ORIGINAL ARTICLE



Breastfeeding and risk for ceasing in mothers of preterm infants—Long-term follow-up

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Abstract

Breastfeeding is challenging for mothers of preterm infants. The aim of this paper is to describe risk factors for ceasing breastfeeding and methods of feeding until 12 months postnatal age in mothers who breastfed their preterm infants at discharge from neonatal intensive care units (NICUs). The data come from a randomised controlled trial, which evaluated the effectiveness on exclusive breastfeeding at 8 weeks of proactive telephone support compared with reactive support offered to mothers of preterm infants following discharge from NICU. Six NICUs across Sweden randomised a total of 493 mothers. We used regression and survival analyses to assess the risk factors for ceasing breastfeeding and the long-term outcomes of the intervention. The results showed that 305 (64%) of the infants were breastfed at 6 months and 49 (21%) at 12 months. Partial breastfeeding at discharge, low maternal educational level, and longer length of stay in the NICU increased the risk for ceasing breastfeeding during the first 12 months. Furthermore, the Kaplan-Meier analysis showed that the proportion of mothers who ceased breastfeeding did not differ between the intervention (n = 231) and controls (n = 262) during the first 12 months (log-rank test p = .68). No difference was found between groups on method of feeding. More than 85% of the infants were fed directly at the breast. These findings provide important insights for health professionals who are supporting mothers of preterm infants to breastfeed long term. Registered in www.clinicaltrials.gov (NCT01806480).

KEYWORDS

bottle, breast milk, feeding, mother, neonatal, RCT

1 | BACKGROUND

Breastfeeding has beneficial immunological, nutritional, and neurodevelopmental effects for the preterm infant (gestational age < 37 weeks; Victora et al., 2016). For example, breast milk has a protective effect against necrotising enterocolitis, bronchopulmonary dysplasia, and late onset sepsis in the very preterm infant (Hair et al.,

2016). Further, breast milk provides cognitive and developmental benefits persisting to adolescence (Lechner & Vohr, 2017). Breastfeeding a preterm infant can be a complicated process with challenging and often slow progression of establishing breastfeeding (Ikonen, Paavilainen, & Kaunonen, 2015). It is highly dependent on the infant's gestational age at birth; the more preterm, the more immature breastfeeding behaviour (Maastrup et al., 2014; Nyqvist, 2008).

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In Sweden, most mothers have the possibility to be with their infants 24/7 and may start breastfeeding as soon as the infant shows feeding cues. Staff in neonatal intensive care units (NICUs) also encourage breastfeeding directly at the breast from the start (Flacking, Ewald, & Wallin, 2011; Nyqvist, 2008); hence, few mothers use an alternative feeding method and most mothers feed directly at the breast (Ericson & Flacking, 2013; Flacking & Dykes, 2013). In other countries for example in the UK, it is relatively common to give expressed breast milk via bottle before starting breastfeeding directly at the breast (Flacking & Dykes, 2013).

The prevalence of exclusive breastfeeding at discharge from NICUs in Sweden is relatively high compared with other Western countries but is decreasing in preterm infants, especially in the group of extremely preterm infants (Ericson, Flacking, Hellstrom-Westas, & Eriksson, 2016). Long-term follow-up data on preterm infant breastfeeding are scarce. A Swedish study from 2007 (Akerstrom, Asplund, & Norman, 2007) showed that the prevalence of exclusive breastfeeding at 2, 4, and 6 months of corrected age were 51%, 37%, and 9%, respectively. In a Danish study from 2014 (Maastrup et al., 2014), the rates of exclusive breastfeeding at 1, 4, and 6 months postnatal age were 66%, 38%, and 13%, respectively.

