

# BMJ Open External barriers for including parents of preterm infants in a randomised clinical trial in the neonatal intensive care unit in Sweden: a descriptive study

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## ABSTRACT

**Objectives** Performing randomised controlled trials (RCTs) in neonatal intensive care is challenging in many ways. While restrictive inclusion criteria or busy study protocols are obvious barriers, external barriers leading to termination of a study are seldom discussed. The aim of this study was to describe barriers for inclusion of families in neonatal intensive care in an RCT aiming to evaluate the effects of continuous skin-to-skin contact on mood and sleep quality in parents of preterm infants, as well as the quality of parent–infant interaction and salivary cortisol concentrations at the time of discharge.

**Design** A descriptive study.

**Setting** Three out of seven tertiary neonatal intensive care units in Sweden participated in a two-arm RCT that was terminated because of low inclusion rate.

**Participants** Before termination of the study, 11 out of 242 families assessed for eligibility were included for participation.

**Results** The major barriers for inclusion in this RCT were external due to (1) lack of intensive care beds in the neonatal ward, causing medically stable infants to be transferred back to the referring hospital quicker than expected, (2) moving directly from the delivery room to a family room without passing an open bay intensive care room or (3) transferring from one neonatal ward to another with the same care level to increase availability of intensive care beds where needed. Other barriers were the inclusion criteria ‘single-birth’ and ‘Swedish-speaking parent’.

**Conclusions** The major barriers for including participants were external constituted by transfers between neonatal wards and cities due to lack of intensive care beds. This is a multifactorial issue related to organisational structures. However, since this affects the possibilities to perform research this study highlights some suggestions to consider when planning prospective intervention studies within a neonatal setting.

**Trial registration number** NCT03004677.

## INTRODUCTION

Around the world, 15 million infants are born preterm every year.<sup>1</sup> In Sweden, approximately 6% of the infants are born before gestational week 38.<sup>2</sup> Thanks to advances in medical

## Strengths and limitations of this study

- Few studies discuss early termination of studies in neonatal intensive care.
- This study describes external barriers for including families in a randomised controlled study.
- A negative outcome related to the termination of this study is that we still do not know if continuous skin-to-skin contact starting after the intensive care period would function as a restart for bonding and therefore improve the parents’ mood, interaction behaviour and coregulation of salivary cortisol between parent and infant.

treatment, there is an increased survival rate for infants born extremely preterm.<sup>3</sup> However, these infants require extensive neonatal intensive care for several weeks and hospital care for several months.<sup>3</sup> Separation between parent and infant is common since many parents do not have the opportunity to stay around the clock in the neonatal intensive care unit (NICU).<sup>4</sup> A separation of the parent–infant dyad is more common during the intensive care period than after, when more hospitals can offer couplet care and single family rooms.<sup>5</sup> Separation in combination with the infants’ health condition and need of intensive care exposes parents to distress, worries and poor sleep. This increases the risk for allostatic overload, postpartum depression and post-traumatic stress disorder<sup>4,6,7</sup> which in turn increases the risk for poor bonding and parent–infant interaction.<sup>8,9</sup>

Practising skin-to-skin contact (SSC) during the NICU stay is one way to minimise separation and instead increase physical contact and possibilities for interaction between the parent and the infant.<sup>10</sup> In SSC, parents carry the infant in an upright position skin to skin on their chest, which improves parents’ mood and reduce stress and symptoms of postpartum depression.<sup>11,12</sup>

Neonatal research often aims to find new interventions to improve care for preterm infants and their families. However, conducting a randomised controlled trial (RCT) in the NICU is challenging in many ways, including recruiting participants. According to Williams *et al*, the most common reason for terminating clinical trials is insufficient accrual rate.<sup>13</sup> A review by McDonald *et al* showed that only 31% of the 114 included trials met their original recruitment goal.<sup>14</sup> In 34% of the trials, the sample size was reduced during the trial, in 11% recruitment was terminated before the formal end of enrolment and in 10% the inclusion criteria were changed as a way of improving recruitment.<sup>14</sup> To better understand the barriers impeding recruitment for patients with cancer, Stafford *et al* conducted interviews with recruiters.<sup>15</sup> Some of the barriers they found for insufficient accrual rate were delays in receiving multisite ethics and governance approval, physical relocation of one of the recruitment sites, timing of the study in relation to the participant's cancer journey and perceived burden of participation.<sup>15</sup> While an obvious problem can be that researchers specify inclusion criteria that are too restrictive or aim to include more tasks than the participant can handle, external circumstances out of the researchers' power to influence, are seldom discussed.

