Welcome to the Integrated Research Application System

IRAS Project Filter

The integrated dataset required for your project will be created from the answers you give to the following questions. The system will generate only those questions and sections which (a) apply to your study type and (b) are required by the bodies reviewing your study. Please ensure you answer all the questions before proceeding with your applications.

Please complete the questions in order. If you change the response to a question, please select 'Save' and review all the questions as your change may have affected subsequent questions.

Please enter a short title for this project (maximum 70 characters)
ORDIT v0.1

1. Is your project research?

(●) Yes ( ) No

2. Select one category from the list below:

( ) Clinical trial of an investigational medicinal product
( ) Clinical investigation or other study of a medical device
( ) Combined trial of an investigational medicinal product and an investigational medical device
( ) Other clinical trial to study a novel intervention or randomised clinical trial to compare interventions in clinical practice
( ) Basic science study involving procedures with human participants
(●) Study administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology
( ) Study involving qualitative methods only
( ) Study limited to working with human tissue samples (or other human biological samples) and data (specific project only)
( ) Study limited to working with data (specific project only)
( ) Research tissue bank
( ) Research database

If your work does not fit any of these categories, select the option below:

( ) Other study

2a. Please answer the following question(s):

a) Does the study involve the use of any ionising radiation?	( ) Yes	(●) No
b) Will you be taking new human tissue samples (or other human biological samples)?	( ) Yes	(●) No
c) Will you be using existing human tissue samples (or other human biological samples)?	( ) Yes	(●) No

3. In which countries of the UK will the research sites be located?*(Tick all that apply)*

[x] England
[x] Scotland
[x] Wales
[ ] Northern Ireland

3a. In which country of the UK will the lead NHS R&D office be located:

- (●) England
- ( ) Scotland
- ( ) Wales
- ( ) Northern Ireland
- ( ) This study does not involve the NHS

4. Which review bodies are you applying to?

- [x] NHS/HSC Research and Development offices
- [ ] Social Care Research Ethics Committee
- [x] Research Ethics Committee
- [ ] Confidentiality Advisory Group (CAG)
- [ ] National Offender Management Service (NOMS) (Prisons & Probation)

For NHS/HSC R&D offices, the CI must create Site-Specific Information Forms for each site, in addition to the study-wide forms, and transfer them to the PIs or local collaborators.

5. Will any research sites in this study be NHS organisations?

(●) Yes ( ) No

5a. Are all the research costs and infrastructure costs for this study provided by an NIHR Biomedical Research Centre, NIHR Biomedical Research Unit, NIHR Collaboration for Leadership in Health Research and Care (CLAHRC) or NIHR Research Centre for Patient Safety & Service Quality in all study sites?

( ) Yes (●) No

If yes, NHS permission for your study will be processed through the NIHR Coordinated System for gaining NHS Permission (NIHR CSP).

5b. Do you wish to make an application for the study to be considered for NIHR Clinical Research Network (CRN) support and inclusion in the NIHR Clinical Research Network (CRN) Portfolio? Please see information button for further details.

( ) Yes (●) No

If yes, NHS permission for your study will be processed through the NIHR Coordinated System for gaining NHS Permission (NIHR CSP) and you must complete a NIHR Clinical Research Network (CRN) Portfolio Application Form immediately after completing this project filter and before completing and submitting other applications.

6. Do you plan to include any participants who are children?

( ) Yes (●) No

7. Do you plan at any stage of the project to undertake intrusive research involving adults lacking capacity to consent for themselves?

( ) Yes (●) No

Answer Yes if you plan to recruit living participants aged 16 or over who lack capacity, or to retain them in the study following loss of capacity. Intrusive research means any research with the living requiring consent in law. This includes use of identifiable tissue samples or personal information, except where application is being made to the Confidentiality Advisory Group to set aside the common law duty of confidentiality in England and Wales. Please consult the guidance notes for further information on the legal frameworks for research involving adults lacking capacity in the UK.

8. Do you plan to include any participants who are prisoners or young offenders in the custody of HM Prison Service or who are offenders supervised by the probation service in England or Wales?

○ Yes ◉ No

9. Is the study or any part of it being undertaken as an educational project?

○ Yes ◉ No

10. Will this research be financially supported by the United States Department of Health and Human Services or any of its divisions, agencies or programs?

○ Yes ◉ No

11. Will identifiable patient data be accessed outside the care team without prior consent at any stage of the project (including identification of potential participants)?

○ Yes ◉ No

Integrated Research Application System
Application Form for Research administering questionnaires/interviews for quantitative analysis or mixed methodology study

NHS Health Research Authority

Application to NHS/HSC Research Ethics Committee

The Chief Investigator should complete this form. Guidance on the questions is available wherever you see this symbol displayed. We recommend reading the guidance first. The complete guidance and a glossary are available by selecting Help.

Please define any terms or acronyms that might not be familar to lay reviewers of the application.

Short title and version number: (maximum 70 characters - this will be inserted as header on all forms)
ORDIT v0.1

Please complete these details after you have booked the REC application for review.

REC Name:
London-central

REC Reference Number:
15/LO/1230

Submission date:
26/06/2015

PART A: Core study information

1. ADMINISTRATIVE DETAILS

A1. Full title of the research:

Organ Dysfunction in Trauma: a national one month point prevalence study

A3-1. Chief Investigator:

	Title	Forename/Initials	Surname
	Professor	Karim	Brohi
Post	Professor of Trauma Science		
Qualifications	FRCS, FRCA		
Employer	Queen Mary University of London		
Work Address	Blizard Institute		
	4 Newark Street		
	London		
Post Code	E1 2AT		
Work E-mail	k.brohi@qmul.ac.uk		
* Personal E-mail			
Work Telephone	02073777044		

* Personal Telephone/Mobile	
Fax	02078822188

** This information is optional. It will not be placed in the public domain or disclosed to any other third party without prior consent.*
A copy of a current CV (maximum 2 pages of A4) for the Chief Investigator must be submitted with the application.

A4. Who is the contact on behalf of the sponsor for all correspondence relating to applications for this project?
This contact will receive copies of all correspondence from REC and R&D reviewers that is sent to the CI.

Title	Forename/Initials	Surname
Mrs	Sally	Burtles

Address	Joint Research Management Office, 5 Walden Street London
Post Code	E1 2EF
E-mail	sponsorsrep@bartshealth.nhs.uk
Telephone	02078827269
Fax	

A5-1. Research reference numbers. *Please give any relevant references for your study:*

Applicant's/organisation's own reference number, e.g. R & D (if available):	
Sponsor's/protocol number:	
Protocol Version:	1.0
Protocol Date:	01/06/2015
Funder's reference number:	
Project website:	

Additional reference number(s):

Ref.Number Description	Reference Number

Registration of research studies is encouraged wherever possible. You may be able to register your study through your NHS organisation or a register run by a medical research charity, or publish your protocol through an open access publisher. If you have registered your study please give details in the "Additional reference number(s)" section.

A5-2. Is this application linked to a previous study or another current application?

○ Yes ◉ No

Please give brief details and reference numbers.

2. OVERVIEW OF THE RESEARCH

To provide all the information required by review bodies and research information systems, we ask a number of specific questions. This section invites you to give an overview using language comprehensible to lay reviewers and members of the public. Please read the guidance notes for advice on this section.

A6-1. Summary of the study. *Please provide a brief summary of the research (maximum 300 words) using language easily understood by lay reviewers and members of the public. Where the research is reviewed by a REC within the UK*

Health Departments Research Ethics Service, this summary will be published on the website of the National Research Ethics Service following the ethical review.