Factors negatively affecting breastfeeding after discharge from the NICU include infant suckling difficulties, unfulfilled information needs, lack of skills, and poor support (Kair, Flaherman, Newby, & Colaizy, 2015; Niela-Vilen, Axelin, Melender, & Salantera, 2015). Evidence on how to support the transition from hospital to home with regard to breastfeeding is scarce. In Sweden, most mothers of preterm infants are referred to the child health care centre or to peer support services if problems with breastfeeding occur after discharge from the NICU. However, mothers with preterm infants may experience a gap in the support or report that the support is not tailored to their needs (Flacking, Ewald, & Starrin, 2007a). Telephone support to facilitate breastfeeding in mothers with term infants has previously shown promising results (Gu, Zhu, Zhang, & Wan, 2016; Lavender, Richens, Milan, Smyth, & Dowswell, 2013). We undertook a randomised controlled trial offering proactive telephone breastfeeding support after NICU discharge to mothers of preterm infants compared with offering reactive mother initiated telephone support (Ericson et al., 2013). The primary outcome, exclusive breastfeeding at 8 weeks after discharge and secondary outcomes of mothers' satisfaction with breastfeeding, attachment, parental stress, and quality of life, has previously been reported (Ericson, Eriksson, Hellstrom-Westas, Hoddinott, & Flacking, 2018). The aim of this paper is to describe risk factors for ceasing breastfeeding and methods of feeding until 12 months postnatal age in mothers of preterm infants who were breastfeeding at NICU discharge. Furthermore, to report the long-term outcomes of proactive breastfeeding support on breastfeeding up to 12 months postnatal age.

2 | METHODS

2.1 | Design

The present study analyses follow-up data at 6 and 12 months postnatal age from a multicentre randomised controlled trial of proactive

Key messages

- Exclusive breastfeeding at discharge, higher maternal educational level, and shorter length of stay in the neonatal intensive care unit were factors associated with higher breastfeeding prevalence during the preterm infants' first year of life.
- The results give insights on long-term outcomes of breastfeeding in mothers who breastfed their preterm infants at discharge from the neonatal intensive care unit, where 64% of the infants were breastfed at 6 months.
- Most infants were fed breast milk directly at the breast; few infants received expressed breast milk by bottle, tube, or cup.

telephone support compared with reactive support. In this paper, we investigated factors associated with risk for ceasing breastfeeding during the first 12 months postnatal age. Furthermore, we report the secondary outcomes from the randomised controlled trial, breastfeeding, and the methods of feeding up at 6 and 12 months of postnatal age. The trial followed the CONSORT recommendations (Moher et al., 2010) and was registered in www.clinicaltrials.gov (NCT01806480).

2.2 | Participants, setting, and data collection

Six NICUs level IIIa or IIIb (American Academy of Pediatrics Committee on Fetus and Newborn, 2012) across Sweden participated. Eligible participants for inclusion were mothers of preterm infants (gestational age < 37 weeks), who had been admitted to one of the participating NICUs for at least 48 hr and who provided breast milk for their infant regardless of amount and method. Exclusion criteria were terminal illness of the infant, serious maternal medical or psychiatric problems at discharge; infants transferred to another hospital/unit after discharge, or language problems that could not be resolved. After receiving oral and written information, all participating mothers signed a written consent. The mothers were informed that participation in the study was voluntary and that they could withdraw at any time. Mothers and infants' confidentiality was ensured at all stages of the research process. The Regional Ethical Review Board, Uppsala, approved the study (Dnr: 2012/292).

Mothers who consented to participate and who met the inclusion criteria were randomised to either the proactive (intervention) or reactive (control) telephone support group. Mothers in the proactive group received a daily telephone call initiated by a member of a breastfeeding support team (who recruited and randomised eligible mothers and delivered the telephone support) from Day 1 until Day 14 after discharge. Mothers could choose sparser calls or stop calls at any time if they preferred. In addition, mothers had the option of reactive telephone support to the same extent as mothers in the control group. Mothers in the reactive group could phone the

breastfeeding support team from Day 1 after discharge until Day 14 after discharge 08.00–16.00 every day (including weekends). The reactive telephone support was defined as standard care. For further information on study design and protocol, see Ericson et al. (2013).

The breastfeeding support team collected the following maternal data at discharge: educational level, parity, country of birth being other than Sweden, multiple births, and mode of delivery. The following infant data were collected: gestational age at birth, small for gestational age (defined as less than –2 SD from the mean), length of stay, group allocation, domiciliary nursing care (i.e., parents are home with the infant before hospital discharge receiving support from the NICU), and breastfeeding at discharge. At 6 months postnatal age, a telephone call was made to participating mothers by the first author (blind to group allocation) to collect breastfeeding outcomes. A questionnaire requesting more detail about feeding was also sent to the mothers. In the questionnaire at 6 months postnatal age, the mothers were provided with an option to agree to receive a further questionnaire at 12 months postnatal age.

Exclusive breastfeeding was defined as feeding with breast milk only regardless of feeding method in the previous 24 hr but could include medications, fortification, and vitamins. Partial breastfeeding was defined as feeding with breast milk in combination with formula and/or solid food in the previous 24 hr. No breastfeeding was defined as full formula feeding and/or solid food with no breast milk intake. The term breastfeeding was used both for breastfeeding at the breast and for breast milk feeding by bottle, tube, or cup (World Health Organization, 2001).

