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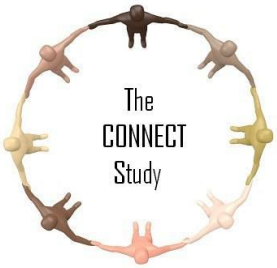

Research without prior consent (deferred consent) in trials investigating the emergency treatment of critically ill children: CONNECT study guidance

Version 2 updated July 2015

http://www.liv.ac.uk/psychology-health-and-society/research/connect/

UNIVERSITY OF LIVERPOOL

MRC Hubs for Trials Methodology Research

Scope and purpose of this guidance

This guidance has been developed to assist the design, review, and conduct of clinical trials investigating the emergency treatment of children (under 16 years of age[*]) and young people (16-18 years) with life-threatening conditions. There are relatively few clinical trials of emergency interventions for children. Problems in seeking parents' consent for research at the point when their child is critically ill have been a significant barrier to conducting trials in this setting[1 2]. As for all paediatric clinical trials, children cannot legally provide consent for their own participation in a trial. Although young people (16-18 years) can legally provide their own consent for a trial, this is not possible in an emergency situation. Instead consent is sought from their legally designated representative (e.g. parent or person with parental responsibility) and assent (agreement) may be sought from the child[†] if appropriate[3-5]. However, there is not always someone with parental responsibility present when a child enters hospital, or a newly delivered mother may be potentially prevented from giving consent to emergency investigations or treatment, such as, for example, by post-delivery sedation or general anaesthetic. Even when someone with parental responsibility arrives in the emergency department with their child, there may not be enough time to seek informed consent[1]. Parents may also be highly stressed in an emergency situation and struggle to make an informed decision about research in the limited time available[2].

Nevertheless, clinical trials are needed to find out whether critical care interventions are safe and can help to save children's lives. Clinical research is governed by European Legislation, which sets the legal framework for valid informed consent as the cornerstone of experimental research involving human beings[6]. Between 2004 and 2008 European Directives made no provision for consent in critical care situations, preventing the conduct of research in this setting. In 2008, UK legislation was introduced to enable doctors and nurses to seek consent for research *after* their child had been given the investigational drug or device when the following conditions are met:

> "*(i) treatment is required urgently;*
> *(ii) urgent action is required for the purposes of the trial;*
> *(iii) it is not reasonably practicable to obtain consent prospectively; and*
> *(iv) an ethics committee has given approval to the procedure under which the action is taken*."[7]

[*] Where Clinical Trial Regulations apply, a child is defined as someone under the age of 16.
[†] Hereafter for simplicity the term 'child' is used for children and young people aged 0-18 years. The exception is in Section 7, which provides separate recommendations for seeking assent from children (under 16 years) and consent from young people (16-18 years).

Across Europe this has been called 'deferred consent', although we would agree with arguments that this is a misnomer, as the child will have already received an intervention as part of a trial before any information is given or consent is sought. Essentially permission is sought post-intervention to use data that has already been collected and consent for the child to continue to take part in the trial. The term deferred consent has recently generated much discussion, leading to proposals to use the term 'research without prior consent' instead. We will therefore use the latter term in this guidance.

Internationally, there has been a lack of research on public experience of research without prior consent and whether it is acceptable to children, parents and practitioners. This guidance has been developed to inform recruitment and consent in this challenging setting to help ensure these processes are appropriate to the needs of children and their parents.

How has the guidance developed?

The recommendations in this guidance are based on findings from a Wellcome Trust funded study called CONNECT (see Appendix A) and were developed by Dr Kerry Woolfall and the CONNECT advisory group (members listed in Appendix B). Statements of key evidence considered when developing each recommendation are shown in Appendix C. As well as the CONNECT study findings, the guidance was also informed by a review of other empirical research and ethical theory. During 2014 the draft guidance was reviewed and developed in consultation with 32 key stakeholders (including critical care practitioners, ethicists and parents of children who have received emergency treatment in a hospital) who attended a one day Medical Research Council Hubs for Trial Methodology Research funded guidance development meeting in Liverpool (23/07/14). The final draft was reviewed by the CONNECT advisory group and members of Paediatric Emergency Research in the United Kingdom & Ireland (PERUKI)[8 9].

What type of trials is this guidance for?

