

This response was submitted to the evidence call issued by the Nuffield Council on Bioethics' Working Party on *Children and clinical research: ethical issues*. Responses were gathered from 7 August to 31 October 2013. The views expressed are solely those of the respondent(s) and not those of the Council.

23. Together for Short Lives and Association for Paediatric Palliative Medicine Joint Research Group
301013

Response to Nuffield Council on Bioethics Call for Evidence on Children and clinical research: ethical issues

Introduction

We welcome this opportunity to submit a response to your consultation on the ethics of children being involved in clinical research. This response is submitted on behalf of the Together for Short Lives and Association of Paediatric Palliative Medicine Joint Research Group¹, which is chaired by Professor Myra Bluebond-Langner, the True Colours Chair in Palliative Care for Children and Young People, University College London Institute of Child Health.

On 10th October 2013 we held a three hour meeting of our Joint Research Group to discuss your consultation document. In the first hour we divided into four discussion groups, each addressing one of your four main consultation questions. In the second hour each group fed back on their group's discussion. This was followed in the third hour by a robust discussion about the key issues that we would like to include in our submission. This written submission complements and supplements the comments that were made by Professor Myra Bluebond-Langner at the Nuffield Working Party meeting in September.

This submission also builds on a response that the Joint Research Group made to the Royal College of Paediatrics and Child Health consultation on the next edition of their "Guidelines for the ethical conduct of medical research involving children". This response is attached at Appendix A for your information.

While many of the issues are applicable to any child involved in clinical research, we have tried to focus our response on the issues that are specific to recruiting neonates, children and young people with life-limiting and life-threatening conditions. There was a strong consensus on two cross-cutting issues:

- We take clinical research to include psychosocial and qualitative research, as well as clinical trials. All of these types of research are necessary for developing an evidence base for children's palliative care policy and practice.
- That neonates as well as children and young people should be included in research. This is important because more neonates die and could benefit from palliative care than any other age group under 18.

Under the four overarching questions in the consultation document we have not provided a response to each of the sub questions, but have raised a number of issues pertinent to research in the field of children and young people's palliative care.

1. How should children be recruited to clinical research?

We believe that the following critical success factors are essential to encouraging and incentivising children and families to participate in children's research:

- Research should be encouraged that involves children of all ages: neonates, children and young people. There are proportionally higher numbers of babies requiring access to palliative care than older children. There are particular difficulties in carrying out research in neonatal palliative care, largely because parents of newborns may not have had time to come to terms with their baby's poor prognosis and the introduction of a palliative care approach, let alone considering participation in research studies.
- Greater recognition needs to be given to the specific health literacy, language and information needs of children and families. Current guidance on the production of children's study information often acts as a disincentive and needs amending so that appropriate language and communication is used when conveying study information to children and parents and so that participation is presented positively not defensively. The language used in research recruitment materials for children, young people and their families, needs to be clear but sensitive to the stage of development and understanding of the nature and prognosis of the illness.
- As in the discussion at the Working Party meeting in September, the Group was divided on the utility and value of assent. There was however unanimous agreement that assent or any other similarly situated principle should not be watered down or 'babyfied' consent.
- Governments and society in general need to give appropriate recognition to the contribution of children and families to research (as appropriate to individual studies). To achieve this we need to know what children and families see as appropriate recognition for taking part in various types of research studies. Many children and young people are willing to take part in research for purely altruistic reasons. Children are capable of altruism from an early age and may also need to find meaning in their illness. Altruism and a search for meaning may inform both the child and other family members in deciding whether or not to take part in research.
- There may be occasions when it is appropriate to provide research participants with a small token of appreciation, such as a voucher.

2. What research proposals should be regarded as ethically acceptable?

All research proposals should describe in a transparent manner what they intend to do and ethics committees should be looking to see if all potential ethical issues have been addressed in the proposal rather than looking for reasons not to do the research. Parental/family proxy data should not be regarded as necessarily representing the views of the child. It should always be assumed that the 'authorised representative' is in the first instance the child, and failing that the person with parental responsibility for that child. There should be safeguards against clinical coercion or gate keeping for participating in research.

Benefits to research participation to the individual child may be more or less obvious and should be left to the discretion of the child and family.

