Guidance to inform communication with bereaved families about their relatives' participation in emergency or critical care research without prior informed consent

ENHANCE

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Foreword

My name is Julie and I'm the patient representative on the NIHR funded ENHANCE study. I have had sepsis and am a volunteer with the UK Sepsis Trust.

I was the patient representative with the PRONTO trial, which involved patients with sepsis. As this trial progressed, I along with the rest of the trial team, became aware that we needed to find out how and whether to let families know if their loved one had died whilst participating in a clinical trial. When a trial involves patients who are critically ill some will die. Sadly 30% of patients with severe sepsis do not survive.

To improve care and patient outcomes clinical trials are necessary and in emergency settings where time is critical patients can be involved in a trial without their consent (if, for example, they need immediate treatment and are too unwell to be consulted).

Through the ENHANCE study we wanted to better understand how to communicate with the loved ones of patients who had died in a way that was open and transparent yet did not add to their grief and distress.

This Guidance has been developed as an attempt to answer that question.

Appreciating that communication is a two-way process we asked bereaved family members for their thoughts, along with views of medical examiners and those who provide information to bereaved relatives.

We hope this guidance will benefit clinical and research staff and improve the experience of bereaved relatives.

Julie Carman
Patient Representative
ENHANCE Study

Reference: Woolfall, K., E. Deja., H. Doughty., B. Young., I. Welters., V. Shepherd., S. Milosevic; K. Pool; J. Carman., V. Sankar., E. Thomas-Jones; J. Euden (2024). Guidance to inform communication with bereaved families about their relatives' participation in emergency or critical care research without prior informed consent. ENHANCE Study Guidance Version 1.0. Liverpool, UK: https://www.liverpool.ac.uk/population-health/research/enhance

What is included in the guidance?

Contents

Glossary of terms and abbreviations

Capacity	Capacity means the ability to make a particular decision at the time it needs to be made. Someone lacking capacity cannot do one or more of the following: (1) understand information given to them about a particular decision; (2) retain that information long enough to be able to make the decision: (3) weigh up the information available to make the decision; (4) communicate their decision (in any way).
CTIMP	Clinical Trial of an Investigational Medicinal Product (e.g. drug trial).
Non-CTIMP	Any study that does not involve an investigational medicinal product is a non-CTIMP (not a drug trial). Examples of non-CTIMPS include medical device trials and observational studies that involve data collection only.
ICU	Intensive Care Unit, also known as critical care (unit).
Informed consent	Providing permission for participation before being entered into the research. For consent to be valid, it must be voluntary and informed, and the person consenting must have the capacity to make the decision.
Emergency and non-emergency research	These terms are in widespread use, but what is defined as an emergency versus non-emergency in a research context is often not clear. This guidance uses the term emergency research when a treatment needs to be given urgently and there is limited or no time to seek informed consent for a study. This definition is used by the Health Research Authority and is closely aligned with the wording of clinical trials legislation. However, emergency research can also be considered to include situations when a study activity does not involve treatment (e.g. the activity is for data collection) but it must happen before an urgent clinical intervention already in progress is complete, or the study activity has a short time window and delaying recruitment to gain consent would invalidate the study. Emergency research often needs to occur within a limited timeframe, but the justification for when it's appropriate to use research without prior consent (RWPC) can vary from study to study in accordance with the potential benefits and harms varying between studies.
Medical Examiner and Medical Examiner Officer	A new statutory medical examiner system is being rolled out across England and Wales to provide independent scrutiny of deaths, and to give bereaved people a voice. From 9 September 2024 all deaths in any health setting that are not investigated by a coroner will be reviewed by NHS Medical Examiners, senior medical doctors in the NHS; supported by Medical Examiner Officers, who manage cases from initial notification through to completion and communication with the registrar offices. Part of the Medical Examiner role is to discuss the cause of death with

