

**Title: Parental experiences of being approached to join multiple neonatal clinical trials: a qualitative study (PARENT)**

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## **Abstract [278 words]**

### **Objective**

To explore parents' perceptions and experience of being approached for enrolment of their preterm infant in more than one trial or study.

### **Design**

A qualitative study involving 17 in-depth semi-structured interviews, with parents who had been approached for multiple studies, and subsequently consented for their infant(s) to join at least one. Parents who declined all studies were not approached.

### **Setting and participants**

Parents of preterm infants receiving care at one of 3 neonatal intensive care units in the north of England.

### **Findings**

Most parents did not view concurrent participation in multiple trials or studies as a significant issue within the wider context of their infant's care. Most parents did not feel pressured into enrolling their infant into more than one study, but some suggested that participation in several provided justification for the subsequent refusal to join others, articulating feeling of guilt at saying 'no', and others appeared fatigued by multiple approaches. Parents focused upon the perceived risks and benefits of each individual study and, whilst acknowledging that making a fully informed decision was not possible, largely agreed due to their belief in the benefits of research, trust in the health professionals caring for their baby and a range of complex personal motivations.

### **Conclusions**

Parents valued the autonomy to make decisions about participation and felt, with hindsight, that their decisions were right. Research teams could be more aware of parental feelings of guilt or gratitude that may motivate them to give consent. Similarly, the capacity of parents to fully remember details of multiple studies when they are stressed, and their infant is sick, should be taken into consideration and continued efforts made to ensure ongoing consent to participation.

## **Background**

Neonatal practice requires a strong evidence base but randomised controlled trials (RCTs) involving enrolment shortly after birth when parents may be anxious are challenging. Research teams must balance this additional stress against the need to achieve successful recruitment<sup>1</sup>, whilst ensuring decisions are made in the infant's best interests. Parents want to be involved in these decisions whilst still seeking guidance from health professionals<sup>2</sup>. Most studies suggest parents feel they made well-informed decisions although achieving fully informed consent can be challenging<sup>3-5</sup>. Parents consider anticipated level of risk and benefit when deciding whether to join a study<sup>6,7</sup>, but in many Neonatal Intensive Care Units (NICUs) it is common for parents to be approached for more than one study. Approach and enrolment to more than one study may raise ethical and scientific issues in the NICU<sup>8</sup> although these are seen in other settings<sup>9</sup>. Working with parents as part of patient public involvement (PPI) when planning, conducting and analysing studies is appropriately considered essential. Where co-enrolment does not compromise scientific integrity it might be considered unfair to deny parents a choice, and may also improve generalisability of study findings<sup>8</sup>. Our aim here was to explore the perceptions and experiences of parents who were approached to take part in more than one research study.

## **Methods**

This study was focused on parents' experiences whose infants were invited to join either of two clinical trials funded by the National Institute for Health Research. These RCTs were: 1) the Speed of Increases in Feeds Trial – an unmasked RCT comparing

two different daily increments in milk feed volumes, and 2) the Enteral Lactoferrin in Neonates trial - a blinded RCT trial of supplemental enteral lactoferrin<sup>10,11</sup>. Further details of other trials and studies that were active at this time are provided in the supplementary table. After PPI discussion we only requested ethics permission to interview parents whose infant/s had joined at least one trial or study, even if they chose to decline others. Therefore, we did not approach parents who had declined participation in all trials or studies they were offered. Parents were recruited when their infant was medically stable and prior to hospital discharge. For further details on participants, procedures and data analysis please see supplementary materials.

Guided by PPI, we developed a topic guide that was iterative and flexible, allowing parents the opportunity to define issues and experiences<sup>14</sup> and we estimated we would need 15-20 interviews until we reached *thematic saturation*<sup>15</sup>. Interviews were conducted by a single trained qualitative researcher with experience of interviewing parents of sick newborn infants, but who was not a health professional.

We used a thematic approach to data analysis<sup>4</sup> whereby two research team members reviewed transcripts to ensure standardisation of thematic coding. We then extracted significant themes and subthemes for further discussion and agreement. The study was approved by the Office for Research Ethics Committees Northern Ireland: ref 15/NI/0021, 02/02/2015 and reporting follows SRQR guidelines.<sup>16</sup>

## **Findings**

We carried out seventeen semi-structured qualitative interviews between 01/04/15 and 28/02/16 with eight parents of twins, eight parents of singletons, and one set of triplets. Seven interviews were with both parents, nine were with the mother alone, and in one interview with a mother the infant grandparent was also present. Data

analysis identified four overarching themes regarding parents' decisions when they considered whether to join more than one study.

