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How do parents perceive their infant's participation in randomized control trials?

**How do parents perceive their infant's participation in randomized controlled trials?**

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## ABSTRACT

**Objective:** To explore parents' perceptions of their infant's participation in a randomized control trial (RCT) and the implications of the RCT for their infant and them. **Design:** A qualitative study using semi-structured interviews. **Setting:** Participants were identified from neonatal intensive care unit (NICU) clinical registers and from responses to an advertisement put on the website of UK special care baby charity, BLISS. Interviews were conducted with parents face-to-face in their homes or over the telephone. **Participants:** Sixteen parents of 12 infants born prematurely or with complications at full term and who had participated in 1 of 3 RCTs while receiving intensive care in 1 of 7 NICUs. **Methods:** Interviews were audio-taped or digitally recorded, transcribed verbatim, and analyzed using systematic thematic analysis using WinMax qualitative software. **Results:** Five main themes emerged from the data. The themes were (a) parents' immediate reactions to being approached about RCT enrollment, (b) interactions between parents and clinicians upon the approach of enrollment and during the RCT, (c) making the decision to enroll their infant, (d) implications of the RCT for parents, and (e) effects of the RCT on the infant. **Conclusions:** Clinicians should be encouraged to approach parents about enrollment of their infants in clinical research given that parents reported mostly positive experiences of their infant's participation in a RCT. However, appropriate measures should be taken to ensure that the individual needs of parents are being met throughout the entire research process from enrollment to follow-up.

*Keywords:* parents, perceptions, infants, participation, randomized controlled trials

## CALLOUTS

**Callout 1** – The literature surrounding neonatal clinical trials needs to capture how parents, including those whose infants have died, experience their newborn infant’s participation in research.

**Callout 2** – Parents whose infants had survived and parents whose infants had died evaluated their infant’s participation in a randomised controlled trial as a positive experience.

**Callout 3** - Multiple factors such as the nature of the randomized controlled trial and their infant’s condition affected parents’ experiences of their infant participating in research.

## INTRODUCTION

Advances in the treatment and outcome of sick newborns usually depend on high quality and well-designed neonatal clinical research (Glantz, 1996). Randomized controlled trials (RCTs) are the accepted 'gold standard' for evaluating the efficacy of treatment strategies, and play an important role in ensuring neonatal practice is evidence-based (Silverman, 1994). At the same time, the birth of a premature or ill newborn is traumatic for parents (Doering, Moser, & Dracup, 2000; Padden & Glenn, 1997). In the case of neonatal research, parents are asked to make important decisions and consent to sometimes highly complex procedures for their newborn infant that may have implications for their infant's health and possibly survival. Trial participation may provide newborn infants with access to the latest medical technology, treatment, and increased contact with healthcare professionals. However, the research design of RCTs also means that parents have no control over whether their infant is allocated to standard care or the treatment arm.

Little is known about how parents experience and make sense of their infant's participation in RCTs. Most published studies have focused on either the consent process (Ballard, Shook, Desai, & Anand, 2004; Burgess, Singhal, Amin, McMillan, & Devrome, 2003; Culbert & Davis, 2005; Mason & Allmark, 2000; Stenson, Becher, & McIntosh, 2004), factors that influence parents' decisions about participating in research (Hoehn et al., 2005; Gammelgard, Knudsen, & Bisgaard, 2006; Zupancic, Gillie, Streiner, Watts, & Schmidt, 1997), or how these decisions are made (Jollye, 2009; Snowdon, Elbourne, & Garcia, 2005). Evidence suggests that neonatologists, midwives and nurses are concerned about the quality of consent in the neonatal setting (Garcia, Elbourne, & Snowdon, 2004; Snowdon, Elbourne, & Garcia, 2004a, 2004b, 2004c). In addition, the consent process has been described as an 'elaborate ritual' (Mason, 1997), perhaps explaining the predominance of studies looking at this specific issue. Greater insight into how parents experience their infant's participation in neonatal research is important if we are to provide them with appropriate support throughout the research process. In addition, previous research in this area has excluded parents' perceptions about research participation when their infants have died.

The Stillbirth and Neonatal Death Society (SANDS) emphasize the importance of also giving parents whose infants have died the opportunity to describe their experiences of their infant's participation in neonatal clinical trials. Stenson et al. (2004) found that parents whose infants died reported high satisfaction with their infant's involvement in a pulmonary function testing trial. It is therefore also important to obtain parents' views of other aspects of their infant's participation in RCTs.

The purpose of this study was to explore the experiences in a neonatal RCT of both parents whose infants have lived and whose infants have died. In particular, we examined parents' thoughts and feelings when approached about enrollment, during and after the RCT, and the implications of their infant's participation for both them and their baby.