This guidance has been developed for randomised controlled trials investigating a drug, medical device or surgical procedure in critically ill children where emergency treatments cannot be delayed to obtain informed consent. These guidelines are to assist the process of research without prior consent in such trials. This guidance may be of interest to those involved in the design and conduct of other types of studies used in children's emergency medicine (e.g. use of biological samples for

research or observational studies), however only randomised controlled trials were considered in the development of the current guidance.

Who is this guidance for?

The guidance is for all those who have a direct or indirect role in the funding, design, conduct and ethical review of paediatric or neonatal trials that involve critically ill children. This includes: doctors, nurses, paramedics, researchers, patient and public involvement (PPI) representatives, members of research ethics committees, funding committees, peer reviewers and Clinical Trial Unit (CTU) staff. The guidance will also be of interest to children and young people, trial sponsors, NHS Research and Development (R&D) staff, parents and other members of the public and to organisations that represent the interests of patients and the public.

Recommendations refer to parents, which for the purposes of the document includes someone who has parental responsibility for a child.

What is included in this guidance?

Section 1 describes the need to conduct research at the pre-trial stage to inform trial design and the process of recruitment for potentially challenging trials.

Section 2 focuses on publicising critical care trials. This is to help raise awareness of research among parents of children with a diagnosis that indicates that they might be entered into research without prior consent.

Section 3 offers guidance on making written trial information easy to understand.

Section 4 describes the need to consider the appropriate timing of a recruitment approach.

Section 5 suggests approaches to consent when a child has died after enrolment in a trial.

Section 6 considers child assent and consent involving young people in this setting.

Recommendations for further research are provided in **Section 7** of the guidance.

CONNECT was funded by Wellcome Trust (WT095874MF) and supported by the MRC Network of Hubs for Trials Methodology Research (MR/L004933/1- R/N42). CONNECT guidance will be reviewed and updated as further research evidence on the recruitment process and stakeholder perspectives becomes available.

Contents

SECTION 1: Pre-trial research for potentially challenging trials

Recommendation 1: Where research without prior consent is being considered for a potentially challenging trial, such as trials involving a new or novel intervention, change in clinical practice or additional blood samples in neonates, the views of children and young people, parents and practitioners should be systematically sought through substantive research at the feasibility or pilot stage to inform the trial design, recruitment and approach to consent. This research should be conducted in addition to, or alongside PPI activities.

- This research is important where there is uncertainty about how to do the proposed trial in a way that acceptable, or there is concern about how the research process will be explained to those involved.
- Involve appropriately skilled researchers in the pre-trial research to explore parent, child and practitioner views on the acceptability of the trial, recruitment and consent procedures. This might include use of quantitative or qualitative methods to examine issues such as: the acceptability of research without prior consent in the context of the particular trial; whether it is appropriate to provide brief information and seeking verbal permission prior to administration of the intervention; maximum timeframe in which to inform parents about research without prior consent; and information materials (e.g. participant information sheet, posters and consent forms).
- Ensure that a diverse sample of parents and their children (where applicable) who experience the health condition being investigated by the trial are represented. Translators may be required to ensure the views of families who do not speak English are accessed.
- Ethical approval can be sought for this research as part of trial feasibility or pilot study ethics applications (where applicable).
- Where trial feasibility or pilot studies are not proposed, seek other funding to conduct substantive research at the pre-trial stage. Resource and time implications of seeking external funding and ethical review for this research should be considered. Wider funding opportunities (e.g. for protocol development funding) and expedited ethical review systems should be put in place so that important pre-trial research is conducted and does not cause unnecessary delays to a trial.
- Use research findings and wider literature on clinical trial recruitment to inform the trial design, protocol (including participant information materials) and recruiter training.
- Publish research findings to inform the design and conduct of future challenging trials.

SECTION 2: Raising awareness about research without prior consent in critical care settings

Recommendation 2: Hospitals conducting emergency research should publicise the use of research without prior consent in critical care settings.

- Use posters and information leaflets in critical care settings (e.g. Intensive Care Units, High Dependency Units and Emergency Departments) explaining that emergency research is carried out in this hospital to help provide the best care for children in the future. This might also explain why consent for research cannot be sought prospectively in emergency situations and advise parents that they may be approached by a researcher (such as a research nurse) to discuss the research after the initial emergency has passed. Translation of information materials into languages other than English should be considered.
- Details of where parents can access further information about research that is being conducted without prior consent should be provided (e.g. where trial information leaflets are located, trial recruiter name and contact details and or website details).