Traumatic injury is a leading cause of death. Severely injured patients who survive their initial injuries and are usually admitted to the intensive care unit (known as critical care). Here a proportion of patients will develop a dysfunction of vital organs (the heart, lungs, liver for example) known as multiple organ failure (MOF). MOF is a dysfunctional systemic inflammatory response to trauma, which increases resource use, prolongs the patients critical care and hospital stay, causes late mortality and further complicates longer term recovery. Trauma care in the UK has improved since the implementation of trauma systems in April 2010. Severely injured patients are now taken to specialist centres for expert management. Studies in Australia and the USA suggest that this leads to a decrease in MOF however the incidence, severity and outcomes of MOF in the UK are yet to be described. The UK national trauma system is perfectly positioned to capture the current situation of organ failure in trauma patients admitted to critical care units. The information can help us to better understand the risks of MOF to potentially reduce the incidence, to accurately target resources and to improve the patient experience post injury.

A6-2. Summary of main issues. *Please summarise the main ethical, legal, or management issues arising from your study and say how you have addressed them.*

Not all studies raise significant issues. Some studies may have straightforward ethical or other issues that can be identified and managed routinely. Others may present significant issues requiring further consideration by a REC, R&D office or other review body (as appropriate to the issue). Studies that present a minimal risk to participants may raise complex organisational or legal issues. You should try to consider all the types of issues that the different reviewers may need to consider.

This study raises few significant issues. Patients will be approached by clinical care staff to invite them to participate in this study and give informed consent. Only those who provide informed consent will be included. Medical case notes will be accessed by the direct clinical care team (such as vital signs, blood test results, microbiology results). This data will be recorded on an anonymised data collection sheet by clinical care staff. Medical case notes will not shared outside of the NHS trusts participating in the study. Using a predesigned short questionnaire (EQ5D), patients who give informed consent will be asked about their recovery following injury at approximately one year following discharge.

No intervention or blood test will be performed outside of routine care.

A6-3. Proportionate review of REC application *The initial project filter has identified that your study may be suitable for proportionate review by a REC sub-committee. Please consult the current guidance notes from NRES and indicate whether you wish to apply through the proportionate review service or, taking into account your answer to A6-2, you consider there are ethical issues that require consideration at a full REC meeting.*

○ Yes - proportionate review ◉ No - review by full REC meeting

Further comments (optional):

Note: This question only applies to the REC application.

3. PURPOSE AND DESIGN OF THE RESEARCH

A7. Select the appropriate methodology description for this research. *Please tick all that apply*:

- ☐ Case series/ case note review
- ☐ Case control
- ☑ Cohort observation
- ☐ Controlled trial without randomisation
- ☐ Cross-sectional study
- ☐ Database analysis
- ☐ Epidemiology
- ☐ Feasibility/ pilot study
- ☐ Laboratory study
- ☐ Metanalysis

- [ ] Qualitative research
- [x] Questionnaire, interview or observation study
- [ ] Randomised controlled trial
- [ ] Other (please specify)

A10. What is the principal research question/objective? *Please put this in language comprehensible to a lay person.*

The overall objective of this study is to explore the incidence, severity, timing and outcomes of organ dysfunction in UK trauma patients.

A11. What are the secondary research questions/objectives if applicable? *Please put this in language comprehensible to a lay person.*

To identify the prevalence of organ dysfunction in trauma patients admitted to critical care units following injury.
To identify the severity and temporal variation of organ dysfunction in this cohort of patients.
To examine the incidence and mode of mortality associated with organ dysfunction following injury.
To investigate the relationship between organ dysfunction and length of stay, and quality of life at one year post injury.

A12. What is the scientific justification for the research? *Please put this in language comprehensible to a lay person.*

Traumatic injury results from incidents such as road traffic collisions, falls and assaults. Patients with severe injury may be admitted to the critical care unit for intensive care in the first hours and days after trauma. A proportion of severely injured patients will develop multiple organ dysfunction (OD) whilst in critical care. Inflammation after injury is part of the normal healing process. OD occurs when the normal inflammatory response to injury becomes deranged or excessive, causing systemic or widespread inflammation in organs such as the lung, brain, liver or kidneys. This will impair the normal functioning of the affected organs, increasing the need for a prolonged critical care stay and for some patients, increasing the risk of death (1, 2).

Recent reports from the USA, Australia and Europe suggest that the incidence of OD following trauma varies between 10 - 33% of patients (3-5), however the UK incidence is unknown. Over the past decade, many new treatments have been introduced into early trauma management and these innovations have increased the survival of many people who would otherwise have died from their injuries (6-9). However this has resulted in greater numbers of severely injured patients surviving with an increased risk of developing OD (3, 10).

OD appears to develop at different time points after the initial traumatic injury (1, 11). Early OD occurs within the first 48-72 hours from injury and is most associated with in-hospital death (5, 12). Other studies describe an early onset OD which is more transient, resolving within four to five days post-injury (3, 10), after which time the patient recovers. Late OD lasts for more than seven after injury, or occurs at a later time point, causing delayed recovery and prolonged hospital stays. Recent American studies suggest that older age greatly increases the risk of this (12-14).

The reasons for and outcomes of OD in the UK are yet to be described. Currently there is no specific prevention or treatment for OD other than supporting the individually affected organs. By conducting this research we hope to understand the the severity, incidence and timing of OD in the UK. We also wish to understand how it affects the patients recovery both in hospital and a year after injury. We hope that findings will identify target areas in order to improve patient outcomes, and also help to with the design of future research to prevent OD.

The way trauma care is delivered within the UK has changed over the past five years, in line with the centralisation and specialisation of cancer and stroke services. Organised regional trauma systems were introduced within England and Wales from April 2010, and Scotland is to implement regionalised care by 2016. A regional trauma system is organised to deliver optimal care at the most appropriate facility at the right time within a specified geographical location (15, 16). Five years post initial implementation the national trauma system is perfectly positioned to capture the current burden of OD after trauma in the UK, in order to better understand the disorder and improve patient outcomes.

References

1. Dewar D, Moore FA, Moore EE et al. Postinjury multiple organ failure. Injury. 2009 Sep;40(9):912-8
2. Ciesla DJ, Moore EE, Johnson JL et al. A 12-year prospective study of postinjury multiple organ failure: has anything changed? Archives of surgery. 2005 May;140(5):432-8
3. Dewar DC, Tarrant SM, King KL et al. Changes in the epidemiology and prediction of multiple-organ failure after injury. The journal of trauma and acute care surgery. 2013 Mar;74(3):774-9

