LUND UNIVERSITY

Breastfeeding of preterm infants. Associated factors in infants, mothers, and clinical practice.

Måstrup, Ragnhild

2014

[Link to publication](#)

Breastfeeding of preterm infants

Associated factors in infants, mothers and clinical practice

RAGNHILD MÅSTRUP

FACULTY OF MEDICINE | LUND UNIVERSITY 2014

Breastfeeding of preterm infants

Associated factors in infants, mothers and clinical practice

Ragnhild Måstrup

LUNDS UNIVERSITET

En del av Förpacknings- och
Tidningsinsamlingen (FTI)

Er lyset for de lærde blot
til ret og galt at stave?
Nej, himlen under flere godt,
og lys er himlens gave,
og solen står med bonden op,
slet ikke med de lærde,
oplyser bedst fra tå til top,
hvem der er mest på færde.

N.F.S. Grundtvig 1839

Contents

Abstract

Breastfeeding has even more pronounced health benefits for preterm infants than for full-term infants, but preterm infants are less breastfed. There is no consensus in Danish neonatal intensive care units (NICUs) about which clinical methods facilitate breastfeeding. Skin-to-skin contact between infant and parent is the first step in the breastfeeding process for preterm infants, but studies of toleration of skin-to-skin contact in extremely preterm infants – less than 28 gestational weeks – are sparse.

The overall aim of this thesis was to study and identify factors associated with breastfeeding of preterm infants, in infants, mothers and clinical practice in order to gain more knowledge of how to guide mothers of preterm infants in breastfeeding. This thesis is based on three studies: Study A, a clinical intervention study with 22 clinically stable extremely preterm infants that investigated infants' tolerance of skin-to-skin contact with their parents; Study B, a national survey of breastfeeding support at all Danish NICUs; and Study C, a national prospective cohort study of breastfeeding preterm infants with the participation of 1,221 mothers and their 1,488 preterm infants at a gestational age of 24-36 weeks. Regression analyses were used to investigate factors associated with early establishment of exclusive breastfeeding, exclusive breastfeeding at discharge and adequate duration in accordance with the Danish Health and Medicines Authority's recommendations.

The results showed that the extremely preterm infants in Study A, with mean weight 702 grams, tolerated skin-to-skin contact with their parents with no significant differences in mean skin temperature, heart rate, respiration rate, or oxygen saturation before, during, and after skin-to-skin contact. In Study B, the NICUs reported that they aimed for early skin-to-skin contact, and in 81% of the infants, skin-to-skin contact was initiated within the first 24 hours of life, but significantly fewer of the extremely preterm infants did so. In Study B, the NICUs described support of breastfeeding as being highly prioritised, reflected in skin-to-skin contact and parents' presence at the NICU, recommendations of breast milk expression, supplementation feedings via feeding tubes, and avoidance of the use of infant feeding bottles as a common practice.

Of the 1,488 preterm infants in Study C, 99% initiated breastfeeding, at discharge, 68% were exclusively breastfed, 17% were partially breastfed, and 31% were exclusively breastfed for an adequate duration following discharge.

Factors in infants, mothers and clinical practice were associated with exclusive breastfeeding. Extremely preterm infants and multiples established exclusive breastfeeding at a higher postmenstrual age (PMA) and had twice the odds of not being exclusively breastfed at discharge. Mothers with low and intermediate education, with less breastfeeding experience, or who smoked had higher odds of inadequate duration of exclusive breastfeeding.

Admitting mothers to the NICU together with the infant immediately after delivery was associated with 1.5 (95% CI 0.3-2.6) days earlier establishment of exclusive breastfeeding. Initiation of breast milk expression showed a dose-response effect: the later the initiation, the higher the odds ratio (OR) for failure of exclusive breastfeeding at discharge and inadequate duration of exclusive breastfeeding.

Nipple shield use was associated with failure of exclusive breastfeeding at discharge (OR 2.3 (95% CI 1.6-3.2)) and inadequate duration of exclusive breastfeeding (OR 1.4 (95% CI 1.1-1.9)). Minimising the use of a pacifier during breastfeeding establishment was associated with 1.2 (95% CI 0.1-2.3) days earlier establishment of exclusive breastfeeding and showed a protective effect for exclusive breastfeeding at discharge (OR 0.4 (95% CI 0.3-0.6)). Test weighing the infant also showed a protective effect for exclusive breastfeeding at discharge (OR 0.6 (95% CI 0.4-0.8)).

Breastfeeding milestones were generally reached at different PMAs for various GA groups, but preterm infants were able to initiate breastfeeding early, with some delay in infants less than GA 32 weeks.

The results indicate that it is possible to establish early skin-to-skin contact with clinically stable extremely preterm infants. Danish preterm infants initiate breastfeeding to the same extent as full-term infants. Breastfeeding competence is not developed at a fixed postmenstrual age, but is influenced by multiple factors in infants, mothers and clinical practice. Admitting mothers to the NICU immediately after delivery seems to contribute to earlier establishment of exclusive breastfeeding. Minimising the use of pacifiers during breastfeeding establishment, restricting the use of nipple shields, encouraging early initiation of breast milk expression, and test weighing of infants may facilitate exclusive breastfeeding in preterm infants.

More support and attention should be given to groups with a higher risk for failure of exclusive breastfeeding: preterm infants with a gestational age of less than 32 weeks, multiples, mothers who smoke, have lower education or less breastfeeding experience.

Abbreviations and definitions

Abbreviations

CI	Confidence interval
CPAP	Continuous Positive Airway Pressure
GA	Gestational age
NICU	Neonatal intensive care unit
OR	Odds ratio
PMA	Postmenstrual age
SD	Standard deviation
SPSS™	Statistical Package for the Social Sciences
UN	United Nations
UNICEF	United Nations Children's Fund
WHO	World Health Organization

Definitions

Preterm infant and gestational age groups[1, 2]

Preterm infant	Born before $37^{0/7}$ gestational weeks broken down into four gestational age groups:
Extremely preterm infant	Born before $28^{0/7}$ gestational weeks
Very preterm infant	Born between $28^{0/7}$ and $31^{6/7}$ gestational weeks
Moderate preterm infant	Born between $32^{0/7}$ and $34^{6/7}$ gestational weeks
Late preterm infant	Born between $35^{0/7}$ and $36^{6/7}$ gestational weeks

Age[3]

Gestational age (GA)	Time elapsed between the first day of the last menstrual period and the day of delivery
Chronological age = postnatal age	Time elapsed from birth
Postmenstrual age (PMA)	Gestational age plus chronological age
Corrected age	Chronological age minus the number of weeks born before 40 weeks of gestation

Breastfeeding

In this thesis, Labbok's definition[4] of exclusive breastfeeding is used, which is the infant feeding directly at and from the breast, and is thereby not equal to feeding the infant with breast milk from a bottle or other device. The definition by Labbok is not identical to the definition by the World Health Organization,[5] which equates breastfeeding and breast milk feeding. For this thesis, exclusive breastfeeding and almost exclusive breastfeeding are equated, as exclusive breastfeeding could include medication and vitamins and, for a few infants, powder fortification mixed with the mother's expressed milk (which for this thesis was considered as medication), but not water, formula or anything else.

Partial breastfeeding includes other feeding methods in addition to breastfeeding (i.e. bottle, cup, lact-aid) regardless of content.

'Any breastfeeding' covers exclusive breastfeeding and partial breastfeeding.

Milestone

A very important stage or event in the development of something[6]

Multiples and multiple birth

Twins and triplets. The birth of twins and triplets (no higher order multiples participated in the studies in this thesis).

Rooming-in

Mothers and infants remain together 24 hours a day in hospital.[7]

Skin-to-skin contact

The infant is placed between the mother's breasts in an upright position, chest to chest. The baby is naked, except for the diaper, a warm hat and socks to allow face, chest, abdomen, arms and legs to remain in skin-to-skin contact with the mother's chest and abdomen.[8] Skin-to-skin contact can also be provided by the father or significant others.[9]

Small for gestaional age

Infant with birth weight more than two standard deviations less than expected according to gestational age.[10]

Test weighing

Measurement of milk intake by weighing the infant immediately before and after a breastfeeding session. The difference in grams equals the volume consumed in millilitres.[11]

Original papers

This thesis for the doctoral degree is based on the following papers, referred to in the text by their Roman numerals:

I   Maastrup R, Greisen G. Extremely preterm infants tolerate skin-to-skin contact during the first weeks of life. Acta Paediatrica 2010;99:1145-1149.

II   Maastrup R, Bojesen SN, Kronborg H, Hallström I. Breastfeeding Support in Neonatal Intensive Care: A National Survey. Journal of Human Lactation 2012;28(3):370-379.

III   Maastrup R, Hansen BM, Kronborg H, Bojesen SN, Hallum K, Frandsen A, Kynaeb A, Svarer I, Hallström I. Factors associated with exclusive breastfeeding of preterm infants. Results from a prospective national cohort study. PLoS ONE 2014;9(2): e89077.

IV   Maastrup R, Hansen BM, Kronborg H, Bojesen SN, Hallum K, Frandsen A, Kynaeb A, Svarer I, Hallström I. Breastfeeding progression in preterm infants is influenced by factors in infants, mothers and clinical practice. The results of a national cohort study with high breastfeeding initiation rates. In manuscript.

Papers I, II and III have been reprinted with the permission of the journals.

Introduction

The rate of preterm births has increased over the last several decades; in 2011, 6.8% of Danish infants were born prematurely.[12] Treatment and care of preterm infants (see Definitions) have been more specialized during this period, saving smaller and smaller infants.[13] When the treatment became more specialized, extremely preterm infants (see Definitions) began to survive. Although treatment and care improved, a large variation in physical and psychosocial outcomes persists.[14, 15]

French obstetrician Budin described in his book *The Nursling* (1907) the practice of breastfeeding preterm infants by wet-nurses in the clinic. In the meantime, the mother sustained her milk production by feeding another infant or child, for the purpose of breastfeeding her preterm infant prior to discharge.[16] There is also a tradition in Denmark of offering human milk to preterm and sick infants. The largest human milk bank in Denmark was established in 1943.[17, 18] Recognition of human milk as the preferred nutrition for preterm and sick infants contributed to encouragement of mothers to express breast milk for their infants – even before they were allowed to visit their baby – and to subsequently try to establish breastfeeding.[19-23] Since the 1960s and 1970s, parents' presence in NICUs gradually increased, and restrictions on parents' presence are diminishing both internationally[24, 25] and in the Nordic countries.[19, 25, 26] Breastfeeding of preterm infants is still a major issue in the Nordic countries.[27-34]

The first step in the breastfeeding progress of preterm infants is skin-to-skin contact between mother and infant[35-37] (see Definitions). This practice was first described internationally in 1985[38] and in Denmark in 1987,[39, 40] spreading to almost all Danish NICUs by 1990,[41] and is still attracting research attention in the Nordic countries.[26, 42-45] Skin-to-skin contact is particularly challenging with extremely preterm infants,[44, 45] and research on these infants before 2010 is sparse.[46, 47]

Even though the literature covers some of the important issues related to breastfeeding of preterm infants, many fields related to this subject are yet to be examined. This thesis will highlight potential influencing factors in infants, mothers and clinical practice that could facilitate the guidance of mothers of preterm infants in breastfeeding.

Background

Preterm infants

Preterm infants are those born before $37^{0/7}$ weeks of gestation. The preterm birth rate has been increasing in recent decades[12, 48] and was estimated at 9.6% (95% CI 9.1-10.1) worldwide and 6.2% (95% CI 5.8-7.9) in Europe in 2005.[49] In Denmark, the preterm birth rate in 2011 was 6.8%: 1.4% extremely and very preterm infants and 5.4% moderate and late preterm infants[12] (see Definitions). There is no consensus in the literature on the line between moderate and late preterm infants. Late preterm infants' lower age ranges from gestational age (GA) (see Definitions) $34^{0/7}$ to $35^{0/7}$.[2, 50-52]

Preterm infants are more fragile and have higher morbidity and mortality than full-term infants,[15, 51] increased risk of respiratory distress syndrome, feeding intolerance, necrotising enterocolitis, periventricular leucomalacia, infections, hypothermia, hypoglycaemia and hyperbilirubinemia.[53] Preterm infants exhibit oromotor hypotonia, rapid fatigue, and general lack of strength.[53] Extremely and very preterm infants suffer from more morbidity and mortality than moderate and late preterm infants,[15] stay for a longer time in incubator and have longer hospitalisations.[15]

Studies have found less myelinated white matter in the brains of preterm infants at corrected term age (see Definitions) compared to healthy full-term infants;[54, 55] this was significantly present in both low-risk and high-risk preterm infants, and the pattern of cerebral alteration was significantly related to degree of prematurity. Slower brain maturation after extremely preterm birth could be due to biological and environmental factors, that the brain matures with different velocity intrauterine and extra uterine and is influenced by quality of experience.[56]

Due to the Scandinavian minimal invasive approach, mechanical ventilation is used less than nasal continuous positive airway pressure (CPAP) in Denmark for treatment of preterm infants with respiratory distress syndrome,[57, 58] which probably contributes to lower rates of severe bronco-pulmonary dysplasia, earlier parent-infant contact, and making it easier for parents to handle the baby during hospitalisation.[58] The commonly used nasal CPAP device in Denmark, the Beneveniste valve, is a simple construction that, due to its small size, does not prevent the infant from latching on to the breast (see Figure 1).

Figure 1. Breastfeeding with CPAP (Beneviniste valve)

Neonatal intensive care units

Most preterm infants are cared for in neonatal intensive care units (NICUs). The classification of NICUs varies internationally. The American Academy of Pediatrics classification (2004) is shown in Table 1.[59] In 2012, the American Academy of Pediatrics revised its definitions and defined level II as caring for preterm infants >32 weeks GA, and levels III and IV as caring for infants <32 weeks GA with no lower limit.[60] NICUs are also classified by "international practice", described by Finström,[61] according to hospital services: IIb: Basic neonatal service, IIa: County hospitals with full resources, and III: Tertiary hospitals with full resources for neonatal intensive care. The definition by the American Academy of Pediatrics is widely used, but the 2012 definitions do not reflect the organisation of Danish NICUs, where caring for infants with GA between 28 and 32 weeks is common in NICUs without the option of mechanical ventilation, as nasal CPAP is the conventional care (see above).

Table 1. American Academy of Pediatrics 2004 classification of NICUs[59]

Level I	Basic care
Level II	Specialty care of infants >1,500 grams and GA >32 weeks, brief mechanical ventilation
Level IIIA	Subspecialty intensive care of infants > 1,000 grams and GA > 28 weeks, conventional ventilation
Level IIIB	Subspecialty intensive care of infants < 1,000 grams and GA < 28 weeks, advanced respiratory support, and pediatric surgical specialist
Level IIIC	Same as IIIB but including extracorporeal membrane oxygenation and surgical repair of complex congenital cardiac malformations

Prevalence of breastfeeding

International studies of preterm breastfeeding vary in outcome measures; some examine exclusive breastfeeding,[29, 62-64] others examine any breastfeeding[65, 66] (see Definitions), and others equate breastfeeding with breast milk feeding.[67-73] The World Health Organization (WHO) equates breastfeeding with breast milk feeding in its definition,[5] while Labbok defines breastfeeding as direct breastfeeding.[4] Direct breastfeeding has been found to have more benefits: Geraghty et al. found in 2005 that early exclusive breastfeeding directly from the breast was associated with longer duration of breast milk feeding overall.[74] Li et al. found in 2010 that infant appetite was less regulated when they were fed from a bottle compared to direct breastfeeding, and that bottle-feeding – not the type of milk in the bottle (expressed breast milk or formula) – may be important in infant self-regulation.[75] Studies have found that preterm infants were more clinically stable during breastfeeding than during bottle-feeding.[76, 77]

Full-term infants
Breastfeeding initiation rates vary among industrialized countries; Australia 88%,[79] Austria 93%, Canada 90%, the UK 76%, and the U.S. 74%.[78] At six months, 14% were exclusively breastfed in Canada and the U.S., and 10% in Austria.[78]

In the Scandinavian countries, 95% to 99% of all mothers begin breastfeeding their infants,[80-83] and the proportion of infants who are exclusively breastfed for four months is relatively high in Denmark (61%),[83] Sweden (53%),[80] and Norway (46%).[81] The six-month rates of exclusive breastfeeding are 12% in Denmark,[83] 14% in Sweden,[80] and 9% in Norway.[81] In Denmark, 11% of the

population are immigrants and their descendants;[84] descendants of immigrants (second and third generation) have lower rates of exclusive breastfeeding at four months (43%) than other Danes.[83] Breastfeeding rates in these studies and statistics concerning full-term infants might include breast milk feeding.

Preterm infants

Breastfeeding rates of preterm infants refer to initiation of breastfeeding, breastfeeding at discharge, and breastfeeding duration. International studies show that mothers of preterm infants have lower breastfeeding initiation rates, 27-62% in the U.S.[65, 66, 85] and 80-86% in Australia.[64, 86] In Scandinavia, there are no available statistics on preterm infant breastfeeding initiation. Preterm infant breastfeeding rates at discharge are found in larger studies to be 86% in Australia, 92% in Sweden, and 65% in Denmark; the corresponding rates for exclusive breastfeeding were 55% in Australia, 53% in Sweden, and 60% in Denmark.[64, 62, 29] Preterm infant breastfeeding duration – including breast milk feeding – has been found to be shorter than full-term infants,[62, 67, 68, 73] and this pattern was more pronounced for preterm infants with lower GA than higher GA at corrected age time points.[62] WHO recommends exclusive breast milk feeding until 6 months of age, regardless of prematurity.[87]

Skin-to-skin contact

Benefits of skin-to-skin contact in breastfeeding

Skin-to-skin contact is the first step in the establishment of breastfeeding.[35-37] The infant is placed between the mother's breasts in an upright prone position. Skin-to-skin contact in full-term infants immediately after birth is positively associated with breastfeeding and mother-infant interaction.[88, 89] The father is also an important person in skin-to-skin contact, as full-term infants who have skin-to-skin contact with their father after caesareans cry less.[90] Not all preterm infants are able to have skin-to-skin contact immediately after birth, and even if they tolerate it, this is not always the practice.[26] However, skin-to-skin contact during hospitalisation is common practice at many NICUs, either intermittent or continuously and with both mothers and fathers.[26, 91, 92] It is well documented that skin-to-skin contact between a preterm infant and his or her mother/parents has a positive influence on breastfeeding initiation and duration.[30, 93-96] Furthermore, very preterm infants who had more skin-to-skin contact (as opposed to less) were breastfed for a longer duration.[30] Only one study has compared initiation time of skin-to-skin contact and breastfeeding.[96] In this study, infants had continuous skin-

to-skin contact for 24 hours a day (or mostly), and more of the infants who initiated skin-to-skin contact within the first day of life were breastfed exclusively for six months (41% vs. 15%). It is not known whether the timing of intermittent skin-to-skin contact is related to breastfeeding in preterm infants.

Other aspects of skin-to-skin contact in preterm infants

Sometimes preterm infants are too unstable to tolerate transfer from incubator to parent, and skin-to-skin contact is delayed. Reported barriers to skin-to-skin contact have been described as fear of accidental extubation of the infant, fear of umbilical catheter dislodgement, safety issues for infants weighing less than 1,500 grams, and to a lesser extent nurses believing that skin-to-skin care will increase their workload. These issues were reported as barriers to a higher extent in the U.S. in 2002 than in the Nordic countries in 2012.[26, 91]

In a global perspective, skin-to-skin contact decreases mortality in resource-limited settings, but this effect is not seen in developed countries.[93] Compared to incubator care, skin-to-skin contact between preterm infants born after 28 gestational weeks and their mothers has shown other benefits than breastfeeding: infants are better at keeping an adequate temperature, have a more stable heart rate and respiration,[97] have calm behaviour,[98] are more often in an inactive alert behavioural state,[99] and have deeper sleep.[100] The development of personal relations and planning functions at 12-month corrected age has been found to be better in children born prematurely that had continuous skin-to-skin contact compared to no skin-to-skin contact.[101] Mothers feel greater responsibility and competence, and they overcome the initial stress and shock associated with premature births more quickly[102] and describe that they feel acknowledged as parents.[103] Fathers describe that they achieve a feeling of well-being by holding their infant skin-to-skin, that the ties between the infant and father are strengthened,[104] and that skin-to-skin contact enhances their ability to play a caring role in their infant's life;[43] this can help increase parental competence. Mothers of preterm infants describe skin-to-skin contact as a way of continuing the pregnancy outside instead of inside the womb, and skin-to-skin contact becomes a transforming bridge between the image of the old life and the new one, and a special ethical action that contributes to repairing the feeling of normality.[105] There were only few studies of skin-to-skin contact that included extremely preterm infants with a postmenstrual age (PMA – see Definitions) of less than 28 weeks,[46, 47] but more studies have been published the last few years.[44, 45] The early studies did not agree about extremely preterm infant toleration of skin-to-skin contact, resulting in different practice at Danish NICUs: at some NICUs, initiation was delayed for two weeks, at other NICUs, skin-to-skin contact was initiated much sooner.