SECTION 3: Written trial information

Recommendation 3: Written trial information should be presented in a format that is easy for parents to understand.

- Ensure the participant information sheet (PIS) and consent form is written clearly and with no unnecessary medical language. Use a short summary section and contents list at the beginning of the PIS to assist understanding (see: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2743679/).
- Ensure brand names are used in addition to generic drug names.
- In addition to information required by research ethics committees include details of key aspects of the trial including why the research was conducted without prior consent (see recommendation 4.2a for suggested content).
- Consider whether translation of written trial information to languages other than English is required.

(See Section 6 for recommendations to inform child assent and consent involving young people)

SECTION 4: Discussing research without prior consent with parents

Recommendation 4.1: Approach parents with trial information at the earliest appropriate opportunity.

- Ensure parents are provided with trial information at the earliest appropriate opportunity after the initial emergency situation has passed, within a maximum recommended timeframe, which should be established on a trial by trial basis (see recommendation 1).
- Trial recruiters should establish an appropriate point in time to approach parents to discuss research. Consultation with nursing staff about the child's condition and their views on how parents are coping is likely to be helpful in gauging what is an appropriate time point. The outcome of the discussion with nursing staff about appropriate timing should be recorded in the patients' clinical notes.
- Trial recruiters should ask a member of the nursing staff known to the family introduce them and ask parents if it is a convenient time to discuss research.
- Trial recruiters should introduce themselves, their role within the trial (e.g. research nurse/principal investigator) and whether or not they are part of the clinical team responsible for treating the child. Ask parents how their child is doing before discussing the trial in detail.

Recommendation 4.2: Discussions about the trial should be conducted sensitively and cover all aspects of the trial, including what research without prior consent is and why it is being used.

a) During the first discussion with parents recruiters should:

- Discuss key aspects of the trial showing parents where further information can be found on the participant information leaflet, whilst paying particular attention to explaining:
    - Why the trial is being conducted and why their child's condition made him/her eligible for the trial.
    - Details of how the intervention is already used in clinical practice (if applicable), any changes to clinical practice and potential risks as a result of being included in the trial.
    - How the trial findings will be used to inform future treatments for critically ill children.

- That it was not possible to seek their consent before the trial intervention was given because their child needed immediate treatment, which could not be delayed.
- That their permission is being sought to use information and/or samples that has already been collected and for their child to continue in the trial. Explain that parents are free to decide whether or not they wish for their child's information is used and how their decision will not affect their child's care. Provide details of any follow up procedures (if applicable).
- How the trial has been approved by an independent research ethics committee whose role is review research to help protect the rights, safety and well-being of research participants.

- Provide parents with sufficient time to consider trial information (e.g. overnight if possible). However, parents' decisions about the use of their child's data and for their child to continue in the trial should be sought before the child is discharged.
- Be prepared to respond to parents who are concerned that participation in the trial may have contributed to poor recovery. Describe how researchers will not know which is the most effective treatment until the trial and analysis of the results is complete (which may take a few years)**.** Offer parents the opportunity to speak to the Principal Investigator (PI) or senior member of the research team to discuss any concerns.

b) During subsequent discussions about the trial recruiters should:

- Check parents have had sufficient time to consider the trial information and that it is an appropriate time to discuss this further.
- Explore parents' views and understanding of the trial and what, if any, follow up procedures will be involved, responding as appropriate.
- Be prepared to respond to parents who are concerned that participation in the trial may have contributed to poor recovery (see 4.2a above).

SECTION 5: Discussing research without prior consent with parents when a child has died

Please note: Research with bereaved parents has emphasised the variability and complexity of their feelings about research when their child was enrolled in a study and subsequently died; a one-size-fits all approach to discussing a clinical trial is unlikely to be sensitive to the needs of grieving parents. Although there are some exceptions, many bereaved parents wish to be informed about their child's involvement and provided with the opportunity to discuss having their child's data analysed in a trial (see Appendix C). However, parents may react to this situation in unpredictable ways. Talking with parents about research which involved their child prior to death is likely to be very difficult for both parents and practitioners. However, it is important to seek consent from these parents - not doing so will mean that parents have no knowledge of their child's participation in research. It will also mean their child's data cannot be included in the trial, which can bias trial findings. The following recommendation includes three options, which aim to help practitioners identify the most appropriate approach for each family. Recommendations are tentative until further research has been conducted.