4. Frohlich M, Lefering R, Probst C et al. Epidemiology and risk factors of multiple-organ failure after multiple trauma: An analysis of 31,154 patients from the TraumaRegister DGU. The journal of trauma and acute care surgery. 2014 Apr;76(4):921-8
5. Sauaia A, Moore EE, Johnson JL et al. Temporal trends of postinjury multiple-organ failure: Still resource intensive, morbid, and lethal. The journal of trauma and acute care surgery. 2014 Mar;76(3):582-93
6. Lord JM, Midwinter MJ, Chen YF et al. The systemic immune response to trauma: an overview of pathophysiology and treatment. Lancet. 2014 Oct 18;384(9952):1455-65
7. Gunst M, Ghaemmaghami V, Gruszecki A et al. Changing epidemiology of trauma deaths leads to a bimodal distribution. Proceedings (Baylor University Medical Center). 2010 Oct;23(4):349-54
8. Davenport RA, Tai N, West A et al. A major trauma centre is a specialty hospital not a hospital of specialties. The British journal of surgery. 2010 Jan;97(1):109-17
9. Twijnstra MJ, Moons KG, Simmermacher RK et al. Regional trauma system reduces mortality and changes admission rates: a before and after study. Annals of surgery. 2010 Feb;251(2):339-43
10. Minei JP, Cuschieri J, Sperry J et al. The changing pattern and implications of multiple organ failure after blunt injury with hemorrhagic shock. Critical care medicine. 2012 Apr;40(4):1129-35
11. Moore FA, Sauaia A, Moore EE et al. Postinjury multiple organ failure: a bimodal phenomenon. The Journal of trauma. 1996 Apr;40(4):501-10; discussion 10-2.
12. Gentile LF, Cuenca AG, Efron PA et al. Persistent inflammation and immunosuppression: a common syndrome and new horizon for surgical intensive care. The journal of trauma and acute care surgery. 2012 Jun;72(6):1491-501
13. Vanzant EL, Lopez CM, Ozrazgat-Baslanti T et al. Persistent inflammation, immunosuppression, and catabolism syndrome after severe blunt trauma. The journal of trauma and acute care surgery. 2014 Jan;76(1):21-9; discussion 9-30.
14. Vanzant EL, Hilton RE Lopez CM et al. Advanced age is associated with worsened outcomes and a unique genomic response in severely injured patients with hemorrhagic shock. Crit Care. 2015 Mar 4;19(1):77
15. Lansink KW, Leenen LP. Do designated trauma systems improve outcome? Current opinion in critical care. 2007 Dec;13(6):686-90.
16. Lansink KW, Gunning AC, Spijkers AT et al. Evaluation of trauma care in a mature level I trauma center in the Netherlands: outcomes in a Dutch mature level I trauma center. World journal of surgery. 2013 Oct;37(10):2353-9

A13. Please summarise your design and methodology. *It should be clear exactly what will happen to the research participant, how many times and in what order. Please complete this section in language comprehensible to the lay person. Do not simply reproduce or refer to the protocol. Further guidance is available in the guidance notes.*

This centre has extensive experience in acute and longer term outcomes research.

Study design
A one month, prospective point prevalence cohort study of adult (≥16 years) patients admitted to critical care following traumatic injury.

Settings
All MTCs in England, Wales and Scotland will be invited to participate. Each site will have a nominated study lead and data collector(s) from within the critical care clinical team. Data collector training will be provided prior to study commencement by the principle investigator. Each site will be supported by an information folder with the protocol, guidance/explanatory notes and contact details of the principal investigator.

At Barts Health MTC (known to be one of the busiest in England) there are approximately 300 trauma patients admitted to critical care per annum. This is 25 patients per month, of which 20-30% develop MOF. There are 32 MTCs in England, Wales and Scotland (yet to be designated but identified). The clinical director, critical care lead and research lead at each MTC will be approached by email inviting them to participate in the study. This will be completely voluntary.

Patient inclusion criteria
All consecutive adult trauma patients (≥16 years of age) admitted to critical care from 08.00 on day one of the study to 07.59 on the final day of the study (six weeks in total) will be entered into the study.

Patient exclusion criteria
Patients will not be included if they are <16 years old, have suffered a burns only injury, decline to participate or is a prisoner.

Consent process
As soon as clinically appropriate (determined by the clinical care team in charge of the patient), consent will be sought for follow up at 12 months post discharge. Participant information will be explained by the designated member of staff from the clinical care team, and left with the patient (and relatives if required) for 24-48 hours. After this time, the patient

will be approached see if they wish to participate, and if so, to sign the study consent form. Consent can be revoked or declined at any stage of the study and the patient will be withdrawn.

Study outcomes
The primary outcome will be the presence of MOF during the study period (Determined by SOFA score). Secondary outcomes include in hospital mortality, ventilator use, organ support, critical care length of stay, total hospital length of stay and quality of life one year post injury.

Data collection
Data will be collected in individual centre critical care units using a paper case record form. The de-identified data required is already recorded as part of routine clinical care and as part of the Intensive Care National Audit and Research Centre (ICNARC) audit. Organ failure scoring is not usually conducted as part of routine clinical care however it uses parameters that are recorded in routine care by critical care clinical staff on a daily basis. This will be completed for every eligible trauma patient in the critical care unit during the study period.

Paper CRFs will be stored within a locked office in each centre only accessible to the centre study lead and data collectors. Each centre will be identified by a numeric code rather than name.Data will be de-identified by local collaborators (part of the clinical care team). A coding log will include identifiable patient data in order to allow follow-up of outcomes and this will only be accessed by local collaborators. This will allow local investigators to identify individual patients whilst other members of the study team cannot trace data back to an individual patient. Each centre will maintain a trial file including a protocol, local investigator delegation log, ethics approval documentation, principal investigator contact details.

Patients will be followed up until hospital discharge to record mortality or alive at discharge. At the end of the initial phase of the study when all patients have been discharged within each site, the anonymous CRFs will be scanned and sent to the principal investigator via an nhs net email account.

Data collection for each patient:
A Hospital admission variables: age, gender, time and date of traumatic injury, ED admission physiology (base deficit, lactate, systolic blood pressure and GCS), ED admission coagulation (INR), intravenous fluids, blood products and antifibrinolytics administered in first 24 hours post injury.
B Injury variables: mechanism of injury, list of injuries, surgical or interventional radiology episodes and a confirmed list of all injuries.
C Critical care data: date of admission to CCU, admission APACHE score, daily organ failure scores using Sequential Organ Failure Assessment (SOFA), days on organ support (inotropes and renal replacement therapy), ventilator free days, daily highest CRP and lowest lymphocyte counts (all blood taken as part of routine care – fields omitted if not taken by clinical care team). If more than one blood test is taken in a 24 hour period, the worst value will be recorded
D Follow up data: date of in-hospital mortality or date of discharge, critical care and hospital length of stay, quality of life at 12 months post injury (EQ5D).

At ten months post study commencement, the principal investigator will access the contact details and preferences for each patient from the participating sites. In England and Wales, the NHS spine and in Scotland the unique patient identifier will be accessed by to ensure that the patient is still alive at this time point. At 12 months post injury, the EQ5D questionnaire (five questions in total - takes 5-10 minutes to complete) will be administered to each patient who has provided informed consent, to determine their quality of life (QoL) at 12 months post injury and MOF. The principal investigator has extensive experience of patient follow up after trauma in both the ACIT trial [Research Ethics Committee 1 in November 2007 (07/Q0603/29)], and the POET outcomes study [Research Ethics Committee in January 2011 (11/LO/1876)].

Data analysis
Statistical analysis will be performed using GraphPad PRISM v5 (GraphPad Software Inc, San Diego CA USA). Analysis plans have been discussed and agreed with the research design service. Statistical analysis will be performed using SPSS v21 (IBM Corporation, Armonk, NY, USA). Univariate analysis of variables between two groups will be conducted using unpaired students t-tests or Mann Whitney U tests (for parametric and non-parametric data respectively). Analysis of more than two groups will be conducted using ANOVA or Kruskal Wallis tests. Percentages or proportions will be analysed using Chi square or Fisher's exact tests. A p value of <0.05 is considered statistically significant for univariate analysis.