### **Theme 1. 'Just another little thing'**

Most parents did not consider joining more than one study as a major issue in the context of their infant's daily medical care (see Box 1 for additional quotes).

*"I, Yeah, it didn't bother me being asked. I think because I had been bombarded with so much stuff that day that it was just kind of 'it's another little thing'"*

The actual number of studies (range 1-5) was not raised as being important and being asked about several studies shortly after NICU admission was not seen as a problem. Most parents held a strong belief in the benefits of research, trusted health professionals that joining a study would not compromise their infants' care, and most viewed joining more than one study positively. Some parents of sick infants where survival was uncertain perceived enrolment as a 'gift' or a way of making their infant's potentially short life matter. Many parents appeared to forget about studies once they were underway, but a small number raised concerns about whether running two trial interventions together might cause problems.

*... 'I thought that em... the RCT 2 one was just one step too far for me personally. I just felt like if they are messing around with her feeding, the amount of feed and then they are putting something new in as well then I thought, I don't want that.'*

### **Theme 2. Information Gathering**

Parents considered the specifics of each study and tried to get as much information as they could in order to make their decision. Parents preferred succinct parent information sheets (PIS) that gave information in a clear, 'jargon-free' fashion and

placed importance on the opportunity to talk through any concerns with a health professional.

*'...coz the leaflets were very well set out and quite sort of succinct which is quite important when you are in such a distractible kind of mood constantly'*

Parents didn't generally seek advice from other parents on the NICU, but some looked for 'stickers' on infant's incubators that signified trial participation. Conversely, others didn't read the PIS in detail but chose to take part for a range of reasons including: feeling a moral obligation to take part for the benefit of future babies; the perception that their baby was benefitting from previous research; or parents desire to repay the clinical teams for their baby's care (see box 2).

*'... in my logical mind I knew that I should probably take part in this kind of thing because if people hadn't done that 40 or 50 years ago then my babies wouldn't be here now. I thought,*  
*"It is my duty to think about the future."*

Parents said they were given all the information they needed but some said they sometimes felt too upset or unwell to fully take in all the information about the study especially if the approach came soon after delivery. Some parents said they couldn't remember what the studies were called or understand what the study involved, but none said they regretted their decisions.

*'I think we did three but - this sounds really awful - I'm not sure of the second one...'*

Although parents considered the PIS important, they considered the approach of the research team member as very influential in their decision, and valued a friendly and informal, but confident manner. Most did not say they felt pressured into joining and appreciated being given as much time as they needed. Whilst many could not

remember the names of studies or what they involved, they clearly remembered the research team member or health professional who first introduced the study.

### ***Theme 3. Making decisions - 'weighing up the pros and cons'***

Parents decided whether to join a study based on the perceived risks of individual studies rather than the number of studies they were asked to consider. (see box 3)

Parents considered the wellbeing of their infant, how medically invasive the trial appeared to be, how important they thought the study was and several personal factors.

*“...we realised, research doesn't know so we don't know so we might as well, we can't make an informed decision about whether one is better than the other so we might as well put her in the trial.”*

Most acknowledged the challenges of making a fully informed decision and in the uncertainty, drew upon more personal, non-medical risk assessments. These included: wondering what decision the 'baby' might have made; considering the study might help their infant; welcoming 'another pair of eyes' to look at the care their baby was receiving; a sense of purpose which helped counteract feelings of helplessness; a way of getting their infant home sooner; and, a debt of gratitude.

### ***Theme 4. Saying 'no'***

Whilst parents were happy being approached to join more than one study, they did not agree to join them all. Some said they felt guilty when declining, often because they felt they owed it to future generations to take part. Many could not remember how many studies their infant joined but taking part in more than one provided justification to refuse others as it gave the impression they had '*done their bit*'.

Parents who declined were divided as to whether they felt they needed to justify their decision.

*'... it felt almost like we'd done our bit, if that make sense.'*

Parents gave several reasons for declining to join, but some said the timing was important, for example if they were approached shortly before hospital discharge they were keen not to jeopardise this and saw joining another study at that stage as a potential threat to their infant leaving hospital on time. A small minority of parents who were asked to join a study when their infant was sick felt this was inappropriate and that the research team had not read the hospital notes properly. Several parents highlighted that it takes confidence to say 'no' to a health professional who might be caring for their infant. Some were relieved to be supported by nurses in their decision to decline, whilst others felt their decision was not initially accepted by the research team, leaving them feeling pressurized and guilty (see Box 4).