Recommendation 5: Discussing research without prior consent with bereaved parents requires considerable care: while research discussions with all parents should be personalised and conducted with sensitivity, this is especially true of parents of children who have died. Use your professional judgement on when and how to discuss research without prior consent with bereaved parents. The approach should be informed by research conducted at the trial design stage (see recommendation 1) and should complement bereavement protocol at each participating trial site.

- The Principal Investigator and/or a clinician known to the family should establish which of the following options is most appropriate for each family:

Option 1: Approach parents with trial information before they leave hospital

- Discuss the trial and provide information before parents leave hospital. However, only approach parents with information and/or seek permission to use data already collected at this point if it is believed that parents have the capacity to absorb information and/or make an informed decision.

Option 2: Contact parents with trial information by letter at a later date

- If it is not thought appropriate to explain about the trial or seek permission to use data already collected before parents leave the hospital, consult with clinical colleagues and bereavement counsellors to identify an appropriate time to contact parents via a posted letter. Sending the letter could be timed to coincide with the bereavement follow up invitation.

- The covering letter, information leaflet and research without prior consent form should be designed and specifically worded for bereaved parents. These documents should be prepared at the trial design stage and written in close consultation with bereaved parents, bereavement specialists and relevant special interest groups (see recommendation 1).
- The covering letter should be personalised and if possible signed by a clinician known to the family. The letter should explain that, understandably, parents will often have questions about the research in the days, weeks or months after the loss of a child and invite them to contact the trial team to arrange for a telephone or face-to-face discussion with the PI about the trial if they wish. Include the bereaved parent information leaflet, research without prior consent form and stamped addressed envelope.
- Letters should explain whether or not the child's data will be included in the trial if parents do not respond to the letter. For example, at the onset of a trial ethical approval may have been sought for inclusion of the child's anonymised data in the trial when no consent form has been received from bereaved parents.
- Copies of letters sent to parents should be placed in the patient's notes.
- Be prepared to respond to parents who are concerned that participation in the trial may have contributed to their child's death. Be careful to avoid giving false reassurance that this is not the case, unless it has been established by the principal/chief investigator or coroner that the cause of death was not related to the trial.

Option 3: Contact parents by telephone or a letter to a arrange a face to face trial discussion

- If it is not thought appropriate to explain about the trial or seek permission to use data already collected before parents leave the hospital, consult with clinical colleagues and bereavement counsellors to identify an appropriate time to contact parents via telephone or letter to arrange a face to face visit to discuss research.
- If a letter is used, these should be written at the trial design stage in close consultation with bereaved parents/bereavement specialists/relevant special interest groups (see recommendation 1).
- The letter should be personalised, signed by a clinician (known to the family if possible) and include a bereaved parent information leaflet.
- Copies of letters sent to parents should be placed in the patients' notes.
- Provide parents with options for meeting location (e.g. at their home or local hospital) as some parents may not wish to return to the hospital where their child died.

- During face to face discussions explore parents' views and understanding of the trial and why consent was not sought prior to the trial so that any concerns can be addressed.
- Be prepared to respond to parents who are concerned that trial participation may have contributed to their child's death. Do not give false reassurance that the trial did not contribute to their child's death, unless it has been established by the principal/chief investigator or coroner that the cause of death was not related to the trial.
- If parents do not wish to have a face to face meeting inform them that a trial information leaflet and consent form will be sent via post (see option 2).

SECTION 6: Child assent and consent involving young people

Recommendation 6: Children (under 16 years) and young people (16-18 years) should be involved in making decisions about the use of their data in the trial and continued enrolment if they have capability.

- Seek parents' permission to involve children (under 16 years) in the consent discussion and assent seeking if their age, condition and cognitive capacity allows.
- Seek permission to use data already collected and consent for continued participation in the trial from young people (16-18 years) if their condition and cognitive capacity allows. When young adults are incapacitated seek consent from parents.
- Ensure written information is available for different age and competence ranges.
- At the pre-trial stage (see recommendation 1) consider what action should be taken if parents do not wish to involve children in the consent discussion.
- When assent (for children) or consent (for young people) cannot be sought due to their condition provide an age appropriate information sheet to assist parents in discussing the trial with their child when they have recovered. Place a copy of the information sheet in the patient's notes and describe the reasons why assent or consent has not been sought.
- Ensure that contact details are provided if parents or children wish to discuss any aspect of the trial with the recruiting doctor or nurse at a later date.