2.3 | Statistical methods

The Student's t test with mean and standard deviation was used on normally distributed variables. Mann-Whitney U-test with median and interquartile range was used on nonnormally distributed variables. Chi-square test was used to show the difference in proportion of dichotomous variables. Unadjusted and adjusted hazard ratios (HRs) were used to analyse the risk for ceasing breastfeeding during the infants first 12 months postnatal age for the combined randomisation groups using Cox proportional hazard regression. In the Cox regression analyses, the HR represents the probability for ceasing breastfeeding. A backward stepwise approach was used to identify confounders, with variables retained at p < .05 (Wald test). To study the effects between exclusive and partial breastfeeding at discharge on exclusive breastfeeding 6 months postnatal age, an unadjusted logistic regression analysis was used. In the logistic regression analyses, exclusive breastfeeding was compared with partial/no breastfeeding, which meant that partial and no breastfeeding were merged into one group. In the logistic regression analysis, the odds ratio (OR) represents the odds for not breastfeeding exclusively at 6 months postnatal age. Data from the logistic and Cox regression models are presented with ORs and HRs with 95% confidence intervals (95% Cls).

A sample size estimation was calculated on the primary outcome (exclusive breastfeeding 8 weeks after discharge) in the randomised controlled trial, however, not on the secondary outcomes (Ericson et al., 2013). Outcome data were analysed according to intention-to-

treat principles. A survival curve was calculated and accompanied by a log-rank test for the risk of ceasing breastfeeding, the Kaplan–Meier method was used to visualise the difference over time (12 months) between the proactive and reactive group. Analyses were also performed on each type of feeding method (i.e., breast and bottle) in the reactive group compared with the proactive group.

Statistical significance level was set at p < .05 for all analyses, and calculations were performed with IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.

3 | RESULTS

3.1 | Participant flow, recruitment, and numbers analysed

The study started in March 2013 and ended in December 2015, in total, 493 mothers participated. The sociodemographic characteristics of participating mothers and infants are shown in Table 1. Fourteen mothers (3%) were lost to follow-up from baseline to 6 months. At 6 months postnatal age, 281 (59%) of the 479 mothers who were asked to continue participation consented to receive the 12 months questionnaire, Figure 1. Out of the 281 mothers who consented, 229 (82%) mothers responded Figure 1. Significantly, fewer mothers with a lower educational level (p < .001) and mothers not born in Sweden (p < .001) returned the questionnaire at 6 months postnatal age. Mothers who did not return the questionnaire at 12 months postnatal age were significantly younger (p = .02), had a lower educational level (p < .001), were not born in Sweden (p = .003), or were partially or not breastfeeding at 8 weeks after discharge and 6 months postnatal age (p = <.001). There were no statistical differences between the randomisation groups with regard to those agreeing/not agreeing to receive the 12 months questionnaire when they were asked at 6 months postnatal age (p = .52).

3.2 | Secondary breastfeeding outcomes for the proactive support trial

There were no differences between the proactive and reactive groups for the method of feeding breast milk at the follow-up points of 6 and 12 months. The Kaplan-Meier analysis revealed that the proportion of women ceasing breastfeeding did not differ between the proactive (n = 231) and reactive (n = 262) groups during the first 12 months postnatal age (log-rank test p = .68; Figure 2). More than 85% of infants who were breastfeeding at any time point were fed directly at the breast only, with no use of bottles, cups, or tubes, Table 2.

3.3 | Risks for ceasing breastfeeding

The proportion of exclusively breastfed infants 6 months postnatal age was 23% (n = 109). Of the infants whose mother responded to the questionnaire at 12 months, 21% (n = 49) were partially breastfed.