	bereaved people and establish if they have questions or any concerns with care before death.
Next of Kin (NOK)	The informal term 'next of kin' in a medical context is someone a patient can nominate to receive information about their medical care. If a next of kin has not been nominated it will usually be assumed to be someone close to the person (e.g. spouse or partner) however duties such as confidentiality still apply. As next of kin they have no rights of access to medical records, or the ability to make decisions about the person's care unless they have Power of Attorney or similar legal arrangements. Separate arrangements apply to decisions about research (see below).
Nominated consultee	Used in non-CTIMPs to refer to a person who is independent of the study appointed in accordance with the Department of Health's guidance on nominating a consultee for research involving adults who lack the capacity to consent. They are consulted to provide advice about the person's participation in a study.
Personal consultee	Used in non-CTIMPs to refer to someone who cares for the patient (not professionally or for payment), or is interested in his/her welfare, and is prepared to be consulted to provide advice about the person's participation in a study. It is usually a family member or a close friend.
Personal legal representative	Used in CTIMPs to refer to a person not connected with the study who is suitable to act as the legal representative by virtue of their relationship with the patient and is available and willing to do so. It is usually a family member or a close friend. They are asked to provide informed consent for a study based on the person's 'presumed will'.
Professional legal representative	Used in CTIMPs to refer to a person who is independent of the study, usually a doctor responsible for the medical treatment of the patient, or a person nominated by the healthcare provider. They are asked to provide informed consent for a study based on the person's 'presumed will'.
Research without prior consent (RWPC)	Research Without Prior Consent is used in emergency research where there is no time to seek informed consent from a legal representative or advice from a consultee before research participation. This is also known as 'deferred consent'.

What is the scope and purpose of the guidance?

Involving critically ill patients in research is important to help find treatments that save lives. If information about patients who die is not included in the research, the results may be unreliable, as it would be unclear if study participation leads to higher rates of death.

In emergency research, where participants are unable to provide consent due to lack of capacity, alternate models of consent are often used. These include approaching those close to the patient, for example a relative or close friend who has been listed as their 'next of kin' (NOK) to seek their advice or consent. Where it is not practicable to do so, it may need to involve an independent professional, such as a doctor, in deciding whether to enrol the patient in research. Patients enrolled in emergency research based on consent or agreement/advice from a healthcare professional may die before the study is discussed with relatives. This leads to situations where bereaved relatives are unaware their family member has participated in a study and that their data will be used.

The National Institute for Health and Care Research: Research for Patient Benefit (NIHR RfPB) funded ENHANCE (ENHANCing Communication with bEreaved relatives about emergency and critical care trials) study assessed and explored potential communication strategies with bereaved families when their relative has died following enrolment into an emergency/critical care trial, without prior informed consent. This ENHANCE guidance has been developed to improve transparency and build trust by assisting and enhancing communication with bereaved families about adult patient participation in emergency or critical care research without informed consent before death. These recommendations aim to assist the design, review and delivery of studies conducted in UK adult emergency and critical care settings. This guidance can be used to inform the development of new study protocols, ethical review of study applications or to accompany/inform amendments to an existing protocol that has been approved by an ethics committee.

This guidance can be used in conjunction with Good Practice Guidance from the Perspectives Study which covers broader approaches to recruitment and consent involving critically ill patients.

Who is this guidance for?

The ENHANCE guidance is for all those with a direct or indirect role in the funding, design, conduct, governance, and ethical review of emergency and critical care studies involving adults. This includes, but is not limited to doctors, nurses, paramedics, researchers, patient and public involvement (PPI) contributors, members of research ethics committees, study sponsors, funding committees, peer reviewers, and clinical trials unit staff. The guidance will also be of interest to patients, family members, NHS Research and Development (R&D) staff, other members of the public and organisations representing the interests of patients and the public.