SECTION 7: Recommendations for further research

- Research is required to explore the acceptability of doing research without prior consent within trials that may involve higher risks, but might provide an option for the treatment of critically ill children.
- Further research involving bereaved parents who have experienced research without prior consent should be conducted to inform recruitment and consent seeking when a child has died. Recommendations made in section 5 should be evaluated by bereaved parents who experience research without prior consent in a critical care trial.
- Recommendations made in section 6 should be evaluated by children who have experience of research without prior consent.

Jargon buster

Term	Acronym	Explanation
Patient and public involvement	PPI	The active involvement of the public in all aspects of research
Principal Investigator	PI	Doctor leading the research at each hospital site.
Clinical Trials Unit	CTU	Specialised research units that design, coordinate and analyse clinical trials and other studies.
Participant information sheet	PIS	Researchers must provide a patient information leaflet to all people they invite to take part in a study. This provides details such as what the research is about and the potential risks and benefits of taking part.
Consent		Agreement or permission to do or allow something. In this document this refers to consent to take part in research
Deferred consent		A term used across Europe to describe the process where research is conducted without prior consent (please see the introduction section for further details).

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Appendices

Appendix A: Outline of the CONNECT Study

The CONsent methods in childreN's emergEncy medicine and urgent Care Trials (CONNECT) study was a Welcome Trust funded post-doctoral fellowship in bioethics awarded to Dr Kerry Woolfall (2012-2015). CONNECT was the first UK study to explore parent and practitioner perceptions and experiences of research without prior consent in children's clinical trials. The aim of CONNECT was to provide new evidence to inform how consent should be sought for children's critical care trials. 354 people took part, including 292 parents, 39, nurses, 19 doctors and 4 clinical trials unit practitioners. Surveys, interviews and focus groups were used to explore their views and experiences on approaches to consent in emergency and urgent care settings. Findings indicated how parents are often unaware that research can be conducted without prior consent and many were momentarily shocked or angered to discover that their child had, or could have, been entered into a trial without their prior consent. Despite initial concerns, practitioner explanations of why consent could not be sought before the emergency intervention was given can help to address parents' initial concerns about the method and help them to reassure them about research without prior consent. Practitioners' views on research without prior consent differ, depending upon whether or not they are experienced in this method. We found that practitioners who have no experience of research without prior consent report negative perceptions of this consent method; these practitioners are concerned about the impact that research without prior consent would have upon the parent-practitioner relationship. In contrast, practitioners experienced in research without prior consent describe how families are receptive to the method, if conducted sensitively and if the timing is appropriate. CONNECT findings have been integrated with wider research and ethical theory to produce guidance to inform approaches to recruitment and consent in paediatric and neonatal critical care trials (See Appendix D).

Links to CONNECT publications to date:
http://bmjopen.bmj.com/content/4/5/e005045.full
http://www.biomedcentral.com/content/pdf/1472-6939-14-45.pdf

Appendix B: CONNECT Advisory Group

Professor Bridget Young, University of Liverpool

Professor Carrol Gamble, University of Liverpool

Dr Lucy Frith, University of Liverpool

Professor Angus Dawson, University of Birmingham

Professor Michael Parker, University of Oxford

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Ms Helen Hickey, University of Liverpool

Dr Claire Snowdon, London School of Hygiene and Tropical Medicine

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Appendix C: Statements of key evidence considered when developing each recommendation

The following statements of key evidence were developed using CONNECT research findings and a review of research and ethical theory. They aim to provide a brief overview of evidence considered when developing each recommendation.

SECTION 1: Pre-trial research for potentially challenging trials

Recommendation 1

- Children's critical care trials are fraught with ethical and practical difficulties (Source: CONNECT[10 11] and other research[12-15]).

- Methods of protecting children from harm and legitimising decision making are required in addition to consent, such as research to inform trial designs[16] and ethical review[17].