In the unadjusted Cox regression analyses, there were no statistically significant differences in the probability for ceasing breastfeeding related to parity, mothers birth country being other than Sweden, mode of delivery, multiple births, gestational age at birth, small for

TABLE 1 Characteristics of the participating mothers (n = 493) and their preterm infants (n = 547)

Demographic variables	Total n (%)	Proactive support n (%)	Reactive support n (%)
Maternal variables			
Randomised to proactive support	493	231 (47)	262 (53)
Age, year; mean (SD)	30 (5.2)	31 (5.3)	30 (5.1)
Maternal educational level			
Higher education	258 (52)	123 (53)	135 (52)
Upper secondary school or less	235 (48)	108 (47)	127 (48)
Primipara	278 (56)	122 (53)	156 (60)
Mothers not born in Sweden	46 (9.3)	27 (12)	19 (7.3)
Vaginal birth	277 (56)	125 (54)	152 (58)
Infant variables			
Gestational age at birth, weeks; median (IQR)	34 (33-35)	34 (33-35)	34 (33-35)
Multiple birth	52 (11)	21 (9.1)	31 (12)
Birthweight, gram; mean (SD)	2,295 (638)	2,262 (657)	2,324 (621)
Small for gestational age	43 (8.7)	21 (9.1)	22 (8.7)
Male	275 (56)	138 (60)	137 (52)
Neonatal illness ^a	18 (3.7)	11 (4.8)	7 (2.7)
Breathing support ^b	233 (47)	108 (47)	125 (48)
Weight at discharge, gram; mean (SD)	2,880 (473)	2,904 (541)	2,858 (403)
Gestational age at discharge; median (IQR)	38 (37-39)	38 (37-39)	38 (37–39)
Length of stay, weeks; median (IQR)	3.3 (2-5)	3.3 (2-5)	3.2 (2-5)
Domiciliary nursing care	448 (91)	212 (93)	236 (90)

Note. SD = standard deviation, IQR = interquartile range.

^bTreatment with ventilator, continuous positive airway pressure (CPAP), or high flow oxygen.

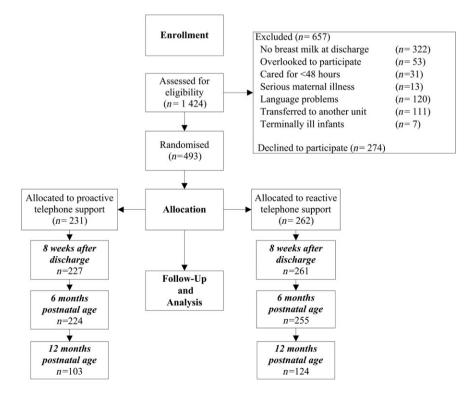


FIGURE 1 Flowchart showing the randomisation, allocation, and analysis stages in the study

^aBronchopulmonary dysplasia, retinopathy of prematurity, necrotising enterocolitis, intraventricular haemorrhage, periventricular leukomalacia.

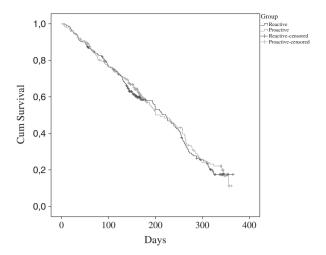


FIGURE 2 Kaplan–Meier curve over event rate of ceasing breastfeeding between the proactive and reactive group (log-rank test p = .68) during the first 12 months postnatal age

gestational age, length of stay, or group allocation. However, the unadjusted analysis showed that lower maternal educational level, no domiciliary nursing care, and partial breastfeeding at discharge increased the risk for ceasing breastfeeding during the first 12 months postnatal age. In the final Cox regression analysis model, partial breastfeeding at discharge from the NICU (HR 1.81, 95% CI 1.35-2.41, p = <.001) was the strongest independent predictor of breastfeeding cessation during the first 12 months postnatal age. Compared with mothers who were breastfeeding exclusively at discharge, mothers who were partially breastfeeding at discharge had ceased breastfeeding to a higher extent at 8 weeks after discharge, OR 5.17 (3.59-7.44; Figure S1), and 6 months postnatal age OR 3.74 (2.47-5.67). The second largest independent predictor of risk for ceasing breastfeeding during the first 12 months postnatal age was a lower maternal educational level (HR 1.42, 95% CI 1.13-1.79. p = .003). Finally, a shorter length of stay reduced the risk of ceasing breastfeeding during the first 12 months postnatal age (HR 0.96, 95% CI 0.92-0.99, p = .021), Table 3.

4 | DISCUSSION

This study provides long-term data on breastfeeding outcome in preterm infants who were breast milk fed at the time of discharge from six NICUs in Sweden and who participated in a randomised controlled trial of proactive compared with reactive telephone breastfeeding support. Partial breastfeeding at discharge was the strongest risk factor independently associated with cessation of breastfeeding during the first 12 months postnatal age, followed by low maternal educational level and longer length of stay in the NICU. This is one of the few studies to report breastfeeding prevalence in mothers of preterm infants for up to a year of postnatal age.