## METHOD

### Design

Semi-structured interviews were conducted with parents whose preterm infants or infants born with complications at full term had participated in a RCT in one of seven different neonatal intensive care units (NICU) in the south of the UK. Parents were identified from NICU clinical registers and responses to an advertisement put on the website of UK special care baby charity BLISS - for babies born too soon, too small, too sick.

### Participants

Sixteen White European parents (10 mothers,  $M_{age} = 31$ , age range: 27-36 years, six fathers, 48  $M_{age} = 32$ , age range: 27-36 years) of 12 infants (eight female, four male, 10 surviving, two deceased) participated in the study. The inclusion criteria for this study included parents could read and speak English fluently, and parents' infants had participated in a RCT in the previous 18

months while receiving intensive care in the NICU. Eleven of the parents who participated were recruited through responses to the website advertisement. Initially, the parents of 17 surviving infants and nine infants who died were identified from NICU clinical registers as eligible to take part in the study. Five parents of three of these infants participated in the study. The remaining parents identified from NICU clinical registers either declined to take part or did not respond to the invitation to participate in the study.

Eight parents were married, six were cohabiting and two were separated. The infants of two parents (one mother, one father) had died while in the NICU. Regarding educational attainment, all mothers and three fathers completed further or higher education, two fathers completed secondary school education, and one father left school at 15 without any qualifications. One mother and one father held managerial or senior official positions, seven mothers and one father held associate professional and technical occupations, two fathers held skilled trades occupations, one father held an elementary occupation, and one father was unemployed. Two mothers were full-time stay at home mothers. Four mothers were health care professionals (nurses) and one father held a managerial position in the National Health Service. The length of time infants spent in the NICU ranged from less than one week to more than 15 weeks. Five infants had participated in the International Neonatal Immunotherapy Study (INIS) which aimed to evaluate the use of non-specific intravenous immunoglobulin (IVIG) in addition to antibiotics in babies with suspected or proven sepsis, two in Neonatal ventilation with INhaled Nitric Oxide versus Ventilatory support withOut inhaled nitric oxide for severe respiratory failure (INNOVO), and five in Whole Body Hypothermia for the Treatment of Perinatal Asphyxial Encephalopathy (TOBY). Parents whose infants participated in the TOBY trial were informed at the outset of their infant's participation which arm their infant had been allocated to. Consent for enrolment of infants into all the RCTs was obtained in person in NICUs. Parents in the current study were asked within six hours of birth for consent for enrollment into the TOBY trial and within a month for INIS and 28 days for INNOVO. Most parents whose infants took part in INIS or INNOVO did not provide or could not recall the specific number of days after the birth of their infant that they were approached about enrollment of their infant into a RCT.

### Procedure

Ethical approval for the study was obtained from UK National Health Service and University

research ethics committees. Eligible participants were mailed a letter of invitation, an information sheet, a consent form and a contact information reply slip. Participants were informed in the letter of invitation and the information sheet the purpose of the study, what it entailed, the risks and benefits of participation, withdrawal procedures, and funding of the research. The contact details of the researcher were provided for participants in case they had questions about the research before consenting to take part. Participants were asked to complete and return the consent form and contact reply slip if they wanted to participate in the study. Following written informed consent, participants were subsequently telephoned by the researcher and an appointment for interview was arranged. The time between when infants participated in the RCT and parents participated in the current study ranged from two weeks to 18 months. Semi-structured interviews of up to 45 minutes duration were conducted with parents face-to-face in their home (n = 8) or over the telephone (n = 8) by a trained research psychologist (KC).

Demographic information including infant gestational age, corrected age, name of NICU, length of time in NICU, name of RCT, parent age, marital status, living situation, educational attainment, occupation, and ethnicity was gathered at the outset of the appointment prior to the interview. Parents who were married or cohabiting and who were both taking part in the study (n = 8) were interviewed separately to ensure they gave their own views and were not influenced by their partner being present. Likewise, married or cohabiting parents whose partners were not taking part in the study were also interviewed in the absence of their partner (n = 6). An interview schedule comprising six key questions divided into five subsections was used to conduct the interviews. Open-ended and broad questions were used to provide parents with the opportunity to raise issues and express their thoughts and feelings freely about their infant's participation in a RCT. The questions were designed in line with the aims of the study. For example, the first question tapped into parents' **thoughts and feelings when approached about enrolling their infant in an RCT**: *"Could you start by telling me what you thought when you were asked to take part in the study?"* All interviews were audio-taped or digitally recorded and transcribed verbatim.

