Death, bereavement and randomised controlled trials (BRACELET): a methodological study of policy and practice in neonatal and paediatric intensive care trials

Claire Snowdon,[1,2*] Peter Brocklehurst,[3,4] Robert Tasker,[5,6] Martin Ward Platt,[7] Sheila Harvey[1,8] and Diana Elbourne[1]

[1]Medical Statistics Department, London School of Hygiene and Tropical Medicine, London, UK
[2]Centre for Family Research, University of Cambridge, Cambridge, UK
[3]Institute for Women's Health, University College London, London, UK
[4]National Perinatal Epidemiology Unit, University of Oxford, Oxford, UK
[5]Departments of Neurology, and Anaesthesia (Pediatrics), Harvard Medical School and Boston Children's Hospital, Boston, MA, USA
[6]Department of Paediatrics, Cambridge University Clinical School, Cambridge, UK
[7]Newcastle Neonatal Service, Royal Victoria Infirmary, Newcastle upon Tyne, UK
[8]Intensive Care National Audit and Research Centre, London, UK

*Corresponding author

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Scientific summary

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Scientific summary

Background

When children are recruited into randomised controlled trials (RCTs) they have dual status as patients and as trial participants. When those children survive they and their parents may join follow-up studies and continue their involvement with the research for many years. This involvement can be sustained through ongoing communications with trial teams and increasingly through feedback of results at the trial end. If a child dies, what then happens for their parents with regard to the trial in which they participated is largely unexplored. The Bereavement and RAndomised ControlLEd Trials (BRACELET) study was therefore funded to consider bereavement subsequent to enrolment in paediatric intensive care (PIC) and neonatal intensive care (NIC) trials.

The BRACELET study addressed this topic through three interlinked components:

- a quantitative survey of trials and clinical centres recruiting to trials in the UK
- a qualitative study of bereavement-related practice and personal experiences in trials
- a methodological study to inform future research in this area.

Objectives

At the outset, objectives were:

Phase I: Quantitative survey

- To determine the extent of clinical RCT activity in UK paediatric intensive care units (PICUs) and neonatal intensive care units (NICUs).
- To describe the number and proportion of deaths among children and babies participating in these trials.
- To identify variation in mortality across units, and across trials.
- To assess whether provision is made for bereavement within trials.

Phase II: Qualitative study

- To start to delineate the relevance of trial enrolment to bereavement, by describing and exploring the experiences and views of people involved in NIC and PIC trials (following Phase I, the focus of Phase II was on NIC trials only).
- To consider similarities and differences in approaches to bereavement by clinicians and trial teams.

Phase II: Methodological study

- To ascertain the feasibility, and acceptability of research with bereaved parents and to consider the methodological challenges of research on this topic.

Methods

Phase I focused on a 5-year period, 2002–6, and surveyed RCT activity, mortality rates, and provision for bereavement for parents in UK PICUs and NICUs.

The Phase II qualitative study focused on four NIC trials identified in Phase I, with a fifth added towards the end of recruitment. Thirty interviews were carried out with 51 bereaved parents and 59 clinicians and trial team members.

Interviews with clinicians and trial team members explored views of parental needs subsequent to enrolment and determined any provision for bereavement in this context. Interviews with bereaved parents explored their diverse experiences of trial enrolment and bereavement, and considered responses to these over time. Parental views were sought regarding support and communication that might be offered in relation to a trial, such as bereavement follow-up, and access to feedback of trial results. Data analysis was carried out using the qualitative package, ATLAS-ti v7.0.77 (GmbH, Berlin, Germany).

Results

The scale and distribution of mortality in randomised controlled trials in UK paediatric intensive care units and neonatal intensive care units

The surveys showed that 50% of PICUs and NICUs participated in ≥1 of 50 RCTs during 2002–6, enrolling over 3000 children. Although 54 NICUs and six PICUs recruited to trials, the majority of participants were recruited via a small group of academic medical units. In NIC trials, 17% of babies died but a lower proportion (6%) of children in PIC RCTs died. Fewer trials were conducted in the paediatric context and far fewer deaths occurred: 12 in the 5-year period compared with 522 in the neonatal context.