Multivariate analysis will be used to determine statistically independent relationships between MOF and other variables. Factors achieving significance of $p<0.15$ in univariate analysis will be entered into the regression models. Multivariate linear regression will be used to analyse continuous dependent variables and binary logistic regression for binary dependent variables. Results of linear regression will be reported as Beta co-efficient with 95% confidence intervals, and for logistic regression adjusted odds ratios (OR) with 95% confidence intervals.

Study completion definition
The study will be completed when twelve month follow up for all patients has been obtained.

Study coordination and local co-ordinators
The study will be coordinated by Elaine Cole, principal investigator. The chief investigator of the study is Professor Karim Brohi, Centre for Trauma Sciences, Blizard Institute, QMUL.

Local named collaborators in individual participating centres will have the following responsibilities:
Provide leadership for the study within the individual MTC, nominate local data collection personnel, act as guarantor for the integrity and quality of the local data and communicate with the national coordinator and principle investigator.

A14-1. In which aspects of the research process have you actively involved, or will you involve, patients, service users, and/or their carers, or members of the public?

- [x] Design of the research
- [ ] Management of the research
- [ ] Undertaking the research
- [ ] Analysis of results
- [x] Dissemination of findings
- [ ] None of the above

Give details of involvement, or if none please justify the absence of involvement.
The Centre for Trauma Sciences has an expert patient panel and members of this have reviewed the protocol. The findings from the study will be disseminated to the public via the After Trauma website (www.aftertrauma.org) and the centre for trauma sciences website (www.c4ts.qmul.ac.uk)

4. RISKS AND ETHICAL ISSUES

RESEARCH PARTICIPANTS

A17-1. Please list the principal inclusion criteria (list the most important, max 5000 characters).

Patient inclusion criteria
All consecutive adult trauma patients (≥16 years of age) admitted to critical care from 08.00 on day one of the study to 07.59 on the final day of the study (six weeks in total) who subsequently provide informed consent will be entered into the study.

A17-2. Please list the principal exclusion criteria (list the most important, max 5000 characters).

Patients will not be included if they:
are <16 years old,
have suffered a burns-only injury,
decline to participate,
decline to provide informed consent,
are a prisoner.

RESEARCH PROCEDURES, RISKS AND BENEFITS

A18. Give details of all non-clinical intervention(s) or procedure(s) that will be received by participants as part of the research protocol. *These include seeking consent, interviews, non-clinical observations and use of questionnaires.*

Please complete the columns for each intervention/procedure as follows:

1. Total number of interventions/procedures to be received by each participant as part of the research protocol.
2. If this intervention/procedure would be routinely given to participants as part of their care outside the research, how many of the total would be routine?

3. Average time taken per intervention/procedure (minutes, hours or days)
4. Details of who will conduct the intervention/procedure, and where it will take place.

Intervention or procedure	1	2	3	4
Introducing and explaining the study	1	0	15 minutes	Local PI and member of clinical care team (critical care nurse), in clinical setting
Seeking consent	1	0	15 minutes	Local PI in clinical setting
Follow up EQ5D questionnaire	1	0	5-10 minutes	Elaine Cole, study PI will either telephone, email or post EQ5D to patient (according to patient preference)

A21. How long do you expect each participant to be in the study in total?

Up to twelve month post injury follow up.

A22. What are the potential risks and burdens for research participants and how will you minimise them?

For all studies, describe any potential adverse effects, pain, discomfort, distress, intrusion, inconvenience or changes to lifestyle. Only describe risks or burdens that could occur as a result of participation in the research. Say what steps would be taken to minimise risks and burdens as far as possible.

There are no risks as a result of participating in this research. All data that we collect will be completely anonymised/de-identified. Elaine Cole, PI will have access to names and contact preferences in order to follow up the participants at twelve months. Consent for this will have been sought whilst the participant is in hospital. Completion of the EQ5D is a potential burden for the participants, however this short, simple questionnaire should take no more than 5-10 minutes to complete.

A23. Will interviews/ questionnaires or group discussions include topics that might be sensitive, embarrassing or upsetting, or is it possible that criminal or other disclosures requiring action could occur during the study?

○ Yes ◉ No

A24. What is the potential for benefit to research participants?

There are no immediate benefits for those people participating in the project. However, we hope that the results will help to increase the understanding of the experience of organ dysfunction, and improve the recovery of future trauma patients.

A26. What are the potential risks for the researchers themselves? *(if any)*

There are no potential risks to the researchers.

RECRUITMENT AND INFORMED CONSENT

In this section we ask you to describe the recruitment procedures for the study. Please give separate details for different study groups where appropriate.

A27-1. How will potential participants, records or samples be identified? Who will carry this out and what resources will be used?*For example, identification may involve a disease register, computerised search of GP records, or review of medical records. Indicate whether this will be done by the direct healthcare team or by researchers acting under arrangements with the responsible care organisation(s).*

Adult patients admitted to the critical care unit during the study period will identified for entry into the study. All of the in hospital data required is collected daily during routine care by the direct care team.

A27-2. Will the identification of potential participants involve reviewing or screening the identifiable personal information of patients, service users or any other person?

○ Yes ◉ No

Please give details below:
Potential participants (adult trauma patients admitted to the critical care unit within the study time frame) will be screened for inclusion by the direct clinical care team.

A28. Will any participants be recruited by publicity through posters, leaflets, adverts or websites?

○ Yes ◉ No

A29. How and by whom will potential participants first be approached?

As soon as clinically appropriate (determined by the clinical care team looking after the patient), consent will be sought by the study local collaborator (who will be a member of the clinical care team) for follow up at 12 months post discharge.

A30-1. Will you obtain informed consent from or on behalf of research participants?

◉ Yes ○ No

If you will be obtaining consent from adult participants, please give details of who will take consent and how it will be done, with details of any steps to provide information (a written information sheet, videos, or interactive material). Arrangements for adults unable to consent for themselves should be described separately in Part B Section 6, and for children in Part B Section 7.

If you plan to seek informed consent from vulnerable groups, say how you will ensure that consent is voluntary and fully informed.

Participant information will be explained by the designated member of staff from the clinical care team, and left with the patient (and relatives if the patient wishes this) for 24-48 hours. After this time, the patient will be approached see if they wish to participate, and if so, to sign the study consent form. Consent can be revoked or declined at any stage of the study and the patient will be withdrawn.

If you are not obtaining consent, please explain why not.

Please enclose a copy of the information sheet(s) and consent form(s).

A30-2. Will you record informed consent (or advice from consultees) in writing?

◉ Yes ○ No

A31. How long will you allow potential participants to decide whether or not to take part?

24-48 hours.

A33-1. What arrangements have been made for persons who might not adequately understand verbal explanations or written information given in English, or who have special communication needs?*(e.g. translation, use of interpreters)*

Local Trust patient advocates or interpreters will be used. It is envisaged that these will be used at a time when they are involved in other aspects of the patients management to avoid inconvenience for both the patient and the advocacy service.

A33-2. What arrangements will you make to comply with the principles of the Welsh Language Act in the provision of information to participants in Wales?

The commitment to the Welsh Language Act in the two Welsh hospitals participating in the study has been

investigated. The Welsh Language Scheme for each of the hospitals relates to the delivery of service through the medium of the Welsh language. The participant information and consent form will be delivered in Welsh and English.