The following types of research were felt to be ethically appropriate for children:

- **Interview studies:** these may provide a forum for children in which their views can be expressed both verbally and non-verbally in a developmentally appropriate way. Children may benefit from the extra attention from research teams.

Interviews with parents should be regarded as separate from research with children, although there may be knock on supportive benefits for the child as a result of parent participation.

- **Observational studies:** verbal and non-verbal clues should be noted, in particular with relation to the child, and issues of consent addressed as a continuous process.
- **Data:** it should be transparent in the research proposal why each item of data is being collected and how it is going to be used in the research.
- **Trials of psycho-social interventions:** rules are similar to those for trials. Randomisation should be allowed. Long term follow up for risk of harm should be applied as with adults.
- **Babies and those children with profound disability:** the person with parental responsibility should make the decision on research participation. Tools should take account of non-verbal means of communication.

Discussion around best interests underscored the complexity of the issues discussed in the Working Party. Attention was given to what constitutes best interests as well as whether or not best interest can be disentangled from the interests of others and with what consequences.

3. How should research in children be encouraged?

The percentage of children in the whole population is getting smaller as people live longer. Despite the changing demographic with an increasingly higher percentage of older people with increasingly complex and emerging new problems, children need to have equal consideration in research prioritisation.

We believe that in every potential research project, it should be mandatory that consideration is given to the implications of including AND excluding children and families from that study.

The following critical success factors are essential to encouraging and incentivising organisations to undertake high quality children's research:

- Research funders, commissioners and children's services have a responsibility to recognise and take responsibility for this proportionately small group within the whole population - many of whom have unique needs

associated with childhood and whose conditions and outcomes impact on health and illness in adulthood and society in general.

- In harsh economic times other private philanthropy is needed to fund research alongside government funding. Governments should further incentivise research funding (for example through tax breaks or match funding).
- Smaller organisations need a platform to be able to articulate their research needs and to access research funding and possible research partnerships.
- The voices of children, parents and families need to be part of lobbying for funding.
- Governments should build a research culture and introduce a policy of engagement with citizens for opt out rather than opt in to receive information about appropriate research studies so that children and families can themselves decide if they would like to find out more about a study.
- Consideration should be given to developing the concept of the academic hospice/hospital/service/organisation, whereby on entering the service children and their families give their consent to receive information on appropriate research studies so that children and families can themselves decide if they would like to find out more about a study.
- Recognition by Government and other key decision-makers of the implications of **not** funding children's research.
- Continuing funding of the National Institute for Social Care and Health research infrastructure for undertaking research with children and young people.
- Removing disincentives from the academic and clinical system.
- Requiring Government and non-Government organisations to make information on current research studies accessible to the public so that children and their families can self-refer or volunteer to participate.
- Recognition by funders that children's research can be more expensive, due to the need to have more research sites to recruit sufficient numbers of children and the unique nature of undertaking children's participatory research, taking account of the long term return on investment.

4. What should happen when the research is over?

It is important to consider the developmental context when addressing issues of research dissemination in work involving children. Researchers need to be mindful that individual information gathered on children at one age might cause distress at a later date. This might be particularly so in the use of photographs. Sharing excerpts of research data with participants where a quotation is to be used in qualitative accounts, prior to publication or dissemination, was discussed as good practice.

Research findings need to be disseminated as agreed at the planning stage and commencement of the research. Children, young people and their families may have contributed actively as part of collaborative input across the duration of the research project and in dissemination. Their involvement may helpfully continue into any policy implications of the final research.

Where relevant, research should be disseminated using age and ability appropriate styles of communication. A flexible and creative approach to dissemination would reflect the diversity of communication needs of participants.

Individual preferences with regard to receiving information should be duly considered and the fact that information needs have the potential to change over time. For example, some families may request a brief research summary whilst others would like to see the range of research outputs, including published papers. We recognise that some families value their child's contribution being openly acknowledged and their child's name included within research outputs, whereas others do not want this.

The responsibility to the research participants when the research is over was addressed. The connection between researcher and participant in certain studies was acknowledged and the supportive role the research might have played for some participants. The participants' psychological well-being at the end of the research was considered. One suggestion was for the opportunity of a one-off debrief/follow-up, after study completion. This was considered particularly important in the context of longitudinal studies.