Bereavement in the context of a neonatal intensive care randomised controlled trial

Phase II involved five trials: INIS, International Neonatal Immunotherapy Study; TOBY, whole-body hypothermia for the treatment of perinatal asphyxia encephalopathy; PROGRAMS, PROphylactic Granulocyte–macrophage colony-Stimulating factor to reduce sepsis in preterm neonates; BOOST-II UK, Benefits Of Oxygen Saturation Targeting in extremely preterm babies; and ExPN, Extreme Preterm Nutrition study.

Parental perspectives

Prominence of the trials in parental experiences

Parents described a range of experiences of trial-related decision-making, with some following extremely preterm births and others made shortly after complicated term deliveries. Some decisions were made under time pressures and in escalating crises. A number of parents of twins had already experienced the death of one baby when asked to decide about enrolment for a sibling. Parents described a number of interacting motives, including saving their baby's life; warding-off or limiting risks of disability; and, helping others families. Parents often described potential benefits of a trial in loose terms as something that '*might help*' and '*won't harm*'.

For most parents, once the decision about enrolment was made, the trial initially receded – it was forgotten, overtaken by other events, or subsumed in their grief. TOBY, however, stayed in the foreground of parental experience. At enrolment, for the parents interviewed in BRACELET, this trial spoke directly to their most pressing concerns; the threat to survival and the possibility of disability, or the ability to transfer away from the hospitals where their difficult births had taken place. These parents saw cooling as a desirable option.

The other trials did not bring about change of the same magnitude. They involved interventions that were not always readily observable to parents. It seemed that once they had agreed to enrol their baby, there was often little, if any, further discussion of their involvement and the trial could fade from parents' experience. Once their baby died, their participation seemed to recede or disappear.

Where trials did not deliver the hoped-for '*help*', this did not seem to cause major difficulties for most of the parents in this study. Often parents had separated the trial from their baby's death, and stated in the interviews that their baby was simply too sick or too small to survive.

Parents' interest in a trial appeared to develop over time as their bereavement receded. Although most had experienced little contact with a trial over the years, parents were often interested in the research, and some would have liked more contact and information than they actually received. They often felt strong connections and a sense of involvement with the trial.

Trial bereavement policies and strategy for feedback of results

Contact with bereaved parents varied across the trials: ExPN involved no contact post bereavement; BOOST-II UK and INIS involved no ongoing contact until feedback of preliminary or main trial results; PROGRAMS offered newsletters and feedback of results. TOBY had a pioneering multipart follow-up package.

Using the TOBY bereavement package as a framework for discussion, parents' views were sought on discussion of a trial at bereavement follow-up; a bereavement leaflet providing contact details, condolences and recognition of participation; a personalised letter offering newsletters; a web-based message board; and feedback of results. Parents expressed a range of views of these options but almost unanimously supported offering parents trial results. Trial communications were valued as a source of information, as an acknowledgement of loss and the contribution to research, as a connection back to their baby and a form of commemoration. Some parents had kept trial paperwork in their baby's memory box.

Views of clinicians and trial team members

Clinicians expressed a range of responses to bereavement in the context of a trial.

Some saw bereavement as a clinical issue, completely separate from research, and the trial as an event in the past, which was not relevant to bereavement follow-up. Clinicians felt their bereavement support systems served parents well. In the experience of most of these clinicians, parents had other priorities at this point, an observation largely supported by the parental interviews.

Parents' growing interest in trials over time, a readiness to engage, and the surfacing of questions about the research which were described in the interviews are not obvious to clinicians who would not be in contact with bereaved parents at this stage.

Trial team members involved in running the trials had responsibility for implementing bereavement-related policies as outlined above. Although we found that these were largely valued by parents, the trial teams had received little feedback and were obliged to work without knowing whether their communications were appreciated or were problematic. With data protection and the research governance-related concerns they faced in maintaining up-to-date records for bereaved parents, it was difficult for them to be sure how many of their communications were actually reaching the parents.

Methodological work

The methodological component focused on the challenges involved in a qualitative study of this sensitive topic. It demonstrated the ineffectiveness of postal recruitment strategies and the value of a more personal approach through involvement of a clinician. It also demonstrated the potential role of publicity in this setting as an adjunct to recruitment, given the value of each testimony for a hard-to-reach population, although the yield through interested charities and special interest groups was low. Online questionnaires on the study website (www.bracelet-study.org.uk) provided a means of participation and a voice for views that would have not otherwise been possible. This approach may prove to be important for other studies

with finite, hard-to-reach populations, for which every contribution counts, and in which interviews may be too challenging for some.