In our study, more than 85% of the infants were fed directly at the breast, which is a high prevalence compared with other countries (Briere, 2015; Dosani et al., 2016; Herich et al., 2017). This is a positive finding, as evidence shows that feeding directly at the breast is important for maintaining long-term breastfeeding duration (Briere, McGrath, Cong, Brownell, & Cusson, 2016) and that bottles may complicate the mothers' breastfeeding attempt (Collins, Gillis, McPhee, Suganuma, & Makrides, 2016).

An important result in the study was that partial breastfeeding at discharge was the strongest risk factor for ceasing breastfeeding. Subsequently, the importance of exclusive breastfeeding at discharge for long-term breastfeeding should underpin support given to mothers during their stay at the NICU where issues such as early initiation of breastfeeding/expressing breast milk, difficult in latching, infant sleepiness, and low milk supply need to be acknowledged and addressed. Further, a systematic review concluded that effective breastfeeding support includes support offered by trained personnel during postnatal care (McFadden et al., 2017).

Findings from our study also showed that a longer length of stay in the NICU increased the risk of ceasing breastfeeding during the first 12 months postnatal age. This may reflect infants' maturation in sucking capacity but also the problems of maintaining a long duration of expressing breast milk for the mother (Flacking, Ewald, Nyqvist, & Starrin, 2006; Ikonen et al., 2015). Thus, it is a balancing act for health

TABLE 2 Method of feeding breast milk at discharge (n = 493), 8 weeks after discharge (n = 428), 6 months (n = 308), and at 12 months (n = 49) postnatal age

			Breast in combination with				
	Only breast n (%)	Only bottle n (%)	Bottle n (%)	Cup n (%)	Tube n (%)	Bottle and cup n (%)	Solid food n (%)
Discharge							
Exclusive breast milk ($n = 406$)	345 (85)	2 (0.5)	52 (13)	3 (0.7)	3 (0.7)	1 (0.2)	0
Partial breast milk ($n = 87$)	0	7 (8)	78 (89)	2 (2)	0	0	0
Eight weeks after discharge							
Exclusive breast milk ($n = 281$)	254 (90)	1 (0.4)	26 (9.5)	0	0	0	0
Partial breast milk ($n = 147$)	0	2 (1)	145 (99)	0	0	0	
Six months postnatal age							
Exclusive breast milk ($n = 109$)	105 (96)	0	4 (4)	0	0	0	0
Partial breast milk ($n = 199$)	0	0	112 (56)	0	0	0	87 (44)
Twelve months postnatal age							
Partial (n = 49)	0	0	0	0	1 (2) ^a	0	48 (98)

^aBreast milk only by tube feeding.

TABLE 3 Risks for ceasing breastfeeding in unadjusted, adjusted, and final model using Cox regression analyses with hazard ratios (HR) and 95% confidence intervals (95% CI)

Variables	Unadjusted HR (95% CI)	p Value	Adjusted ^a model HR (95%)	p Value	Final model HR (95%)	p Value
Maternal educational level						
Upper secondary school or less	1.42 (1.13-1.79)	.003	1.49 (1.16-1.90)	.002	1.42 (1.13-1.79)	.003
Higher education	Ref		Ref		Ref	
Parity						
Primipara	1.06 (0.84-1.34)	.63	1.11 (0.86-1.42)	.43		
Multiparous	Ref		Ref			
Mothers born in Sweden						
Yes	0.66 (0.42-1.06)	.09	0.63 (0.38-1.04)	.07		
No	Ref		Ref			
Caesarean section						
Yes	1.01 (0.80-1.27)	.95	1.14 (0.88-1.47)	.31		
No	Ref		Ref			
Multiple birth						
Yes	1.19 (0.84-1.67)	.33	1.27 (0.88-1.84)	.21		
No	Ref		Ref			
Gestational age at birth (weeks)	1.02 (0.97-1.07)	.44	0.99 (0.90-1.09)	.84		
Small for gestational age						
Yes	1.13 (0.78-1.66)	.52	1.09 (0.72-1.63)	.69		
No	Ref		Ref			
Length of stay (weeks)	0.98 (0.94-1.01)	.20	0.95 (0.89-1.02)	.17	0.96 (0.92-0.99)	.019
Domiciliary nursing care						
No	1.54 (1.03-2.31)	.04	1.41 (0.90-2.20)	.13		
Yes	Ref		Ref			
Breastfeeding at discharge						
Partial	1.61 (1.23-2.12)	.001	1.70 (1.24-2.32)	.001	1.81 (1.35-2.41)	<.001
Exclusive	Ref		Ref		Ref	
Randomised to						
Reactive group	1.04 (0.83-1.32)	.71	1.05 (0.82-1.34)	.69		
Proactive group	Ref		Ref			

^aAdjusted for all variables presented in model.

care staff to optimally facilitate breastfeeding in mothers of preterm infants without creating pressure on the mother, sometimes for several months of hospitalisation.

