might reflect not only the maternal motivation but also the units' policy of early BMF support. However, results from the unit questionnaire study did not show an association between a unit policy of early expression and BMF at discharge. This finding is limited by the lack of information about when mothers actually started to express breast milk. Furthermore, other factors are associated with the decisions to express milk and adequacy of the milk supply including grief, which can be present after very preterm birth, and the stress associated with NICU hospitalizations (Flacking, Ewald, & Starrin, 2007a; Shah, Clements, & Poehlmann, 2011; Shin & White-Traut, 2007; Spinelli et al., 2016).

Our finding that infants born at a lower GA and infants with neonatal morbidities had a lower likelihood of receiving any BMF at discharge is consistent with previous studies (Bonet et al., 2011). However, among infants receiving any BMF, GA and infant morbidity were not associated with the likelihood of exclusive BMF. In addition, pregnancy complications were not associated with exclusive BMF, which is in agreement with previous findings (Husebye et al., 2014). We speculate that it might be more of a maternal decision to provide exclusive BMF, and any BMF may be driven more by the infant's clinical condition or by unit/staff policies. Our finding that multiple birth was negatively associated with exclusive BMF is a factor that needs to be taken into consideration when giving BMF support in this already vulnerable subgroup. This finding is in line with a study from Maastrup et al. (2014).

In a study about breastfeeding competence in infants born very preterm, Nyqvist et al. showed that feeding at the breast could be introduced at 29 weeks of PMA (2008). An in-hospital priority should be to encourage initiation and establishment of breastfeeding without delay. Unlimited visiting hours in the hospital for the mother, supporting the mother to take responsibility for the breastfeeding when the mother is ready, and semidemand feeding have been suggested to increase breastfeeding at breast (exclusive or partial) at

discharge (Nyqvist, 2008). In addition, Briere et al. described goal setting as a contributing factor for achieving breast feeding at breast after preterm birth (infants born <34 weeks GA); their study indicated that mothers who prior to birth were aiming to breastfeed for a specific duration, breastfed their infants more often at breast (2015).

Our results that units providing donor milk increased exclusive BMF rates at discharge are consistent with a recent U.S. study that showed a sixfold increased odds of receiving mother's own milk if a donor milk programme was implemented (Parker et al., 2016). More than half of the units in our cohort did not use donor milk to feed very preterm infants. The use of donor milk positively impacts BMF overall and may be a strong signal to mothers and families that breast milk and breastfeeding is important and that the staff has a positive attitude and experience instructing mothers how to express breast milk.

In contrast to a large cluster randomized PROBIT trial in term infants (Kramer et al., 2001), we did not find that BFH accreditation was associated with improved exclusive BMF at discharge but improved any BMF. This may indicate that the BFHI does not sufficiently address factors that are key to obtain exclusive breastfeeding after very preterm birth, such as skin-to-skin care/kangaroo-mother care (Hurst et al., 1997; Nyqvist et al., 2010) and the importance of aiming at establishing a sufficiently high breast milk production within the first weeks after delivery to maintain exclusive BMF of the growing infant (Meier, Johnson, Patel, & Rossman, 2017).

Nevertheless, our results stress the need to implement BFHI in neonatal units. A breast milk feeding friendly environment (BFH accreditation, written protocols for BMF and use of donor milk) influenced the chance of receiving breast milk at discharge. An expanded version of the BFHI dedicated for infants in the neonatal intensive care is a step towards awareness and support for health care professionals caring for the very preterm infant and their families (Nyqvist et al., 2013).

The limitations of our study are that it did not include information on mother's intention/motivation to breastfeed, medication use, socio-economic status, and smoking. All these factors have been associated with breastfeeding duration (Flacking, Ewald et al., 2007a; Flacking, Wallin et al., 2007b; Herich et al., 2017; Perrella et al., 2012). BMF at discharge was investigated without differentiating between mother's own milk and donor milk, although it is most unlikely that infants would be discharged home on donor's milk, we cannot exclude that this occurred in a few cases.

We were unable to adjust socio-economic factors and therefore the associations between individuals' characteristics, unit policies, and BMF might have suffered from residual socio-economic confounding. Another limitation is that we did not include maternal pre-pregnancy BMI and maternal diabetes. Because these are risk factors for both preterm birth and poor lactation outcomes (Goldenberg, Culhane, Iams, & Romero, 2008; Matias, Dewey, Quesenberry, & Gunderson, 2014), there may be residual confounding.

In some regions, the unit questionnaire was administrated prior to the inclusion of the cohort study ended, which could have made it possible to change policies and practices during the time of inclusions introducing misclassification of the exposure. This would lead to a bias towards the null.

We did not find that having a dedicated staff influenced BMF at discharge. This may be related to the fact that this and the advice of

early expression are implemented and applied in practice differently across countries. These questions were not standardized and therefore not able to detect any differences in type and timing of support as in contrast to the BFHI question being a standardized working tool regardless of setting.

Despite these limitations, our study included a large European cohort with prospectively collected data and examined both individual level and unit level characteristics that might influence the receipt of breast milk among very preterm infants.

Our study showed that having a BMF protocol was associated with a higher chance of infants receiving exclusive BMF at discharge. This indicates that policies are translated into practice of breastfeeding support. However, the availability of dedicated lactation personnel did not influence BMF at discharge. This might be explained by the fact that we were not able to differentiate what actual support was provided by lactation personnel, that is, what was communicated to the mothers. BMF support can be influenced by staff preferences and unit norms, resulting in inconsistent and not always effective feeding strategies in the NICU (McInnes, Shepherd, Cheyne, & Niven, 2010). Multi-disciplinary nutrition and lactation teams engaged in the work of implementing protocols has showed higher rates of mother's own milk received at discharge from NICU (Meier et al., 2017).

Given the benefits of breast milk for the very preterm infant, clinicians need to provide information and education about breast milk/breastfeeding to parents in order to promote informed decision making. In addition, it is important that the maternal and neonatal units offer support to mothers who aim at breastfeeding. It is not ethical to inform the parents about the benefits of breastfeeding without giving the tools to support and realize their breastfeeding goals.

5 | CONCLUSION

The large variations in BMF across regions in Europe illustrate the high potential for improving breastfeeding rates in very preterm infants. This study confirms the importance of early breastfeeding support and acknowledges the impact of having a breastfeeding friendly environment to improve BMF at discharge thereby illustrating the key role that the NICU can play in achieving this goal.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

CONTRIBUTIONS

EW contributed to designing the data collection instrument, collected the data in Stockholm region, analysed and interpreted the data, drafted and revised the manuscript. A-KEB contributed to designing the data collection instrument, coordinated data collection in Stockholm, supervised statistical analyses, interpreted data, participated in drafting the paper, and critically reviewed the manuscript for important intellectual content. MB contributed to designing the data collection instrument, had the original conceptions for the paper, and critically reviewed the manuscript. LT contributed to designing the data collection instrument, coordinated data collection in Estonia, participated in the preparation of the manuscript,

and critically reviewed the manuscript. CR coordinated data collection in Portuguese regions, participated in the preparation of the manuscript, and critically reviewed the manuscript. EAHJ contributed to the design of the study, participated in the interpretation of the findings, and critically reviewed the manuscript. MC contributed to designing the data collection instrument, coordinated data collection in the Emilia Romagna and Marche regions, participated in the preparation of the manuscript, contributed to the interpretation of the findings, and critically reviewed the manuscript. JZ drafted the data collection instrument, had the original conceptions for the paper, supervised statistical analyses, interpreted the data, and critically reviewed the manuscript for important intellectual content. All authors have seen this version and approved the final content.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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APPENDIX

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