Only a few studies had studied prevalence of skin-to-skin contact. National studies from the U.S. and Nordic countries found that 82% of NICUs in the U.S. survey, and 100% of NICUs in the Nordic survey practiced skin-to-skin contact.[26, 91] Swedish infants with GA 28-34 weeks initiated skin-to-skin contact earlier (82% within 24 hours)[42] than extremely preterm infants less than GA 27 weeks (median postnatal age, six days – see Definitions).[44] Only the study of extremely preterm infants was national.[44] Studies from Sweden and the U.S. reported that preterm infants in NICUs had average daily skin-to-skin contact for 120-400 minutes.[30, 42, 106]

Benefits of breastfeeding

Breastfeeding provides health benefits to both the infant and mother[107-109] with even more pronounced benefits for preterm infants.[110] Breastfeeding (or tube-feeding with the mother's expressed milk) reduces the risk of severe disease such as early severe infections, necrotising enterocolitis and retinopathy[111-116] probably due to the immunological components of breast milk, the protein composition of whey and casein that makes breast milk easier to digest than infant formula, and fatty acids.[117-118] Comparing breastfed and formula-fed preterm infants, breastfed infants have a lower percentage of hard stools[119] and formula-fed infants are more often treated with laxatives.[120] Breastfeeding has a positive influence on intelligence quotient (IQ) in children,[121, 122] and the effect persists during adolescence[123] and adulthood.[124] The explanation could be associated with the feeding situation or the content of long-chain polyunsaturated fatty acid, especially the n-3 fatty acid, of which cellular membranes in the brain and the retina contain high levels. Or it could be associated with undefined factors that correlate with both cognitive development and breastfeeding.[118]

Premature birth and admission to an NICU may have a negative influence on the mother's view of herself; skin-to-skin contact and breastfeeding are actions in which the mother feels important.[125] Mothers of preterm infants may feel that they failed when they give premature birth and that the only task left to do right is to breastfeed.[126] Breastfeeding repairs the disruption caused by preterm birth and gives the mother the opportunity of carrying out responsibilities and tasks, which contributes to her construction of herself as a good mother in spite of the preterm birth.[105] Mothers described that breastfeeding rewards them with feelings of closeness and bonding with their infant,[127] making it even more important to mothers of preterm infants. Even if the mothers establish breastfeeding, they do not always regard it as being mutual pleasurable.[126]

Establishment of breastfeeding in preterm infants is important to infants, mothers, and society.

Mothers who do not breastfeed

In the Scandinavian countries, breastfeeding is supported and promoted by the healthcare professionals during pregnancy, delivery and postnatal/neonatal care, as well as by long maternal leave.[128, 129] Breastfeeding is the cultural norm, and almost all mothers initiate breastfeeding.[80-82] It is the task of the healthcare professionals to support mothers in making and implementing their own informed decisions about milk production, breastfeeding and feeding.[27] The group that does not breastfeed consists of mothers who do not want to breastfeed, mothers who are not allowed to breastfeed (because of medication, etc.), mothers who are not able to breastfeed (because of breast surgery, etc.), and mothers who plan to breastfeed but, for reasons often related to the infant or milk production, do not establish breastfeeding. When mothers who plan to breastfeed do not establish breastfeeding, their expectations are shattered; they often feel guilty and have low confidence in their own abilities and feelings of shame, disappointment and being useless.[31, 34, 126, 130] They turn the failure towards themselves, asking themselves if they have tried hard enough or if they could have done more.[31] Mothers who do not breastfeed sometimes find the attitudes of the healthcare system too pro-breastfeeding.[126]

Breastfeeding milestones for preterm infants

In a Nordic context, a preterm infant's breastfeeding development is often referred to as the "breastfeeding wheel".[35, 36] In Denmark, the wheel was transformed to the "Milky Way" in 2000 (see Figure 2);[37] the content was the same, beginning with skin-to-skin contact, moving to the first breastfeeding experience, then the infant will gradually "walk the Milky Way" by sucking and swallowing, taking a little breast before tube feeding, taking half a breastfeed sometimes before tube-feeding, taking more breastfeeds than tube feeds, and finally be exclusively breastfed (see Figure 2).

The Breastfeeding Process:

- Exclusively breastfed
- Takes more breast than tube
- Takes half a meal some times before tube
- Takes a little breast before tube
- Sucks and swallows
- Seeks, finds and sucks for pleasure
- Licks and tastes
- Nuzzles breast
- Skin-to-skin kontact
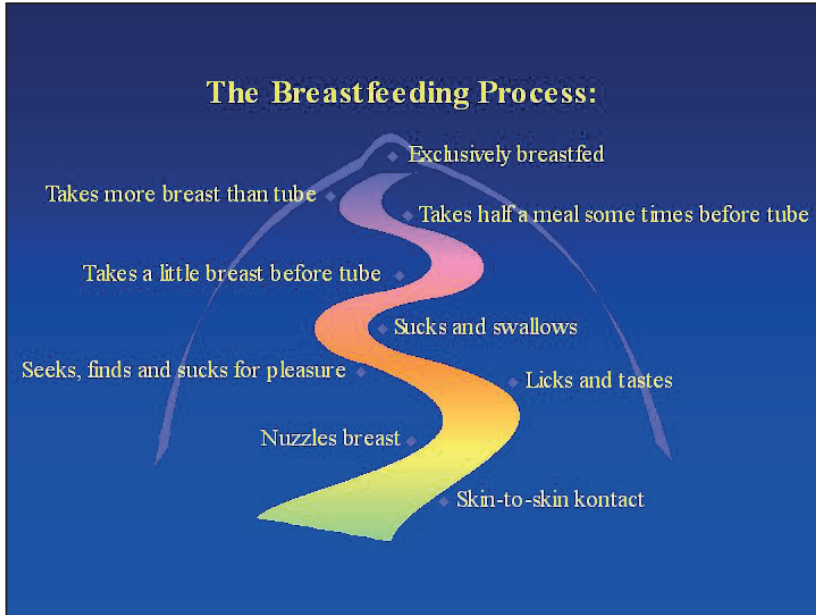
Developed by Ragnhild Måstrup, Hvidovre Hospital 2000

Figure 2. A preterm infant's breastfeeding process or"The Milky Way

All these feeding milestones (see Definitions) are simplified in: breastfeeding initiation, breastfeeding a given amount of milk, and establishment of exclusive breastfeeding.

Nyqvist conducted pioneering research in 1999 when she published results of the development of preterm infant breastfeeding behaviour,[131] showing that breastfeeding could be initiated in relatively healthy preterm infants from 27.9 gestational weeks, how breastfeeding competences developed with PMA, and that exclusive breastfeeding was established at a median of 36.0 gestational weeks. The research was followed by a similar study of extremely and very preterm infants,[132] but no comparison of PMA at the various breastfeeding milestones was made between various GA groups. Breastfeeding milestones in bottle-fed preterm infants are well-studied, but infant sucking skills seems to differ between bottle feeding and breastfeeding, and data gathered from bottle feeding are not necessarily applicable to breastfeeding.[133]

Facilitators and barriers to breastfeeding of preterm infants

There are several facilitators and barriers to breastfeeding in preterm infants. Some of them are related to infants and mothers, while others are related to ward-specific factors i.e. the support the hospital and the NICU offer and the clinical methods used at the NICU. These factors will be described in the following sections.

Factors in infants

The barriers for infants include low gestational age,[71, 73] infants from multiple births,[67, 69-71] and delayed initial breastfeeding attempt.[134] Slower brain maturation, indicated by the infant's rapid fatigue, limited periods in alert behavioural state, low muscle tone, and general lack of strength may contribute to difficulties in breastfeeding establishment.[53, 99, 135] Latching on the breast and sustaining the latch is challenged by the infant's small mouth, weak intra-oral vacuum, and the fact that the infant is easily overstimulated by numerous stimuli at the NICU (sounds, light), touch, handling and social interaction.[135] Also, the higher risk of low blood glucose,[53] which requires early feeding before the mother has sufficient quantities of milk, could interfere with breastfeeding establishment.

On the base of a Newborn Individualised Developmental Care and Assessment Program (NIDCAP) observation, Nyqvist suggested that a preterm infant could be facilitated in breastfeeding by planning the infant's day, providing a supportive physical environment, showing the mother how to support the infant in a flexed position, pointing out to the mother how her infant communicates with signs of approach and avoidance, and teaching her to respond adequately and help the infant to regain control, being patient, giving the mother and infant plenty of time and letting the infant's cues determine the pace.[135]

Factors in mothers

Barriers for mothers include low socio-economic status[29, 65, 66, 68-70] and smoking.[29] The establishment of sufficient milk production is delayed in mothers of preterm infants,[136] and lactation must be initiated by expressing milk rather than the infant sucking at the breast. In addition, lack of privacy and the mother's stress due to the premature birth while having a baby who has poor sucking skills make it harder for the mother to adapt to the infant's needs.[137] Previous long breastfeeding experience facilitates later breastfeeding.[73] Mothers need balanced help from the

nursing staff, i.e. the staff gives support and advice, but also steps back when the mother feels she can handle breastfeeding by herself. [31]

Early separation due to NICU admission is related to increased parental NICU-related stress,[138] and higher stress levels in the dimension of incompetence have been found in mothers not at co-care facilities.[139] Mothers separated from their newborn infants experience emotional strain and anxiety; they feel that they are outsiders, and experience a lack of control when the infant is admitted to the NICU.[140] On the other hand, the possibility of rooming-in can help parents feel like a family and not just visitors to their own baby.[141] Paternal emotional, practical and physical support are important factors in successful breastfeeding,[142] and the mother needs the infant's father to be present at the NICU to support her,[143] which is why no restrictions on the presence of both parents may facilitate breastfeeding.

Although mothers of preterm infants generally experience breastfeeding as a positive act that normalizes the premature birth, mothers exhibit both positive and negative emotional manifestations in the process of breastfeeding a preterm infant.[126]

Factors in clinical practice

Recognition of the impact of clinical practice on breastfeeding success was the background for the United Nations Children's Fund (UNICEF) and WHO launch of the Baby-Friendly Hospital Initiative in 1989 of "Ten Steps" to protect, promote and support breastfeeding in maternity services.[7] A study from Belarus has shown that the Baby-Friendly Hospital Initiative improved breastfeeding duration.[144] Reports and research on local initiatives modifying the "Ten Steps" to a NICU context have been published.[143, 145-147] A Nordic working group is now expanding the Baby-Friendly Hospital Initiative for Neonatal Intensive Care at an international level.[27, 28]

Supporting breastfeeding at the NICU
The NICU had historically been an unfriendly environment for breastfeeding, with separation (see the next section), restrictions on parental presence,[24] a highly technological space with large noisy rooms, but the trend is now turning[148] and the "Baby-Friendly Hospital Initiative for neonatal intensive care" is creating recommendations for NICUs to support breastfeeding.[27, 28] First of all, NICUs should respect the rights, responsibilities, and duties of parents to provide appropriate direction and guidance for their infant according to Article 5 of the United Nations (UN) Convention on the Rights of the Child and not to separate infants from their parents against their will according to Article 9.[149] The Convention covers all children irrespective of the child's birth or other status. All

193 countries that have signed the convention are obliged to comply with the convention. Only The U.S. and Somalia have not signed the convention.

A low level of light, sound and activity according to the infant and mother's individual needs, and providing the mother with a bed or a comfortable armchair, are important to enable the mother to support her preterm infant in the development of effective breastfeeding behaviour.[135, 143] For the mother to breastfeed, it is essential that she have free access to her infant and that her planning of breastfeeding sessions be respected, including waking her up during the night when her infant needs to breastfeed.[31, 103] The unrestricted presence of parents at the NICU and opportunities for parents to rest, sleep and eat at the NICU are also recommended by "the Baby-Friendly Hospital Initiative for Neonatal Intensive Care" to support breastfeeding.[27, 28]

Separation or rooming-in

Since medical care of preterm infants commenced in the late 1880s, it has been the norm to separate the mother and infant at the NICU even after the parents' role as caregivers was acknowledged at paediatric wards in the 1980s. Today, unrestricted presence of parents is emerging but is far from the norm.[25, 26] Unrestricted presence of parents is not always the same as offering the parents a bed at the NICU, but some NICUs in Europe and the U.S. have beds for parents too.[25, 148]

Rooming-in (see Definitions) of the mother together with the infant in maternity wards has been associated with better breastfeeding outcomes.[150] One older study found the same positive association with rooming-in of mothers in the NICU,[151] and more studies have added to the evidence the last years.[33, 152]

Breast milk expression

Lack of breast milk is one of the greatest barriers to establishing breastfeeding in preterm infants.[153] It is recommended that mothers initiate breast milk expression soon after delivery but there is no consensus as to how early this should be done, or to the outcome that should be promoted. A U.S. study showed that initiating breast milk expression within six hours after delivery was positively related to continued breast milk expression at 40 weeks PMA,[154] whereas another study found that initiating expression within 24 hours was positively related to adequate milk volume six weeks later.[155] A recent randomised controlled trial in mothers of preterm infants found that initiation of breast milk expression within one hour after delivery, compared to six hours, doubled the mothers' volume of milk for the first three weeks.[156]

Skin-to-skin contact

Skin-to-skin contact is regarded as a facilitator of breastfeeding preterm infants as described above.

Pacifier and bottle feeding

The use of a pacifier in preterm infants has been shown to relieve pain and reduce stress in the absence of the mother,[157, 158] and is therefore widely used for preterm infants, although the use of a pacifier is not recommended for full-term newborns[7] as it is associated with lower breastfeeding outcomes.[182, 160] An Australian study showed that the use of pacifiers for preterm infants was not associated with breastfeeding at discharge,[161] and a Brazilian study found that the use of a pacifier increased the odds of preterm infants not being exclusively breastfed at six months.[162]

Preterm infants are less physiologically stable during bottle feeding than breastfeeding,[76] and preterm infants who have been bottle-fed during hospitalisation are less likely to be exclusively breastfed at discharge than infants who have been cup-fed.[161] Tube-feeding preterm infants during the transition from exclusive tube feeding to breastfeeding has been shown to increase the likelihood of breastfeeding.[163] Bottle feeding is not recommended for preterm infants.[28]

Nipple shield

In general, the use of a thin silicone nipple shield is not recommended for full-term infants,[7] as the use is thought to decrease milk production, make it difficult to wean from nipple shield, and result in earlier unplanned weaning of breastfeeding.[117] Reports on the use of nipple shield in preterm infants facilitating latch on, increasing milk transfer and compensating for weak infant suction appeared around 2000,[164, 165] suggesting that preterm infants need temporary strategies like nipple shield to facilitate milk intake until reaching corrected term age.[165] For this reason, nipple shields have been widely recommended for preterm infants.[28, 145, 166, 167] A more recent literature review concludes that current research does not provide evidence for the safety or effectiveness of nipple shield use for either full-term or preterm infants.[168] For some mothers, the use of a nipple shield rescues breastfeeding when the infant would otherwise have been unable to breastfeed. When neonatal nurses meet in Denmark, the use of nipple shields is sometimes discussed, and the pros and cons are very strong and based on personal convictions.

Test weighing

Mothers of preterm infants (and nurses) may have a need of quantifying the infant's intake of breast milk during and after transition from tube feeding to breastfeeding, as the volume intake during the tube feeding period had been measured to the nearest millilitre, and mothers are concerned about their infant getting enough milk from the breast.[169] Measurement of milk intake by test weighing (see Definitions) is the most precise method.[170] and has been recommended for preterm infants.[145, 167, 171] A Swedish study showed that preterm

infants at a NICU using test weighing as a routine established exclusive breastfeeding at an earlier PMA than infants at a NICU not using test weighing, but there were no differences in exclusive breastfeeding rates or postnatal age at the establishment of exclusive breastfeeding.[172] Another Swedish study using a quasi-experimental design found that infants in the "non-test weighing group" had twice the risk of not being exclusively breastfed at discharge.[32] Test weighing could also be regarded as mechanical, unnatural and stressful to mothers.[11] Mothers have described that they became "addicted" to and relying on test weighing instead of having confidence in their own judgement.[31] Maybe that is a contributing factor to mothers preferring to continue the procedure once test weighing has been initiated.[11] In full-term infants, test weighing is associated with a shorter duration of exclusive breastfeeding,[173] and the conflicting results make it hard to guide mothers in this respect.

Research is needed

To sum up, facilitation of breastfeeding in preterm infants at the NICU is important, but knowledge about the best way of guiding the mother is unclear imprecise, contradictive or sparse for some clinical methods. Successful breastfeeding is probably influenced by multiple factors, and several clinical methods have been studied one by one. Knowledge about extremely preterm infant toleration of skin-to-skin contact is sparse.

Aims

The overall aim of this thesis was to study and identify factors associated with breastfeeding of preterm infants, in the infant, the mother and the NICU in order to gain more knowledge on which to base guidance of mothers of preterm infants in breastfeeding. For each study, a specific aim was formulated.

Study A

The aim was to determine whether clinically stable extremely preterm infants could maintain their temperature during skin-to-skin contact and to screen for other negative effects (Paper I).

Study B

The aim was to describe breastfeeding support at neonatal intensive care units in Denmark (Paper II).

Study C

The primary aim was to investigate the association between early breast milk expression, early initiation of skin-to-skin contact, rooming-in, nipple shield use, test weighing, and pacifier use, and the establishment of exclusive breastfeeding at discharge, as well as at a predefined interval after discharge (Paper III). A further aim was to describe rates of breastfeeding duration at predefined times in various preterm GA groups, to analyse the PMA at breastfeeding milestones in various preterm GA groups, and to analyse factors associated with PMA at establishment of exclusive breastfeeding (Paper IV).

Methods

Design

This thesis includes one intervention study (Study A), and two national surveys (Study B and C). An overview of the studies is shown in Table 2.

Table 2. Overview of the studies

Study	Design	Time period	Sample	Instruments	Paper
A	Intervention study	March-Dec. 2008	22 extremely preterm infants	Continuously skin-temperature measurement	I
B	National survey	Aug.-Oct. 2009	Head nurses from 19 NICUs, 2 M-I wards and one children's department	Breastfeeding support questionnaire	II
C	National survey Longitudinal cohort study	Sept. 2009 - Dec. 2011	1,221 mothers and their 1,488 preterm infants	Questionnaire 1 and 2 to the mother. Telephone interview 1, 4, 6 and 12 months corrected age	III, IV

M-I wards = Mother-infant wards

A prospective design was used for the clinical intervention study (Paper I), in which the 22 infants served as their own control group in a pre-test, test, post-test design. The intervention was skin-to-skin contact (flexible time duration), and the pre-test and post-test were each 2 hours of incubator care immediately before and after the intervention.

Surveys were used for Study B and C. Study B included one questionnaire answered jointly by the head nurse and nurses with extensive experience in

supporting mothers in the breastfeeding of preterm infants from each of the participating wards. In addition to a national survey, Study C was a longitudinal cohort study. The study was based on three questionnaires; two answered by the mothers during the infant's hospitalisation, and the third used for a maximum of four structured telephone interviews until breastfeeding ceased or the infant reached 12 months corrected age – whichever occurred first.