In 2018, we published a study protocol for an RCT with the aim to evaluate the effect of continuous SSC on sleep quality and mood in parents of preterm infants as well as the quality of parent–infant interaction and salivary cortisol concentrations at the time of discharge.<sup>16</sup> The hypothesis was that continuous SSC starting after the intensive care period would function as a restart for bonding and therefore improve the parents' mood, interaction behaviour and coregulation of salivary cortisol between parent and infant. Furthermore, it was hypothesised that the parents' possibility to take turns and assist each other with practical support during SSC would facilitate parents' sleep quality. The study started and opened for recruitment in January 2017 but due to low inclusion rate, the study was finally terminated in March 2020.

## AIM

The purpose of this paper was to describe barriers for inclusion of families in neonatal intensive care in an RCT aiming to evaluate the effects of continuous SSC on sleep quality and mood in parents of preterm infants, as well as the quality of parent–infant interaction and salivary cortisol concentrations at the time of discharge.

## METHODS

### Description of the terminated study

The protocol for the terminated two-arm (intervention and control) RCT is published.<sup>16</sup>

## Participants

Three out of seven tertiary university hospitals in Sweden providing care for extremely preterm infants were included. The settings were family-centred NICUs with single family rooms where the family can stay together with their infant around the clock when extensive intensive care is no longer required. The parents' presence at NICUs in Sweden are facilitated through the Swedish national insurance system, which allows both parents to share parental benefit for 480 days per child. In addition, both parents of an infant requiring care at an NICU are entitled to temporary parental benefit until the infant is discharged. This means that during the infant's entire NICU stay, both parents have the legal right to be together with their infant at the NICU. Moreover, hospital care in Sweden is free of charge for all children.

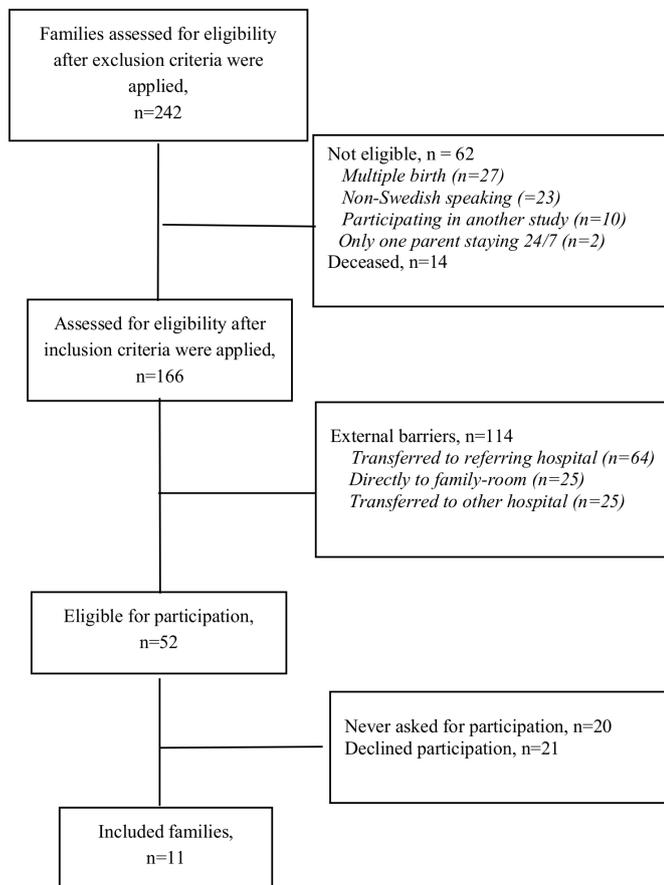
Inclusion criteria were parents (mother and father/partner) of single preterm infants born <30 weeks of gestation. The infant should have moved out from the open bay intensive care room and into a single family room where both parents could stay and care for their infant all hours of the day. Parents should be able to read and understand Swedish. Exclusion criteria were parents with sleeping disorders, psychiatric problems or drug abuse and infants with major congenital malformation, grade III–IV intraventricular haemorrhage or a chromosomal defect that could affect the infant's ability to interact. In agreement with a power calculation, the aim was to include 50 parents (=25 families). Based on previous numbers of admittance, it was estimated to take 1 year to recruit these families from the three different sites.