The recommendations in this guidance are based on the findings of the ENHANCE study. Researchers and ethics committee members can struggle to know when, or whether, it is

appropriate to disclose a deceased patient's research involvement to grieving families and next of kin. The ENHANCE study is the first UK study to explore whether bereaved relatives wish to be informed about their family member's participation in research and if so, when and how they would prefer to be told. We also sought the perspectives of professionals who communicate with bereaved relatives in this setting, including researchers, medical examiners and bereavement nurses.

ENHANCE participants were recruited from across the UK. Please see Appendix 1 for an outline of the study methods. All recommendations comply with English and Welsh legislative frameworks and should be used with close reference to those. Appendix 2 provides a description of approaches to recruitment and consent in emergency situations by study type (e.g. Clinical trials of investigational medicinal products (CTIMPs) and non CTIMPs). While frameworks in Scotland and Northern Ireland differ from those in England and Wales, we expect the guidance to be broadly transferable throughout the UK and beyond.

Key ENHANCE findings and principles that underpin the guidance

The ENHANCE study assessed and explored potential communication strategies with bereaved families when a patient has died following enrolment into an emergency/critical care study, without prior informed consent. See Appendix 1 and 3 for study details. Key findings and principles that underpin this guidance include:

- There is no legal obligation to discuss research participation with bereaved families ('next of kin' where they are nominated).
- Researchers are concerned about the potential burden of informing bereaved families about patient enrolment into a study under an emergency (RWPC) where consent has not been obtained from a patient or relative before death.
- There has been uncertainty about whether and how to inform bereaved families, which has led to many studies, including CTIMPs, not including a process of notifying families about participation after death in their protocol.
- Ethical concerns have been raised about a lack of transparency when relatives are not informed, as well as the duty of candour, which emphasises the importance of being open and transparent about the quality and type of care patients receive.
- The ENHANCE study found that bereaved family members had mixed views on whether they or their relatives would want to know about research involvement. Whilst most of the people we interviewed or who were contacted by a Medical Examiner, stated they would wish to know, there were exceptions.
- This supports evidence from the few studies on this topic conducted in paediatric and adult critical care settings. Most family members do wish to know about their relatives' involvement in research.

- A minority of families in the ENHANCE study did not wish to be informed about research participation. It is therefore important to respect their wishes and find a solution that accommodates all perspectives.
- Researchers, Medical Examiners, and relatives in our sample acknowledged that bereaved families could find out about research participation through different means, such as a request to see medical notes, which may compromise trust.
- Staff and families felt that it should be one of the clinical, research or bereavement team who provides bereaved relatives with information about research participation, ideally involving a person known to the family who has knowledge of the study to address potential questions.
- Family members who wished to know about research involvement stated they would prefer to find out early in the grieving period. However, they acknowledged it is difficult to identify 'the right time' for the information to be delivered.
- Discussing the cause of death with bereaved families and establishing if there are concerns with care is a routine practice of established medical examiner services. Medical Examiners and Medical Examiner Officers held mixed views about whether their role should be holistic and extend to clinical and research aspects of care.
- At the final guidance development workshop bereaved families emphasised the importance of early research discussions. Key stakeholders, including medical examiners, research nurses and the bereaved were concerned that embedding such discussions within medical examiner calls was not soon enough and that any mention of research in a conversation about the cause of death could make the bereaved think that research was linked to death and cause an unnecessary burden. There were also concerns that research participation may not be accurately recorded in the medical notes leading to miscommunication.
- Study findings highlight the importance of providing bereaved relatives with the option of being notified about research involvement without prior consent before death, if they wish to receive such information. The need for honesty and transparency was paramount.

Recommendations

Research and/or clinical teams (with knowledge of the study) should discuss emergency or critical care research involvement with bereaved relatives as soon as appropriate after enrolment. We acknowledge that it is not always suitable or possible to speak to family members about research involvement before death, or before the bereaved family leaves the hospital.