Context of the studies

Denmark has 5.5 million inhabitants and about 56,000 births per year (2011).[12] Denmark has public health care and all citizens have access to treatment at public hospitals free of charge.[174] In connection with birth, parents in Denmark are entitled to paid parental leave. Mothers have paid leave for a minimum of four weeks before delivery and up to 10.5 months after delivery, of which 7.5 months can be shared with the father/partner. Maternal leave can be extended with the length of the hospital stay to a maximum of 3 months if the infant is born preterm or stays at the hospital due to illness. Partners have two weeks of leave following birth. An additional year of parental leave is optional without payment.[128]

Most preterm infants are admitted to one of Denmark's 19 NICUs, except for stable late preterm infants, who are cared for at maternity wards. Preterm infants at an NICU are hospitalised until breastfeeding is established, or until exclusive breastfeeding is given up, and mixed feeding or bottle feeding is established. The Danish NICUs have a family-focused approach, including parents giving informed consent for their infant's treatments, high degree of parental presence, and parents participating in the infant's care.

Study A was conducted at the NICU at Rigshospitalet, Copenhagen University Hospital, a 36-bed high-intensive NICU with 2-bed and 5-bed rooms. The NICU had a parent-bed beside most incubators.

All Danish NICUs contributed data in Study B and all NICUs except one contributed data in Study C.

Study population

The study population was preterm infants, their mothers/parents and the NICUs at which they were hospitalised.

In study A, a power calculation allowing exclusion of a difference in mean skin temperature of one standard deviation with a p-value of 0.05 and a power of 80% showed that 22 infants were needed. No power calculation was made in

Study B, as it was a descriptive study. In Study C, we had no a priori estimates of either outcome or multiple exposures and no power calculation was made. The study was planned to enrol infants in a 12-month period to include as many mother-infant pairs as possible.

In Study A, 57 extremely preterm infants were admitted to the study NICU between March and December 2008. The author of this thesis enrolled parents and infants, started each measurement, and supervised transfer. She was not available for 22 of the infants (due to circumstances beyond her control); 11 infants were too unstable to participate and not enrolled. Two infants became unstable after enrolment and did not participate. The 22 infants who participated in the study had lower mean GA and lower mean birth weight than the group as a whole, but not different from infants who were too unstable to participate (see flowchart, Paper I, Figure 1). None of the parents refused to participate with their infant. The mean PMA at study time was 26 weeks and five days, and the mean weight was 702 grams; ten infants participated in their first week of life, but only one infant was studied during the very first skin-to-skin session, and six infants during the second session. Eleven infants were studied during the 3rd, 4th and 5th skin-to-skin sessions, and the remaining four infants had previously been skin-to-skin seven or more times.

Figure 3.

Extremely preterm infant skin-to-skin with her father

In study B, 22 wards participated. NICUs in Denmark are organized in relation to the GA from which they care for preterm infants. As this does not fit into the American classification,[59, 60] the NICUs were classified as low, medium and high intensive care in this thesis (see Table 3), and they are all called NICUs, as they all provide at least nasal CPAP treatment for preterm infants. One high intensive care NICU did not provide surgery. All 19 NICUs in Denmark participated. Three other wards that routinely take care of preterm infants during breastfeeding establishment also participated. They were two mother-infant wards (non-intensive wards where the mother and preterm infant were admitted together for breastfeeding establishment) and one children's ward. In order to compare with future studies, homogeneity of wards was chosen for Paper II, and only results from the 19 NICUs were reported in Paper II.

Table 3. Classification of NICUs

Finström[61]	AAP 2004[59]	AAP 2012[60]	DK NICUs care from GA	Paper II
IIb	II	II	32	Low
IIa	IIIA	II	30	Medium
IIa	IIIA	II	28	Medium
IIa	IIIA	II	28	Medium
IIa	IIIA	II	28	Medium
IIa	IIIA	II	28	Medium
IIa	IIIA	II	28	Medium
IIa	IIIA	II	28	Medium
IIa	IIIA	II	28	Medium
IIa	IIIA	II	28	Medium
IIa	IIIA	II	28	Medium
IIa	IIIA	II	28	Medium
IIa	IIIA	II	26	Medium
IIa	IIIA	II	26	Medium
IIa	IIIA	II	26	Medium
IIa	IIIA	II	No limit	High
III	IIIB	III	No limit	High
III	IIIC	IV	No limit	High
III	IIIC	IV	No limit	High

AAP = American Academi of Pediatrics, DK= Danish

In study C, 21 wards participated, which were all Danish wards that routinely took care of preterm infants during breastfeeding establishment. This included all participating wards in Study B except one high intensive care NICU, which transferred all preterm infants to other NICUs before breastfeeding establishment. Seven wards showed some reluctance in participating in the study, as they thought it was too time-consuming. These wards were encouraged to participate without performing structured telephone interviews and/or data entry, which made them consent to participation.

All preterm infants, who were admitted to the participating wards from 1st of September 2009 to 31st of August 2010 in their first five days of life, could be included in Study C. During the study time 2,579 preterm infants from 2,150 mothers were admitted to the participating wards. Infants were excluded if they were discharged to maternity wards before five days of age (161 mothers/188 infants), if they died (161 mothers/188 infants), or if an interpreter was not available for the mother (35 mothers/42 infants).

Participants are described in the flow chart (Paper III and IV, Figure 1). Of the eligible infants, 1,488 (65%) participated until discharge (Paper III, Table 1). The number of participating mothers was 1,221.

The preterm infants were divided into the four gestational age groups; extremely preterm infants with GA <28 weeks, very preterm infants with GA $28^{0/7} – 31^{6/7}$ weeks, moderate preterm infant with GA $32^{0/7} – 34^{6/7}$ weeks, and late preterm infants with GA $35^{0/7} – 36^{6/7}$ weeks. As most preterm infants with GA less than $35^{0/7}$ weeks as a routine are admitted to NICUs in Denmark, regardless of the infants' physical situation, the lower limit of gestational age in the late preterm group in this thesis was set to $35^{0/7}$ weeks.

Data collection

Measurement of physical parameters

In study A, each extremely preterm infant participated once when he or she was stable for transfer to the skin-to-skin position. Skin temperature values for each minute were saved electronically from the start of the pre-test (two hours before), during the intervention (all the skin-to-skin time) and to the end of the post-test (two hours after skin-to-skin contact). Heart rate, respiration rate, and oxygen saturation were monitored electronically (Paper I).

Questionnaires

Coded questionnaires were mailed to each head nurse of the 22 wards participating in Study B. They were asked to respond to the questionnaire in cooperation with nurses at the ward with extensive experience in supporting mothers in

breastfeeding of preterm infants. Reminders were sent after one and two months (Paper II).

In Study C, identified contact persons from all 21 participating wards registered all preterm infants admitted to the ward with date of birth, GA, gender and singleton/twin/triplet; informed mothers, distributed and collected Questionnaire 1 and 2. Contact persons often took advantage of the opportunity to be supervised by the project leader (RM) by phone or e-mail. In addition, e-mails were sent out regularly to all contact persons to support and motivate them to continue data collection.

Telephone interviews were performed by 15 of the 21 wards, and data were entered in the database by 12 of the 21 wards, (some intended to enter the data, but were short of time at the end of the study). To ensure consistency, a structured questionnaire was used for telephone interviews, and an easy-to-use database was constructed, followed by written guidance and the option of e-mail and phone support. The National Expert Panel in charge of the study conducted structured telephone interviews for the remaining six wards in cooperation with one NICU, and a student assistant entered the data for the remaining nine wards in cooperation with another NICU. The author of this thesis checked all the data and crosschecked any extreme, misleading data against the original responses.

Instruments

Study protocols and information

Specific protocols were prepared for the three studies. For each study, written information and consent forms and an Excel database were prepared. In addition, for study A, a transfer and position guideline to ensure standardised, safe, and optimised transfer of extremely preterm infants between parent and incubator to prevent heat loss (see Appendix A), and a data and observation scheme was prepared to ensure uniform data collection (see Appendix B). In study C, materials prepared for the NICU contact persons included written guidelines on how to conduct the study and how to enter data, code number forms and standard letters to mothers if it was necessary to send the questionnaires by mail.

Questionnaires

No previous questionnaires were found that investigated breastfeeding support at NICUs (Study B), and no questionnaires were found that covered the aim of Study C; therefore, four questionnaires were developed – one for the head nurses at the NICU (Paper II) and three for mothers of preterm infants (Paper III and IV) – based on a review of the literature and several meetings and discussions by a National Expert Panel. The National Expert Panel consisted of eight neonatal nurses, each with 10-20 years of experience in the breastfeeding of preterm

infants, four of whom were International Board Certified Lactation Consultants (IBCLCs).

The questionnaire for the head nurses in study B had 59 questions covering categories of patients, physical conditions of families, clinical guidelines for staff and informational materials for parents, practices concerning breastfeeding, breast milk expression, test weighing and skin-to-skin contact (see Appendix C).

Questionnaire 1 contained 38 questions, including demographic questions about the mother and infant and questions about breastfeeding plans, experiences and self-efficacy, breast milk expression and skin-to-skin contact. The questionnaire was to be answered by the mothers approximately seven days after the infant's birth (see Table 4). The questions about ethnic origin were formulated as "In which country were you born?" and "What language do you speak at home?" (see Appendix D).

Questionnaire 2 were to be answered by mothers at the infant's discharge and contained 56 questions about breastfeeding initiation and progression, feeding method at discharge, breast milk expression, test weighing, the infant's condition, the mother's perceived support and any breastfeeding problems. There were also questions about reasons and timing for the use of pacifiers, bottle feeding and nipple shield (see Appendix E).

A third questionnaire, which contained 15 questions about breastfeeding duration (exclusive and any), reasons for ceasing breastfeeding, duration of breast milk expression and nipple shield use, and breastfeeding problems, was used for telephone interviews with breastfeeding mothers at 1, 4, 6 and 12 months corrected age or until breastfeeding ceased – whichever occurred first (see Appendix F). The third questionnaire was designed to be read out loud as a structured telephone interview; or in the absence of telephone contact, it could be sent to the mother in a stamped, addressed envelope. In total, the questionnaires included 38 interval scale variables, 124 categorical variables and five open questions.

Table 4. Overview of questionnaires in Study C and when they were issued

Q1	Q2	Q3	Q3	Q3	Q3
After delivery	At infant discharge	1 month corr. age	4 months corr. age	6 months corr. age	12 months corr. age

Corr. = corrected, Q = questionnaire

Two senior academic experts reviewed the questionnaires. The questionnaire for the head nurses were pilot tested by two neonatal nurses, while the questionnaires for mothers were tested by 21 mothers for comprehension and relevance. Mothers were chosen from various wards, representing infants with different gestational age and mothers with different educational backgrounds. The process led to minor changes in the questionnaires (Paper III and IV). In the questionnaire for head nurses, five questions about accommodations for parents were changed to one open question and three simplified questions. In the questionnaires for mothers, for example, the question about breastfeeding experience was changed from "Did anyone in your family breastfeed? Yes/no." to "What experience do you have of breastfeeding in your family? Good/bad/none", or "Does your partner support your breastfeeding choice?" adding an alternative of, "I am alone with my baby".

Monitor

Besides ordinary monitoring of infant physical parameters, one additional instrument was used in Study A: skin temperature was measured continuously with a Philips skin temperature probe attached to the infant's lower back with Mepilex® border lite and covered with a Neo Guard® thermal reflector. Temperature values were saved every minute in the monitor (Philips CareView), printed and entered in Excel 2000, and mean values for each infant's pre-test, test and post-test period were calculated.

Outcomes and variables

Main outcomes were mean skin-temperature (Paper I), the distribution of breastfeeding support measures at Danish NICUs (Paper II), exclusive breastfeeding at discharge and adequate duration (Paper III), and mean PMA in the four various GA groups at selected breastfeeding milestones (Paper IV).

The length of adequate duration of exclusive breastfeeding was determined according to the Danish Health and Medicines Authority's recommendation for exclusive breastfeeding in preterm infants, which is exclusive breastfeeding for four months plus half of the period of time the infant was born before the estimated date of delivery[175] (Paper III).

The four selected milestones were:
1. Breastfeeding initiation, defined as the mother's description of when the baby was first placed at her breast for licking, tasting and possible latching, but not necessarily sucking and sinking

2. First complete breastfeeding, defined as the mother's description of when the baby first completed a breastfeeding session (the prescribed volume, or if it was deemed that the infant did not need supplementation feeding)

3. Establishment of exclusive breastfeeding defined as the mother's description of when the baby took all at and from the breast

4. Discharge from NICU to home

Besides main outcome, the variables in Study A were heart rate, respiration rate, and oxygen saturation before, during and after skin-to-skin contact, together with the number of stimulation-required apnoeas. Variables in Study B were various breastfeeding support measurements (Paper II, Table 3).

In the logistic regression analyses, variables concerning the infant and the mother that were known at birth and that were expected to be associated with breastfeeding, as well as variables reflecting the clinical practice used to establish breastfeeding, were entered.

The variables were:
- Gestational age groups broken down into four subgroups: extremely, very, moderate, and late preterm infants
- Multiple births
- Small for gestational age (see Definitions)
- The educational level of the mother broken down into three groups: high (more than 16 years), intermediate (14-16 years), and low (fewer than 14 years)
- Experience of breastfeeding, broken down into five groups: first-time mothers, mothers who had not breastfed their previous infant(s), previous exclusive breastfeeding of an infant for less than one month, previous exclusive breastfeeding of an infant for 1-4 months, and previous exclusive breastfeeding of an infant for more than four months
- Maternal smoking
- Mode of delivery (Caesarean section)
- Initiation of breast milk expression after delivery, broken down into five groups: before six hours, 6-12 hours, 12-24 hours, 24-48 hours, and later than 48 hours
- First skin-to-skin contact before six hours after birth
- Admitting mother and infant together to the NICU
- Nipple shield use during hospitalisation
- Test weighing the infant at most breastfeeding sessions during transition from tube feeding to breastfeeding

- Pacifier use during hospitalisation, broken down into three groups: no use of a pacifier, minimizing the use of a pacifier during breastfeeding transition, and unrestricted use of a pacifier

In the general linear regression, all explanatory variables with a p-value of less than 0.2 in univariate analyses were entered in the stepwise backwards model:

- Gestational age groups broken down into four groups: extremely, very, moderate, and late preterm infants

- Multiple births

- Small for gestational age

- First-time mothers

- Mode of delivery (Caesarean section)

- Admitting mother and infant together to the NICU immediately after delivery

- Pacifier use during hospitalisation, broken down into three groups: no use of a pacifier, minimising the use of a pacifier during breastfeeding transition, and unrestricted use of a pacifier

One or more of the following practices could be regarded as minimizing the use of a pacifier during the transition from tube feeding to breastfeeding: predominantly using the pacifier during tube feedings, painful or stressful events, predominantly using the pacifier in the mother's absence, or removing the pacifier completely.

Data analyses

Descriptive statistics

Excel 2003 and SPSS^{TM} version 19.0, 20.0, and 21.0 were used for statistical analyses. Descriptive statistics were used in all of the studies for the study populations and descriptive variables; the normally distributed results were reported with mean and standard deviation (SD), and the remaining results were reported with median and (interquartile) range.[176] Two questions in study B were open; in the first question, respondents were asked to describe typical maternal accommodation during the infant's hospitalisation; in the second question, respondents were asked to describe limitations on the use of donor milk. Remarks of similar content were grouped together. The open questions in Study C have not been analysed yet.

Analytic statistics

Repeated measures analysis of variance was used to test for differences in normally distributed scale data among groups (skin temperature and physiological variables in Paper I, and PMA at breastfeeding milestones in Paper IV). Pearson's Chi-Square test was used to determine statistically significant differences for nominal data (Paper III, IV). Student's t-test was used for analysing the effect on temperature, and mother/not mother was used as a 'between subject factor'. The number of apnoeas in each infant (varying between 0 and 2) before, during and after skin-to-skin contact was compared with the Kruskall-Wallis' test (Paper I). P-values less than 0.05 were considered as statistically significant in all of the studies.[176]

Failure of exclusive breastfeeding at discharge was analysed by means of logistic regression models; first the explanatory variables were analysed in univariate models, and second the explanatory variables with a p-value of less than 0.1 were analysed simultaneously in a multiple model. The variables from the multivariate model that analysed failure of exclusive breastfeeding at discharge were also used for analysing associations with inadequate duration of exclusive breastfeeding to see whether any associations persisted (Paper III).

PMA at establishment of exclusive breastfeeding was analysed in a general linear model. First, maternal and infant characteristics and clinical practices were analysed in univariate models, and second the explanatory variables with a p-value of less than 0.2 were entered in a stepwise backward model and removed stepwise until all remaining variables were significant at the <0.05 p-level (Paper IV). A scatter plot was performed, and a curve was fitted for correlation between GA and PMA at establishment of exclusive breastfeeding. Breastfeeding duration for infants lost to follow-up was adjusted to the time at the most recently answered questionnaire and the analyses performed with all infants (Paper IV).

The R Square-value, which corresponds to the multiple correlation coefficient R, was used as a measure of how well the model fit the data in the general linear model. In logistic regression a corresponding measure is Nagelkerke's R Square, which should be treated with caution, as it is a less accurate measure.[177]

The regression analyses were performed with one infant per mother, to ensure that mothers of multiples were not counted twice;[176] the first-born infants of multiples were included in the analyses (Paper III, IV).

Ethical considerations

All of the studies were conducted in accordance with the Declaration of Helsinki[178] – ethical principles for medical research involving human subjects – and approved by The Danish Data Protection Agency. The Biomedical Research Ethics Committee Capital Region approved Study A (no. H-A-2007-0110). According to Danish law, surveys do not need to be approved by the Biomedical Research Ethics Committee.

Benefits and burdens for the research subject

The basic principle of human research is to benefit patients without harming them. Medical research involving humans may only be conducted if the importance of the objective outweighs the risk and burden to research subjects.[178] Extremely preterm infants are particularly vulnerable patients, and research is justified only if it is responsive to the health needs or priorities of these infants and cannot be carried out in a non-vulnerable group.[178] Extremely preterm infants are even more immature and fragile than other preterm infants, and research on physiological stability during skin-to-skin contact is not always transferable from preterm infants older than 27 gestational weeks to younger ones, which is why Study A had to be carried out with the participation of extremely preterm infants. Because extremely preterm infants need the gentlest care, there is reason to investigate how to optimise conditions for this fragile population.

Furthermore vulnerable groups such as extremely preterm infants should receive thoroughly considered protection and should stand to benefit from the knowledge generated by the research.[178] Therefore, inclusion criteria in Study A were first of all that the infant was deemed to be stable for transfer between incubator and parent and that skin-to-skin contact was planned regardless of the study. The infant's skin temperature, heart rate, respiration and oxygen saturation were continuously monitored throughout the study, also in order to intervene immediately if the temperature dropped below 36.5°C or other adverse events occurred. We believed that each extremely preterm infant in the project would be treated better, because nonparticipating infants did not have their skin-temperature measured continuously when they were skin-to-skin. The burden of having a temperature probe attached to the skin was judged to be minimal. If the study were to find that extremely preterm infants tolerated skin-to-skin contact, the results could help other extremely preterm infants and their parents in early establishment of contact, leading to early bonding.

Informed written consent

Participation in medical research must be voluntary, and the research subject must be adequately informed of the aims, methods, any possible conflicts of interest, the anticipated benefits and potential risks of the study and the discomfort it may entail. Furthermore they have to be able to make a reasoned judgement and be emotionally stable before written consent is obtained.[178, 179] When giving consent on behalf of another person (surrogate decision-making) the surrogate has to be free of conflicts of interest,[179] and parents of a newborn may be presumed to seek the infant's best interests. As mothers experience the first days after premature delivery as traumatic and stressful,[103] the information for parents in Study A was delayed until the infant was clinically stable and skin-to-skin contact would be possible – or had already occurred.