## Procedure

Research coordinators on each unit identified potential families and provided the parents with written and oral information about the study prior to moving to a family room. The families who accepted to participate were randomised to the intervention or control group before they moved into the family-room. In families assigned to the intervention, the infants should be cared for in continuous SSC on parents' chests, 24 hours a day, for four consecutive days, alternating between the parents. Families randomised to the control group were free to continue to practise intermittent SSC as much as they wanted since this was part of the standard care in the participating NICUs.<sup>17</sup> Outcome measurements included: parents' mood, sleep (actigraphy) and sleep quality, parent–infant interaction, and salivary cortisol reactivity, recovery and coregulation (for further information please see the study protocol).<sup>16</sup>

## Patient and public involvement

The protocol was pilot tested with two families before the study commenced. The families provided feedback on the study sequence and feasibility.<sup>16</sup>



**Figure 1** Flow chart of eligibility, barriers for inclusion and included families.

## RESULTS

A total of 242 families were assessed for eligibility whereof 11 were included (figure 1). The major barriers for inclusion in this study were external barriers (n=114). External barriers were related to (1) the lack of neonatal intensive care beds in Sweden at the time, causing medically stable infants to be transferred back to the referring hospital quicker than usual (n=64), (2) moving directly from the delivery room to a family room without the need for intensive care (n=25) or (3) moving from hospital to hospital across the country to increase availability of neonatal intensive care beds where needed (n=25).

Another identified barrier for enrolment was the inclusion criteria (n=62). Multiple birth was not included in this study because of the higher demands of practising continuous SSC with more than one infant (n=27). Non-Swedish-speaking parents were not included due to lack of validated translations of the included questionnaires (n=23).

Some families were never asked for participation despite eligibility (n=20). The reasons were that the research coordinators did not manage to approach the families in time because of a high patient volume, lack of staff, or a short admission time at the included NICU before moving to another hospital.

Twenty-one parents declined participation, reasons for declining were not recorded. Some efforts were made

to adjust the protocol in order to facilitate recruitment. Gestational age of inclusion criteria was changed from <30 weeks to <33 weeks to increase the number of potential candidates. The time in continuous SSC was decreased from four consecutive nights to 24 hours because some parents had expressed that four nights was a long time period for them to manage the intervention, or that they did not have the energy to comply to a study for several days. Moreover, in an attempt to ease the burden of participation, the documentation of sleep and time in SSC were simplified and the actigraph device was set on the ankle instead as some parents had complained over itching and difficulties to sleep when they wore the device around the waist. Despite these changes, there were no noticeable change in recruitment. In total, 11 families were included in the study before termination because of insufficient inclusion rate (figure 1).

## DISCUSSION

The overall reason for terminating this study was due to the external barrier of a lack of intensive care beds in the participating hospitals. In some countries, infants and their families may be transferred from one NICU to another during their hospitalisation either because of a lack of available beds or the need for another level of care. Transfer of infants who no longer require intensive care, from tertiary to non-tertiary NICUs is routine in Sweden today because extremely preterm infants are at less risk of mortality and morbidity if born in a tertiary hospital.<sup>18</sup> In times of high patient volume and lack of staff, there may be a need to identify which infants have least need for intensive care thus transferal from an intensive care room to a family room within the same NICU may be an option. Transferal between NICUs with the same level of care is more difficult to explain and often unpredictable for families as well as for researchers, increasing the risk for parental stress and problems with recruitment. Multiple transferals may lead to families receiving neonatal care in several NICUs across the country, making it difficult to comply to clinical intervention protocols especially if the intervention is a prospective single site study. For this purpose, it is important that non-tertiary NICUs also participate and fulfil clinical intervention protocols initiated at tertiary hospitals, which warrants more clinical researchers in these hospitals. However, transferals between same level NICUs are more an organisation issue partially due to lack of staff to meet a high patient volume.