The following recommendations provide options for researchers to consider when designing emergency or critical care studies where consent may not be obtained from a patient or relative before death. Recommendations are presented to inform study protocols, research ethics committee applications and staff training. Recommendations are structured to recognise the varying systems and staffing structures across NHS Trusts and Health Boards. The following recommendations use the term bereaved family members. In this context, we are referring to a person (or persons) who are close to the patient and may be listed as their 'next of kin'.

Section 1: Pre- Research Activity

Recommendation 1: Tailor the approach to notifying families about research involvement to the research setting and the preferences of patients and family members sought through patient and public involvement at the study design stage.

- Seek the views of patients and families at the research planning stage to consider the most appropriate and practicable approach (of those stated below) to notifying bereaved relatives where it has not been possible to seek consent for research participation before death from a professional and/or personal legal representative or a professional and/or personal consultee. When seeking patients and public involvement contributors for your study aim for diversity of experience and background e.g. variance in experience or knowledge of research, different ethnic or cultural backgrounds as well as previous ICU admission.
- Ensure that time and resources required for the chosen notification processes are considered and include them in the research funding application.
- Consider how research participation, type of consent to be sought (e.g. if applicable, professional legal representative or professional consultee) and study names are recorded within NHS Trust/Health Board records and potential gaps. For example, consider how ambulance-led studies that use alternative consent pathways are recorded in hospital records so these patients can be identified in addition to those conducted within the ED and ICU.
- Consider which letters for bereaved families need to be developed (see templates in Appendix 4 and 5) and tailor communication for your study in collaboration with PPI. Letters will need to be approved by a research ethics committee. Ensure your

protocol considers options for families who may live abroad or do not attend hospital (e.g. digital versions).

- Use posters to advertise that this is a research-active hospital if these are not already used in participating NHS Trusts and Health Boards.
- Research teams using NHS data should also consider in their protocol what should happen if a patient has opted out of NHS National data sharing before death and whether this may have implications for the bereaved family notification process.

Section 2: For NHS research in Trusts and Health Boards involved in emergency or critical care research

Recommendation 2: A designated clinician or a member of the bereavement team should provide the bereaved family with an opportunity to find out IF their relative was involved in emergency or critical care research before they died

- At an individual study level, establish whether it will be the clinical team or bereavement team who will establish **IF** the bereaved family member would like to find out about research participation.
- Ensure this role is clarified in the study protocol and on study delegation logs.
- The designated person/team should use their professional judgment on when to ask the bereaved family member. They should explain that this is a research active hospital and how some patients may have been involved in emergency or critical care research before they passed away. Then ask the bereaved if they would like to know whether their relative was involved in research during their hospital admission.
- Asking the bereaved **IF** they would like to know about research involvement should be consistent with the ethically approved study protocol, take place as soon as practically possible, and complement bereavement guidance at each participating hospital.
- If it is not thought appropriate to discuss the study, consult with colleagues to identify an appropriate time to contact family members by a research ethics committee approved personalised letter from the research team in the appropriate language. This communication should take place sooner rather than later (e.g. within a week).
- If the family member states they would like to know about research involvement, check the medical records and confirm whether the deceased patient did take part in the research and who approved their involvement (e.g. independent doctor).

Option 1: Obtain contact details to send to a designated research team and/or clinician

- Ask the bereaved family member if they would like the designated member of the research team and/or clinician (whoever is deemed appropriate for the individual study) to contact them with information about the research.
- Ask how and when they would like to be contacted (e.g. face-to-face discussion or letter and identify any communication or language needs).
- Seek consent to provide their preferred contact details and preferred method of contact to the research team member and/or designated clinician.
- Be prepared to respond to family members who are concerned that study participation may have contributed to their relative's death.