### **Data analysis**

The data were analyzed using an inductive (data-driven) approach to systematic thematic analysis to identify main themes (Boyatzis, 1998) using WinMax qualitative software. Using an inductive approach to thematic analysis meant that data-driven codes were constructed from the raw information. First, transcripts were read by a researcher (KC) to familiarize herself with the data. Second, a sub-sample of transcripts was selected and used as a basis to develop the coding schedule. The raw information from these transcripts was coded for all possible themes. Codes were then examined by two researchers (KC & SA), subcategorized and refined to agree a coding schedule. As a result of this coding process, five main themes were identified. In the coding schedule, each theme was given a label (name), a description or definition, indicators of how to identify the theme, a description of any qualifications and exclusions to the identification of the theme, and examples of the theme. All interview transcripts were then reread, analyzed and coded using this coding schedule.

## RESULTS

Five main themes were identified from the data: (a) parents' immediate reactions to being approached about RCT enrollment, (b) interactions between parents and clinicians upon the approach of enrollment and during the RCT, (c) making the decision to enroll their infant, (d) implications of the RCT for parents, and (e) effects of the RCT on the infant. These themes are described in more detail and illustrated with quotes from participants. Quotes are coded according to the interview number, whether the parent was a mother or father, the RCT and whether the infant died or survived.

### **Parents' immediate reactions to being approached about RCT enrollment**

Parents' immediate responses when approached about enrolling their infant into a RCT were mixed, with some parents being shocked and anxious about enrollment, and others being less concerned due to their medical background or because of everything else happening at that time. Every parent reported being emotionally overwhelmed and struggling to get their head around the situation of having a sick infant. Many parents recognized that their distress and worry about both the infant and mother's recovery meant they could not think straight under the circumstances which made it difficult for them to take on board the RCT. One mother whose infant survived and participated in the TOBY trial stated: *"I was still dealing with the fact that they told me that he was brain damaged. I was still not particularly able to comprehend myself because I wasn't too well...."* Parents reported being confused and finding it difficult initially to understand what the clinician was asking them to do and what the RCT involved. In particular, for parents without a medical background, being in a specialized environment and not having limited medical knowledge made the RCT hard to understand. Most mothers also described how they were recovering from traumatic births.

*Initially it's sort of hard to take in, to think about it because he was so ill. Obviously your primary concern is with him and how he's doing and also sort of the distress and that sort of the emotions that are going on at the time. It's hard to take in. (Interview 5: Father: INIS: Survived)*

Parents who were initially against their infant's participation said they were worried about the uncertainty of the consequences of participation for their infant. The mother of an infant who died did not want her infant to be interfered with any further and explained: *"I mean at the beginning I was a bit against it because I was thinking does this mean you know if it means it's going to be extra manipulation..."*

Other mothers had thoughts and images running through their head of their infant being tested on as if a "guinea-pig", or of the media later on reporting research studies that went wrong. *I suppose you know very quickly thoughts go through your head of you're not experimenting on my son. He's not a guinea-pig. He's too small. He's already battling hard you know. What if it goes wrong? (Interview 15: Mother: INIS: Survived)*

Parents who were less anxious about their infant's participation were either from a medical background so had knowledge of clinical trials and research in general, or thought the RCT was of little significance given the intensive care their infant had already received and was receiving at the time they were approached about enrollment of their infant into the RCT.



*I think maybe because I'm a nurse and I've done all my research stuff and a lot of our nursing is evidence based that it wasn't a problem. (Interview 1: Mother: INIS: Survived)*

### **Interactions between parents and clinicians upon the approach of enrollment and during the RCT**

Most parents did not think it was inappropriate that they were asked to enroll their infant in the RCT. They appreciated the uneasiness clinicians experience in approaching parents and that there is never going to be a right time to ask parents of sick infants. Parents who thought that the clinician came across as confident reported that it made them feel more comfortable and reassured about enrolling their infant into a trial. In addition, one mother explained that by coming across as hesitant, the clinicians' approach caused more anxiety than the trial itself.

*The fact that it was kind of like so "Oh you don't have to but oh you know". I could feel there was a little bit of tension about asking, you know, if the baby, if it was ok to do the research on our baby; and in a way the tension created the problem more than the actual procedure which is carried out. (Interview 3: Mother: TOBY: Died)*

One father thought parents should be approached sooner rather than later to optimize their Infant's chance of survival. Some parents suggested that if information about the RCT and indeed other perinatal and neonatal research were given earlier – perhaps prenatally or on admission to hospital – it might give them more time to consider the information and better understand the purpose and procedure of the RCT and research being conducted more generally in the NICU.