A35. What steps would you take if a participant, who has given informed consent, loses capacity to consent during the study? *Tick one option only.*

- ○ The participant and all identifiable data or tissue collected would be withdrawn from the study. Data or tissue which is not identifiable to the research team may be retained.
- ◉ The participant would be withdrawn from the study. Identifiable data or tissue already collected with consent would be retained and used in the study. No further data or tissue would be collected or any other research procedures carried out on or in relation to the participant.
- ○ The participant would continue to be included in the study.
- ○ Not applicable – informed consent will not be sought from any participants in this research.
- ○ Not applicable – it is not practicable for the research team to monitor capacity and continued capacity will be assumed.

Further details:

If a patient loses capacity after initially giving informed consent, then the de-identified critical care data would still be included in order to report incidence, temporal variations etc, however the patient follow up at 12 months will not be conducted.

If you plan to retain and make further use of identifiable data/tissue following loss of capacity, you should inform participants about this when seeking their consent initially.

CONFIDENTIALITY

In this section, personal data means any data relating to a participant who could potentially be identified. It includes pseudonymised data capable of being linked to a participant through a unique code number.

Storage and use of personal data during the study

A36. Will you be undertaking any of the following activities at any stage (including in the identification of potential participants)? *(Tick as appropriate)*

- ☐ Access to medical records by those outside the direct healthcare team
- ☐ Electronic transfer by magnetic or optical media, email or computer networks
- ☐ Sharing of personal data with other organisations
- ☐ Export of personal data outside the EEA
- ☑ Use of personal addresses, postcodes, faxes, emails or telephone numbers
- ☐ Publication of direct quotations from respondents
- ☐ Publication of data that might allow identification of individuals
- ☐ Use of audio/visual recording devices
- ☐ Storage of personal data on any of the following:
  - ☑ Manual files including X−rays
  - ☑ NHS computers
  - ☐ Home or other personal computers
  - ☐ University computers
  - ☐ Private company computers
  - ☐ Laptop computers

Further details:

Identifiable data and consent forms will be kept within each Trust site. This will be kept in a locked cabinet, within a locked room under the responsibility of the site PI. Prior to 12 months post injury, the main CI and PI will seek patient contact details from each participating Trust site PI (as per the patients preference: either address or telephone number or email address). This will allow the administration of the EQ5D quality of life follow up for those patients who have consented to participate. Prior to the 12 month follow up, NHS Health and Social Care Information Centre will be contacted to ensure that the patient is still alive at this time point. This will avoid erroneous follow up and exposing relative to undue distress. In England and Wales, the NHS spine and in Scotland the unique patient identifier will be accessed.

A38. How will you ensure the confidentiality of personal data? *Please provide a general statement of the policy and procedures for ensuring confidentiality, e.g. anonymisation or pseudonymisation of data.*

Each centre will be identified by a numeric code rather than name.

Data will be de-identified by local collaborators (part of the clinical care team). A coding log only be accessible by local collaborators will include identifiable patient data in order to allow quality of life follow-up. This will allow local investigators to identify individual patients whilst other members of the study team cannot trace data back to an individual patient.

At the end of the initial phase of the study when all patients have been discharged within each site, the de-identified CRFs will be scanned and sent to the principal investigator via an nhs net email account.

A40. Who will have access to participants' personal data during the study? *Where access is by individuals outside the direct care team, please justify and say whether consent will be sought.*

The only time that personal contact details will be accessed outside of the direct care team is when they are supplied to the site PI for 12 month post discharge follow up. This will then be passed onto the main study PI Elaine Cole will conduct the follow up (according to the patients wishes - email, letter or telephone). Informed consent for this process will have been sought.

Storage and use of data after the end of the study

A43. How long will personal data be stored or accessed after the study has ended?

- ○ Less than 3 months
- ○ 3 – 6 months
- ○ 6 – 12 months
- ○ 12 months – 3 years
- ◉ Over 3 years

If longer than 12 months, please justify:
In accordance with the sponsor policy, all study data will be archived for a period of 20 years.

INCENTIVES AND PAYMENTS

A46. Will research participants receive any payments, reimbursement of expenses or any other benefits or incentives for taking part in this research?

○ Yes ◉ No

A47. Will individual researchers receive any personal payment over and above normal salary, or any other benefits or incentives, for taking part in this research?

○ Yes ◉ No

A48. Does the Chief Investigator or any other investigator/collaborator have any direct personal involvement (e.g. financial, share holding, personal relationship etc.) in the organisations sponsoring or funding the research that may give rise to a possible conflict of interest?

○ Yes ◉ No

NOTIFICATION OF OTHER PROFESSIONALS

A49-1. Will you inform the participants' General Practitioners (and/or any other health or care professional responsible for their care) that they are taking part in the study?

○ Yes ◉ No

If Yes, please enclose a copy of the information sheet/letter for the GP/health professional with a version number and date.

PUBLICATION AND DISSEMINATION

A50. Will the research be registered on a public database?

○ Yes ◉ No

Please give details, or justify if not registering the research.
ORDIT is not a randomised controlled trial, nor is it designed to assess the efficacy of a healthcare intervention therefore it is not eligible to be registered on the ISRCTN Register or ClinicalTrials.gov.

Similarly, as an unfunded study it is not eligible for the UKCRN Portfolio.

ORDIT does not have active public involvement therefore is not suitable for registration with INVOLVE

Registration of research studies is encouraged wherever possible.
You may be able to register your study through your NHS organisation or a register run by a medical research charity, or publish your protocol through an open access publisher. If you are aware of a suitable register or other method of publication, please give details. If not, you may indicate that no suitable register exists. Please ensure that you have entered registry reference number(s) in question A5-1.

A51. How do you intend to report and disseminate the results of the study? *Tick as appropriate:*

- ☑ Peer reviewed scientific journals
- ☑ Internal report
- ☑ Conference presentation
- ☑ Publication on website
- ☐ Other publication
- ☐ Submission to regulatory authorities
- ☐ Access to raw data and right to publish freely by all investigators in study or by Independent Steering Committee on behalf of all investigators
- ☐ No plans to report or disseminate the results
- ☐ Other (please specify)

A53. Will you inform participants of the results?

◉ Yes ○ No

Please give details of how you will inform participants or justify if not doing so.
via the Centre for Trauma Sciences website (the link is provided in the participant information sheet).

5. Scientific and Statistical Review

A54. How has the scientific quality of the research been assessed? *Tick as appropriate:*

- [ ] Independent external review
- [ ] Review within a company
- [x] Review within a multi−centre research group
- [x] Review within the Chief Investigator's institution or host organisation
- [x] Review within the research team
- [ ] Review by educational supervisor
- [ ] Other

Justify and describe the review process and outcome. If the review has been undertaken but not seen by the researcher, give details of the body which has undertaken the review:
All draft trial documents (e.g. protocol, patient information sheets, consent forms) were developed in an iterative manner across the trauma research team and steering group. The study protocol was reviewed by Charlotte Wilson, Andrea Takeda and Lauren Bell of the Research Design Service.
Professor Tim Harris has completed a peer review of the research proposal and protocol.
The study documents were submitted to the Site's Joint Research & Management Office for their review. The study protocol was discussed and reviewed with two members of our AfterTrauma PPI group (MR and NR)

For all studies except non-doctoral student research, please enclose a copy of any available scientific critique reports, together with any related correspondence.

For non-doctoral student research, please enclose a copy of the assessment from your educational supervisor/ institution.