Option 2: Send a letter to the bereaved next of kin

- Send a letter to the bereaved family member from the study team.
- Template letters should be developed at the study design stage, approved by a research ethics committee and made available to the designated person/team. These should be written in close consultation with PPI representatives/bereaved family members/bereavement specialists/relevant interest groups. The letter should be personalised, signed by a research lead (known to the family if possible), including a named contact, email address (e.g. research team email to help prevent delays in responding) and telephone number and emphasise that a face-to-face meeting is optional.
- Consider which letter translations will be required for the local population.
- The letter should explain that if the bereaved family do not wish to have a face-to-face meeting, further information about the study can be made available (e.g. by post or study website). Provide contact details to the bereaved family in case they wish to discuss the research at a later date. Add a potential time frame for the research team to respond to the family. An example letter is provided in Appendix 4.
- A copy of the letter sent should be placed in the patient's notes.

Section 3: For NHS Trusts and Health Boards involved in emergency or critical care research who provide bereavement information to families after death

Recommendation 3: Include a letter in the bereavement information materials that states the possibility of research involvement

- Add a sensitively worded letter to bereavement information (e.g. bereavement pack or booklet) stating that this is a research-active hospital and that their family member may have been involved in emergency or critical care research during the

hospital admission or ambulatory care before they died. An example letter is provided in Appendix 5.

- Consider which letter translations will be required for the local population.
- Identify who would be the most appropriate person for families to contact in your Trust/Health Board if they would like to find out more information about research involvement.
- Include contact details (e.g. key contact with the Trust/Health Board or research team email address and/or phone number) in the letter.
- To respond appropriately to relative enquiries, the key contact will need knowledge of emergency and critical care research within their Trust/Health Board, including information on the studies that are conducted without prior informed consent and have notification of bereaved next of kin in their protocol.

Section 4: For research and/or clinical teams when discussing research participation with bereaved family members

Recommendation 4: Discussing research conducted without prior consent with bereaved family members should be carefully considered and tailored to the individual

- During face-to-face discussions or telephone calls explore bereaved family members views and understanding of the study, as well as why informed consent could not be sought, so that any immediate concerns can be addressed.
- Tailor communication for each individual with consideration of their communication and language needs. Use interpreter services if required.
- Ensure staff involved in discussing research with bereaved families have received relevant protocol training.
- Tailor conversations with bereaved family members to the study and their questions or concerns. The following points may be helpful to consider. Please note that this is not a checklist as some points will not be relevant and may depend on the study type, data collected and family awareness of the research:
    - That consent is commonly sought from a patient before involvement in research however, in an emergency, which requires rapid assessment and treatment, legislation allows research studies to enrol participants without prior consent.
    - Clarify how alternate models of consent are often used. These include approaching the patient's family to seek their advice or consent or, where it is not possible, involving a nominated independent professional, such as a doctor, in deciding whether to enrol the patient in research.
    - Explain how patients enrolled in emergency research based on consent or agreement/advice from an independent professional may sadly die before

the study is discussed with relatives.

- Explain that permission from an NHS research ethics committee was sought to enrol patients in this way.
- Explain that research into treatments given in emergencies is important to help save lives in the future and how the information collected from your relative's medical records can be used to improve the care of patients.
- Provide information about the study interventions and how they compare with usual clinical care.
- Clarify that all information collected is anonymous meaning that no one outside of the hospital team has access to any personal identifiable information.
- Confirm that under the legal framework (in England & Wales), no additional written permissions are needed at this time.
- If families question whether the death was related to study participation involve the clinical team in these discussions and check if the family have spoken to a Medical Examiner. Do not give false reassurance that the study did not contribute to their family member's death unless it has been established by the principal/chief investigator or coroner that the cause of death was not related to the study.
- Provide an information sheet for bereaved relatives, which details a timeframe for when the study findings will be available and how they can be accessed (e.g. study website or research team contact details) if they wish to do so.

Appendix 1: Overview of the ENHANCE study

Rationale for the study

Clinical research in emergency or critical care settings is vital, yet the recruitment and consent processes are highly complex. In emergency research, where participants cannot provide consent, alternate models of consent are used. However, patients may die before the study is discussed with relatives, leading to bereaved families being unaware that their family member participated in a clinical study. There is a lack of knowledge about whether relatives wish to be informed of participation in research, or when and how they would prefer to be informed.