Overall, parents expressed gratification for being given the option of participating. The "loss of parental role" and helplessness experienced by parents in the NICU was seen as an important reason for giving parents responsibility to decide about participation. Parents were mostly satisfied with the clinician's approach, with many saying the information was communicated in a clear, sensitive, and empathetic manner, and that adequate information was provided.

*I was glad that they had asked because I knew it was probably his only chance of survival because of the level of intensive care that he was being given once he got there and so I'll you know just having the chance of him surviving, I was grateful. (Interview 11: Mother: TOBY: Survived)*

*They were very good actually. They were very kind of empathetic, if that's the right word, about the whole situation, kind of very aware that they were putting added stress on us when we've already got enough things to think about. (Interview 16: Mother: INNOVO: Survived)*

*The doctor who actually came to spoke to us initially, his whole approach to it was you know excellent. We didn't feel pressurized at all. We felt like we had lots of information and I think for other parents who take part that's a really important thing. You know it's a difficult time. They obviously want to have babies recruited into trials but they need to make sure that they're not pressurizing people and make sure that they get the right information which in our experience was a positive one. (Interview 14: Mother: TOBY: Survived)*

A few mothers were not satisfied initially with the way in which they were approached by the clinician. One mother thought the clinician was insensitive and lacked essential communication skills. Some mothers had been approached about the RCT and were subsequently transferred to another hospital to where their infant had been born. Two of these mothers said that when approached they felt their newborn would be transferred to another hospital for the sole reason of the RCT and benefit to the clinicians, rather than putting their baby's welfare first. However, none of the parents thought they were coerced into making a decision and consenting. Most parents felt reassured by the clinician, were comfortable asking the clinician questions and were content with responses given.

### **Making the decision to enroll their infant**

Parents talked about the importance of having time to think and discuss the RCT with their partner/spouse, and of having their concerns and questions answered by the clinician. This was especially important to those who were initially apprehensive. Once parents had spoken with their partner and/or had their questions answered about the study, they reported being comfortable with enrolling their infant into the trial and that the initial anxiety they experienced about enrollment reduced. Decisions were made jointly by parents. Some parents relied on their partner to read the information provided about the RCT and to explain it to them or vice versa. This is because they found it difficult to understand the purpose of the RCT and what it involved due to being distressed with everything else that was happening to them and their infant at the time and a traumatic birth. Parents considered the benefits and risks of the RCT, but tended to focus their attention on the benefits. One father said: *"We both agreed the positives outweighed the negatives."* Some parents valued the advice of clinicians when making the decision, with one mother asking the clinician what he would do if in the same situation.

*We didn't have a clue what it was about at first so we said to the doctor you know "if your child was in the same situation would you put yours in there? Would you do it?" So we did put him in the end. (Interview 4: Mother: TOBY: Survived)*

Parents decided to enroll their newborn infant for a variety of reasons. First, they thought the RCT would either benefit their infant or do nothing (i.e., it would not make any difference to their infant's condition). One parent stated: *"In the end it just came down to, if he doesn't go on this trial he's going to be the same. If he does go on this trial then maybe it will help him."* Another parent reported: *She was so poorly and they'd tried so many different things, so many different antibiotics and things weren't working that basically putting her on a trial was either gonna benefit her or it wasn't going to do anything. (Interview 6: Mother: INIS: Survived)*

Second, they believed it would benefit and help future infants and their families. *So if it's going to help other babies in the future, they can find a way of helping premature babies get stronger and get off the incubators quicker we just thought that would be a good thing to take part in. (Interview 8: Father: TOBY: Died)*

Third, parents perceived no or few risks and did not think the RCT would harm their infant. One mother of a surviving infant who participated in INIS said: *"It couldn't do her any harm"*.

Most parents feared the death of their infant, described themselves as *"clutching at straws"*, and were willing to do whatever they could to help their infant, particularly if other treatments did not

seem to be working. One father described: “*They said to me was “he’s definitely got brain damage, it may or may not help” and I remember distinctly saying “whatever it takes”.*” When parents reflected back on the whole research experience, none of them regretted their decision to enrol their infant in the RCT and many cited they would make the same decision again.

### **Implications of the RCT for parents**

Although parents who knew their infant had been allocated to the control arm were disappointed, they understood the reasons behind randomization and were pleased that their infant could help future babies. Some of these parents also thought that although their infant was not allocated to the control arm, it afforded them access to better medical care and technology in a different hospital to where their infant was born. Parents of surviving infants who were unaware of whether their baby had been allocated to the treatment or control arm did not think the RCT significantly affected them during the RCT. These parents said they forgot about the trial once consent had been given because they were preoccupied with the welfare of their infant.