Parents were informed that participation was voluntary, that they could drop out of the studies at any time without giving any reasons, and that it would not influence the care of their baby. Just before the skin-to-skin intervention, parents were again actively given the opportunity to drop out. In Study C, the mothers were to be informed about the research around days 5 to 7, and the information was to be delayed even longer if the infant's condition was severe.

Informed written consent was obtained from both parents as the infant's legal guardians in Study A, from the head nurses of the participating NICUs in Study B, and from the mothers of the preterm infants in Study C.

Justice

Justice refers to recruiting participants without discrimination.[179] No one in Study A and C was excluded in advance because they did not speak Danish. This was not relevant in Study B. The NICUs were encouraged to enrol non-Danish speaking mothers on an equal basis as Danish speaking mothers. Interpreters could be used by the NICUs to inform mothers and fill out the questionnaires with the mothers. As expenses for interpreters were incurred by the NICUs, each NICU used their own guidelines for interpreter assistance. The infant's father could also assist the mother with interpreting.

Confidentiallity

According to the Helsinki Declaration, it is the duty of healthcare professionals who are involved in medical research to protect the personal information of research subjects.[178] For the surveys, mothers/parents and head nurse(s) were promised confidential handling of the data. The results were reported at the group level so that no single person or NICU could be identified. The questionnaires and coded forms were kept separately, safe, and secure in a locked room. Questions that could be perceived as intruding mothers' personal integrity –questions about ethnic origin, smoking habits, etc. – were formulated as neutrally as possible.

Results

Extremely preterm infants tolerate skin-to-skin contact

We found that clinically stable, extremely preterm infants tolerated skin-to-skin contact with their parents (Paper I). Sixteen infants were skin-to-skin with the mother, five with the father and one with a teenage sister. Skin-to-skin contact lasted between 51 minutes and 6½ hours (mean of 98 minutes) and infant mean skin temperature during skin-to-skin contact was 37.0° C (± 0.33). There were no significant differences in mean skin temperature, heart rate, respiration rate, or oxygen saturation before, during, and after skin-to-skin contact. While staying within normal range, mean skin temperature increased 0.1° C during skin-to-skin contact with the mother and decreased 0.3° C during skin-to-skin contact with the father (p =0.01 without post-hoc correction). Regarding change of temperature, no other trends or significant differences were found in gestational age, postnatal age, weight, weight loss, incubator temperature, incubator humidity, oxygen requirements or instability. The group mean skin temperature calculated per minute decreased by an average of 0.1° C, when infants were transferred from the incubator to their parents and decreased by an average of 0.3°C when they were transferred from their parents back to the incubator. After the return transfer, the period of decrease was longer and infants took longer to regain their "pre-temperature".

Skin-to-skin contact

Skin-to-skin contact between preterm infants and parents was encouraged at all Danish NICUs. Infant instability was a common barrier to skin-to-skin contact at the NICUs (Paper II), but low gestational age was not an absolute barrier, although fewer extremely and very preterm infants initiated skin-to-skin contact within 24 hours of life (Paper IV, Table 2). Most NICUs (95%) aimed to initiate skin-to-skin contact within the infant's first 24 hours of life if the infant was clinically stable (Paper II), and 81% of infants did so (Paper IV). Additionally, 16% of infants initiated skin-to-skin contact later on during the first week of life.

The duration of skin-to-skin contact on a given day (median: day 6 of life) was 2-4 hours for 26% of the infants, with late preterm infants having less skin-to-skin contact than other preterm infants (see Table 5). Some mothers made a note, that the duration of skin-to-skin contact that day had been shortened because of phototherapy. Univariate analyses showed an association between early initiation of skin-to-skin contact and exclusive breastfeeding at discharge (Paper III), but the association did not persist in the adjusted analysis. Continuing skin-to-skin contact after incubator care was associated with 1.1-day (95% CI 0.0-2.1, p =0.046) earlier establishment of exclusive breastfeeding.

Table 5. Duration of skin-to-skin contact on a given day

Infant median postnatal age: 6 days (IQR 5 - 10). N 1,644

Duration	Total (%)	Gestational age groups (%)			
		24-27	28-31	32-34	35-36
No skin-to-skin contact	15	12	4	14	22
< 1 hour	16	9	3	14	25
1-2 hours	19	30	17	19	20
2-4 hours	26	26	38	26	18
4-6 hours	15	15	24	15	9
6-8 hours	7	8	12	7	4
8-12 hours	3	0	2	3	3
> 12 hours	1	0	0	1	1

IQR = Interquartile range

Breastfeeding support at Danish NICUs

The survey of breastfeeding support at Danish NICUs showed that there were differences between NICUs, but in general they described support for breastfeeding as a high priority. This was reflected in the reported practice of aiming for early skin-to-skin contact between preterm infants and their parents, few limitations on skin-to-skin contact, support for parental presence at the NICU, the practice of breast milk expression and supplementation via feeding tubes, and avoidance of the use of infant feeding bottles as a common practice (Paper II). Creating an unweighted breastfeeding support score from 0 to 36 reflecting the variables in Paper II (a higher score meant more breastfeeding support measurements) resulted in Danish NICUs having a mean breastfeeding support

score of 24.2 (SD 4.6). As it is shown in Figure 4, the score failed to be associated with breastfeeding rates at discharge (Pearson Correlation 0.23, p =0.34), and the score was not developed further.
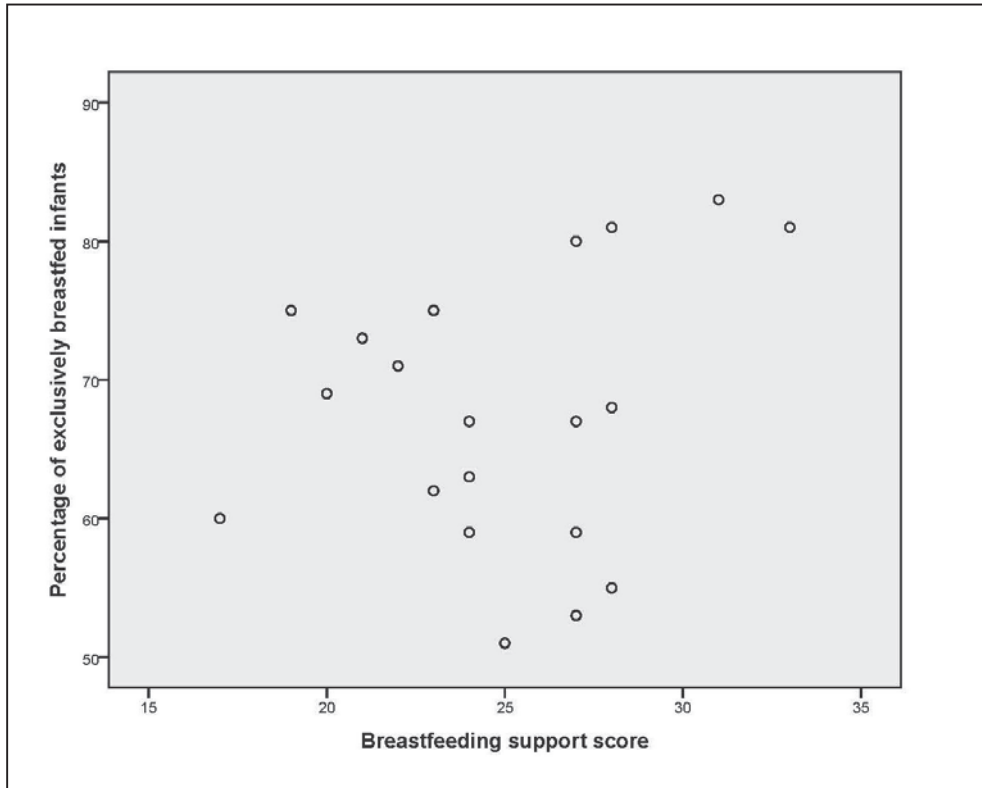
Figure 4. For each ward, the Breastfeeding Support score is plotted against the percentage of exclusively breastfed infants at discharge.

Breastfeeding

Characteristics of participating infants and mothers in study C are shown in Table 6.

Table 6. Infant and maternal characteristics Study C

	N	
Infant		
Gestational age in weeks + days, median (range)	1,488	34+1 (24+0 - 36+6)
Birth weight in grams, mean (SD)	1,471	2,067 (587)
Infants from multiple birth, %	1,488	36%
Small for gestational age, %	1,474	18%
Gender, boys, %	1,488	51%
Initiated breastfeeding, %	1,484	99%
Mother		
Age in years, mean (SD)	1,216	31 (5)
Lives together with infant's father, %	1,216	96%
Education, high (>16 years), %	1,204	20%
Education, intermediate (14 - 16 years), %		47%
Education, low or none (<14 years), %		34%
Smoking, %	1,207	10%
First-time mother, %	1,204	65%
Speaks a non-Scandinavian language at home, %	1,214	7%
Mode of delivery, caesarean section, %	1,219	50%
Mother admitted to the NICU immediately after delivery, %	1,207	29%
Planned to breastfeed, %	1,210	98%
Breastfed other infants exclusively >4 months, %	1,168	17%

Of the 1,488 preterm infants in Study C, 99% initiated breastfeeding, 68% were exclusively breastfed at discharge and 31% were exclusively breastfed for an adequate duration. Participating wards differed in exclusive breastfeeding rates at discharge from 51%[*] to 83%. Nine percent of the infants received expressed breast milk in addition to breastfeeding at discharge, which meant that 77% of them were

---

[*]This figure was mistakenly reported as 53% in Paper III

exclusively breast milk fed (see Table 7). Comparing exclusive breastfed infants with the 9% of infants receiving expressed breast milk in addition to breastfeeding, significantly more of the infants who were exclusively breastfed at discharge were still breastfeeding (to any extent) at six-month corrected age (45 and 23% respectively, p <0.0001).

Table7. Feeding method at discharge. N=1488

	Breastfed (%)	Breast milk fed (%)
Exclusively	68	77
Partially	17	15
Not at all	15	8

Exclusively breastfed infants are included in breast milk fed infants.

Factors associated with breastfeeding

Breastfeeding of preterm infants was associated with multiple factors in infants, mothers and clinical practices at the NICUs. The Nagelkerke's R Square in the regression analyses in Paper III was 0.19 and 0.18 and could cautiously be interpreted such that the models could explain 19% and 18% respectively of the differences in breastfeeding outcome. In the linear regression, the adjusted R Square was 0.29, interpreted such that the model could explain 29% of the difference in PMA at establishment of exclusive breastfeeding (Paper IV).

Factors in preterm infants

Gestational age was highly associated with exclusive breastfeeding. Extremely preterm infants initiated breastfeeding at relatively low mean PMA, but they were delayed in mean PMA at first complete breastfeeding, establishment of exclusive breastfeeding, and discharge compared to other GA-groups (Paper IV, Figure 2). Being extremely preterm at birth was associated with an increased risk of not being exclusively breastfed at discharge (odds ratio (OR) 2.8 (95% CI 1.3-6.4)). On the other hand significantly fewer mothers of extremely preterm infants had given up breastfeeding within one month after delivery, and more extremely preterm infants were exclusively breastfed at six-month chronological age (see

Definitions). When correcting age for preterm birth, the opposite was found: significantly fewer of extremely preterm infants were exclusively breastfed for one-month and four-month corrected age (Paper IV, Table 4). Other infant factors negatively associated with exclusive breastfeeding were being multiples, small for gestational age, and male gender (Paper III, Tables 3 and 4).

PMA at the establishment of exclusive breastfeeding was not associated with exclusive breastfeeding at discharge. The four GA groups had significantly different PMA at the four breastfeeding milestones (Paper IV, Figure 2). Median postnatal age was inversely related to GA as the extremely, very, moderate and late preterm infants were 39, eight, two and zero postnatal days respectively at breastfeeding initiation (p <0.0001) (Paper IV, Table 2). Very preterm infants reached the milestone "first complete breastfeed" at the significantly lowest mean PMA (35.5 weeks), whereas moderate preterm infants had the significantly lowest mean PMA (36.3 weeks) at the establishment of breastfeeding (Paper IV, Table 2).

Factors in mothers

A maternal factor strongly associated with exclusive breastfeeding was smoking. Smoking mothers had more than twice the risk (OR 2.2 (95% CI 1.4-3.7)) for not breastfeeding exclusively at infant discharge, and more than three times the risk (OR 3.4 (95% CI 1.8-6.5)) for inadequate breastfeeding duration (Paper III, Table 3 and 4). First-time mothers established breastfeeding 1.4 days (95% CI 0.4-2.4) later than other mothers (Paper IV) and had 2.7 times (95% CI 1.8-4.0) the risk of inadequate breastfeeding duration compared to mothers with previous experience of more than four months of exclusive breastfeeding. Mothers with breastfeeding experience of less than four months had markedly higher (3.5-11 times) risk of inadequate breastfeeding duration, and mothers with lower education (<14 years) also had higher risk (OR 2.6 (CI 1.7-3.9) (Paper III). There were no significant differences in exclusive breastfeeding at discharge and adequate duration between mothers speaking a Scandinavian language at home and mothers speaking a language other than Scandinavian at home, but the latter established breastfeeding earlier (2.8 days (95% CI 0.6-5.0)).

Factors in clinical practice

Rooming-in
Part of breastfeeding support included supportive family measures. At all NICUs, it was possible for some parents to stay overnight; two wards had a one-hour daily restriction on parental presence. Five NICUs provided maternity care for mothers, who were admitted to the NICU together with their infants immediately after

delivery (Paper II). This resulted in 29% of the mothers being admitted immediately after delivery and was associated with 1.5 (95% CI 0.3-2.6) days earlier establishment of exclusive breastfeeding (Paper IV). Rooming-in of the mother and the infant for a few days before discharge in order to establish breastfeeding both day and night was common at all NICUs. An additional eight wards offered mother-infant rooming-in after maternity care. Fathers could room-in to a lesser extent (Paper II).

Breast milk expression

Breast milk expression was an important issue at Danish NICUs, 89% of the head nurses stating that mothers were advised to initiate breast milk expression within six hours after delivery (Paper II), but only 22% of mothers doing so (Paper III, Table 3). Significantly more mothers who initiated breast milk expression before 12 hours after delivery expressed more than 400 millilitres of breast milk at median day six after delivery than mothers who initiated breast milk expression later (51% vs. 36%, p <0.0001).

Delayed initiation of breast milk expression showed a persistent dose-response effect: the later the initiation, the higher the OR for failure of exclusive breastfeeding at discharge and adequate duration (Paper III) and for later establishment of exclusive breastfeeding. The adjusted analyses showed variations in time periods later than 12 hours after delivery being significant for the three outcomes (Paper III, Figures 2 and 3; Paper IV, Figure 4).

The majority of head nurses (79%) responded that mothers were advised to express breast milk 6-8 times a day, and 64% of mothers did so on a designated day (median: day 6 after delivery).

Use of tube feeding, bottles and pacifiers

During transition from exclusive tube feeding to exclusive breastfeeding, the most common method for supplementation at all NICUs was tube feeding. The use of bottle feeding was avoided for infants to be exclusively breastfed at all but two wards (Paper II). NICUs' self-reported restriction on use of bottle-feeding in Study B was supported by the responses of mothers in Study C: of infants who had the first complete oral feeding solely at the breast, bottle-feeding was subsequently used for less than 2% (Paper IV).

Pacifiers for preterm infants were used at all NICUs if the parents approved, but 10 wards encouraged minimising the use of pacifiers during the breastfeeding transition (Paper II). Of the infants, 12% did not use a pacifier; 30% had the use minimised during the breastfeeding transition, which was positively associated with exclusive breastfeeding at discharge (OR 0.4 (95% CI 0.3-0.6)) (Paper III), and with 2.1 (95% CI 0.8-3.3) days earlier establishment of exclusive breastfeeding (Paper IV).

Use of nipple shield

Nipple shield was used by 58% of infants altogether, but use differed significantly between infants discharged at the various participating wards (35-67%, p <0.0001). Nipple shield use was negatively associated with exclusive breastfeeding at discharge (OR 2.3 (95% CI 1.6-3.2)) and adequate duration (OR 1.4 (95% CI 1.1-1.9)) (Paper III), but there was no association to PMA at the establishment of exclusive breastfeeding (Paper IV).

Use of Test weighing

The use of test weighing for most breastfeeds was routine in 10 (53%) of the Danish NICUs (Paper II). Of the infants 30% were test weighed for most breastfeeds, but use differed between infants discharged from the various wards (0-87%, p <0.0001). Test weighing infants for most breastfeeds was associated with a lower risk (OR 0.6 (95% CI 0.4-0.8)) of not being exclusively breastfed at discharge (Paper III), but the benefit disappeared within a month after discharge, and was not associated with adequate breastfeeding duration – nor with how early exclusive breastfeeding was established (Paper IV).
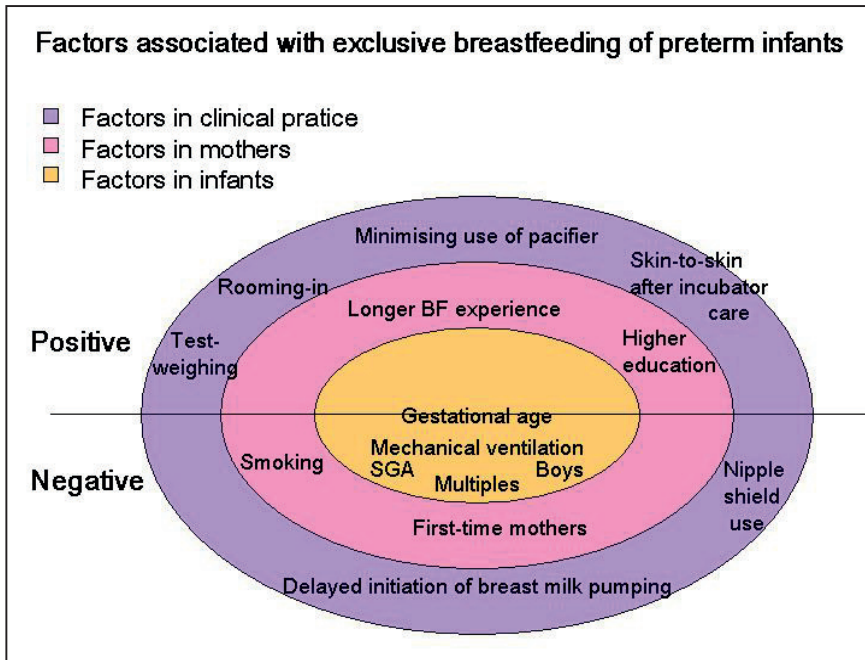
Figure 5. A model of factors associated with exclusive breastfeeding of preterm infants.

Discussion

Methodological considerations

The strengths of the studies are that all Danish NICUs participated in Study B, and all NICUs and wards that routinely care for preterm infants during breastfeeding establishment enrolled mother-infant pairs in Study C. The nationwide design resulted in a large number of participating preterm infants and mothers at NICUs with differing clinical practice.

Validity

Validity refers to the ability of a study to answer the research question.[180] Validity and precision are both components of accuracy.[181] Internal validity or reliability refers to whether the results pertain to the study subject, and external validity or generalizability if the results pertain to people outside the study population.[181] Valid statistical association refers to the role of chance, bias and confounding being minimal.[182]

Internal validity related to data collection

Validity of instruments
Validity of instruments refers to the degree to which an instrument measures what it is supposed to be measuring. Face validity refers to whether the questionnaire looks as though it is measuring the topic being investigated. Content validity is concerned with how representative the questions in the questionnaire are for the topic being investigated.[183] The advantage of developing new questionnaires for study C, in the absence of questionnaires covering the aspects, was that we had all the items of interest covered. The disadvantage was that it was not tested on a large scale before use and ended up with many questions. The large number of questions could have contributed to the dropout rate after consent (Paper III, Figure 1). The questionnaires for mothers did not represent a scale or score, and face and content validity were assumed to be sufficient. In future, the number of

questions in the questionnaire could be reduced, and further clarification of some questions would contribute to reducing the amount of missing data, such as duration of exclusive breastfeeding (see below).