In the NIHR RfPB funded ENHANCing Communication with bEreaved relatives about emergency and critical care trials (ENHANCE) study, we aimed to assess and explore potential communication strategies with bereaved relatives when a patient has died following enrolment into an emergency/critical care study, without prior informed consent.

ENHANCE was approved by the Yorkshire & The Humber- Leeds West Research Ethics Committee, 17th March 2023, Reference 23/YH/0052. Sponsor: University of Liverpool

Methods

Mixed-methods study involving:

1) a Medical Examiner-led survey of relatives of deceased trial participants. This was a short survey of recently bereaved next of kin who were informed of their relatives involvement in either the NIHR funded PRONTO trial (PRONTO - Centre for Trials Research - Cardiff University) or UKROX trial (ICNARC – UK-ROX) and asked if they would like to receive further information from the research team and/or take part in an interview at a later date
2) semi-structured interviews with bereaved relatives, Medical Examiners, research, and clinical staff involved in emergency and critical care trials in England and Wales. Relatives were recruited via social media and the Medical Examiner survey. Staff were recruited via social media and research networks.
3) two stakeholder workshops (one online, one face to face in Liverpool) to review draft guidance for future were conducted in May 2024 involving all key stakeholder groups.

Qualitative data were analysed using thematic analysis and quantitative data was analysed using descriptive statistics. Findings informed draft guidance, which was reviewed and developed during the workshops.

Participants

Sixty-five participants took part between June 2023 and May 2024. Eleven bereaved relatives completed the survey; fifty-three participants (18 bereaved relatives, 14 Medical Examiners/Officers, 13 Research nurses, 4 doctors, and 4 Bereavement nurses) took part in semi-structured interviews; and one bereaved relative participated in both phases.

A total of 38 stakeholders (8 relatives, 6 Medical Examiners/Officers, 7 research nurses, 1 HRA representative, 2 ethics board members, 6 clinical nurses, 5 doctors, 3 bereavement nurses and 8 researchers with 7 individuals self-identifying as having 2 or more stakeholder roles) attended one of two guidance development meetings, 12 of whom had also taken part in interviews.

Appendix 2 Summary of approaches to recruitment and consent seeking with incapacitated patients in England and Wales by study type

Summarised interpretation of legal frameworks from the Health Research Authority website and relevant legislation, 2013, 2018, 2019

Clinical trials of investigational medicinal products (CTIMPs)

CTIMPS in emergency situations

When investigating treatments that must be administered urgently and it is not reasonably practicable to obtain consent from a legally designated representative, patients can be recruited into a trial without prior consent. This is known as research without prior consent (RWPC). As patients recruited under this process may regain capacity to give consent, researchers are required to plan how they will involve patients in the on-going consent process. Trial participation and any relevant consent required (e.g. consent for continued participation and disclosure of confidential information) should be discussed with the legally designated representative, or patient if they regain capacity, as soon as possible after the patient's recruitment to the trial.

CTIMPs in non-emergency situations

Investigators can seek prospective consent from an incapacitated patient's legally designated personal representative. Personal legal representatives are personally known to the patient, such as a family member or a close friend. However, if there is no personal legal representative, they are not available or they are unwilling to act (i.e. you can't contact them or they don't want to make that decision) a doctor who is independent of the study can act as a legally designated professional legal representative, and consent to a patient's enrolment in a trial in certain circumstances. Researchers will usually seek consent (e.g. for continued participation and further disclosure of confidential information) from the patient, if and when they regain capacity.

In the context of this guidance, a patient may have been entered into a clinical trial with professional legal representative consent and subsequently die without their family member being aware of their participation.

Other study types

Other study types are those that involve the processing of personal data, administration of interviews or observations, and clinical trials that are not CTIMPs (for example, medical devices).