The opportunity for feedback to researchers from research participants on different aspects of the research process could help researchers reflect upon and evaluate their research practice. Finally the impact was acknowledged on the researchers themselves, and on the issue of boundaries, particularly when the research has involved close working relationships over significant periods of time.

Conclusion

Whilst safeguards obviously need to be in place, research indicates that parents want to participate in research (see appendix A) and do so for altruistic reasons, as part of a way of making sense of their experience and as a lasting legacy to their children.

Appendix A

To: Professor Neena Modi and the RCPCH Committee revising RCPCH “Guidelines for the ethical conduct of medical research involving children” *Arch Dis Child* 2000;82:177-182.

From: Professor Myra Bluebond-Langner, True Colours Chair in Palliative Care for Children and Young People on behalf of the Together for Short Lives and Association of Paediatric Palliative Medicine Joint Research Group

Re: 1. Background and Statement Regarding Research with Children and Families With Life-Limiting Conditions and Life-Threatening Illnesses
2. Summary and Proposed Paragraph for Inclusion in Revised Document

Date: 06 January 2013

1. Background and Statement Regarding Research with Children and Families with Life-Limiting Conditions and Life-threatening Illnesses

The 2000 RCPCH statement on the conduct of research involving children was bold, forward looking and supportive of high quality research with children and families. It stresses the importance and benefits of such research and has done much to facilitate it.

In 2000 paediatric palliative care was an emerging specialty with a very limited research base. While some research has been done since that time on the physical aspects of care (e.g. symptom relief) there have been real difficulties in getting studies into the psychosocial aspects of care underway. Securing approval from LRECS and MRECS for their proposed studies has been a barrier to research and the development of a robust evidence base for practice and policy.

While the physical aspects of care are being addressed there is also a clear need to address issues around the functioning of the child and family. One example are the difficulties professionals, patients and families face around decisions about care and treatment. There have been several high profile cases in recent years where challenges to decision making have reached the press and the high court (e.g. newborn care and more recently with oncology).

Key to dealing with critical issues around decision making and formulating meaningful guidance is a better understanding of all aspects of the decision making process. This can only come about by detailed, in depth, often observational, interview and ethnographic prospective studies throughout the illness trajectory. Because these studies will be on-going at difficult points of the trajectory Research Ethics Committees may flag them as intrusive, potentially harmful and not necessarily in the best interest of the child. Yet a small but growing body of evidence about the experience of participation in research paints a very different picture. Most participants have expressed a positive view of being interviewed, for example, particularly recognising the need “to get it right” for those coming behind (see discussion below).

Given how essential these studies are to delivering the highest standard of care we recommend that the Research Ethics Committees base their approach on the evidence and work with researchers and clinicians to facilitate the conduct of research with children with life-limiting conditions and life-threatening illnesses their parents and those who care for and treat them at all stages in the illness trajectory from diagnosis on through death and bereavement.

We express our concerns in the following **statement**:

Since the publication in 2000 of the RCPCH statement “Guidelines for the ethical conduct of medical research involving children” palliative care and other qualitative and psycho-social researchers have been frustrated by their inability to obtain timely approval for their research projects, the need for repeated submissions and/or changes to the protocols or information sheets which adversely impact the quality of the study and the resulting evidence.⁽¹⁾

Researchers report that Research Ethics Committees (REC) concerns include the inability to obtain proper informed consent from participants and that harms outweigh benefits. Review of the evidence in the peer reviewed literature of the last twelve years shows both that ethical standards for participation can be met^(2,3) and that evidence for participant reported benefit is substantial if not overwhelming^(3,4,5,6,7).

Participants report benefits of participation to include: a validation of their experiences⁽⁵⁾ and a first opportunity to speak about their child’s illness and death, a release from isolation⁽³⁾ Some studies report that participants report no adverse effects^(2,6) others that some adverse effects were, on balance, part of an essentially positive experience⁽⁸⁾.

Researchers point out that RECs may be drawing an analogy between the emotional, tearful state of participants in interviews with the physical pain and mental distress associated with venepuncture or, say, bone marrow aspiration. The analogy is flawed. In fact participants report that they are simply expressing emotions which they always carry with them, not experiencing pain caused by the researcher. Strong majorities rate the experience as positive and fractions over 90% report that they would participate again and support continuing research⁽⁵⁾.