As part of the recruitment processes, general practitioners (GPs) were informed of the plan to invite parents to participate, and given the opportunity to object. Some parents questioned whether this was necessary, feeling that their GP could not have made a valid judgement about their particular situation.

An important consideration for BRACELET is the possibility that the sample is biased in two ways. Parents who were invited to participate were identified from trial records which could not generally be updated post trial enrolment. Those who responded were therefore more likely to be living in the same home and in the original relationship. Participating parents were also prepared to discuss difficult experiences and the majority were interviewed as a couple. Questionnaires completed post interview suggested that they valued the opportunity to revisit their experiences. The sample may therefore have been skewed towards those whose relationships remained stable in the aftermath of bereavement, and those who were more comfortable with discussing their bereavement. This stability and comfort may, in turn, have affected our data on trial participation. We therefore place clear caveats around the findings and highlight this potential limitation in our sample.

Conclusions

Death is a sufficiently frequent outcome in NIC and PIC RCTs to warrant research into how this is experienced and what provision is made for this outcome. Accounts from bereaved parents in this study demonstrate the difficult circumstances that surround trial enrolment in a range of trials. Interviews with clinicians and trial teams showed that there is currently no agreed or integrated response to bereavement, and clinicians and different trial teams respond to bereavement in different ways, from no response to a multipart strategy. We recommend that a co-ordinated response to bereavement is a necessary part of RCTs that anticipate mortality in their population, which should be considered at trial inception and written into the trial documents.

Bereaved parents were engaged with both the trial in which their baby participated and in their own participation in BRACELET. Although there have been few previous examples of trial-related research involving bereaved parents, researchers and research ethics committees can be reassured that research with bereaved parents involved in NIC trials is feasible, that these parents bring an important perspective, and that they should not be excluded from future studies.

Implications for health care

Randomised controlled trials are an important aspect of health care as they advance knowledge in critical care for infants and children. An unfortunate reality is that death is a relatively common outcome in some PIC and NIC RCTs. BRACELET suggests that those whose children die after having been enrolled in a trial may have information and support needs, and this raises new questions for clinical and research communities as to how these might be met.

Responses to bereavement are not well developed, partly because there is no consensus on whether or not a response is necessary. Clinicians often felt that their bereavement policies need not be changed because a child was enrolled in a trial. If, as a result of BRACELET, it is considered that a co-ordinated response to bereavement is needed, it will be important to consider who might be responsible for this and how it might be implemented.

Bereaved parents in this study appreciated some involvement in the research in which their baby participated, and were often interested in more contact and information than they actually received.

As this was not a constant position, with interest in a trial ebbing and flowing over time, providing for bereavement with the sensitivity it deserves will be a challenge. Important inroads into provision for bereaved parents have been made by trial teams and these examples may be used to guide further research in this area.

Feedback of trial results was valued by parents as it offered important opportunities for information, closure and '*comfort*'. Parents also recognised that feedback is potentially challenging in terms of the information that might be conveyed or for the connection made to a difficult time. Parents who have entered into a 'contract' with clinical researchers by enrolling their baby into a trial should at least be offered the opportunity to learn the outcome as a matter of respect for their trust and engagement in research.

Recommendations for research

More research is needed into the experiences of bereavement subsequent to trial enrolment, with study of bereavement strategies in NIC trials as they are introduced.

It is also important to determine whether parents and triallists in PIC trials (and trials in adults) face the same issues identified for NIC trials.

To achieve a more complete appreciation of views and experiences of trial participation researchers should seek to represent views of samples of all parents, bereaved and not.

It is important that careful studies of feedback of results are carried out to show how individual trial teams manage this situation, and to explore how results are received and understood by bereaved and non-bereaved parents.

There are important questions to be answered about parental experiences of parenting twins and higher order births in trials. This is potentially a highly complicated and particularly sensitive situation and needs to be understood through careful study.

Developmental research should continue to explore means of involving a wider range of parents in future research, including via publicity and specialist websites.

Methodological research is needed to ensure that we have the tools to explore with parents and other relatives as partners in research a range of trial-related topics which might be challenging as the information is complex or the focus is sensitive.

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