No previous questionnaires were found that investigated breastfeeding support at NICUs, and developing a questionnaire for breastfeeding support at NICUs was first of all explorative and descriptive (Study B). Although each item was found to be associated with breastfeeding in infants in other studies, only the item of availability of a lactation consultant at the NICU had been tested between NICUs at the time of the development of the questionnaire. Studies of the Baby-Friendly Hospital Initiative have analysed differences in breastfeeding rates, but that was between maternity wards through analysing a whole concept of breastfeeding support. The expansion of the Baby-Friendly Hospital Initiative to neonatal intensive care was not available at the time of the development of the questionnaire for Study B. The modest attempt to measure NICU breastfeeding support from an unweighted score failed, and development of a valid score is more complex and beyond the scope of this thesis. NICUs could differ in other respects associated with breastfeeding from those covered in the questionnaire. Also, responses by the NICUs about what they usually do or what they encourage mothers to do are not the same as measuring what is actually done. An example is that 89% of the NICUs responded that they would encourage mothers to initiate breast milk expression within six hours after delivery, but only 22% of the mothers did so.

Reliability of instruments

Reliability refers to the consistency of instruments – that the results are reproducible.[184] The skin-temperature probe was found by the manufacturer to have an accuracy of +/- 0.1°C.[185] In Study B and C, efforts were made to construct precise questions with mutually exclusive and exhaustive response alternatives in order to get reliable data and create a "permissive atmosphere" in the questionnaires to encourage frankness.[183] The questionnaires were not meant to be repeated by the head nurses or mothers, and reliability analyses were not performed. The weak definition of "first complete oral feeding" could generate unreliable results. To ensure more accurate data, a narrower definition would be needed; however, as not all infants were test weighed, a definition that included a precise quantity of milk might be answered by fewer participants. The weak definition of "first complete feeding" did not seem to influence mothers, given that the variation in PMA at this milestone was not larger than for the other milestones, indicating that Danish mothers of preterm infants tend to interpret "first complete breastfeeding" in a similar way. In Questionnaire 3, mothers were asked if they would describe their breastfeeding after discharge as mainly functioning or mainly problematic. Some mothers would have liked to have a choice in between.

Changing the response alternatives to a Likert scale may have generated more reproducible results.

Risk of information bias

Systematic errors are commonly referred to as biases; the opposite of bias is validity. The opposite of random error is precision and reliability. Information bias refers to systematic errors in the data obtained.[181]

All self-administered questionnaires run the risk of response biases, such as the tendency of some respondents to present themselves in a more favourable light. The use of fixed response alternatives enhances the chance of an accurate description,[183] and was therefore used for most questions in Studies B and C.

The survey in Paper II had only four missing values, indicating that the questionnaire was easy to understand and use by head nurses. The questionnaires answered by the mothers had more missing values (Paper III, Table 3, and Paper IV, Table 1 and 2), which could be because the questionnaires were long and it was hard for some mothers to remember the infant's weight or age, etc., at breastfeeding milestones.

Recall bias is systematic bias due to a long time span between the event of interest and the collection of data.[176] To reduce recall bias of breastfeeding duration in Study C, repeated telephone interviews were performed.

In intervention studies, validity also refers to the fact that the subjects are treated equally except for the intervention.[186] Study A was a pre-test – test – post-test study in which the infants served as their own control group, and none of the infants were skin-to-skin during the pre-test or post-test period, whereas all were skin-to-skin during the test-period. The guidelines for transfer and position should ensure standardised transfer.

Validity of analyses

Chance

Chance is measured as the probability of finding a similar or more extreme result when the null hypothesis of comparing groups is true, and the level of significance is normally set to less than 5% (p <0.05). When the p-value is >0.05 there is not enough evidence to reject the null hypothesis. Results with a p-value less than 0.05 are not necessary true, but worth a second look. Strong statistical significance is evident when the p-value is less than 0.001, and the p-value is also related to the sample size.[176] In Paper I, the difference in infant mean skin temperature during skin-to-skin contact with the mother and father was significant (p=0.011) without post-hoc correction, and tested together with 12 other variables, which increased the probability of an overestimate of the effect. A statistically significant result is not automatically clinically significant. Clinical significance is the practical

importance of an effect.[176] The clinical significance of the difference in skin temperature between skin-to-skin contact with the father and mother is debatable, as the difference in mean skin temperature was within the normal temperature range.

Regression analyses that include many variables in small sample sizes run the risk of finding a model that appears to fit well but is unreliable.[176] In Papers III and IV, the large sample size made it possible to test more variables in the regression analyses. Large sample sizes increase the precision of an estimate[181] but could make it easier to yield statistically significant results with small effects of no practical importance.[176]

Confounding

Confounding may be considered as a confusion of effects[181] and involves the possibility of the observed association being due to other differences between the study groups than the exposure under study.[182] There are three criteria for a confounding factor: it must be an extraneous risk factor for the outcome, associated with the exposure under study, and not be affected by the exposure, i.e. not be an intermediate factor.[181] If we look at the initiation time of breast milk expression in Paper III, breastfeeding experience could be regarded as a confounder, as it is a risk for the outcome (less breastfeeding experience is associated with not breastfeeding exclusively at discharge). Breastfeeding experience is also associated with exposure, as mothers who have long breastfeeding experience probably initiate breast milk expression earlier, either because they know stimulation of the breast is important or simply because lactogenesis II occurs earlier. Also, in our study, mothers with longer previous breastfeeding experience initiated breast milk expression earlier (p =0.044).

Third, breastfeeding experience precedes the initiation of breast milk expression and cannot be an intermediate step between initiation of breast milk expression and exclusive breastfeeding. An example of an intermediate factor is maternal confidence in breastfeeding. As mothers answered the questionnaire at median day 7 after delivery, early or late breast milk initiation could have resulted in high or low milk production (which was correlated), affecting their confidence in breastfeeding and thereby affecting exclusive breastfeeding at discharge. For this reason, maternal factors that could have changed during the first few days as a result of clinical practice were not used in the regression analyses of Papers III and IV.

Uncontrolled confounding can lead to overestimates or underestimates of the true association between exposure and outcome.[182] In the logistic regression analyses of paper III, we controlled for confounders and other variables known to be associated with breastfeeding length.

External validity

Risk of selection bias

Selection bias refers to whether the association between exposure and outcome differs between study participants and subjects eligible for the study,[181] and needs to be taken into consideration when generalising the results. The selection of subjects is important to outcome; studies of highly selected subjects may generate misleading results,[176] – for example, approaching only mothers who want to breastfeed could lead to artificially high breastfeeding rates.

In study A, some infants were randomly not approached and some infants were deselected as they were too unstable to participate. Nevertheless, deselected infants were comparable in GA and birth weight to the infants in the study group, and the results were not biased by selecting the largest infants. Selection bias was not a problem in Study B, as all Danish NICUs participated.

Of the 21 participating wards in study C, 18 adhered to the project protocol in the enrolment of mother-infant pairs (see Paper III for details). The proportion of mothers of eligible infants not approached in study C was 13% and varied between wards from 0% to 66%. In total, 11% of the informed mothers declined to participate, which varied between wards from 0% to 63%. The wards approaching fewer infants could have selected mothers systematically, who were keen to breastfeed and favourably disposed to breastfeeding surveys, but the percentage of mothers declining to participate was high (24%, 59% and 63%) in the three wards not adhering to the project protocol, indicating that the selection of mothers was not systematically biased by only approaching mothers who were favourably disposed to surveys.

It is well known that participants with poorer health outcomes are more reluctant to participate in surveys and more often drop out of cohorts.[187] Losses to follow-up in cohort studies weaken the analysis by reducing the number of subjects supplying information. The main problem is whether subjects are lost to follow-up for reasons related to the outcome or to risk categories.[176] Although it was the purpose in study C, only one NICU systematically recorded the feeding method at discharge for infants not participating or dropping out of the study. In this NICU, 98 infants were eligible for the study and 73 were participating at discharge. More of the eligible infants were not breastfed at discharge. The distribution of exclusively, partially (see Definitions) and not breastfed infants were 53%, 8% and 39% among the eligible infants and 59%, 10% and 32% among infants participating at discharge (p =0.04). We do not know if the same pattern was true for infants at the other NICUs, but our best guess is that more of the non-participating and lost infants were not breastfed.

A drop out analysis showed that significantly fewer of the eligible extremely preterm infants participated in study C (p <0.0001) and in the regressions analyses, but there was no difference in the proportion of declining mothers among

GA groups; thus, fewer mothers of extremely preterm infants were approached and more of them dropped out after consent. There were no differences in the participation of multiples and singletons. There is the possibility that more mothers who declined to participate had planned shorter breastfeeding duration, and therefore our breastfeeding rates could be artificially high. This selection bias may also be present in other breastfeeding surveys with which comparisons were made.[62, 64, 82] Further dropout analyses comparing mothers participating in Questionnaire 1 to those included in regression analyses showed that mothers who dropped out or gave incomplete answers had lower education (p =0.001), more were smokers (p =0.001), and more spoke a language other than Scandinavian at home (p <0.0001). No differences were found in multiples or small for gestational age infants, first-time mothers, maternal self-efficacy, admitting mothers to the NICU or initiation time of breast milk expression. There was a significant correlation between mothers with low education and smokers (R=0.197); however the correlation was not high enough to rule out one of the variables and allow it to be predicted by the other one.

The high dropout rate of extremely preterm infants from Study C could indicate that they have an even greater risk of not being exclusively breastfed than this study could show, and our breastfeeding rates could be artificially high because of the higher dropout rate. On the other hand, extremely preterm infants represent a very small proportion of the total number of infants. Study C had breastfeeding outcomes for 65% of all eligible infants, but only for 46% of extremely preterm infants. If the dropout rate of extremely preterm infants were equal to the total dropout rate and we assume that none of the "extra numbers" of extremely preterm infants who dropped out were exclusively breastfed, the total proportion of exclusively breastfed infants would decrease only by 1% (from 68% to 67%).

The differences between mother-infant pairs who did and did not participate in the regression analyses could have affected the results, as some of these variables explained exclusive breastfeeding. Therefore, it cannot be ruled out that maternal education was associated with exclusive breastfeeding at discharge even though no significant associations were found. The negative association between maternal smoking and exclusive breastfeeding could be even stronger than our results showed.

Limitations of generalisation

In Study A, only one infant was studied during the first skin-to-skin session, and we are not able to generalise the results to early skin-to-skin contact. Although the infants could participate in the study while they were on mechanical ventilation, only one infant did. The results can be generalised only to clinically stable extremely preterm infants.

Study B is a description of Danish NICUs and cannot be generalised to other countries. In Study C, generalisation of breastfeeding rates in extremely preterm infants should be performed with caution. The results of study C of late preterm infants cannot be generalised to all late preterm infants, as late preterm infants admitted to NICUs are a group with more health problems than late preterm infants cared for at maternity wards.

Breastfeeding rates in Papers III and IV could also be influenced by the structured telephone interviews conducted by NICU nurses experienced in breastfeeding, as they could serve as an intervention – even if this was not the purpose – in which mothers could get answers to their breastfeeding questions, as there were no limitations on a nurse's answers to a mother's questions. Or mothers may have breastfed longer just because they participated in a cohort study, also known as the Hawthorne effect.[183] Thus, breastfeeding rates in Papers III and IV could be overestimated compared to all eligible infants. This bias could also be present in other breastfeeding studies as described above. Mothers who did not want to breastfeed were not included in the cohort (1% of the mothers who had consented).

The breastfeeding rates in Study C could be underestimates, as mothers of 117 infants, who were exclusively breastfed at discharge but completely weaned at the first structured telephone interview at one month corrected age, did not report duration of exclusive breastfeeding; thus, the duration was adjusted to the date of discharge. This did not influence rates of exclusive breastfeeding at one month corrected age, but could contribute to a small underestimate of exclusive breastfeeding rates at one and four months chronological age.

Causality in epidemiologic studies

Causality is the relationship between cause and effect. Unlike randomised controlled trials, the presence of valid statistical associations between exposure and disease in epidemiologic studies does not imply causality. However, a cause-effect relationship can be assumed, depending on several criteria; the most cited list is of Hill's criteria.[188] The criteria are strength of association, consistency with other studies, specificity of factor and effect, temporality (the exposure of interest precedes the outcome by an appropriate period of time), biologic gradient (a dose-response relationship), plausibility (a biological explanation), coherence, experimental evidence and analogy.[188] All of the criteria have exceptions, and the process of causal inference is difficult and should be performed very carefully. Although initiation time of breast milk expression was significantly associated with exclusive breastfeeding at discharge and adequate duration, different time periods were significant for the two outcomes (Paper III, Tables 3 and 4). For both outcomes, a dose-response relationship was found: the later the initiation of breast

milk expression, the higher the OR for not breastfeeding exclusively at discharge (Paper III, Figures 2 and 3), and even if it was not significant for all the different time periods, the dose-response relationship strengthened the probability of a true association.

Even if cause and effect relationships cannot be established, a large study like Study C provides important evidence from the daily clinic that supports, or questions, the recommendations based on data from smaller studies.

General discussion of results

Skin-to-skin contact

The results in Paper I showed that it is possible for extremely preterm infants to have and tolerate skin-to-skin contact before PMA 28 weeks. It was not possible to completely prevent temperature loss during transfer, but it was minimised to means of 0.1° C and 0.3° C. Within the normal range, they may be better at retaining skin temperature when skin-to-skin with the mother compared to with the father, which should not prevent fathers from having skin-to-skin contact with their infant, but requires more awareness of the infant's temperature during skin-to-skin contact. However, the results need further investigation, as this difference was small and has not been found in other studies of extremely preterm infants.[46, 47] A biological explanation is reasonable, as breast and chest temperature is higher in breastfeeding mothers than in other women and in men. This is due to both changes during pregnancy (hormones and increased breast gland tissue) and the increased blood circulation in and around the breast in mothers who produce breast milk.[189] (Paper I).

The timing of initiation of skin-to-skin contact in Paper IV was comparable to the results in a Swedish study.[42] Possible explanations for late preterm infants having less skin-to-skin contact on median day 6 after birth compared to other GA groups could be that late preterm infants have short stays in incubators and not all wards encourage parents to continue skin-to-skin contact after incubator care (Paper II). Continued skin-to-skin contact on a daily basis after incubator care was associated with earlier establishment of exclusive breastfeeding (Paper IV). It has been assumed that skin-to-skin contact supports development in preterm infants, as accelerated neurophysiological development has been reported in preterm infants receiving daily skin-to-skin contact.[190] Skin-to-skin contact during breastfeeding establishment also means that the infant is close to the breasts, and the mother can observe early hunger cues. Continuing skin-to-skin contact after incubator care is not a precise measurement of the amount of skin-to-skin contact, but it could be an

indicator of increased duration. The total duration of skin-to-skin contact during the entire hospitalisation was not measured, but it has previously been shown to be associated with duration of breastfeeding in very preterm infants.[30]

Skin-to-skin contact has previously been associated with increased breastfeeding rates in preterm infants,[30, 93-96] but did not show significant association with breastfeeding rates in Paper III. It seems that even if mothers were not able to have early skin-to-skin contact with their preterm infants, this was not an essential barrier to the establishment of breastfeeding, maybe because most infants had skin-to-skin contact later during the NICU stay. The effect of skin-to-skin contact on breastfeeding could be stronger in settings with lower breastfeeding rates.[8] It should be mentioned that an effect of skin-to-skin contact is also seen in settings with high breastfeeding rates[30, 96]

Preterm breastfeeding rates

Exclusive breastfeeding from the breast at different time points was chosen as main outcomes in Paper III and IV. The rates of direct breastfeeding are equal to or lower than the rates of breast milk fed infants, which is why breastfeeding rates in this thesis could be lower than in breast milk fed infants. Comparisons in Paper III, IV and this thesis are, however, mainly made with studies reporting direct breastfeeding; otherwise, breast milk feeding is stated.

Study C was the first national survey to investigate the initiation rate of breastfeeding in preterm infants in the Scandinavian countries, and we found that preterm infants initiated breastfeeding to the same extent as full-term infants: 99% and 95-99%.[80, 82] The high initiation rates in Paper IV may be due to Danish NICUs' high priority of breastfeeding support (Paper II), the cultural norm of breastfeeding,[82, 83] and the fact that most mothers in the cohort had planned to breastfeed. The 68% rate of exclusively breastfed preterm infants at discharge is relatively high compared to 27-55% of preterm infants in U.S. and Scandinavian studies.[62-65]

Thirty-one per cent were breastfed exclusively for the recommended duration. The Danish Health and Medicines Authority's recommendation of exclusive breastfeeding in preterm infants for four months plus half of the period of time the infant was born before estimated date of delivery[175] is lower than WHO's recommendation of six months regardless of prematurity.[87] The reason for the Danish recommendation is a preterm infant's higher growth velocity, resulting in increased needs for energy, protein and minerals.[175] It is questionable whether this recommendation should also apply to preterm infants with GA >32 weeks, as it reduces the total period more for older preterm infants, and these infants may have less specialised needs. But as health visitors support and guide mothers in breastfeeding duration after discharge from the NICU, and as their guidance is

based on the Danish Health and Medicines Authority's recommendations, another limit for exclusive breastfeeding duration would be problematical. Exclusive breastfeeding in full-term infants beyond six months is not recommended.[191]

Our results support the importance of direct breastfeeding, as more infants who were exclusively breastfed at discharge were breastfed (to any extent) at six months corrected age compared to infants receiving expressed breast milk in addition to breastfeeding at discharge.

Breastfeeding support score

Mapping various aspects of breastfeeding support at NICUs at a national level has not been performed before to our knowledge and can serve as a comparison for further surveys, both nationally and internationally.

The breastfeeding support score failed to be associated with breastfeeding rates at discharge and was not further developed. Analyses showed differences in exclusive breastfeeding rates between NICUs (53-83%), but the breastfeeding support score could not detect these differences. Six items were answered affirmatively by 100% of the NICUs (Paper II, Table 3) eliminating the possibility of detecting any influence of these items. It cannot be ruled out that the breastfeeding support score could be associated with breastfeeding at discharge in countries with more varied breastfeeding support between NICUs.

Breastfeeding milestones in preterm infants

Paper IV showed that it is possible for preterm infants to initiate breastfeeding at a low age. Infants born before GA 32 weeks initiated breastfeeding at a mean PMA of approximately 32 weeks. Early initiation has previously been reported in Swedish preterm infants.[131, 132] However, breastfeeding progression was inversely related to GA (Paper IV). Extremely and very preterm infants' higher PMA at establishment of exclusive breastfeeding may be related to these infants suffering from more morbidity and having slower or altered brain maturation.[15, 54-56] The mean PMA at establishment of exclusive breastfeeding in Paper IV was 36.7 weeks overall, extremely preterm infants having the highest mean PMA. The results are supported by a large Australian study in which preterm infants established exclusive suckle feeding at mean PMA 36.4 weeks and extremely preterm infants were found to have higher mean PMA.[64] A Swedish study showed earlier establishment of exclusive breastfeeding (median PMA: 36.0 weeks);[131] however, it lacked participation of preterm infants with severe morbidity, extremely preterm infants and preterm infants with GA 36 weeks.

Paper IV reports how mean PMA and median postnatal age at various breastfeeding milestones differ according to GA group in a large national population of preterm infants. Breastfeeding competencies are thus not developed at a fixed PMA or a fixed postnatal age, but are influenced by multiple factors in the infant, mother and clinical practice.

Infant and maternal factors associated with breastfeeding

Most of the infant and maternal factors that Study C showed to be associated with breastfeeding are supported by other studies and give us an idea of whom to provide with extra breastfeeding support: infants with lowest GA,[71, 73] multiples,[69-71] mothers with low socio-economic status,[29, 65, 66, 68-70] with less breastfeeding experience,[73] and smoking mothers.[29] We do not know the reasons that mothers who spoke a non-Scandinavian language at home established breastfeeding earlier. We did not distinguish between immigrants and their descendants, and mothers could speak non-Scandinavian languages at home for reasons other than immigration, which is why this needs further investigation. Furthermore, these results should be interpreted with caution because of the higher dropout rates among these mothers.