Other study types in emergency situations

Patients can be recruited without prior advice from a consultee, provided it is not reasonably practicable to seek such advice in advance. Investigators need to seek agreement of a registered medical practitioner who is not involved in the organisation or conduct of the study - unless there is insufficient time to obtain that agreement. A consultee's advice (personal consultee or nominated

consultee if there is no personal consultee available) should be sought on the participant's likely views and feelings about the study as soon as possible after recruitment. If objections are raised, the patient must be withdrawn unless doing so would pose a risk to the participant's health. If and when a patient recruited under a consultee process subsequently regains capacity, study participation should be discussed.

Other types of study in non-emergency situations

Before a patient is recruited to such a study, investigators are required to seek advice from the patient's personal consultee, usually a family member, about the patient's likely wishes. If investigators are unable to identify a personal consultee they can consult with a nominated consultee, which is usually a member of the patient's care team who has no connection to the research. When a patient recruited under a consultee process subsequently regains capacity, study participation should be discussed.

As noted above, in the context of this guidance, a patient may have been entered into research with the agreement of a medical practitioner or advice from a nominated consultee advice and subsequently die without their family members being aware of their participation.

For legal provisions for recruitment and consent of incapacitated patients in:

- Scotland see http://www.hra-decisiontools.org.uk/consent/principles-ALC-Scotland.html
- Northern Ireland see http://www.hra-decisiontools.org.uk/consent/principles-ALC-NIreland.htm

Appendix 3 ENHANCE Study Management Group and Advisory Group

ENHANCE Study Management Group

Name	Role/expertise	Institution/Organisation
Prof Kerry Woolfall	Chief Investigator, trials methodologist	University of Liverpool
Dr Joanne Euden	Co-lead, clinical trials management	Centre for Trials Research, Cardiff University
Dr Beth Deja	Co-investigator, ENHANCE Research Associate	University of Liverpool
Dr Hannah Doughty	ENHANCE Research Associate	University of Liverpool
Mrs Julie Carman	PPI Representative	Sepsis Trust
Prof Bridget Young	Co-investigator, trials methodologist	University of Liverpool
Prof Ingeborg Welters	Co-investigator, Intensive Care doctor	University of Liverpool
Dr Victoria Shepherd	Co-investigator, qualitative, trials methodologist	Cardiff University
Dr Vinoth Sanker	Co-investigator, Medical Examiner	Liverpool University Hospitals NHS Foundation Trust
Karen Poole	Co-investigator, Medical Examiner	Liverpool University Hospitals NHS Foundation Trust
Dr Emma Thomas-Jones	Co-investigator	Cardiff University
Dr Sarah Milosevic	Co-investigator	Cardiff University

ENHANCE Study Advisory Group

Name	Role/expertise	Institution/Organisation
Benjamin Davies	Ethicist	University of Sheffield
Hugh Davies	Ethicist	HRA/Chair of Oxford Research Ethics Committee
Oliver Jones	PPI Representative	Sepsis Trust
Grace Blows	ED Junior Sister EGH	Epsom and St Helier University Hospitals NHS Trust
Donna Durrant	Research Nurse working primarily with ITU studies	Northampton General Hospital
Rosalie McDonald	Senior Clinical Research Nurse, Emergency Department	St George's University Hospital
Rebekah Burnham	Research Nurse	LEEDS Teaching Hospitals NHS Trust
Catherine Woodward	Medical Examiner	Liverpool University Hospitals Foundation Trust, Liverpool University Hospitals Foundation Trust
Maria Guerin	Bereavement nurse	SWAN End of Life and Bereavement Care Team
Honorine Jobain	Research Nurse	LEEDS Teaching Hospitals NHS Trust

Appendix 4 Template of a Bereavement letter from the study team

The template below is adapted from the letter developed by the NIHR funded PRONTO trial and feedback from ENHANCE workshop participants. Please adapt for your study, ideally with input from PPI partners.