*It didn’t have any impact on me I don’t think. It was just kind of because it wasn’t directly, you couldn’t see it helping her or not helping her.....I think there was just so much else going on at the time that, like I said, I didn’t really give it much thought and I’m sure half the time I forgot about the trial. (Interview 16: Mother: INNOVO: Survived)*

Parents reported that the one 285 time they did give thought to the RCT was when their infant’s health deteriorated or once their baby was discharged from NICU. In these instances, parents wondered whether the RCT might be helping or had helped their infant. Stress experienced by parents while their infant was in the NICU was described as caused by the situation of having a sick infant in the NICU, rather than the RCT per se.

*We were devastated. Not because he was on the trial though, because of the way he was; plus he was always asleep which wasn’t very nice. But I think the whole experience has left a scar on us, but I wouldn’t say it was the trial particularly, it was what he went through. (Interview 4: Mother: TOBY: Survived)*

Some of these parents reported that although they did not think their infant’s participation had any consequences for them, the consequences for future infants and families would be considerable. In contrast, parents whose infants survived and who knew their infants had been allocated to the treatment arm of the TOBY trial described how their levels of anxiety significantly increased whilst the treatment was administered.

*It was much harder during those days. All those times he was on the mat and he didn’t show any signs of improvement, so you’ve basically got to sit there with your baby for three days thinking “he could, he could die at any time” really and it just lasts until he gets warmed up so it is quite a hard time. (Interview 5: Father: TOBY: Survived)*

Parents whose infants died and participated in the TOBY trial believed the extra monitoring of an electroencephalogram (EEG) or Magnetic Resonance Imaging (MRI) scan identified the extent of their infant’s brain damage which enabled them to make the decision to stop life support, prevented them from clinging on to false hope, and allowed them to grieve.

*They did an MRI and I think they did it so early on because she was part of the study... in our case it was fairly determinant really because I think we kind of in a way, you know - once the damage was shown to be like that bad we had to take a decision on, you know, how we wanted to.... I feel grateful, you know, because I feel that it kind of showed [the extent of brain damage] earlier that maybe that, if we hadn't been part of the study, it would have taken ages and we have been building lots of hope, you know, that she was going to be fine... so in this case I feel, you know, fairly positive. (Interview 3: Mother: TOBY: Died)*

*I think well it kind of at least when we had to make decisions I mean when we were at the [NICU], they were kind of like well "What do you want to do?" you know "We can keep her on life support for quite a while" and we were like "Well, there's no point. We know the outcome. We know what needs to be done." and it kind of made the process a lot easier because you, your mind's so distorted. (Interview 8: Father: TOBY: Died)*

### **Effects of the RCT on the infant**

Every parent expressed their satisfaction with the quality of intensive care their infant was given in the NICU and during the RCT. Parents thought that while their infant was enrolled in the RCT, their infant received either the same care, more care or better care compared to infants not enrolled in the trial. Parents who thought that their infant received more care while enrolled in the RCT noted additional monitoring of their infant including extra observations and tests.

*I think he probably would have received more care being on the cooling arm [pauses]. The only reason I say that is because of the side-effects of being cooled is that it slows down his breathing rate and heart rate and his blood pressure for three days...so he probably has to have more care than he would normally. (Interview 5: Father: TOBY: Survived)*

Parents who believed their infant received better care while enrolled in the RCT, particularly mothers of infants transferred to other hospitals, thought participation in the trial afforded their infant access to the latest medical technology and better equipped NICUs. Supplementary follow up assessments following discharge from hospital were also perceived as beneficial to their infant.

*Had he not been part of the trial, he would have stayed at our local hospital and if he had stayed there I, despite the care they offer, I don't think he it would have been the same and I don't think he would have survived... they have more techniques, more equipment. It was a new unit so they had a lot more they could offer [infant] in terms of intensive care.*

Parents of surviving infants, except those who knew their infant had been allocated to the control arm, were confident that their infant's condition improved immediately after participating in the trial. Some parents who were blind to randomization believed their infant had been assigned to the treatment arm because of subsequent marked improvements to their health in the short-term and long-term.