It is well known that mothers with higher educational level have higher breastfeeding prevalence (Flacking, Nyqvist, & Ewald, 2007b; Victora et al., 2016). This was also a finding in the present study where mothers with lower educational level were 42% more likely to cease breastfeeding during the first 12 months postnatal age compared with mothers with a high educational level. The underlying mechanisms for the association between education and breastfeeding are obscure. One suggestion relates to a biological effect of socio-economic status (SES), for which educational level can be regarded as a good proxy. It has been hypothesised that SES influences our health through changes in our physiology through different pathways, with mothers of lower SES experiencing poorer health, for example, obesity (Chen & Miller, 2013). Obesity in turn may result in delayed lactogenesis and/or low milk supply (Lee & Kelleher, 2016; Nommsen-Rivers, 2016). Another suggestion is that mothers with a lower SES have less intention and/or self-efficacy to breastfeed as a result of fewer internal and external resources (de Jersey, Mallan, Forster, & Daniels, 2017; Karall et al., 2015). Further research is needed to explore this association and to identify strategies for how to facilitate breastfeeding in this group of mothers.

The strength of the study is the large study population, the long-term follow-up, and the high response rate. A limitation with regard to the results on duration and risk factors is that the sample only included mothers who were breastfeeding at discharge. Hence, although the results may look very positive at a glance with 23% (n = 109) exclusively breastfed at 6 months postnatal age and 21% (n = 49) partially breastfed at 12 months postnatal age, the overall breastfeeding prevalence would be lower if mothers who were not breastfeeding at discharge had been included. The 12 months' time point of data collection was not in the published study protocol (Ericson et al., 2013), and this late addition of 12 months data required additional consent from the mother at 6 months to send the 12 months questionnaire. There was a low response rate at the 12 months followup, and the data should be interpreted knowing that significantly more mothers who sent in the questionnaire had a higher education, were

older, born in Sweden, and were exclusively breastfeeding 8 weeks after discharge and 6 months postnatal age than the mothers who did not respond.

Previous findings from this randomised controlled trial of proactive breastfeeding telephone support showed no short-term increase of exclusive breastfeeding at 8 weeks after discharge compared with reactive telephone support (Ericson et al., 2018). There were no differences in the secondary outcomes of exclusive breastfeeding or method of feeding comparing proactive and reactive support at 6 or 12 months postnatal age. A limitation of this study is that the recruitment of participants ended before reaching the calculated sample-size due to time constraints. Thus, according to the priori power calculation, the trial was underpowered for primary and secondary outcomes. To our knowledge, there were no published studies on comparable interventions aiming to increase breastfeeding after discharge in countries with high breastfeeding prevalence when we calculated a priori power analysis. Thus, the estimated differences between the two randomisation groups were based on differences in exclusive breastfeeding at 2 months postnatal age in mothers with different educational levels and of preterm infants (Flacking et al., 2011). This was probably an overestimated effect of the intervention in a country with high breastfeeding prevalence. The pilot study of the intervention that inspired this trial (Hoddinott, Craig, Maclennan, Boyers, & Vale, 2012) showed promising results with a 22% difference in exclusive breastfeeding 6-8 weeks after discharge, but the result was not statistically significant. The study was performed in a disadvantaged area and in a country with low breastfeeding prevalence to mothers with infants born at term.

5 | CONCLUSION

In conclusion, the findings from this study give important insights about predictors of long-term breastfeeding in mothers who breastfed their preterm infants at discharge from NICUs. Partial breastfeeding at discharge from the NICU, low maternal educational level, and longer hospital stay significantly increased the risk for ceasing breastfeeding during the first 12 months postnatal age. This study raises awareness of which groups of mothers may benefit from additional interventions and support to facilitate longer and exclusive breastfeeding during the first 12 months postnatal age.

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CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

CONTRIBUTIONS

All five authors (JE, ME, PH, LH-W and RF) designed the study, reviewed and revised the manuscript, and approved the final

manuscript as submitted. JE performed the analyses of the data and drafted the final manuscript.

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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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