A56. How have the statistical aspects of the research been reviewed? *Tick as appropriate:*

- [ ] Review by independent statistician commissioned by funder or sponsor
- [x] Other review by independent statistician
- [ ] Review by company statistician
- [x] Review by a statistician within the Chief Investigator's institution
- [x] Review by a statistician within the research team or multi−centre group
- [ ] Review by educational supervisor
- [ ] Other review by individual with relevant statistical expertise
- [ ] No review necessary as only frequencies and associations will be assessed – details of statistical input not required

In all cases please give details below of the individual responsible for reviewing the statistical aspects. If advice has been provided in confidence, give details of the department and institution concerned.

	Title	Forename/Initials	Surname
	Ms	Lauren	Bell
Department	Research Design Services, London and the Pragmatic Clinical Trials Unit, Centre of Primary Care and Public Health		
Institution	Queen Mary University of London		
Work Address	Research Design Service London		
	Yvonne Carter Building		
	58 Turner Street London		
Post Code	E1 2AB		
Telephone	020 7882 2481		
Fax			

Mobile

E-mail l.bell@qmul.ac.uk

Please enclose a copy of any available comments or reports from a statistician.

A57. What is the primary outcome measure for the study?

The presence of MOF post injury, identified during the critical care stay using Sequential Organ Failure Scoring (SOFA).

A58. What are the secondary outcome measures? *(if any)*

Maximum SOFA score over 7, 10 and 14 days (dependent on the patients length of stay)
Total number of days on organ support
Number of ventilator free days
In hospital mortality
Total length of critical care stay
Total length of hospital stay
Quality of life at one year post injury (measured by EQ5D)

A59. What is the sample size for the research? *How many participants/samples/data records do you plan to study in total? If there is more than one group, please give further details below.*

Total UK sample size: 550

Total international sample size (including UK): 550

Total in European Economic Area:

Further details:
See A60.

A60. How was the sample size decided upon? *If a formal sample size calculation was used, indicate how this was done, giving sufficient information to justify and reproduce the calculation.*

This is a convenience sample for the one month study period. The rate of admission to critical care is likely to vary between MTCs nationally. Each MTC is required to submit annual trauma patient figures to the Trauma Audit and Research Network (TARN). We used the severely injured cohorts (ISS>15) from TARN as a surrogate measure of annual trauma admissions to critical care. From this we calculated monthly critical care admissions. Local critical care unit pilot data analysis (From ACIT II and POET studies) showed that there are approximately 300 severely injured patient admissions per annum, which is approximately 25 patients in a month period. This number was then multiplied by the maximum number of MTCs that may participate (32) = 800 if all units participate. We understand that not all patients will provide informed consent however local data suggests that decline-to-participate rates in ACIT II and POET are 1%. We therefore set a conservative estimate of two thirds of the potential total but hope to exceed this target to get the most representative cohort.

A61. Will participants be allocated to groups at random?

○ Yes ◉ No

A62. Please describe the methods of analysis (statistical or other appropriate methods, e.g. for qualitative research) by which the data will be evaluated to meet the study objectives.

Statistical analysis will be performed using SPSS v21 (IBM Corporation, Armonk, NY, USA).

Univariate analysis between two groups will be conducted using unpaired students t-tests or Mann Whitney U tests (dependent on whether the data is parametric or non parametric). Analysis of more than two groups will be conducted using ANOVA or Kruskal Wallis tests. Percentages or proportions will be analysed using Chi square or Fisher's exact tests. A p value of <0.05 is considered statistically significant for univariate analysis.

Multivariate analysis will be used to determine statistically independent relationships between MOF and other variables. Multivariate linear regression will be used to analyse continuous dependent variables and binary logistic regression for binary dependent variables. Factors achieving significance of p<0.15 in univariate analysis will be entered into the regression models.

6. MANAGEMENT OF THE RESEARCH

A63. Other key investigators/collaborators. *Please include all grant co−applicants, protocol co−authors and other key members of the Chief Investigator's team, including non-doctoral student researchers.*

	Title	Forename/Initials	Surname
	Dr	Elaine	Cole
Post	Post doctoral trauma research fellow		
Qualifications	PhD, MSc, BSc, RN		
Employer	Queen Mary University of London		
Work Address	5 Walden Street London		
Post Code	E1 2AT		
Telephone	07808400582		
Fax	02078822180		
Mobile			
Work Email	e.cole@qmul.ac.uk		

A64. Details of research sponsor(s)

A64-1. Sponsor

Lead Sponsor

Status:
- ○ NHS or HSC care organisation
- ◉ Academic
- ○ Pharmaceutical industry
- ○ Medical device industry
- ○ Local Authority
- ○ Other social care provider (including voluntary sector or private organisation)
- ○ Other

Commercial status:

If Other, please specify:

Contact person

Name of organisation	Queen Mary University of London
Given name	Sally
Family name	Burtles
Address	Joint Research Management Office, Queen Marys innovation Centre, 5 Walden Street
Town/city	London
Post code	E1 2EF
Country	UNITED KINGDOM

Telephone	02078827260
Fax	02078827276
E-mail	sponsorsrep@bartshealth.nhs.uk

Is the sponsor based outside the UK?

◯ Yes ◉ No

Under the Research Governance Framework for Health and Social Care, a sponsor outside the UK must appoint a legal representative established in the UK. Please consult the guidance notes.

A65. Has external funding for the research been secured?

☐ Funding secured from one or more funders

☐ External funding application to one or more funders in progress

☑ No application for external funding will be made

What type of research project is this?

◉ Standalone project

◯ Project that is part of a programme grant

◯ Project that is part of a Centre grant

◯ Project that is part of a fellowship/ personal award/ research training award

◯ Other

Other – please state:

A67. Has this or a similar application been previously rejected by a Research Ethics Committee in the UK or another country?

◯ Yes ◉ No

Please provide a copy of the unfavourable opinion letter(s). You should explain in your answer to question A6-2 how the reasons for the unfavourable opinion have been addressed in this application.

A68-1. Give details of the lead NHS R&D contact for this research:

Title	Forename/Initials	Surname
Dr	Sally	Burtles

Organisation	Queen Mary University of London/Barts Health NHS Trust
Address	Joint Research Management Office, 5 Walden Street London
Post Code	E1 2EF
Work Email	sponsorsrep@bartshealth.nhs.uk
Telephone	02078827260
Fax	02078827276
Mobile	

Details can be obtained from the NHS R&D Forum website: http://www.rdforum.nhs.uk

A69-1. How long do you expect the study to last in the UK?

Planned start date: 01/06/2015
Planned end date: 30/10/2016
Total duration:
Years: 1 Months: 4 Days: 30

A71-2. Where will the research take place? *(Tick as appropriate)*

- [x] England
- [x] Scotland
- [x] Wales
- [x] Northern Ireland
- [ ] Other countries in European Economic Area

Total UK sites in study 31

Does this trial involve countries outside the EU?
○ Yes ◉ No

A72. What host organisations (NHS or other) in the UK will be responsible for the research sites? *Please indicate the type of organisation by ticking the box and give approximate numbers of planned research sites:*

[x] NHS organisations in England	25
[x] NHS organisations in Wales	2
[x] NHS organisations in Scotland	4
[ ] HSC organisations in Northern Ireland	
[ ] GP practices in England	
[ ] GP practices in Wales	
[ ] GP practices in Scotland	
[ ] GP practices in Northern Ireland	
[ ] Social care organisations	
[ ] Phase 1 trial units	
[ ] Prison establishments	
[ ] Probation areas	
[ ] Independent hospitals	
[ ] Educational establishments	
[ ] Independent research units	
[ ] Other (give details)	

Total UK sites in study: 31

A76. Insurance/ indemnity to meet potential legal liabilities

Note: in this question to NHS indemnity schemes include equivalent schemes provided by Health and Social Care (HSC) in Northern Ireland

A76-1. What arrangements will be made for insurance and/or indemnity to meet the potential legal liability of the sponsor(s) for harm to participants arising from the management of the research? *Please tick box(es) as applicable.*

Note: Where a NHS organisation has agreed to act as sponsor or co-sponsor, indemnity is provided through NHS schemes. Indicate if this applies (there is no need to provide documentary evidence). For all other sponsors, please describe the arrangements and provide evidence.