*I don't know what she had, but I feel that she actually had the immunoglobulin because the following day she was better or getting better so for us it was really positive... it's*

*weird that she had, she went on the INIS trial and she was so so poorly and then the next day was improving, getting better so it suggests that she didn't have the placebo. (Interview 6: Mother: INIS: Survived)*

*I really strongly believe that um [our baby] actually had the nitric and this [other] little boy... he had so many respiratory problems um he was in hospital for, I think he came home a day before his first birthday um and is still having problems. [Our baby] just seemed to do so well and I mean she's got a little bit of asthma now and had a little bit of oxygen when she first came home but in comparison, considering she was sicker when she was born than he was, yeah, I think it's had good effects. I'd be surprised if she didn't actually have it. (Interview 16: Mother: INNOVO: Survived)*

Many parents believed the survival of their infant was attributable to the trial. Parents of deceased infants did not usually think the trial benefited their baby and believed that even if randomized to the treatment arm, the extent of their infant's ill-health was too severe for the RCT to make a difference.

*I don't think it would have made any difference. I mean [baby] was severely brain damaged. I mean actually when we got to the [NICU] and they did an EEG she had zero brain function anyway. So to be honest I don't think it would have made any difference what arm she would have been in after that because I don't think there was anything there to, to save um so for us it, it didn't really make any difference at all. (Interview 8: Father: TOBY: Died)*

Parents of both surviving and deceased infants described participating in the RCT as a positive experience when they reflected back on the event as an entirety.

## **DISCUSSION**

This is one of the first studies to qualitatively examine the experiences of parents of surviving and deceased infants of the whole process of participating in a trial from the moment of invitation until trial completion. The findings of this study illustrate that parents perceive the effects of clinical trials on their infant and themselves differently according to a number of different factors including the nature of the trial, randomisation, the severity of the infant's illness, and the survival or death of their infant. However, overall parents found the experience of the trial to be positive. Many parents of surviving infants believed that participation immediately benefited their infant and played an important role in their infant's survival. The finding that parents perceived long-term benefits for their infant's health is broadly consistent with previous research. In a study by Hoehn et al. (2005), parents of infants having cardiothoracic surgery revealed that parents perceived the extra monitoring of an EEG as a clear and immediate benefit for their neonate. Similar findings were reported in parents interviewed after allowing their infant into the TOBY trial (Allmark & Mason, 2006). It has been recognised that sick newborn infants may actually benefit from participation in a RCT based on evidence that that the placebo group had a better outcome than the eligible but non-randomised group (Lantos, 1999). However, the question of why the "inclusion benefit" phenomenon exists is yet to be answered. In contrast, bereaved parents did not think participation made a difference to their newborn or was able to alter their infant's outcome for the better. Instead, these parents believed the RCT discursively shortened their infant's life due to the extra EEG or MRI scan,

which determined brain damage severity. For these bereaved parents the extra EEG or MRI scan served an important purpose as it enabled them to come to terms with their infant's death sooner and prevented them from feeling false hope. Also, a small number of parents of surviving babies, particularly those who knew their infant had been allocated to the control arm of the TOBY trial, did not perceive the clinical trial to have any effects on their infant.

The current findings demonstrated that parents thought their infant received the same, additional or better care than the standard level of intensive care when their infant was enrolled in the RCT. Parents across all three RCTs cited that their newborn infant had access to the latest medical technology, a better NICU as well as more observations and tests. Such findings are reflected within the neonatal and pediatric clinical research literature (Morley, Lau, Davis, & Morse, 2005; Stenson et al., 2004).

Parents often cite the possibility of personal benefit to their infant as a reason for deciding to enroll their newborn infant in research (Allmark & Mason, 2006; Ballard et al., 2004; Hoehn et al., 2005), which is consistent with our findings. Most parents in the current study did not associate participation with risks or harm to their infant. Instead, they thought the trial would either be beneficial or make no difference to their infant. As one might expect for an individual in stressful circumstances, these findings suggest that parents tend to focus on the potential good and ignore the bad. The majority of parents of infants who took part in the NEOPAIN study decided to join the study in the hope of helping their baby, but fewer than half expressed fears (Ballard et al., 2004). Thus, it appears that parents were unaware of the risks and demonstrates parents' potential vulnerability when being asked to enroll their newborn into a RCT. Furthermore, a survey of 72 parents of newborns in the NICU who were presented with hypothetical research scenarios, illustrated that although parents were more likely to enroll their newborn in a study involving moderate risk and possible major direct benefit, a third were willing to consent to research with moderate risk and no direct benefit (Singhal, Oberle, Burgess, & Huber-Okraimec, 2002).

Altruism was one of the most frequently reported reasons for consenting to a RCT and that participation would hopefully help infants, their families, and also researchers in the future even if it did not help their own infant. Qualitative research and questionnaire studies also indicate that altruism is a reason for including newborn infants in RCTs (Hoehn et al., 2005; Mason & Allmark, 2000; Morley et al., 2005; Zupancic et al., 1997). However, findings from the TOBY trial found only a minority of parents thought their giving consent was influenced by a desire to contribute to future knowledge (Allmark & Mason, 2006).