- The majority of parents and practitioners support the use of research without prior consent in paediatric and neonatal critical care trials to enable critical care research to proceed. However, parents indicated that research without prior consent is more acceptable for trials of medical interventions that have been used in standard clinical practice than trials that involve new interventions. Some practitioners and parents have concerns about research without prior consent for blood samples, particularly in neonates. Parents support the conduct of research for the common good, without direct benefit for their child as long as child safety is not compromised. (Source: CONNECT[11]).

- Parents regard seeking prospective informed consent as inappropriate in the critical care setting as the stress of the situation prevents them from absorbing, understanding or even wanting information about research when their child is critically ill (Source: CONNECT[11 18] and other research[2 19-22]).

- Providing trial information that is tailored to what parents consider important in making a decision about a clinical trial may improve recruitment practice and ultimately benefit evidence based paediatric medicine (Source: other research[23 24]).

- In both the emergency and the non-emergency settings parents may sign consent forms and consider themselves informed without an adequate understanding of what the trial entails or how involvement will impact on family life (Source: CONNECT and other research[23 25-28]).

- Qualitative and/ or quantitative research can inform trial development in challenging settings, including the identification of barriers and potential solutions to successful recruitment (Source: CONNECT[11] and wider research[16 29 30]).

SECTION 2: Publicising trials that use research without prior consent

- Organisations involved in clinical research should promote this more widely with patients and the public. Those departments involved in paediatric emergency medicine research should consider the 'brand' that is used to promote this important work (Source: wider research[31])

- Some parents may be initially surprised or concerned to find out that their child has been entered into a clinical trial without their prior consent (Source: CONNECT).

- Parents want to discuss research in a timely fashion but only when the child's condition has stabilised (Source: CONNECT).

SECTION 3: Written trial information

Recommendation 3: Written trial information should be presented in a format that is easy to understand

- In both the emergency and the non-emergency settings parents may sign consent forms and consider themselves informed without an adequate understanding of what the trial entails or how involvement will impact on family life (Source: CONNECT and other research[23 25-28]).

- Patient information should be clearly written and not too long (Source: CONNECT and other research[32-34])

- Providing trial information that is tailored to what parents consider important in making a decision about a clinical trial may improve recruitment practice and ultimately benefit evidence based paediatric medicine (Source: other research[23 24]).

- Parents recommend that brand names as well as generic drug names should be used when giving verbal and written information, as this may help them to may recognise the drugs (Source: CONNECT[11]).

SECTION 4: Discussing research without prior consent with parents

Recommendation 4.1

-Improvements to life-saving treatments for critically ill children have been prevented by ethical and practical challenges. In particular, the process of informed consent requires time, but this is severely constrained in the critical care setting. Any delays in the treatment of children for consent seeking purposes are unethical and can obscure trial findings (Source: ethical literature[35 36]and other research[1 12 37]).

- UK legislation was amended in 2008 to enable the use of research without prior consent in children's critical care trials so that children can benefit from treatments that have been tested (Source: UK legislation[7]).

- The majority of parents regard seeking prospective informed consent as inappropriate in the critical care setting as the stress of the situation prevents them from absorbing, understanding or even wanting information about research when their child is critically ill. Parents and practitioners support the use of research without prior consent in paediatric and neonatal critical care trials to enable critical care research to proceed. (Source: CONNECT[11 18] and other research[2 19-22]).

- One of the main reasons parents report as influencing their decision to provide consent for their child's participation in critical care research is the hope that the research will be of future benefit to other critically ill children (Source: CONNECT*).

- Clinical trials of interventions to save the lives of critically ill children are important to make sure their care is evidence-based. Children, like adults have the right to the highest standard of healthcare and for their care to be evidence-based where possible. They also have the right to be informed about their involvement in research and to take part in research decisions (Source: other research[38] and ethical literature[17 39]).

- Parents want research without prior consent to be sought in a timely fashion but only when the child's condition has stabilised (Source: CONNECT[11]).

- Before discussing research parents recommend that trial recruiters should check with the nurse or doctor who is looking after their child that the timing is appropriate (Source: CONNECT[11])

- The stressful critical care environment may compromise some parents ability to fully absorb research information and may cause a burden (Source: ethical literature[40 41]).