- ☐ NHS indemnity scheme will apply (NHS sponsors only)
- ☑ Other insurance or indemnity arrangements will apply (give details below)

Queen Mary University London indemnity and insurance cover

Please enclose a copy of relevant documents.

A76-2. What arrangements will be made for insurance and/ or indemnity to meet the potential legal liability of the sponsor(s) or employer(s) for harm to participants arising from the design of the research? *Please tick box(es) as applicable.*

Note: Where researchers with substantive NHS employment contracts have designed the research, indemnity is provided through NHS schemes. Indicate if this applies (there is no need to provide documentary evidence). For other protocol authors (e.g. company employees, university members), please describe the arrangements and provide evidence.

- ☑ NHS indemnity scheme will apply (protocol authors with NHS contracts only)
- ☐ Other insurance or indemnity arrangements will apply (give details below)

Queen Mary University London indemnity and insurance cover

Please enclose a copy of relevant documents.

A76-3. What arrangements will be made for insurance and/ or indemnity to meet the potential legal liability of investigators/collaborators arising from harm to participants in the conduct of the research?

Note: Where the participants are NHS patients, indemnity is provided through the NHS schemes or through professional indemnity. Indicate if this applies to the whole study (there is no need to provide documentary evidence). Where non-NHS sites are to be included in the research, including private practices, please describe the arrangements which will be made at these sites and provide evidence.

- ☑ NHS indemnity scheme or professional indemnity will apply (participants recruited at NHS sites only)
- ☐ Research includes non-NHS sites (give details of insurance/ indemnity arrangements for these sites below)

Please enclose a copy of relevant documents.

PART C: Overview of research sites

Please enter details of the host organisations (Local Authority, NHS or other) in the UK that will be responsible for the research sites. *For NHS sites, the host organisation is the Trust or Health Board. Where the research site is a primary care site, e.g. GP practice, please insert the host organisation (PCT or Health Board) in the Institution row and insert the research site (e.g. GP practice) in the Department row.*

Research site		Investigator/ Collaborator/ Contact	
Institution name	Barts Health NHS Trust	Title	Dr
Department name	Critical Care Unit	First name/ Initials	Elaine
Street address	Whitechapel Road	Surname	Cole
Town/city	London		
Post Code	E1 1BB		
Institution name	Aberdeen Royal Infirmary, NHS Grampian	Title	Dr
Department name	Critical Care Unit	First name/ Initials	Peter
Street address	Foresterhill Rd,	Surname	Williams
Town/city	Aberdeen		
Post Code	AB25 2ZN		
Institution name	Addenbrooke's Hospital Cambridge NHS Trust	Title	Dr
Department name	Critical Care Unit	First name/ Initials	Roderick
Street address	Hills Road	Surname	MacKenzie
Town/city	Cambridge		
Post Code	CB2 0QQ		
Institution name	Derriford Hospital Plymouth NHS Trust,	Title	Dr
Department name	Critical Care Unit	First name/ Initials	Elfyn
Street address	Derriford Road	Surname	Thomas
Town/city	Plymouth		
Post Code	PL6 8DH		
Institution name	Edinburgh Royal Infirmary, NHS Lothian	Title	Dr
Department name	Critical Care Unit	First name/ Initials	Dave
Street address	51 Little France Crescent	Surname	Caesar
Town/city	Edinburgh		
Post Code	EH16 4SA		
Institution name	Frenchay Hospital Bristol, North Bristol NHS Trust	Title	Dr
Department name	Critical Care Unit	First name/ Initials	Matt
Street address	Frenchay Park Road	Surname	Thomas
Town/city	Bristol		
Post Code	BS16 1LE		

Institution name	Hull Royal Infirmary,	Title	Dr
Department name	Critical Care Unit	First name/ Initials	Neil
Street address	Anlaby Road	Surname	Smith
Town/city	Hull		
Post Code	HU3 2JZ		

Institution name	James Cook University Hospital Middlesbrough,	Title	Dr
Department name	Critical Care Unit	First name/ Initials	Judith
Street address	Marton Road	Surname	Wright
Town/city	Middlesborough		
Post Code	TS4 3BW		

Institution name	John Radcliffe Hospital Oxford,	Title	Dr
Department name	Critical Care Unit	First name/ Initials	Stuart
Street address	Headley Way, Headington	Surname	McKecknie
Town/city	Oxford		
Post Code	OX3 9DU		

Institution name	King’s College Hospital London,	Title	Dr
Department name	Critical Care Unit	First name/ Initials	Phil
Street address	Denmark Hill	Surname	Hopkins
Town/city	London		
Post Code	SE5 9RS		

Institution name	Leeds General Infirmary,	Title	Dr
Department name	Critical Care Unit	First name/ Initials	John
Street address	Great George Street	Surname	Adams
Town/city	Leeds		
Post Code	LS1 3EX		

Institution name	Manchester Royal Infirmary,	Title	Dr
Department name	Critical Care Unit	First name/ Initials	Jane
Street address	Oxford Road	Surname	Eddleston
Town/city	Manchester		
Post Code	M13 9WL		

Institution name	Morriston Hospital Swansea,	Title	Dr
Department name	Critical Care Unit	First name/ Initials	Paul
Street address	Heol Maes Eglwys, Morriston	Surname	Temblett
Town/city	Swansea		
Post Code	SA6 6NL		

Institution name	Ninewells Hospital Dundee, NHS Tayside	Title	Dr
Department name	Critical Care Unit	First name/ Initials	Mike
Street address	Dundee	Surname	Johnston
Town/city	Dundee		

Post Code	DD1 9SY		
Institution name	Northern General Hospital Sheffield	Title	Dr
Department name	Critical Care Unit	First name/ Initials	Angela
Street address	Herries Road	Surname	Pinder
Town/city	Sheffield		
Post Code	S5 7AU		
Institution name	Queen Elizabeth Hospital Birmingham	Title	Dr
Department name	Critical Care Unit	First name/ Initials	Tom
Street address	Edgbaston	Surname	Gallacher
Town/city	Birmingham		
Post Code	B15 2TH		
Institution name	Queen’s Medical Centre Nottingham	Title	Dr
Department name	Critical Care Unit	First name/ Initials	Daniel
Street address	Derby Road	Surname	Harvey
Town/city	Nottingham		
Post Code	NG7 2UH		
Institution name	Royal Liverpool University Hospital	Title	Dr
Department name	Critical Care Unit	First name/ Initials	Elizabeth
Street address	Prescott Street	Surname	Flockton
Town/city	Liverpool		
Post Code	L7 8XP		
Institution name	Aintree University Hospital Liverpool	Title	Dr
Department name	Critical Care Unit	First name/ Initials	Ged
Street address	Longmoor Lane	Surname	Dempsey
Town/city	Liverpool		
Post Code	L9 7AL		
Institution name	Preston Royal Infirmary	Title	Dr
Department name	Critical Care Unit	First name/ Initials	E
Street address	Sharoe Green Lane North	Surname	Denison-Davies
Town/city	Preston		
Post Code	PR2 9HT		
Institution name	Royal Sussex County Hospital Brighton	Title	Dr
Department name	Critical Care Unit	First name/ Initials	John
Street address	Eastern Road	Surname	Kilic
Town/city	Brighton		
Post Code	Bn2 5BE		
Institution name	Royal Victoria Infirmary Newcastle	Title	Dr