High consent rates are obtained for trials in many NICUs, as 96% of neonatal trials reported total acceptance (Campbell, Surry, & Royle, 1998). Parents of critically ill infants may be more willing to agree to any additional treatment that could possibly save their baby's life. The findings of the present study reflect this. Most parents talked about enrolling their infant because of the severity of their baby's sickness, the uncertainty of survival and thus their willingness to try anything to help. Levene, Wright and Griffiths (1996) showed that the poorer the infant's outcome, the more likely parents are to consent; and that parents were more likely to consent to a trial when their infant was critically ill soon after birth than a week later. This study and past research suggest that the majority of parents will consent to RCTs if their infant is critically ill at birth or shortly afterwards, perhaps as a way to try to save their infant. However, these studies

also highlight again the desperation of parents of sick newborns and their vulnerability.

The birth of a premature or critically ill infant can result in debilitating parental responses (Doering, Moser, & Dracup, 2000), and as a result, parents often have difficulty comprehending what is happening (Allmark & Mason, 2006; Nicklin & Spencer, 2004). The findings of the present study reflected this. Parents were emotionally overwhelmed and expressed difficulty in fully comprehending what they were being asked to do when the RCT was initially mentioned to them. Jollye (2009) found that parents were unable to understand the situation they were in for up to a week. In light of this, perhaps concerns expressed in previous publications about the capacity of parents to make rational decisions and thus give fully informed consent (Ballard et al., 2003; Manning, 2000) need to be readdressed. Despite suggestions to waive consent in scenarios such as neonatal research (Truog, Robinson, Randolph, & Morris, 1999), the literature illustrates that most parents think they should be asked to give consent and be involved in making the decision to enroll an infant into a study (Burgess et al., 2003; Mason & Allmark, 2000; Morley et al., 2005). In our study, parents thought they should be approached about RCTS and make the decision to enroll their infant in research, particularly as most other aspects of the parenting role and the responsibilities had been taken away from them. Recent research has indicated the process of continuous consent may help gain valid informed consent and help parents to understand clinical trials better during an emotive period of time (Allmark & Mason, 2006). Such a method may provide parents with more information and increase the sense of control a parent feels, which may help parents, fathers in particular, to cope (Arockiasamy, Holsti, & Albersheim, 2008).

Parents expressed understanding of the difficulty of approaching parents about RCTs and most were not upset, but appreciative of being given the opportunity to enroll their infant in research. Some mothers stated a preference for a confident approach, which aided them to place their trust in the clinician and the trial. A qualitative study by Jollye (2009) found that the more confident the researcher was in their approach, the happier the parents were to enroll their infant. Furthermore, parents considered the best approach of the clinician to be polite and proficient. In the current study most, but not all, parents also expressed satisfaction with the proficient and empathetic approach of the clinician and the way in which information was conveyed. In agreement with previous literature exploring parents' perspectives of neonatal research (Ballard et al., 2004; Hoehn et al., 2005), parents did not feel pressured to take part in the RCT and knew they had the right to decline enrollment.

### **Limitations**

A number of limitations should be borne in mind in review of the results and their interpretation. First, given the gap in the literature on parents whose infants have died, this study aimed to explore the perceptions of RCTs of both parents whose infants had lived and whose infants had died. Although the two parents whose infants had died were parents of different infants and the infants had been in different NICUs, the small sample size of parents whose infants died reduced the potential to achieve saturation with emerging themes in relation to this important group of parents that so often get excluded from studies. In addition, the infants who died had participated in the same RCT and as demonstrated by the results of this study, the nature of a RCT may affect how parents perceive their experiences of their deceased infant's participation in a RCT. Second, to optimize recruitment of participants into the current study, the design of the study allowed for variations in the time that passed between the parental interview

in the current study and the infants' participation in the RCTs. Parental responses may have been affected by the time lag between actual participation in the RCT and the interview because parents' interpretations of the experience may have been altered by the infant's subsequent course and by later experiences in neonatal intensive care. Despite these limitations, the study did include both mothers and fathers and was able to capture both mothers' and fathers' perceptions of their infant's participation in a RCT.

### **Implications for current practice**

Clinicians and trial recruiters should be encouraged to approach parents of infants in the NICU who fit research protocol criteria because parents in the current study were supportive of neonatal research, were appreciative of being given the opportunity to participate in the RCT and viewed their own experiences in a positive light. Due to the vulnerability of parents and given that not all parents were satisfied with the manner in which clinicians approached them about the RCT, appropriate measures should be taken to ensure that parents are approached in a confident but empathetic manner, and that parents fully understand the purpose of the study, the randomization process, the medical procedures involved and importantly the risks of the trial given that parents tend to focus on the benefits in desperate circumstances. Importantly, such measures should be applied consistently across different neonatal settings and by different clinicians.