Clearly the conduct of such research must be carried by skilled interviewers and conform to standards which are well documented by the researchers themselves⁽³⁾. REC scrutiny is indeed appropriate here. But, we submit, the mere designation of a particular group of subjects-ill children, bereaved families nor the mention of a range of topics-end of life or bereavement, for example, should not in themselves flag studies as of above minimal risk to participants.

The research regarding harm and benefit to research participation cited above was carried out with parents of ill or deceased children, not with the children and young people themselves. We take the position that children are not simply small adults and that research on adults should not generally be extrapolated to children. We also point out that the views and experiences of parents cannot stand in for those of the

children themselves and as such can lead to wrong conclusions^(10,11). So, we should ask again, now with regard to children, about the two areas of particular concern to RECs: consent and harms/benefits.

The 2000 guidelines already address issues of consent to research on children. With regard to the question of whether the harms and benefits might weigh differently for children with life-limiting conditions or life-threatening illnesses, children who are in terminal phases of illness or dying what do we say? While not studied head on with these children to the same extent as with their parents there are findings which suggest that ethical standards can be met and that there can be benefit.

For example, Hinds et al⁽⁹⁾ found in a study of 10-20 yr olds making end of life decisions that they expressed a wish, in their decisions, to benefit others-both their parents and 'unknown others.' They cite what has been described as the 'maturational effect' of a life ending illness. This is but one example of research which supports the idea that children and young people would accept and benefit from meaningful encounters which benefit others. Protecting them by isolating or sequestering them would deny them this benefit and while well intentioned is also at odds with what has actually been observed. In sum, in our view the risk of not doing research with these children themselves is great.

2. Summary and Proposed Paragraph for Inclusion in Revised Document

Continuing to improve care for children with life-threatening illnesses, their families and bereaved families is vital. There is a dearth of research in this area and yet it is essential if we are to have a firm and robust evidence base for both the physical and psychosocial aspects of care. Until now research ethics committees have been reluctant to sanction projects in this population lest they intrude on families and increase their stress. However recent studies show that this is not the case. The vast majority of families who have taken part in studies have expressed a positive view and valued the opportunity to discuss their experiences and contribute to improving care for the future.

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ⁱ The membership of the Together for Short Lives and Association of Paediatric Palliative Medicine Joint Research Group is as follows:

Jan Aldridge, Consultant Clinical Psychologist, Martin House Children's Hospice
Helen Bennett, Director of Care, Alexander Devine Children's Hospice Service
Prof Bryony Beresford, Research Director (Children and Families Team), Social Policy Research Unit, University of York
Dr Rachel Black, Nurse Consultant, Demelza Hospice Care for Children
Maddie Blackburn, PhD Student, Open University
Prof Myra Bluebond-Langner Professor and True Colours Chair in Palliative Care Children and Young People, Louis Dundas Centre for Children's Palliative Care, UCL-Institute of Child Health. *Chair of Together for Short Lives and Association for Palliative Medicine Joint Research Group*
Dr Lynda Brook, Consultant in Children's Palliative Care, Alder Hey Children's Hospital
Lizzie Chambers, Director of Development, Together for Short Lives
Prof Jane Coad, Professor of Children and Family Nursing, Coventry University
Prof Sir Alan Craft, Emeritus Professor of Child health, Newcastle University
Dr Lorna Fraser, Anniversary Research Lecturer, Department of Health Sciences, University of York
Dr Ann Goldman, Retired Consultant in Children's Palliative Care, Great Ormond Street Hospital for Children
Dr Nicky Harris, Former Medical Director, Children's Hospice South West
Dr Jane Hunt, Senior Lecturer in Children & Young People's Nursing, Bournemouth University

Dr Louise Jones, Head of Marie Curie Palliative Care Research Unit, University College
London

Dr Susie Lapwood, Head of Research, Education and Professional Development, Helen and
Douglas House

Dr Linda Maynard, Head of Education and Development/ Lead Nurse, East Anglia Children's
Hospices

Dr Toni Menezes, Head of Practice Education and Quality, Shooting Star CHASE Children's
Hospice

Prof Jane Noyes, Professor of Nursing and Health Services Research, Bangor University

Two observers were present at the meeting: Aaron Pritchard and Virginia Bennett from
Bangor University.