(Date) XXXXXX

Dear [*add name*]

This letter is regarding [*insert name*] and their participation in the (Insert study name). We offer our deepest sympathies for your loss and thank you for taking the time to read this letter during such a difficult time.

When [*insert name*] was admitted to hospital, one of the possibilities the clinical team were concerned about was (add medical condition/suspected condition). As a result of this they were eligible to be enrolled into the [*add study name*). The aim of [*add study name and aims*] Because [*add medical condition/suspected condition*] is an emergency which requires rapid assessment and treatment, [*add study name*] has permission from an NHS research ethics committee to enrol participants before we have obtained full informed consent. We then approach patients (or their relatives if they are unable to consent for themselves) to discuss the study and gain permission. Sadly [*insert name*] died before we were able to complete this process. (if applicable: A person/doctor who was independent of the study was consulted to provide consent for your relative's participation in the study based on their presumed will.

[*Please amend below to reflect data collection for your study in line with relevant approvals*]

The information from medical records that was collected for the purpose of the [add study name] up until the time of [*insert name*]'s death is invaluable for the trial team and can be used to improve care of patients who might have [*add medical condition/suspected condition*] on arrival at the Emergency Department/Intensive Care Unit in the future.

We would like to assure you that all retained information is anonymous meaning that no one outside of the hospital team have access to any personal identifiable information. This information is incredibly important and will contribute to our understanding of whether this intervention can help save lives in the future. In accordance with the legal framework in England & Wales, no additional written permissions are needed at this time.

We hope that this letter answers any questions you may have regarding the [*add study name*]. You do not have to respond to this letter. However, we do encourage you to contact a member of the Research Team on the number or email below if you would like more information about the study, to discuss the information you have received if you find it in any way stressful or would like further

support. If the team are not available or you contact them via email, please be assured the team will get back to you as soon as possible *[add time frame]*

We would like to take this opportunity to thank you and [insert name] for your contribution to the [*add study name*] trial, and again, please accept our deepest sympathies for your loss.

Yours sincerely

Dr XXXXXXXXX

Principal Investigator on behalf of the *[add study name and hospital/organisation]*

Should you have any further questions or require further information about the study you can contact the Research team (during normal working hours):

Contact Number: XXXXXXX

Appendix 5 Template of a letter for inclusion in bereavement information

The template below was developed in collaboration with bereaved families and bereavement nurses. Please adapt this letter for your Trust/Health Board, ideally with input from PPI partners.

Dear relative,

We offer our deepest sympathies for your loss and thank you for taking the time to read this letter during such a difficult time.

You may or may not already know that research takes place in this hospital. Being a research-active hospital is important to help inform the future clinical care of NHS patients.

If your family member was admitted in an ambulance or through the emergency department they may have been involved in emergency or critical care research during their hospital admission or ambulatory care.

In some cases, where there is an emergency that requires rapid treatment and assessment, some studies have permission from an NHS research ethics committee to enrol patients without prior informed consent. This means that time-critical treatments and assessments are not delayed for research discussions. Patients enrolled in emergency research based on consent or agreement/advice from a healthcare professional may die before the study is discussed with relatives. This leads to situations where bereaved relatives are unaware their family member has participated in a study and that their data will be used.

There are *(add number)* of these studies currently open in our Trust including: (*add logo and very brief patient-friendly description of studies that have RWPC and notification in protocol*).

If you would like to find out if your relative was involved in emergency or critical care research without prior informed consent, please contact (*add telephone number and email for key contact person in the Trust/Health Board or research team who has oversight of studies conducted without prior consent that have notification of bereaved next of kin within their protocol*).

[Add contact details] If the team are not available or you contact via email, please be assured the team will get back to you as soon as possible *[add time frame]*

Thank you for reading this letter, and again, please accept our sincere condolences for your loss.

Yours sincerely

(add bereavement team contact)