Recommendation 4.2 (a and b)

- The critical care situation can impact upon parental capacity to fully absorb and understand trial information even when the critical situation has passed (Source: CONNECT*, ethical literature[36 42] and other research[2 19-22])

- Parents may sometimes sign consent forms and consider themselves informed without an adequate understanding of what the trial entails or how involvement will impact on family life (Source: CONNECT*, other research[23 25-28]).

- Some parents may be initially surprised or concerned to be informed that their child has been entered into a clinical trial without their prior consent. However, practitioner explanations about why a research without prior consent approach is used in critical care settings can help to address parents' initial concerns about the method and help them understand why research without prior consent has been used (Source: CONNECT*).

- When considering whether or not to provide research without prior consent for a critical care trial parents prioritise: child safety; an explanation as to why research without prior consent was used; any changes to standard clinical practice and how their child would have been treated had the trial not been running (Source: CONNECT[11])

- Providing trial information that is tailored to what parents consider important in making a decision about a clinical trial may improve recruitment practice and ultimately benefit evidence based children's medicine. Encouraging more parental participation in the discussions may help practitioners identify key issues and concerns for parents and provide appropriate information and clarification (Source: CONNECT* and other research[23 24]).

SECTION 5: Discussing research without prior consent with parents when a child has died

Recommendation 5:

- Excluding children who die, without any attempt to obtain consent from their parents can jeopardize trial results (Source: other research[13 37 43]).

- Practitioners have described how contacting parents to discuss research participation is personally challenging (Source: CONNECT and other research[44]).

- Bereaved parents can value the contribution that their child has made to research and it is important that they are given the opportunity, without pressure, to make the gesture of consenting

to the including of their data, and have the opportunity to be thanked for doing so. A minority strongly oppose such disclosure (Source: CONNECT[11] and other research[45 46]).

- Parents' interest in receiving information about a trial may recede initially after their child's death but re-emerge over time (CONNECT[11] and wider research[45]).

- Opinions vary regarding the right time for practitioners to contact bereaved parents about the inclusion of their child's data in a trial. However, parents state that disclosure should not be too soon (e.g. days) after death (Source: CONNECT[11] and other research[46]).

- Bereaved parents strongly support medical research to help save the lives of critically ill children and help to prevent other parents from experiencing child death (Source: CONNECT[11] and other research[45]).

- Research involving bereaved parents at the pre-trial stage can inform a co-ordinated and family centred approach to consent seeking (Source: CONNECT[11] and other research[45])

-Bereaved parents describe the individuality of grief and how this poses difficulties in making broad recommendations for consent seeking. They recommend that a doctor or nurse already known to the family should individually assess whether or not to make contact with parents to discuss research. Decisions to contact bereaved parents should be balanced against the potential burden that a recruitment discussion may pose (Source: CONNECT[11] and other research[46]).

- Parents may not attend bereavement follow up visits or access bereavement counselling. Those who do attend bereavement follow up may not prioritize research during discussions about events that occurred around their child's death or have the capacity to discuss trial participation. However some parents would like to have the opportunity to discuss research at this point in time (Source: CONNECT[11] and other research[45]).

- Recruitment of bereaved parents by postal contact without providing the option for telephone or face to face discussion with the PI is insufficient. (Source: CONNECT*[11] and other research[45])

- Doctors and nurses contacting parents in this situation should be aware that parents' responses may be unpredictable due to the grief they will be suffering. Approaches to consent should be personalised and conducted with considerable care and sensitivity (Source: CONNECT[11] and other research[46]).

- Parents describe how practitioners seeking research without prior consent should be prepared to address potential concerns from parents that the interventions administered as part of the trial may have contributed to their child's death (Source: CONNECT[11]).

- There are ethical and safety arguments that the advantages of using data without consent in these situations outweighs any harms relating to a lack of consent. However, some may oppose the use of data without consent (Source: other research and ethical literature[44 46 47]).

SECTION 6: Child assent and consent involving young people

- International guidelines require that if a child is able, assent should be sought for their participation in research in addition to parental consent (Source: ethical literature[48 49], research guidelines[50-52]).

- In the critical care setting it may be impossible to seek assent as children may be too poorly or heavily sedated (Source: CONNECT).

- Children may be discharged from hospital before doctors and nurses have an opportunity to discuss the trial (Source: CONNECT).

- Parents may oppose discussion of research with children. Researchers should consider what to do if parents do not wish to disclose research information with children (Source: other research[53]).