Risks and benefits with transferal from a tertiary to a non-tertiary hospital has been discussed for years<sup>19</sup> and a meta-analysis comprising 12 articles of parents' experiences show that neonatal transfer can be scary and threatening but also a relief to be closer to home.<sup>20</sup> Less is known about parents' experiences of transferals between different NICUs with same level of care due to a lack of intensive care beds.

Having twins and language barriers were the most common reason for ineligibility for the terminated study.



Twins have a higher risk of being born preterm and needing neonatal care and constitutes a large proportion of NICU admissions.<sup>21</sup> However, to include families of twins in the terminated study was not feasible since the parents were supposed to assist and support each other by taking turns providing continuous SSC. Non-Swedish-speaking parents is a growing group and the use of translators and interpreters need to be considered in the future in order to be inclusive and increase generalisability.<sup>22</sup>

DeMauro *et al* suggest that strategies to reduce the burden of research participation in the NICU may facilitate participation. Furthermore, that low maternal education, larger families, site and public insurance affect attrition rate.<sup>23</sup> Due to ethical restrictions, we have no data on families who declined participation and can therefore only relate to the factor of public insurance. As public insurance applies to all families in Sweden it is not suggested to be a factor that explains attrition rate in the present study. Lack of demographic data also limits the possibility to compare parents who declined with parents who agreed to participate. However, the major problem with the terminated study was the inclusion rate. Even though a pilot test for feasibility was performed before the start of the study and efforts were made to ease the burden of participation, the inclusion rate remained low.

When and how to approach parents for consent can impact their decision. According to Korotchikova *et al*, a significantly higher number consent to participation in research if both parents are present when approached.<sup>24</sup> In the terminated study, parents were approached in connection to the move from the intensive care room to the single family room which might have provided some stress for the parents with a lot of changes happening at the same time. However, 114 families were never approached due to external barriers.

Being a parent to a premature infant in the NICU is an emotional experience extending for a long period of time. Couplet care and family-centred care is a relatively new phenomenon in neonatal intensive care after a history of separation between parents and preterm infants during admission to an NICU. This is appreciated by the parents but is also a demanding task and sometimes a stressful experience.<sup>12 25</sup> We did not ask the 21 families who declined participation about the reasons. It is possible that the stressful situation was a contributing factor since one third of parents refusing consent in another study of neonatal research did so because of tiredness and stress.<sup>24</sup> One objective with the terminated study was to evaluate if sleep quality was facilitated when the parents took turns and assisted each other with practical support during SSC. This is a dilemma where parents are potentially too exhausted to engage in research that potentially could be beneficial for their well-being. Parents' previous experiences of intermittent SSC could also have influenced the parents' choice in participating in the study. We did not collect data on parents' previous experiences or to what extent they had practised intermittent SSC since this is part of the standard care. Sweden has a long tradition of

practising intermittent SSC<sup>26</sup> and most of the extremely preterm infants experience their first intermittent SSC session within the first week of life.<sup>17</sup>

The issues raised in this paper are important to consider when planning an experimental study in an NICU in Sweden and other countries that share similar characterisation of the public health system. In different hospital structures, there might be other internal or external factors hindering consent.<sup>14 15</sup> However, studies within an NICU context are few and focus on withdrawal and attrition rather than barriers for inclusion,<sup>23 27</sup> which warrant more research within this field.

## CONCLUSIONS

The major reason why some participants were not included was due to the external barrier constituted by transfers between NICUs. This is a multifactorial issue related to organisational structures. Still, an important issue for researchers to consider when planning prospective intervention studies within an NICU setting. Drawn from the results of this study, our advises for future trials comprise of: performing multicentred studies including several tertiary NICUs, including researchers from non-tertiary hospitals, considering if it is possible to include families with multiple birth, increasing the use of interpreters in order to be inclusive of all families, and including parents in the study design. A negative outcome related to the termination of this study is that we still do not know if continuous SSC starting after the intensive care period would function as a restart for bonding and therefore improve the parents' mood, sleep quality, interaction behaviour and coregulation of salivary cortisol between parent and infant.

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