*"And he kept coming back to me. You know? That's why I felt guilty. I felt like I was, kind of, letting him down a little bit'."*

## **Discussion**

Approaching parents for permission to enrol their infant into more than one study is an important challenge on many NICUs<sup>8</sup>, and whilst some data suggests this may not be problematic for many, there are few in-depth qualitative studies<sup>6,17-19</sup>. Our study provides an in-depth analysis of parental experiences and motivations and supports the idea that joining more than one study is not necessarily problematic. Many suggested complex personal reasons which helped them see research



positively, whilst others provided important insights into their decisions including feelings of guilt or obligation.

Our study has several strengths. The semi-structured nature of the interviews allowed parents to consider their experiences, typically several weeks after they were approached. Parents articulated issues in their own words that they felt important to an impartial researcher who was not a health professional and acted as a 'naive observer'. Furthermore, we used methods that reassured parents of complete anonymity.

Nevertheless, our findings require careful interpretation. The design and types of studies may limit generalisability to other settings such as the specifics of the hospitals, the timing of approach, the interventional nature of the studies, the experience of having an infant who joined a study and survived, and the attitudes, behaviours and beliefs of the clinical and research teams involved. Although we used a form of purposive sampling, we did not record socio-demographic information about our parents and were not able to explore how those or other factors such as ethnicity or religion impact upon their experiences and decisions. Around half of our parents had twin or triplet pregnancies, but we did not explore how this affects decisions, although data suggest parents have important views on co-randomisation<sup>20</sup>. We did not seek ethics permissions to speak to parents who declined to join any study offered, or where the infant subsequently died<sup>21</sup>.

Our study suggests parents make separate decisions about each study in turn, judging each by its own perceived 'pros and cons',<sup>6,22</sup> and emphasise that parents want to make final decisions about enrolment, in contrast with data that suggested

some parents expected health professionals to make the decision<sup>2,23</sup>. Whilst most felt they made decisions they didn't later regret, some said that they had not initially understood trial information properly and that subsequent trial procedures came as a surprise. This highlights the challenges of gaining fully informed consent, the importance of continued involvement of the research team in explaining ongoing procedures, and the rights of parents to withdraw or to decline specific procedures<sup>2,5,6,19,23</sup>. Importantly, most parents acknowledged that despite feeling stressed, they were still happy with their decisions, frequently citing their faith in health professionals to protect their infant. Many suggested they would have liked information about the studies before the baby was born, and whilst many acknowledged there were time pressures on decision making, they did not feel they made decisions inadvisably either at the time or on reflection.

## **Conclusions**

This in-depth study emphasises the need for researchers to be aware of several factors when speaking to parents especially in the context of co-enrolment. Few parents expressed regrets, but some decisions may have been motivated by guilt, a debt of gratitude or lack of confidence to refuse. Parents recognised the challenges of gaining fully informed consent, but most felt their decisions were 'good enough' given the circumstances. A better understanding of this may help health professionals to support parents better.

Data from this study could be used in Good Clinical Practice training, ongoing education for 'front-line' researchers and others involved in designing or supporting research. This study highlights the importance of involving PPI representatives when developing a PIS and with all aspects of research design and suggests that changing the PIS may be useful if co-enrolment is likely. Our study highlights the

'overwhelming' nature of having a sick infant, the additional challenge of being asked to join multiple research studies, and the need for all researchers to consider how best to improve parent satisfaction and understanding of the need for research.

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## **Contributorship statement**

All authors contributed to the design of the study, contributed to drafting and revising the manuscript for relevant intellectual content, approved the final version for publication, and agree to be accountable for all aspects of the work.

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### **“What is already known on this topic”**

1. Parents of newborn infants may be asked to consider joining more than one study or trial: this is important for timely completion of studies and a reflection of real-world practices.
2. Researchers have concerns about asking parents to take part in more than one study for ethical and scientific reasons and due to the potential for overburdening families at a stressful time.
3. There are mixed views amongst health care professionals and research ethics committees about what is felt to be appropriate in the context of sick newborn infants.

### **“What this study adds”**

1. Parents did not usually report regretting their decisions, but some reported feelings of guilt or anxiety due to declining or agreeing to study participation.
2. Participant information leaflets may benefit from being written differently where multiple study participation is anticipated, and these are best co-designed with parents and the public
3. Research teams should be aware of the potential for overwhelming families and the need to actively provide ongoing opportunities to discuss continued participation in research studies.

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