Department name	Critical Care Unit	First name/ Initials	Angus
Street address	Queen Victoria Road	Surname	Vincent
Town/city	Newcastle		
Post Code	NE1 4LP		

Institution name	Salford Royal Hospital	Title	Dr
Department name	Critical Care Unit	First name/ Initials	Jane
Street address	Stott Lane	Surname	Eddleston
Town/city	Salford		
Post Code	M6 8HD		

Institution name	Southampton General Hospital	Title	Prof
Department name	Critical Care Unit	First name/ Initials	M
Street address	Tremona Road	Surname	Grocott
Town/city	Southampton Road		
Post Code	SO16 6YD		

Institution name	Southern Glasgow University Hospital	Title	Dr
Department name	Critical Care Unit	First name/ Initials	Bill
Street address	1345 Govan Road	Surname	Leach
Town/city	Glasgow		
Post Code	G51 4TF		

Institution name	St George's Hospital London	Title	Dr
Department name	Critical Care Unit	First name/ Initials	M
Street address	Blackshaw Road	Surname	Cecconi
Town/city	London		
Post Code	SW17 0QT		

Institution name	St Mary's Hospital London	Title	Dr
Department name	Critical Care Unit	First name/ Initials	Martin
Street address	Praed Street	Surname	Stotz
Town/city	London		
Post Code	W2 1NY		

Institution name	University Hospital Coventry	Title	Dr
Department name	Critical Care Unit	First name/ Initials	Christopher
Street address	Clifford Bridge Road	Surname	Bassford
Town/city	Coventry		
Post Code	Cv2 2DX		

Institution name	University Hospital of Wales	Title	Dr
Department name	Critical Care Unit	First name/ Initials	Matt
Street address	Heath Park	Surname	Wise
Town/city	Cardiff		
Post Code	CF14 4XW		

Institution name	University Hospital South Manchester	Title	Dr
Department name	Critical Care Unit	First name/ Initials	Jane
Street address	Southmoor Road	Surname	Eddleston
Town/city	Manchester		
Post Code	M23 9LT		

Institution name	University Hospital of North Staffordshire	Title	Dr
Department name	Critical Care Unit	First name/ Initials	B
Street address	Newcastle Road	Surname	Carr
Town/city	Stoke on Trent		
Post Code	ST4 6QG		

PART D: Declarations

D1. Declaration by Chief Investigator

1. The information in this form is accurate to the best of my knowledge and belief and I take full responsibility for it.

2. I undertake to abide by the ethical principles underlying the Declaration of Helsinki and good practice guidelines on the proper conduct of research.

3. If the research is approved I undertake to adhere to the study protocol, the terms of the full application as approved and any conditions set out by review bodies in giving approval.

4. I undertake to notify review bodies of substantial amendments to the protocol or the terms of the approved application, and to seek a favourable opinion from the main REC before implementing the amendment.

5. I undertake to submit annual progress reports setting out the progress of the research, as required by review bodies.

6. I am aware of my responsibility to be up to date and comply with the requirements of the law and relevant guidelines relating to security and confidentiality of patient or other personal data, including the need to register when necessary with the appropriate Data Protection Officer. I understand that I am not permitted to disclose identifiable data to third parties unless the disclosure has the consent of the data subject or, in the case of patient data in England and Wales, the disclosure is covered by the terms of an approval under Section 251 of the NHS Act 2006.

7. I understand that research records/data may be subject to inspection by review bodies for audit purposes if required.

8. I understand that any personal data in this application will be held by review bodies and their operational managers and that this will be managed according to the principles established in the Data Protection Act 1998.

9. I understand that the information contained in this application, any supporting documentation and all correspondence with review bodies or their operational managers relating to the application:

    - Will be held by the REC (where applicable) until at least 3 years after the end of the study; and by NHS R&D offices (where the research requires NHS management permission) in accordance with the NHS Code of Practice on Records Management.
    - May be disclosed to the operational managers of review bodies, or the appointing authority for the REC (where applicable), in order to check that the application has been processed correctly or to investigate any complaint.
    - May be seen by auditors appointed to undertake accreditation of RECs (where applicable).
    - Will be subject to the provisions of the Freedom of Information Acts and may be disclosed in response to requests made under the Acts except where statutory exemptions apply.
    - May be sent by email to REC members.

10. I understand that information relating to this research, including the contact details on this application, may be held on national research information systems, and that this will be managed according to the principles established in the Data Protection Act 1998.

11. Where the research is reviewed by a REC within the UK Health Departments Research Ethics Service, I understand that the summary of this study will be published on the website of the National Research Ethics Service (NRES), together with the contact point for enquiries named below. Publication will take place no earlier than 3 months after issue of the ethics committee's final opinion or the withdrawal of the application.

Contact point for publication*(Not applicable for R&D Forms)*

NRES would like to include a contact point with the published summary of the study for those wishing to seek further information. We would be grateful if you would indicate one of the contact points below.

(●) Chief Investigator

( ) Sponsor

- ○ Study co-ordinator
- ○ Student
- ○ Other – please give details
- ○ None

Access to application for training purposes *(Not applicable for R&D Forms)*

Optional – please tick as appropriate:

☑ I would be content for members of other RECs to have access to the information in the application in confidence for training purposes. All personal identifiers and references to sponsors, funders and research units would be removed.

This section was signed electronically by Professor Karim Brohi on 14/07/2015 12:39.

Job Title/Post:

Organisation:

Email:

D2. Declaration by the sponsor's representative

If there is more than one sponsor, this declaration should be signed on behalf of the co−sponsors by a representative of the lead sponsor named at A64-1.

I confirm that:

1. This research proposal has been discussed with the Chief Investigator and agreement in principle to sponsor the research is in place.

2. An appropriate process of scientific critique has demonstrated that this research proposal is worthwhile and of high scientific quality.

3. Any necessary indemnity or insurance arrangements, as described in question A76, will be in place before this research starts. Insurance or indemnity policies will be renewed for the duration of the study where necessary.

4. Arrangements will be in place before the study starts for the research team to access resources and support to deliver the research as proposed.

5. Arrangements to allocate responsibilities for the management, monitoring and reporting of the research will be in place before the research starts.

6. The duties of sponsors set out in the Research Governance Framework for Health and Social Care will be undertaken in relation to this research.

   Please note: *The declarations below do not form part of the application for approval above. They will not be considered by the Research Ethics Committee.*

7. Where the research is reviewed by a REC within the UK Health Departments Research Ethics Service, I understand that the summary of this study will be published on the website of the National Research Ethics Service (NRES), together with the contact point for enquiries named in this application. Publication will take place no earlier than 3 months after issue of the ethics committee's final opinion or the withdrawal of the application.

8. Specifically, for submissions to the Research Ethics Committees (RECs) I declare that any and all clinical trials approved by the HRA since 30th September 2013 (as defined on IRAS categories as clinical trials of medicines, devices, combination of medicines and devices or other clinical trials) have been registered on a publically accessible register in compliance with the HRA registration requirements for the UK, or that any deferral granted by the HRA still applies.

This section was signed electronically by Dr Sally Burtles on 14/07/2015 10:41.

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