Clinical practice

The most interesting results concern clinical practice. Even though only 18-29% of the differences in breastfeeding outcome were explicable by the regression analyses in Paper III and IV, changing practice might influence breastfeeding of preterm infants, and the nursing staff is interested in guiding mothers without harming breastfeeding; therefore, the following discussion will focus on clinical practice to facilitate breastfeeding.

Rooming-in

Admitting the mother together with the infant to the NICU immediately after delivery was associated with earlier establishment of exclusive breastfeeding, but no association was found with exclusive breastfeeding at discharge or breastfeeding duration. As all mothers in Danish NICUs are included in the practice of rooming-in to a greater or lesser degree (Paper II), and we did not ask mothers if they slept beside their infants in study C, this could be the reason that we found significant results only at breastfeeding establishment (Paper IV). The reason for earlier establishment of exclusive breastfeeding may be that the mother is able to observe and respond to the infant's early hunger cues, the opportunity for more breastfeeding sessions around the clock, and the fact that the mother and

infant are not stressed out by separation, as (early) separation is perceived to be stressful by mothers of preterm infants.[138, 139] A U.S. study of a Level-III NICU shifting from open ward to single-family rooms showed that breastfeeding at discharge improved from 50% to 70% and the proportion of days with breast milk feeding increased significantly (p =0.001).[152] A more recent Norwegian study of neonatal family care 24 hours per day showed that significantly more preterm infants in the intervention group were breastfed at three months (74%) than preterm infants in the control group (43%, p = 0.04);[33] thus, breastfeeding seems to improve in both low and high breastfeeding cultures. A Swedish study found that infants had significantly shorter hospital stays when parents were admitted to the NICU,[192] and a Danish study found that parents prefer rooming-in with the infant at the NICU to feel like a family.[141] In addition, the UN Convention on the Rights of the Child and "the Baby-Friendly Hospital Initiative for Neonatal Intensive Care" stresses the non-separation paradigm.[28, 149] In the light of the near-unanimous support for the UN Convention on the Rights of the Child, it is surprising that separation of the mother and infant is still common at NICUs in Denmark (Paper II) and the rest of Europe.[25] It seems as though the way care is organised in term of rooming-in improves many dimensions in preterm infants and their mothers. For these reasons, further efforts should be made to avoid separating the mother and preterm infant.

Breast milk expression

The timing of breast milk expression was associated with breastfeeding. The timing of initiation of breast milk expression showed a dose-response effect on two outcomes in Paper III, and a kind of dose-response effect on the outcome in Paper IV: the later the initiation the higher the OR of not being exclusively breastfed at discharge, and for inadequate breastfeeding duration (Paper III), and the later the establishment of exclusive breastfeeding (Paper IV). The consistency in associations with all three outcomes indicates the importance of initiation time of breast milk expression – or an undefined factor that correlates with both initiation of breast milk expression and exclusive breastfeeding.

These results are supported by other studies that have found that breast milk expression should be initiated at an early stage after delivery.[154-156] Early initiation could contribute to higher milk production later on[155, 156] and thereby protect exclusive breastfeeding. Even though our results could be biased by other factors such as maternal illness or perceived importance of breastfeeding, it appears that initiating breast milk expression even before six hours after delivery would be helpful for mothers who want to breastfeed their preterm infant. The currently most prevalent recommendation for initiation of breast milk expression at Danish NICUs was within six hours after delivery (Paper II), but only 22% of the mothers initiated breast milk expression within six hours after delivery (Paper III). It is not known whether the mothers were informed before six hours after delivery, and it

cannot be determined whether the delay was due to late information or maternal adaptation of information. Study C was the first to our knowledge to examine several different time intervals of initiation of breast milk expression; however, it did not shed clear light on how early breast milk expression should be initiated to support exclusive breastfeeding. But it appears that the earlier the better, and there is no adverse effect of initiating breast milk expression within six hours after delivery.

Minimising the use of a pacifier

The results of Study C showed that minimising the use of a pacifier during breastfeeding establishment was positively associated with exclusive breastfeeding at discharge and with earlier establishment of exclusive breastfeeding. The reasons could be that the infant is more eager to suck at the breast and shows more hunger cues when use is minimised. Pacifier use has been found to be negatively associated with breastfeeding in full-term infants[159, 160] and occasionally found to be negatively associated with breastfeeding in preterm infants,[162] but the most common findings are that pacifier use is not associated with breastfeeding in preterm infants.[158, 161] The lack of association could be due to differing definitions of breastfeeding; exclusive breastfeeding could be more affected by pacifier use than non-exclusive breastfeeding, and direct breastfeeding could be more affected than breast milk feeding. The general lack of association has led to a recommendation of pacifier use for preterm infants when breastfeeding is not possible and in the mother's absence,[28, 158] as pacifier use has a calming effect, reduces infant stress, and provides pain relief during painful procedures to preterm infants.[157, 158] To our knowledge, minimising the use of a pacifier during breastfeeding transition has not previously been studied in preterm infants but could be a useful intervention for facilitating breastfeeding.

Use of nipple shield

Nipple shield use was found to be negatively associated with exclusive breastfeeding at discharge and adequate duration (Paper III), but no association was found to how early exclusive breastfeeding was established (Paper IV). These results are not in line with previous findings,[164, 165] which could be due to previous studies having been small (15 and 34 infants), with no comparison group, or measuring any breastfeeding instead of exclusive breastfeeding. Our results do not support the hypothesis that preterm infants need temporary facilitation of milk intake with use of a nipple shield until corrected term age, as exclusive breastfeeding was established at a mean of PMA 36.7 weeks, and not earlier by infants using nipple shields. Also the study by Meier did not define breastfeeding (direct breastfeeding or breast milk feeding). The impact of nipple shield use could be more negative on exclusive breastfeeding, as the use of nipple shields is suspected to compromise milk production due to less oxytocin stimulation;[168] the

infant could get used to the nipple shield, making it difficult to wean it from the nipple shield,[117] and long-term use could be perceived as troublesome by the mother. These mechanisms are not affected by exclusive breast milk feeding, as they do not particularly affect the mother's ability to express breast milk.

A nipple shield is often used to solve latching problems, and the latching problem could lead to failure of breastfeeding regardless of nipple shield use, but the huge variation in nipple shield use between NICUs (35-67% of discharged infants) indicates that a nipple shield was not always used for the same degree of latching problems. Thus, although our results could be biased by nipple shields used in infants with latching problems they suggest that the use of a nipple shield does not promote breastfeeding in preterm infants.

Use of test weighing

Test weighing the infant at most breastfeeds during transition was protective of exclusive breastfeeding at discharge but had no association with breastfeeding duration (Paper III) or PMA at establishment of exclusive breastfeeding (Paper IV). The protective effect was eliminated within one month of discharge, indicating that mothers using test weighing at the NICU ceased exclusive breastfeeding earlier after discharge when they could not measure the amount of milk their infant breastfed. The protective effect was also found in a Swedish study using a quasi-experimental design.[32] Our results could not support the results of another Swedish study comparing two NICUs, which found earlier establishment of exclusive breastfeeding in the ward using test weighing.[172] Neither study C nor the two Swedish studies were designed to strongly establish a cause-effect relationship. A U.S. study supported our results, as it found that test weighing had no association with breastfeeding duration.[11] Is the protective effect of test weighing at breastfeeding establishment related to restoring feelings of security in mothers of preterm infants? Kavanaugh found that breastfeeding mothers of preterm infants were very concerned about the infant's getting enough milk and gaining weight;[169] perhaps the mechanism of test weighing eases the task of nourishing an infant with low birth weight. More research is needed to shed light on the use of test weighing.

Conclusion and clinical implications

We can conclude that clinically stable extremely preterm infants tolerate skin-to-skin contact with their parents. The intervention was not associated with adverse effects and should be regarded as safe.

Danish NICUs described the support of breastfeeding as a high priority, as reflected in aiming for early skin-to-skin contact, few limitations on skin-to-skin contact, support of parental presence at the NICU, the practice of breast milk expression and supplementation via feeding tubes, and avoiding the use of infant feeding bottles as a common practice. Maternal rooming-in for the infant's entire hospitalisation is still not common practice.

Danish preterm infants initiate breastfeeding to the same extent as full-term infants. Breastfeeding competences are not developed at a fixed PMA, but are influenced by multiple factors in infants, mothers and clinical practice; the same applies to exclusive breastfeeding.

Admitting a mother together with her infant immediately after delivery seems to contribute to earlier establishment of exclusive breastfeeding. Minimising the use of pacifiers during breastfeeding establishment is an easy and cheap intervention that might support exclusive breastfeeding of preterm infants and is not deemed to have any adverse effects. It appears that nipple shield use in preterm infants does not support breastfeeding; instead patience is needed on the part of both mothers and staff. The results indicate that delayed initiation of breast milk expression is a barrier to exclusive breastfeeding; even though it appears that the earlier the better, we are not able to clarify how early it should be initiated. Most importantly, the infant needs his or her mother's milk from the very beginning, which supports early initiation within six hours. Test weighing seems to be positively associated with exclusive breastfeeding at discharge, but more research is needed on how to support mothers when test weighing is discontinued at discharge.

More support and attention should be given to groups with a greater risk of breastfeeding failure, including extremely and very preterm infants and multiples, as well as mothers who smoke, have lower education or less breastfeeding experience.

Further research

Further research is needed in order to consolidate some of the results found in this thesis. Conducting a randomised controlled trial of nipple shield use in preterm infants could be helpful in solving the problem of contradictive results in available research. Likewise, a randomised controlled trial of minimising the use of a pacifier during breastfeeding transition could confirm or deny the unique results of this thesis. The difference in mean skin temperature in extremely preterm infants skin-to-skin with their mother and father needs further research.

Working with these studies has raised new questions. What is breastfeeding support at NICUs like in other countries? How do we adequately support mothers in sustaining the good effect of test weighing when it stops? What are a mother's reasons for not breastfeeding a preterm infant at NICU discharge in a culture of high breastfeeding? What factors are associated with continued exclusive breastfeeding one month after discharge? What are the reasons for, and duration of, nipple shield use in preterm infants, and how does it associate with breastfeeding? The answer to the last question could shed more light on a controversial tool in breastfeeding.

Furthermore, it would be interesting to follow up the cohort of preterm infants, exploring whether exclusive breastfeeding at discharge from NICU and adequate duration of exclusive breastfeeding are associated with less re-hospitalisation during the infant's first year of life.

Summary in Danish

Amning har sundhedsmæssige fordele for mor og barn og mere udtalte fordele for præmature børn, men udenlandske undersøgelser viser, at færre præmature børn påbegynder amning, og færre præmature børn ammes i 4 og 6 måneder sammenlignet med mature børn. Der findes ikke danske undersøgelser om andelen af præmature børn, som påbegynder amning, men en dansk undersøgelse viser, at 60 % af de præmature børn ammes fuldt ved udskrivelse til hjemmet. Der er ikke enighed mellem danske neonatalafdelinger eller international forskningslitteratur om, hvilken klinisk praksis der fremmer amning. Hud-mod-hud-kontakt mellem det præmature barn og forældrene er det første skridt i ammeetablering hos præmature børn, men undersøgelser af hud-mod-hud-kontakt med ekstremt præmature børn under 28 gestationsuger er sparsomme.

Afhandlingens overordnede formål var at identificere og undersøge faktorer der har sammenhæng med amning af præmature børn - både faktorer hos børn, mødre og i den kliniske praksis - for at danne mere viden og kunne vejlede mødre til præmature børn om amning på et evidensbaseret grundlag.

Afhandlingen består af tre undersøgelser. Studie A: et interventionsstudie om ekstremt præmature børn tolererer hud-mod-hud-kontakt med deres forældre med deltagelse af 22 stabile børn født før 28 gestationsuger, Studie B: en national spørgeskemaundersøgelse af ammeforhold på alle 19 danske neonatalafdelinger, og Studie C: en national spørgeskemaundersøgelse af amning af præmature børn med deltagelse af 1.221 mødre og deres 1.488 præmature børn med gestationsalder (GA) 24-36 uger. Vi undersøgte hvilke faktorer, der havde sammenhæng med tidlig etablering af fuld amning, fuld amning ved udskrivelse til hjemmet, og varigheden af fuld amning i henhold til Sundhedsstyrelsens anbefalinger.

De ekstremt præmature børn i Studie A havde på undersøgelsestidspunktet en gennemsnitlig postmenstruel alder (PMA) på 26 uger og 5 dage og en gennemsnitlig vægt på 702 gram. Børnene tolererede hud-mod-hud-kontakten med forældrene uden betydende forskelle i gennemsnitlig hudtemperatur, puls, respiration eller ilt-saturation før, under og efter hud-mod-hud-kontakten, hvilket betyder, at det er muligt at etablere tidlig hud-mod-hud-kontakt med stabile ekstremt præmature børn.

Neonatalafdelingerne beskrev, at de stræber efter tidlig etablering af hud-mod-hud-kontakt, og 81 % af de præmature børn påbegyndte dette indenfor det første levedøgn, men væsentlig færre af de ekstremt præmature børn.

Neonatalafdelingerne beskrev at forholdene for amning generelt var gode afspejlet i hud-mod-hud-kontakt, forældres tilstedeværelse, anbefalinger for udmalkning, tilskud med sonde, og tilbageholdenhed med brug af sutteflasker.

Af de deltagende børn påbegyndte 99 % amning, ved udskrivelse var 68 % fuldt ammede og 17 % var delvist ammede, 31 % af børnene levede op til Sundhedsstyrelsens anbefaling om varigheden af fuld amning.

Faktorer hos børn, mødre og i klinisk praksis havde sammenhæng med amning af præmature børn. Ekstremt præmature børn samt tvillinger og trillinger, etablerede fuld amning senere (ved en højere PMA), og havde dobbelt så høj risiko for ikke at være ammet ved udskrivelse. Mødre med kort og mellemlang uddannelse, med kortere ammeerfaring, og mødre der røg havde større risiko for utilstrækkelig længde af fuld amning. Førstegangsfødende etablerede fuld amning halvanden dag senere end flergangsfødende.

Klinisk praksis havde også betydning. At medindlægge moderen på neonatalafdelingen direkte efter fødslen viste større mulighed for at etablere fuld amning nogle dage tidligere, 29 % af mødrene blev medindlagt direkte. Børn der anvendte suttebrik havde dobbelt så stor risiko for ikke at være ammet fuldt ved udskrivelse og halvanden gang så stor risiko for utilstrækkelig længde af fuld amning, men anvendelsen af suttebrik havde ikke indflydelse på, hvor tidligt børnene etablerede fuld amning. Børn, hvor brugen af narresut blev minimeret under ammeetableringen, etablerede amning en dag hurtigere, og havde dobbelt så stor chance for at være fuldt ammede ved udskrivelsen. Brug af kontrolvejning, dvs. at veje barnet lige før og efter en amning, viste halvanden gang større chance for at være fuldt ammet ved udskrivelsen, men havde ingen sammenhæng med hvor tidligt eller hvor længe barnet blev fuldt ammet. Der var stor forskel mellem neonatalafdelingerne på, hvor mange børn der havde anvendt suttebrik, narresut og kontrolvejning under indlæggelsen.

Hvor tidligt moderen påbegyndte udmalkning af modermælk viste en dosis-responseffekt på fuld amning ved udskrivelse og anbefalet varighed af fuld amning, jo tidligere, jo mere positivt for amning, men ikke alle resultater havde statistisk styrke. Mødre, der påbegyndte udmalkning senere end 48 timer efter fødslen, havde fem gange forhøjet risiko for ikke at amme fuldt ved udskrivelse, og mødre der påbegyndte udmalkning mellem 12 og 24 timer efter fødslen havde halvanden gang større risiko for utilstrækkelig længde af fuld amning. Dosis-responseffekten tillader dog at anbefale, at udmalkning påbegyndes tidligt efter fødslen.

Vi kan konkludere, at stabile ekstremt præmature børn tolererer hud-mod-hud-kontakt med deres forældre. Danske præmature børn påbegynder amning i samme grad som mature børn.

Præmature børns ammekompetencer bliver ikke udviklet ved en fast alder, men har sammenhæng med forhold hos børn, mødre og i klinisk praksis. At medindlægge mødrene på neonatalafdelingen direkte efter fødslen, kan formentlig

medvirke til tidligere etablering af fuld amning. Det ser ud til, at minimering af brug af narresut under ammeetableringen, begrænsning i brug af suttebrikker, påbegyndelse af udmalkning tidligst muligt efter fødslen og anvendelse af kontrolvejning fremmer amning af præmature børn. Der savnes dog forskning i, hvordan mødre støttes, når kontrolvejning stoppes ved barnets udskrivelse, da disse mødre hurtigere holder op med at amme fuldt.

Ekstra støtte og opmærksomhed bør gives til grupper med større risiko for ikke at amme fuldt, dvs. de ekstremt og meget præmature børn, tvillinger/ trillinger, mødre der ryger, har kortere uddannelse eller kortere ammeerfaring.

Acknowledgement

References

1. World Health Organization, Fact sheet N°363, Preterm birth. Updated November 2013. Available: http://www.who.int/mediacentre/factsheets/fs363/en/. Accessed 2014 April 1.

2. Winterstein AG, Knox CA, Kubilis P, Hampp C. Appropriateness of Age Thresholds for Respiratory Syncytial Virus Immunoprophylaxis in Moderate-Preterm Infants: A Cohort Study. JAMA Pediatr. 2013 Dec 1;167(12):1118-24.

3. Engle WA; American Academy of Pediatrics Committee on Fetus and Newborn. Age terminology during the perinatal period. Pediatrics. 2004 Nov;114(5):1362-4.

4. Labbok MH, Starling A. Definitions of breastfeeding: call for the development and use of consistent definitions in research and peer-reviewed literature. Breastfeed Med. 2012 Dec;7(6):397-402.

5. World Health Organization. Indicators for assessing infant and young child feeding practices: conclusions of a consensus meeting held 6–8 November 2007 in Washington D.C., USA. WHO, Geneva; 2008. Available: http://www.unicef.org/nutritioncluster/files/IYCFE_WHO_Part1_eng.pdf . Accessed 2014 March 29.

6. Hornby AS. Oxford Advanced Learner's Dictionary. 6th edition. New York: Oxford University Press; 2000.

7. World Health Organization, UNICEF. Protecting, promoting and supporting breast-feeding -The special role of maternity services. Geneva: WHO Publication; 1989.

8. World Health Organization. Kangaroo mother care: a practical guide. Department of reproductive health and research. WHO, Geneva; 2003. Available: http://whqlibdoc.who.int/publications/2003/9241590351.pdf. Accessed 2014 March 29.

9. Nyqvist KH; Expert Group of the International Network on Kangaroo Mother Care, Anderson GC, Bergman N, Cattaneo A, Charpak N, Davanzo R, Ewald U, Ludington-Hoe S, Mendoza S, Pallás-Allonso C, Peláez JG, Sizun J, Widström AM. State of the art and recommendations. Kangaroo mother care: application in a high-tech environment. Acta Paediatr. 2010 Jun;99(6):812-9.

10. Heinonen K, Matilainen R, Koski H, Launiala K. Intrauterine growth retardation (IUGR) in pre-term infants. J Perinat Med. 1985;13(4):171-8.

11. Hurst NM, Meier PP, Engstrom JL, Myatt A. Mothers performing in-home measurement of milk intake during breastfeeding of their preterm infants: maternal reactions and feeding outcomes. J Hum Lact. 2004 May;20(2):178-87.

12. Danish Health and Medicines Authority. [Number and analysis: Birth statistics 2011]. Danish Health and Medicines Authority, Copenhagen; 2012. Available: http://www.ssi.dk/Sundhedsdataogit/~/media/Indhold/DK%20-%20dansk/Sundhedsdata%20og%20it/NSF/Analyser%20og%20rapporter/TalOgAnalyser/2012/F%C3%B8dselsstatistik%202011.ashx. Accessed 2014 April 1. Danish.