Many parents forgot about the trial following consent and were not always aware of what was happening in terms of the RCT. This may indicate the need for clinician-parent communication to continue beyond the consent process throughout the trial and during follow-up so that parents are aware of what is happening throughout the entire research process and have continued support that is tailored to their individual needs. This is important as the results of the current study demonstrate that several factors affect parents' experiences of their infant's participation in research and that these factors affect parents in different ways.

A father of a deceased baby suggested the need for communication following the point of consent. Previous research suggests that parents are unsure about clinical trial follow-up procedures (Chappuy et al., 2006; Jollye, 2009). Neonatal intensive care units conducting research may benefit from making it standard practice to provide parents with feedback forms to fill in as well as routinely asking parents at the last follow-up about their experiences of participation in the RCT. This would afford parents the opportunity to voice concerns or equally express satisfaction with the way in which RCTs are conducted. Data generated from parental feedback would be a useful means to routinely evaluate whether or not the individual needs of parents who enroll their infant into neonatal research are being met.

### **Conclusions**

Overall, both parents whose infants survived and whose infants died were supportive of neonatal research and were pleased with their decision to enroll their newborn in the RCT. Parents appeared to appreciate being approached about research and that studies need to be performed to improve the care and outcome of sick premature and/or sick newborns. Parents interpret their experiences differently according to the nature of the RCT, randomization, the severity of the newborn's illness and whether or not their newborn survived or died. Further research exploring associations between these factors and parents' experiences of their



newborn's participation in neonatal research are warranted.

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**Table 1. Demographic characteristics of the parents**

|   | <b>Mother<br/>(n = 10)</b> | <b>Father<br/>(n = 6)</b> |
|---|----------------------------|---------------------------|
| <b>Age</b> (mean, SD)   | 31 (3)                     | 32 (3)                    |
| <b>Marital status</b>   |                            |                           |
| Married   | 6 (60%)                    | 2 (33%)                   |
| Separated   | 1 (10%)                    | 1 (17%)                   |
| Cohabiting  | 3 (30%)                    | 3 (50%)                   |
| <b>Ethnicity</b>  |                            |                           |
| White British   | 9 (90%)                    | 6 (100%)                  |
| White Other Background  | 1 (10%)                    | 0 (0%)                    |
| <b>Highest level of education</b>   |                            |                           |
| Secondary school (15 or under)  | 0 (0%)                     | 1 (17%)                   |
| Secondary school (16 or under)  | 0 (0%)                     | 2 (33%)                   |
| Secondary school/further education (18 or under)                          | 0 (0%)                     | 1 (17%)                   |
| Further education/higher education (18+ certificate/diploma/first degree) | 1 (10%)                    | 2 (33%)                   |
| <b>Occupation</b>   |                            |                           |
| Managers and senior officials   | 1 (10%)                    | 1 (17%)                   |
| Associate professional and technical occupations                          | 7 (70%)                    | 1 (17%)                   |
| Skilled trades occupations  | 0 (0%)                     | 2 (33%)                   |
| Elementary occupations  | 0 (0%)                     | 1 (17%)                   |
| Home duties   | 2 (20%)                    | 0 (0%)                    |
| Not known, unemployed   | 0 (0%)                     | 1 (17%)                   |
| <b>Length of time infant in NICU</b>                                      |                            |                           |
| ≤ 1 week  | 0 (0%)                     | 1 (17%)                   |
| 1-2 weeks   | 2 (20%)                    | 1 (17%)                   |
| 3-6 weeks   | 3 (30%)                    | 0 (0%)                    |
| 7-10 weeks  | 0 (0%)                     | 0 (0%)                    |
| 11-14 weeks   | 4 (40%)                    | 3 (50%)                   |
| ≥ 15 weeks  | 1 (10%)                    | 2 (17%)                   |
| <b>Neonatal RCT infant participated in</b>                                |                            |                           |
| INIS  | 3 (30%)                    | 3 (50%)                   |
| TOBY  | 5 (50%)                    | 2 (33%)                   |
| INNOVO  | 2 (20%)                    | 1 (17%)                   |
| <b>Infant outcome</b>   |                            |                           |
| Survived  | 9 (90%)                    | 5 (83%)                   |
| Died  | 1 (10%)                    | 1 (17%)                   |