13. Mathiesen R. Hansen BM, Løkke A, Greisen G. [Handling of preterm children at Rigshospitalet Copenhagen University Hospital 1955 – 2007]. Bibl Læger. 2008;200:528-46. Danish.

14. Hansen BM, Hoff B, Greisen G, Mortensen EL; Danish ETFOL Study Group. Early nasal continuous positive airway pressure in a cohort of the smallest infants in Denmark: neurodevelopmental outcome at five years of age. Acta Paediatr. 2004 Feb;93(2):190-5.

15. Horbar JD, Carpenter JH, Badger GJ, Kenny MJ, Soll RF, Morrow KA, Buzas JS. Mortality and neonatal morbidity among infants 501 to 1500 grams from 2000 to 2009. Pediatrics. 2012 Jun;129(6):1019-26.

16. Budin P. The Nursling. The feeding and hygiene of premature and full-term infants. London: The Caxton publishing compagny; 1907. Available: http://www.neonatology.org/classics/nursling/nursling.html. Accessed 2014 April 1.

17. Christensen JF. [The first two years of the milk bank]. Ugeskr. Læger. 1946;18:443. Danish.

18. Arnold LD. Donor milk banking in Scandinavia. J Hum Lact. 1999 Mar;15(1):55-9.

19. Mørch DT. [Winther babies]. Copenhagen, Gyldendal; 1976. Danish.

20. Damgaard B. [Large development in the nursing care of preterm infants]. Sygeplejersken 1983;83(41):4−8. Danish.

21. Fegran L, Helseth S, Slettebø A. Nurses as moral practitioners encountering parents in neonatal intensive care units. Nurs Ethics. 2006 Jan;13(1):52-64.

22. Hansen Å. Personal communication 2014.

23. Sarring, B. Personal communication 2014.

24. Davis L, Mohay H, Edwards H. Mothers' involvement in caring for their premature infants: an historical overview. J Adv Nurs. 2003 Jun;42(6):578-86.

25. Greisen G, Mirante N, Haumont D, Pierrat V, Pallás-Alonso CR, Warren I, Smit BJ, Westrup B, Sizun J, Maraschini A, Cuttini M; ESF Network. Parents, siblings and grandparents in the Neonatal Intensive Care Unit. A survey of policies in eight European countries. Acta Paediatr. 2009;98:1744-50.

26. Olsson E, Andersen RD, Axelin A, Jonsdottir RB, Maastrup R, Eriksson M. Skin-to-skin care in neonatal intensive care units in the Nordic countries: a survey of attitudes and practices. Acta Paediatr. 2012;101:1140-6.

27. Nyqvist KH, Häggkvist AP, Hansen MN, Kylberg E, Frandsen AL, Maastrup R, Ezeonodo A, Hannula L, Koskinen K, Haiek LN. Expansion of the ten steps to successful breastfeeding into neonatal intensive care: expert group recommendations for three guiding principles. J Hum Lact. 2012 Aug;28(3):289-96.

28. Nyqvist KH, Häggkvist AP, Hansen MN, Kylberg E, Frandsen AL, Maastrup R, Ezeonodo A, Hannula L, Haiek LN. Expansion of the Baby-Friendly Hospital Initiative Ten Steps to Successful Breastfeeding into Neonatal Intensive Care: Expert Group Recommendations. J Hum Lact. 2013 Aug;29(3):300-9.

29. Zachariassen G, Faerk J, Grytter C, Esberg B, Juvonen P, Halken S. Factors associated with successful establishment of breastfeeding in very preterm infants. Acta Paediatr. 2010;99:1000-4.

30. Flacking R, Ewald U, Wallin L. Positive Effect of Kangaroo Mother Care on Long-Term Breastfeeding in Very Preterm Infants. J Obstet Gynecol Neonatal Nurs. 2011;40:190-7.

31. Björk M, Thelin A, Peterson I, Hammarlund K. A journey filled with emotions – mothers' experiences of breastfeeding their preterm infant in a Swedish neonatal ward. Breastfeed Rev. 2012 Mar;20(1):25-31.

32. Ericson J, Flacking R. Estimated breastfeeding to support breastfeeding in the neonatal intensive care unit. J Obstet Gynecol Neonatal Nurs. 2013 Jan-Feb;42(1):29-37.

33. Wataker H, Meberg A, Nestaas E. Neonatal family care for 24 hours per day: effects on maternal confidence and breast-feeding. J Perinat Neonatal Nurs. 2012 Oct-Dec;26(4):336-42.

34. Niela-Vilén H, Axelin A, Melender HL, Salanterä S. Aiming to be a breastfeeding mother in a neonatal intensive care unit and at home: a thematic analysis of peer-support group discussion in social media. Matern Child Nutr. 2014 Feb 13. doi: 10.1111/mcn.12108. [Epub ahead of print].

35. Häggkvist AP. [Breastfeeding infants with special needs]. Board of Health, Oslo; 1998. Norwegian.

36. Jacobsen U, Virgin C. [Neonatology – nursing care and nearness]. Sygeplejersken. 1992 Jul 1;92(27):4-6. Danish.

37. Nilsson I, Schack-Nielsen L, Jerris T. [Breastfeeding – a handbook for health care professionals]. Danish Health and Medicines Authority, Copenhagen; 2013. Danish.

38. Whitelaw A, Sleath K. Myth of the marsupial mother: home care of very low birth weight babies in Bogota, Colombia. Lancet. 1985 May 25;1(8439):1206-8.

39. Møller-Jensen H, Hjort-Gregersen K, Matthiessen M, Vestergaard HF, Jepsen BH. [Kangaroo method used in practice at Sønderborg Hospital]. Sygeplejersken. 1987 May 6;87(19):16-8. Danish.

40. Virgin C. [Kangaroo method returns children to mothers]. Sygeplejersken. 1987 May 6;87(19):10-4. Danish.

41. Virgin C. [The value of close contact]. Sygeplejersken. 1990 Feb 28;90(9):24-5. Danish.

42. Blomqvist YT, Ewald U, Gradin M, Nyqvist KH, Rubertsson C. Initiation and extent of skin-to-skin care at two Swedish neonatal intensive care units. Acta Paediatr. 2013 Jan;102(1):22-8.

43. Helth TD, Jarden M. Fathers' experiences with the skin-to-skin method in NICU: Competent parenthood and redefined gender roles. J Neonatal Nurs. 2013;19(3):114-21.

44. Mörelius E, Angelhoff C, Eriksson J, Olhager E. Time of initiation of skin-to-skin contact in extremely preterm infants in Sweden. Acta Paediatr. 2012 Jan;101(1):14-8.

45. Karlsson V, Heinemann AB, Sjörs G, Nykvist KH, Agren J. Early skin-to-skin care in extremely preterm infants: thermal balance and care environment. J Pediatr. 2012 Sep;161(3):422-6.

46. Van Zanten HA, Havenaar AJ, Stigt HJH, Ligthart PAH, Walther FJ. The kangaroo method is safe for premature infants under 30 weeks of gestation during ventilatory support. J Neonatal Nurs. 2007 Oct;13(5):186-90.

47. Bauer K, Pyper A, Sperling P, Uhrig C, Versmold H. Effects of gestational and postnatal age on body temperature, oxygen consumption, and activity during early skin-to-skin contact between preterm infants of 25-30-week gestation and their mothers. Pediatr Res. 1998 Aug;44(2):247-51.

48. Callaghan WM, MacDorman MF, Rasmussen SA, Qin C, Lackritz EM. The contribution of preterm birth to infant mortality rates in the United States. Pediatrics. 2006;118:1566-73.

49. Beck S, Wojdyla D, Say L, Betran AP, Merialdi M, Requejo JH, Rubens C, Menon R, Van Look PF. The worldwide incidence of preterm birth: a systematic review of maternal mortality and morbidity. Bull World Health Organ. 2010 Jan;88(1):31-8. Review.

50. Martin JA, Hamilton BE, Sutton PD, Ventura SJ, Menacker F, Kirmeyer S, Mathews TJ. Births: Final data for 2006. National vital statistics reports; vol 57 no 7. Hyattsville, MD: National Center for Health Statistics. 2009. Available: http://www.cdc.gov/nchs/data/nvsr/nvsr57/nvsr57_07.pdf Accessed 2014 April 1.

51. Ananth CV, Friedman AM, Gyamfi-Bannerman C. Epidemiology of moderate preterm, late preterm and early term delivery. Clin Perinatol. 2013 Dec;40(4):601-10.

52. MedlinePlus, The U.S. National Library of Medicine, National Institutes of Health. Available: http://www.nlm.nih.gov/medlineplus/ency/article/001562.htm. Accessed 2014 March 23.

53. Sahni R, Polin RA. Physiologic underpinnings for clinical problems in moderately preterm and late preterm infants. Clin Perinatol. 2013 Dec;40(4):645-63.

54. Inder TE, Warfield SK, Wang H, Hüppi PS, Volpe JJ. Abnormal cerebral structure is present at term in premature infants. Pediatrics. 2005 Feb;115(2):286-94.

55. Mewes AU, Hüppi PS, Als H, Rybicki FJ, Inder TE, McAnulty GB, Mulkern RV, Robertson RL, Rivkin MJ, Warfield SK. Regional brain development in serial magnetic resonance imaging of low-risk preterm infants. Pediatrics. 2006 Jul;118(1):23-33.

56. Als H, Duffy FH, McAnulty GB, Rivkin MJ, Vajapeyam S, Mulkern RV, Warfield SK, Huppi PS, Butler SC, Conneman N, Fischer C, Eichenwald EC. Early experience alters brain function and structure. Pediatrics. 2004 Apr;113(4):846-57.

57. Kamper J, Ringsted C. Early treatment of idiopathic respiratory distress syndrome using binasal continuous positive airway pressure. Acta Paediatr Scand. 1990;79:581-6.

58. Verder H. Nasal CPAP has become an indispensable part of the primary treatment of newborns with respiratory distress syndrome. Acta Paediatr. 2007 Apr;96(4):482-4.

59. American Academy of Pediatrics, Committee on Fetus and Newborn. Levels of Neonatal Care. Pediatrics. 2004 Nov;114(5):1341-7.

60. American Academy of Pediatrics Committee on Fetus And Newborn. Levels of neonatal care. Pediatrics. 2012 Sep;130(3):587-97.

61. Finnström O, Olausson PO, Sedin G, Serenius F, Svenningsen N, Thiringer K, Tunell R, Wennergren M, Wesström G. The Swedish national prospective study on extremely low birthweight (ELBW) infants. Incidence, mortality, morbidity and survival in relation to level of care. Acta Paediatr. 1997;86:503-11.

62. Akerstrom S, Asplund I, Norman M. Successful breastfeeding after discharge of preterm and sick newborn infants. Acta Paediatr. 2007 Oct;96(10):1450-4.

63. Bragelien R, Røkke W, Markestad T. Stimulation of sucking and swallowing to promote oral feeding in premature infants. Acta Paediatr. 2007 Oct;96(10):1430-2.

64. Dodrill P, Donovan T, Cleghorn G, McMahon S, Davies PS. Attainment of early feeding milestones in preterm neonates. J Perinatol. 2008 Aug;28(8):549-55.

65. Smith MM, Durkin M, Hinton VJ, Bellinger D, Kuhn L. Initiation of breastfeeding among mothers of very low birth weight infants. Pediatrics. 2003 Jun;111(6 Pt 1):1337-42.

66. Pineda RG. Predictors of breastfeeding and breastmilk feeding among very low birth weight infants. Breastfeed Med. 2011 Feb;6(1):15-9.

67. Flacking R, Nyqvist KH, Ewald U, Wallin L. Long-term duration of Breastfeeding in Swedish Low Birth Weight Infants. J Hum Lact. 2003;19:157-165.

68. Flacking R, Wallin L, Ewald U. Perinatal and socioeconomic determinants of breastfeeding duration in very preterm infants. Acta Paediatr. 2007 Aug;96(8):1126-30.

69. Hill PD, Aldag JC, Zinaman M, Chatterton RT. Predictors of preterm infant feeding methods and perceived insufficient milk supply at week 12 postpartum. J Hum Lact. 2007 Feb;23(1):32-8.

70. Ostlund A, Nordström M, Dykes F, Flacking R. Breastfeeding in preterm and term twins--maternal factors associated with early cessation: a population-based study. J Hum Lact. 2010 Aug;26(3):235-41.

71. Lee HC, Gould JB. Factors influencing breast milk versus formula feeding at discharge for very low birth weight infants in California. J Pediatr. 2009 Nov;155(5):657-62.e1-2.

72. Bonet M, Blondel B, Agostino R, Combier E, Maier RF, Cuttini M, Khoshnood B, Zeitlin J; MOSAIC research group. Variations in breastfeeding rates for very preterm infants between regions and neonatal units in Europe: results from the MOSAIC cohort. Arch Dis Child Fetal Neonatal Ed. 2011 Nov;96(6):F450-2.

73. Perrella SL, Williams J, Nathan EA, Fenwick J, Hartmann PE, Geddes DT. Influences on breastfeeding outcomes for healthy term and preterm/sick infants. Breastfeed Med. 2012 Aug;7:255-61.

74. Geraghty SR, Khoury JC, Kalkwarf HJ. Human milk pumping rates of mothers of singletons and mothers of multiples. J Hum Lact. 2005 Nov;21(4):413-20.

75. Li R, Fein SB, Grummer-Strawn LM. Do infants fed from bottles lack self-regulation of milk intake compared with directly breastfed infants? Pediatrics. 2010 Jun;125(6):e1386-93.

76. Meier P Bottle- and breast-feeding: effects on transcutaneous oxygen pressure and temperature in preterm infants. Nurs Res. 1988 Jan-Feb;37(1):36-41.

77. Chen CH, Wang TM, Chang HM, Chi CS. The effect of breast- and bottle-feeding on oxygen saturation and body temperature in preterm infants. J Hum Lact. 2000 Feb;16(1):21-7.

78. The WHO Global Data Bank on Infant and Young Child Feeding. Available: http://who.int/nutrition/databases/infantfeeding/en/index.html . Accessed 2014 April 1.

79. Australian Bureau of Statistics. Breastfeeding in Australia 2001. Available: http://www.abs.gov.au/ausstats/abs@.nsf/ca79f63026ec2e9cca256886001514d7/4db9 a8a50fef826cca256d1100053523!OpenDocument . Accessed 2014 April 1.

80. Official statistics of Sweden. [Breastfeeding, children born 2006]. Statistics – Health and Diseases. Swedish. Available: http://www.socialstyrelsen.se/Lists/Artikelkatalog/Attachments/8711/2008-125-12_200812512_rev.pdf . Accessed 2014 April 1.

81. Helsedirektoratet, Mattilsynet og Universitetet in Oslo. [Infant food - 6 months. Country-wide dietary survey among 6 months old children, 2006-2007]. Oslo: Norwegian Directorate for Health, University of Oslo & Norwegian Food Safety Authority; 2008. Norwegian. Avilable: http://www.matportalen.no/kosthold_og_helse/article3345.ece/BINARY/Helsedirekto ratet+-+Landsomfattende+kostholdsunders%C3%B8kelse+blant+6+m%C3%A5neder+gaml e+barn. Accessed 2014 April 1.

82. Kronborg H, Vaeth M. The influence of psychosocial factors on the duration of breastfeeding. Scand J Public Health. 2004;32:210-6.

83. Christensen AM, Brixval CS, Svendsen M, Laursen B, Holstein BE. [Annual rapport of children born in 2008 and 2009 from The Database of Children's Health: Breastfeeding in 14 communities]. The steering committee of The Database of Children's Health and National Institute of Public Health. Copenhagen, 2011. Available: http://www.si-folkesundhed.dk/upload/%C3%A5rsrapport_fra_databasen_b%C3%B8rns_sundhed_j uni_2011.pdf. Accessed 2014 April 1.

84. Statistics Denmark. Immigrants in Denmark 2013. Available: http://www.dst.dk/pukora/epub/upload/17961/indv2013.pdf . Accessed 2014 April 1.

85. Demirci JR, Sereika SM, Bogen D. Prevalence and predictors of early breastfeeding among late preterm mother-infant dyads. Breastfeed Med. 2013 Jun;8(3):277-85.

86. Smithers LG, McPhee AJ, Gibson RA, Makrides M. Characterisation of feeding patterns in infants born < 33 weeks gestational age. Asia Pac J Clin Nutr. 2003;12 Suppl:S43.

87. World Health Organization. Global Strategy for Infant and Young Child Feeding. WHO, Geneva; 2003. Available at : http://www.who.int/nutrition/publications/gs_infant_feeding_text_eng.pdf. Assessed 2014 March 23.

88. Moore ER, Anderson GC, Bergman N, Dowswell T. Early skin-to-skin contact for mothers and their healthy newborn infants. Cochrane Database Syst Rev. 2012 May 16;5:CD003519.

89. Dumas L, Lepage M, Bystrova K, Matthiesen AS, Welles-Nyström B, Widström AM. Influence of skin-to-skin contact and rooming-in on early mother-infant interaction: a randomized controlled trial. Clin Nurs Res. 2013 Aug;22(3):310-36.

90. Erlandsson K, Dsilna A, Fagerberg I, Christensson K. Skin-to-skin care with the father after cesarean birth and its effect on newborn crying and prefeeding behavior. Birth. 2007 Jun;34(2):105-14.

91. Engler AJ, Ludington-Hoe SM, Cusson RM, Adams R, Bahnsen M, Brumbaugh E, Coates P, Grieb J, McHargue L, Ryan DL, Settle M, Williams D. Kangaroo care: national survey of practice, knowledge, barriers, and perceptions. MCN Am J Matern Child Nurs. 2002 May-Jun;27(3):146-53.

92. Pallás-Alonso CR, Losacco V, Maraschini A, Greisen G, Pierrat V, Warren I, Haumont D, Westrup B, Smit BJ, Sizun J, Cuttini M; European Science Foundation Network. Parental involvement and kangaroo care in European neonatal intensive care units: a policy survey in eight countries. Pediatr Crit Care Med. 2012 Sep;13(5):568-77.

93. Conde-Agudelo A, Belizán JM, Diaz-Rossello J. Kangaroo mother care to reduce morbidity and mortality in low birthweight infants. Cochrane Database Syst Rev. 2011 Mar 16;(3):CD002771.

94. Hake-Brooks SJ, Anderson GC. Kangaroo care and breastfeeding of mother-preterm infant dyads 0-18 months: a randomized, controlled trial. Neonatal Netw. 2008 May-Jun;27(3):151-9.

95. Gathwala G, Singh B, Singh J. Effect of Kangaroo Mother Care on physical growth, breastfeeding and its acceptability. Trop Doct. 2010 Oct;40(4):199-202.

96. Nagai S, Yonemoto N, Rabesandratana N, Andrianarimanana D, Nakayama T, Mori R. Long-term effects of earlier initiated continuous Kangaroo Mother Care (KMC) for low-birth-weight (LBW) infants in Madagascar. Acta Paediatr. 2011 Dec; 100(12):e241-7.

97. Bergman NJ, Linley LL, Fawcus SR. Randomized controlled trial of skin-to-skin contact from birth versus conventional incubator for physiological stabilization in 1200- to 2199-gram newborns. Acta Paediatr. 2004 Jun;93(6):779-85.

98. Ludington SM. Energy conservation during skin-to-skin contact between premature infants and their mothers
Heart Lung. 1990 Sep;19(5 Pt 1):445-51.

99. Chwo MJ, Anderson GC, Good M, Dowling DA, Shiau SH, Chu DM. A randomized controlled trial of early kangaroo care for preterm infants: effects on temperature, weight, behavior, and acuity. J Nurs Res. 2002 Jun;10(2):129-42.

100. Ludington-Hoe SM, Johnson MW, Morgan K, Lewis T, Gutman J, Wilson PD, Scher MS. Neurophysiologic assessment of neonatal sleep organization: preliminary results of a randomized, controlled trial of skin contact with preterm infants. Pediatrics 2006 May;117(5):e909-e923.

101. Tessier R, Cristo M, Velez S, Giron M, Nadeau L, Figueroa Z, Ruiz JG, Charpak N. Kangaroo Mother Care: a method of protecting high risk premature infants against developmental delay. Infant Behav Dev. 2003;26:384–97.

102. Charpak N, Ruiz JG, Zupan J, Cattaneo A, Figueroa Z, Tessier R, Cristo M, Anderson G, Ludington S, Mendoza S, Mokhachane M, Worku B. Kangaroo Mother Care: 25 years after. Acta Paediatr. 2005 May;94(5):514-22.

103. Lupton D, Fenwick J. 'They've forgotten that I'm the mum': constructing and practising motherhood in special care nurseries. Soc Sci Med. 2001 Oct;53(8):1011-21.

104. Lundqvist P, Jakobsson L. Swedish men's experiences of becoming fathers to their preterm infants. Neonatal Netw. 2003 Nov-Dec;22(6):25-31.

105. Haslund H. An anthropological analysis of parenthood after prematurity. Moral experiments in the borderland between illness and everyday-life. Ph.D thesis. The Department of Culture and Socielty, Aarhus University, Denmark; 2013.

106. Anderson GC, Chiu SH, Dombrowski MA, Swinth JY, Albert JM, Wada N. Mother-newborn contact in a randomized trial of kangaroo (skin-to-skin) care. J Obstet Gynecol Neonatal Nurs. 2003 Sep-Oct;32(5):604-11.

107. Hoddinott P, Tappin D, Wright C. Breast feeding. BMJ. 2008;336:881-7.

108. Schack-Nielsen L, Michaelsen KF. [The effects of breastfeeding I: effects on the immune system and the central nervous system]. Ugeskr Laeger. 2007 Mar 12;169(11):985-9. Review. Danish.

109. Schack-Nielsen L, Michaelsen KF. [The effects of breastfeeding II: effects on lifestyle illnesses, mother's health and negative effects]. Ugeskr Laeger. 2007 Mar 12;169(11):989-93. Review. Danish.

110. Schandler RJ, Schulman RJ, Lau C. Feeding strategies for preterm infants: Beneficial outcomes of feeding fortified human milk versus preterm formula. Pediatrics. 1999;103:1150-7.

111. Hylander MA, Strobino DM, Dhanireddy R. Human milk feedings and infection among very low birth weight infants. Pediatrics. 1998 Sep;102(3):E38.

112. Rønnestad A, Abrahamsen TG, Medbø S, Reigstad H, Lossius K, Kaaresen PI, Egeland T, Engelund IE, Irgens LM, Markestad T. Late-onset septicemia in a Norwegian national cohort of extremely premature infants receiving very early full human milk feeding. Pediatrics. 2005 Mar;115(3):e269-76.

113. Cristofalo EA, Schanler RJ, Blanco CL, Sullivan S, Trawoeger R, Kiechl-Kohlendorfer U, Dudell G, Rechtman DJ, Lee ML, Lucas A, Abrams S. Randomized trial of exclusive human milk versus preterm formula diets in extremely premature infants. J Pediatr. 2013 Dec;163(6):1592-5.

114. Lucas A, Cole TJ. Breast milk and neonatal necrotising enterocolitis. Lancet, 1990, 336:1519–23.

115. Updegrove K. Necrotizing enterocolitis: the evidence for use of human milk in prevention and treatment. J Hum Lact. 2004 Aug;20(3):335-9. Review.

116. Hylander MA, Strobino DM, Pezzullo JC, Dhanireddy R. Association of human milk feedings with a reduction in retinopathy of prematurity among very low birthweight infants. J Perinatol. 2001 Sep;21(6):356-62.

117. Riordan J. Breastfeeding and human lactation. 3rd edition. Boston: Jones and Barlett Publishers, Inc; 2005.

118. Michaelsen KF, Lauritzen L, Mortensen EL. Effects of breast-feeding on cognitive function. Adv Exp Med Biol. 2009;639:199-215.

119. Duman N, Utkutan S, Ozkan H, Ozdoğan S. Are the stool characteristics of preterm infants affected by infant formulas? Turk J Pediatr. 2000 Apr-Jun;42(2):138-44.

120. Zachariassen G, Fenger-Gron J. Preterm dietary study: meal frequency, regurgitation and the surprisingly high use of laxatives among formula-fed infants following discharge. Acta Paediatr. 2014 Mar;103(3):e116-22.

121. Eriksen HL, Kesmodel US, Underbjerg M, Kilburn TR, Bertrand J, Mortensen EL. Predictors of intelligence at the age of 5: family, pregnancy and birth characteristics, postnatal influences, and postnatal growth. PLoS One. 2013 Nov 13;8(11):e79200.

122. Fonseca AL, Albernaz EP, Kaufmann CC, Neves IH, Figueiredo VL. Impact of breastfeeding on the intelligence quotient of eight-year-old children. J Pediatr (Rio J). 2013 Jul-Aug;89(4):346-53.

123. Kafouri S, Kramer M, Leonard G, Perron M, Pike B, Richer L, Toro R, Veillette S, Pausova Z, Paus T. Breastfeeding and brain structure in adolescence. Int J Epidemiol. 2013 Feb;42(1):150-9.

124. Mortensen EL, Michaelsen KF, Sanders SA, Reinisch JM. The association between duration of breastfeeding and adult intelligence. JAMA. 2002 May 8;287(18):2365-71.

125. Flacking R, Ewald U, Nyqvist KH, Starrin B. Trustful bonds: a key to "becoming a mother" and to reciprocal breastfeeding. Stories of mothers of very preterm infants at a neonatal unit. Soc Sci Med. 2006 Jan;62(1):70-80.

126. Flacking R, Ewald U, Starrin B. "I wanted to do a good job": experiences of 'becoming a mother' and breastfeeding in mothers of very preterm infants after discharge from a neonatal unit. Soc Sci Med. 2007 Jun;64(12):2405-16.

127. Kavanaugh K, Meier P, Zimmermann B, Mead L. The rewards outweigh the efforts: breastfeeding outcomes for mothers of preterm infants. J Hum Lact. 1997 Mar;13(1):15-21.

128. Danish legal information. [Law on maternity leave]. Danish. Available: https://www.retsinformation.dk/Forms/R0710.aspx?id=143853. Accessed 2014 April 1.

129. The Swedish constitution. [Law on parental leave]. Swedish. Available: http://www.riksdagen.se/sv/Dokument-Lagar/Lagar/Svenskforfattningssamling/Foraldraledighetslag-1995584_sfs-1995-584/. Accessed 2014 April 1.

130. Larsen JS, Hall EO, Aagaard H. Shattered expectations: when mothers' confidence in breastfeeding is undermined – a metasynthesis. Scand J Caring Sci. 2008 Dec;22(4):653-61.

131. Nyqvist KH, Sjöden PO, Ewald U. The development of preterm infants' breastfeeding behavior. Early Hum Dev. 1999 Jul;55(3):247-64.

132. Nyqvist KH. Early attainment of breastfeeding competence in very preterm infants. Acta Paediatr. 2008 Jun;97(6):776-81.

133. Lau C, Geddes D, Mizuno K, Schaal B. The development of oral feeding skills in infants. Int J Pediatr. 2012;2012:572341.

134. Wheeler J, Chapman C, Johnson M, Langdon R. Feeding outcomes and influences within the neonatal unit. Int J Nurs Pract. 2000;6:196-206.

135. Nyqvist KH, Ewald U, Sjoden PO. Supporting a preterm infant's behaviour during breastfeeding: a case report. J Hum Lact. 1996 Sep;12(3):221-8.

136. Cregan MD, De Mello TR, Kershaw D, McDougall K, Hartmann PE. Initiation of lactation in women after preterm delivery. Acta Obstet Gynecol Scand. 2002 Sep;81(9):870-7.

137. Swanson V, Nicol H, McInnes R, Cheyne H, Mactier H, Callander E. Developing maternal self-efficacy for feeding preterm babies in the neonatal unit. Qual Health Res. 2012 Oct;22(10):1369-82.

138. Franck LS, Cox S, Allen A, Winter I. Measuring neonatal intensive care unit-related parental stress. J Adv Nurs. 2005 Mar;49(6):608-15.

139. Flacking R, Thomson G, Ekenberg L, Löwegren L, Wallin L. Influence of NICU co-care facilities and skin-to-skin contact on maternal stress in mothers of preterm infants. Sex Reprod Healthc. 2013 Oct;4(3):107-12.

140. Nystrom K, Axelsson K. Mother's experience of being separated from their newborns. J Obstet Gynecol Neonatal Nurs. 2002 May-Jun;31(3):275-82.

141. Beck SA, Weiss J, Greisen G, Andersen M, Zoffmann V. Room for family-centered care – a qualitative evaluation of a neonatal intensive care unit remodeling project. J Neonatal Nurs 2009;15:88-99.

142. Tohotoa J, Maycock B, Hauck YL, Howat P, Burns S, Binns CW. Dads make a difference: an exploratory study of paternal support for breastfeeding in Perth, Western Australia. Int Breastfeed J. 2009 Nov 29;4:15.

143. Nyqvist KH, Kylberg E. Application of the Baby Friendly Hospital Initiative to neonatal care: Suggestions by Swedish mothers of very preterm infants. J Hum Lact. 2008;24:252-262.

144. Kramer MS, Chalmers B, Hodnett ED, Sevkovskaya Z, Dzikovich I, Shapiro S, Collet JP, Vanilovich I, Mezen I, Ducruet T, Shishko G, Zubovich V, Mknuik D, Gluchanina E, Dombrovskiy V, Ustinovitch A, Kot T, Bogdanovich N, Ovchinikova L, Helsing E; PROBIT Study Group (Promotion of Breastfeeding Intervention Trial). Promotion of Breastfeeding Intervention Trial (PROBIT): a randomized trial in the Republic of Belarus. JAMA. 2001;285:413-420.

145. Spatz DL. Ten steps for promoting and protecting breastfeeding for vulnerable infants. J Perinat Neonatal Nurs. 2004;18:385-396. Review.

146. do Nascimento MB, Issler H. Breastfeeding the premature infant: experience of a baby-friendly hospital in Brazil. J Hum Lact. 2005;21:47-52.

147. Dall'Oglio I, Salvatori G, Bonci E, Nantini B, D'Agostino G, Dotta A. Breastfeeding promotion in neonatal intensive care unit: impact of a new program toward a BFHI for high-risk infants. Acta Paediatr. 2007;96:1626-31.

148. Shahheidari M, Homer C. Impact of the design of neonatal intensive care units on neonates, staff, and families: a systematic literature review. J Perinat Neonatal Nurs. 2012 Jul-Sep;26(3):260-6.

149. Office of the United Nations High Commissioner for Human Rights. Convention on the rights of the child. Available: http://www.ohchr.org/en/professionalinterest/pages/crc.aspx. Accessed 2014 April 1.

150. Pechlivani F, Vassilakou T, Sarafidou J, Zachou T, Anastasiou CA, Sidossis LS. Prevalence and determinants of exclusive breastfeeding during hospital stay in the area of Athens, Greece. Acta Paediatr. 2005 Jul;94(7):928-34.

151. Elander G, Lindberg T. Hospital routines in infants with hyperbilirubinemia influence the duration of breast feeding. Acta Paediatr Scand. 1986;75:708-712.

152. Domanico R, Davis DK, Coleman F, Davis BO. Documenting the NICU design dilemma: comparative patient progress in open-ward and single family room units. J Perinatol. 2011 Apr;31(4):281-8.

153. Callen J, Pinelli J. A review of the literature examining the benefits and challenges, incidence and duration, and barriers to breastfeeding in preterm infants. Adv Neonatal Care. 2005;5:72-88.

154. Furman L, Minich N, Hack M. Correlates of lactation in mothers of very low birth weight infants. Pediatrics. 2002;109:e57.

155. Hill PD, Aldag JC. Milk volume on day 4 and income predictive of lactation adequacy at 6 weeks of mothers of nonnursing preterm infants. J Perinat Neonatal Nurs. 2005 Jul-Sep;19(3):273-82.

156. Parker LA, Sullivan S, Krueger C, Kelechi T, Mueller M. Effect of early breast milk expression on milk volume and timing of lactogenesis stage II among mothers of very low birth weight infants: a pilot study. J Perinatol. 2012 Mar;32(3):205-9.

157. Cignacco E, Hamers JP, Stoffel L, van Lingen RA, Gessler P, McDougall J, Nelle M. The efficacy of non-pharmacological interventions in the management of procedural pain in preterm and term neonates. A systematic literature review. Eur J Pain. 2007 Feb;11(2):139-52.

158. Pinelli J, Symington A, Ciliska D. Nonnutritive sucking in high-risk infants: benign intervention or legitimate therapy? J Obstet Gynecol Neonatal Nurs. 2002;31:582-91. Review.

159. Kronborg H, Vaeth M. How are effective breastfeeding technique and pacifier use related to breastfeeding problems and breastfeeding duration? Birth. 2009 Mar;36(1):34-42.

160. Howard CR, Howard FM, Lanphear B, Eberly S, deBlieck EA, Oakes D, Lawrence RA. Randomized clinical trial of pacifier use and bottle-feeding or cupfeeding and their effect on breastfeeding. Pediatrics. 2003 Mar;111(3):511-8.

161. Collins CT, Ryan P, Crowther CA, McPhee AJ, Paterson S, Hiller JE. Effect of bottles, cups, and dummies on breast feeding in preterm infants: a randomised controlled trial. BMJ. 2004;329:193-8.

162. Benevenuto de Oliveira MM, Thomson Z, Vannuchi MT, Matsuo T. Feeding patterns of Brazilian preterm infants during the first 6 months of life, Londrina, Parana, Brazil. J Hum Lact. 2007;23:269-74.

163. Kliethermes PA, Cross ML, Lanese MG, Johnson KM, Simon SD. Transitioning preterm infants with nasogastric tube supplementation: increased likelihood of breastfeeding. J Obstet Gynecol Neonatal Nurs. 1999;28:264-73.

164. Clum D, Primomo J. Use of a silicone nipple shield with premature infants. J Hum Lact. 1996 Dec;12(4):287-90.

165. Meier PP, Brown LP, Hurst NM, Spatz DL, Engstrom JL, Borucki LC, Krouse AM. Nipple shields for preterm infants: effect on milk transfer and duration of breastfeeding. J Hum Lact. 2000 May;16(2):106-14.

166. Dougherty D, Luther M. Birth to breast – a feeding care map for the NICU: helping the extremely low birth weight infant navigate the course. Neonatal Netw. 2008 Nov-Dec;27(6):371-7. Review.

167. Meier PP, Patel AL, Bigger HR, Rossman B, Engstrom JL. Supporting breastfeeding in the neonatal intensive care unit: Rush Mother's Milk Club as a case study of evidence-based care. Pediatr Clin North Am. 2013 Feb;60(1):209-26.

168. McKechnie AC, Eglash A. Nipple shields: a review of the literature. Breastfeed Med. 2010 Dec;5(6):309-14.

169. Kavanaugh K, Mead L, Meier P, Mangurten HH. Getting enough: mothers' concerns about breastfeeding a preterm infant after discharge. J Obstet Gynecol Neonatal Nurs. 1995 Jan;24(1):23-32.

170. Meier PP, Engstrom JL, Fleming BA, Streeter PL, Lawrence PB. Estimating milk intake of hospitalized preterm infants who breastfeed. J Hum Lact. 1996 Mar;12(1):21-6.

171. Nyqvist KH. Breast-feeding in preterm twins: Development of feeding behavior and milk intake during hospital stay and related caregiving practices. J Pediatr Nurs. 2002 Aug;17(4):246-56.

172. Funkquist E-L, Tuvemo T, Jonsson B, Serenius F, Nyqvist KH. Influence of test-weighing before/after nursing on breastfeeding in preterm infants. Adv Neonat Care. 2010;10:33-9.

173. Centuori S, Burmaz T, Ronfani L, Fragiacomo M, Quintero S, Pavan C, Davanzo R, Cattaneo A. Nipple care, sore nipples, and breastfeeding: a randomized trial. J Hum Lact. 1999 Jun;15(2):125-30.

174. Danish legal information. [Law on Health Care]. Danish. Available: https://www.retsinformation.dk/forms/r0710.aspx?id=130455. Accessed 2014 April 1.

175. Koch B et al. [Recommendations for infant nutrition. Guidelines for healthcare professionals]. 2nd edition. Denmark: The Danish Health Board; 2005. Danish.

176. Altman DG. Practical statistics for medical research. London: Chapman & Hall; 1991.

177. Field A. Discovering statistics using SPSS. 3rd edition. London: SAGE Publications Ltd; 2009.

178. World Medical Association. Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects. WMA 2013. Available: http://www.wma.net/en/30publications/10policies/b3/index.html. Accessed 2014 April 1.

179. Beauchamp TL. Principles of Biomedical ethics. New York: Oxford University Press; 1994.

180. Kazdin, A. Research Design in Clinical Psychology. 4th edition. Boston: Allyn and Bacon; 2010.

181. Rothman KJ, Greenland S, Lash TL. Modern epidemiology. 3rd edition. Philadelphia: Lippincott Williams & Wilkins; 2008

182. ahennekens CH, Buring JE. Epidemiology in Medicine. Boston: Little Brown & Co; 1987

183. Polit DF, Hungler BP. Nursing research, principles and methods. 6th edition. Philadelphia: Lippincott Williams & Wilkins; 1999.

184. Bartlett JW, Frost C. Reliability, repeatability and reproducibility: analysis of measurement errors in continuous variables. Ultrasound Obstet Gynecol. 2008 Apr;31(4):466-75.

185. Philips. User manual IntelliVue Patient monitor MP20/30, MP40/50, MP60/70/80/90. Release E.= with software revision E.01.xx. Germany: Phillips; 2006.

186. Boutron I, Moher D, Altman DG, Schulz KF, Ravaud P; CONSORT Group. Extending the CONSORT statement to randomized trials of nonpharmacologic treatment: explanation and elaboration. Ann Intern Med. 2008 Feb 19;148(4):295-309.

187. Howe LD, Tilling K, Galobardes B, Lawlor DA. Loss to follow-up in cohort studies: bias in estimates of socioeconomic inequalities. Epidemiology. 2013 Jan;24(1):1-9.

188. Rothman KJ. Epidemiology, an introduction. 2nd edition. New York: Oxford University Press; 2012.

189. Ludington-Hoe SM, Nguyen N, Swinth JY, Satyshur RD. Kangaroo care compared to incubators in maintaining body warmth in preterm infants. Biol Res Nurs. 2000 Jul;2(1):60-73.

190. Scher MS, Ludington-Hoe S, Kaffashi F, Johnson MW, Holditch-Davis D, Loparo KA. Neurophysiologic assessment of brain maturation after an 8-week trial of skin-to-skin contact on preterm infants. Clin Neurophysiol. 2009 Oct;120(10):1812-8.

191. ESPGHAN Committee on Nutrition, Agostoni C, Braegger C, Decsi T, Kolacek S, Koletzko B, Michaelsen KF, Mihatsch W, Moreno LA, Puntis J, Shamir R, Szajewska H, Turck D, van Goudoever J. Breast-feeding: A commentary by the ESPGHAN Committee on Nutrition. J Pediatr Gastroenterol Nutr. 2009 Jul;49(1):112-25.

192. Ortenstrand A, Westrup B, Broström EB, Sarman I, Akerström S, Brune T, Lindberg L, Waldenström U. The Stockholm Neonatal Family Centered Care Study: effects on length of stay and infant morbidity. Pediatrics. 2010 Feb;125(2):e278-85.

Factors associated with exclusive breastfeeding of preterm infants

- Factors in clinical pratice
- Factors in mothers
- Factors in infants

Positive

Negative

Minimising use of pacifier

Rooming-in

Skin-to-skin after incubator care

Longer BF experience

Test-weighing

Higher education

Gestational age

Mechanical ventilation

SGA   Boys

Multiples

Smoking

Nipple shield use

First-time mothers

Delayed initiation of breast milk pumping

LUND UNIVERSITY
Faculty of Medicine