NETSCC, HTA

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PROTOCOL

CRASH-2 SUBSTUDY

The effect of tranexamic acid on intracranial bleeding among CRASH-2 trial participants

CONTENTS

CRASH-2 substudy

The effect of tranexamic acid on intracranial bleeding among CRASH-2 trial participants

1. Background

CRASH-2 is a large randomised controlled trial of the effect on mortality and transfusion requirements of tranexamic acid (TXA) in trauma patients with significant bleeding (www.crash2.Lshtm.ac.uk). Over 9,000 patients have been enrolled so far and recruitment will continue until 20,000 patients have been randomised. Many of the patients included in the CRASH-2 trial have multiple injuries and in about 40% of patients this includes traumatic brain injury (TBI). The CRASH-2 trial will assess as sub-group analyses, the effect of TXA in patients who also have TBI. These analyses will examine the effect of TXA on mortality, on the need for a neurosurgical operation and on neurological impairment, using a modified version of the Oxford Handicap Score (our previous analyses have shown that this score is strongly correlated with outcome on the Glasgow Outcome Scale at six months).

Traumatic intracranial bleeding: TBI is commonly accompanied by intracranial bleeding, which can be epidural, subdural, subarachnoid or parenchymal. Of the 7,814 patients with TBI enrolled in the MRC CRASH trial who had a computerised tomography (CT) scan, 31% had subarachnoid haemorrhage and 40% had an intracranial haematoma. Overall 56% of TBI patients had some type of intracranial bleeding.[1]

Prognostic studies show that intracranial bleeding is associated with increased mortality and disability six months after injury. In the MRC CRASH trial, the presence of subarachnoid haemorrhage, petechial haemorrhage or intracranial haematoma were independently associated with poor outcome at 2 weeks and 6 months.[2] Similarly, the IMPACT study found that after controlling for age, Glasgow Coma Score (GCS) motor score and pupil reactions, subarachnoid and subdural haemorrhages more than doubled the odds of poor outcome at six months.[3] The larger the intracranial bleeding, wherever the location, the worse prognosis it is associated with. The Brain Trauma Foundation Guideline for Surgery takes into account the bleeding size to recommend surgical

evacuation: 50 cm^3 for parenchymal haematoma, 30 cm^3 for epidural and 10 mm for subdural haematoma.[5]

In patients with TBI, intracranial bleeding can develop or worsen after hospital admission. Studies involving repeated CT scanning have found that intracranial bleeds can develop or expand in the 24 hours after injury. Ortel studied a group of patients in whom two CT scans were obtained within 24 hours of injury to determine the prevalence of progressive intracranial haemorrhage.[4] Among patients who had their first CT scan within 2 hours of injury, 49% had radiological evidence of progressive haemorrhage. Yadav conducted repeat CT scanning of TBI patients at hospital admission and 24 hours later, and found that 16% of 262 parenchymal haematomas and contusions increased in size in the first 24 hours.[6] Similarly, Sullivan et al found that traumatic epidural haemorrhages enlarged in 23% of 160 TBI patients treated non-operatively.[7] The mean enlargement was 7 mm, and the mean time to enlargement was 8 hours from injury and 5.3 hours from CT diagnosis. Although these studies provide estimates of the occurrence of intracranial bleeding and expansion they all have limitations. All included patients who have an abnormal initial CT scan and there is little information on the proportion of patients that develop new intracranial bleeds in the first 24 hours who have the potential to benefit from early treatment.

Tranexamic acid and intracranial bleeding: Tranexamic acid is commonly used in surgery to reduce blood loss. A systematic review of randomised controlled trials of TXA in elective surgery showed that it reduces the need for transfusion by one third, reduces donor exposure by one unit, and halves the need for further surgery to control bleeding.[8] A systematic review of randomised trials of TXA in patients with *aneurismal* subarachnoid haemorrhage showed that TXA reduced the rate of re-bleeding by approximately 40%, but because of an increase in cerebral ischaemia there was no overall benefit.[9] However, the duration of TXA treatment in these trials was six weeks and it is possible that a shorter treatment might prevent re-bleeding whilst avoiding the risk of ischaemia. The systematic review was conducted in 2003 but since then a randomised controlled trial of the early administration of a short course (3 days) of TXA in aneurysmal subarachnoid haemorrhage found that TXA reduced the occurrence of re-bleeding from 10.8% to 2.4% with no evidence of increased side effects.[10] Almost all of the effect on re-bleeding was observed within the first few hours after hospital admission. Tranexamic acid could also improve outcome after TBI by reducing systemic blood loss. Hypotension is an established risk factor for poor outcome after TBI.

Hypothesis: Early administration of TXA can prevent the occurrence or increase of intracranial bleeding in patients with TBI and significant bleeding.

Aim: The aim of the proposed substudy is to quantify the effect on intracranial bleeding of the early administration of TXA, in CRASH-2 trial participants with traumatic brain injury.

Primary outcome:

1) Increase in volume of intracranial bleeding

Secondary outcomes:

1) Frequency of progressive haematomas
2) Frequency of delayed haematomas
3) New focal ischaemic lesions

Other relevant outcomes including mortality, disability, need of neurosurgical operation and non fatal thromboembolic events are collected in the CRASH-2 trial and will be reported for the TBI subgroup in the main analysis.

2. Study design

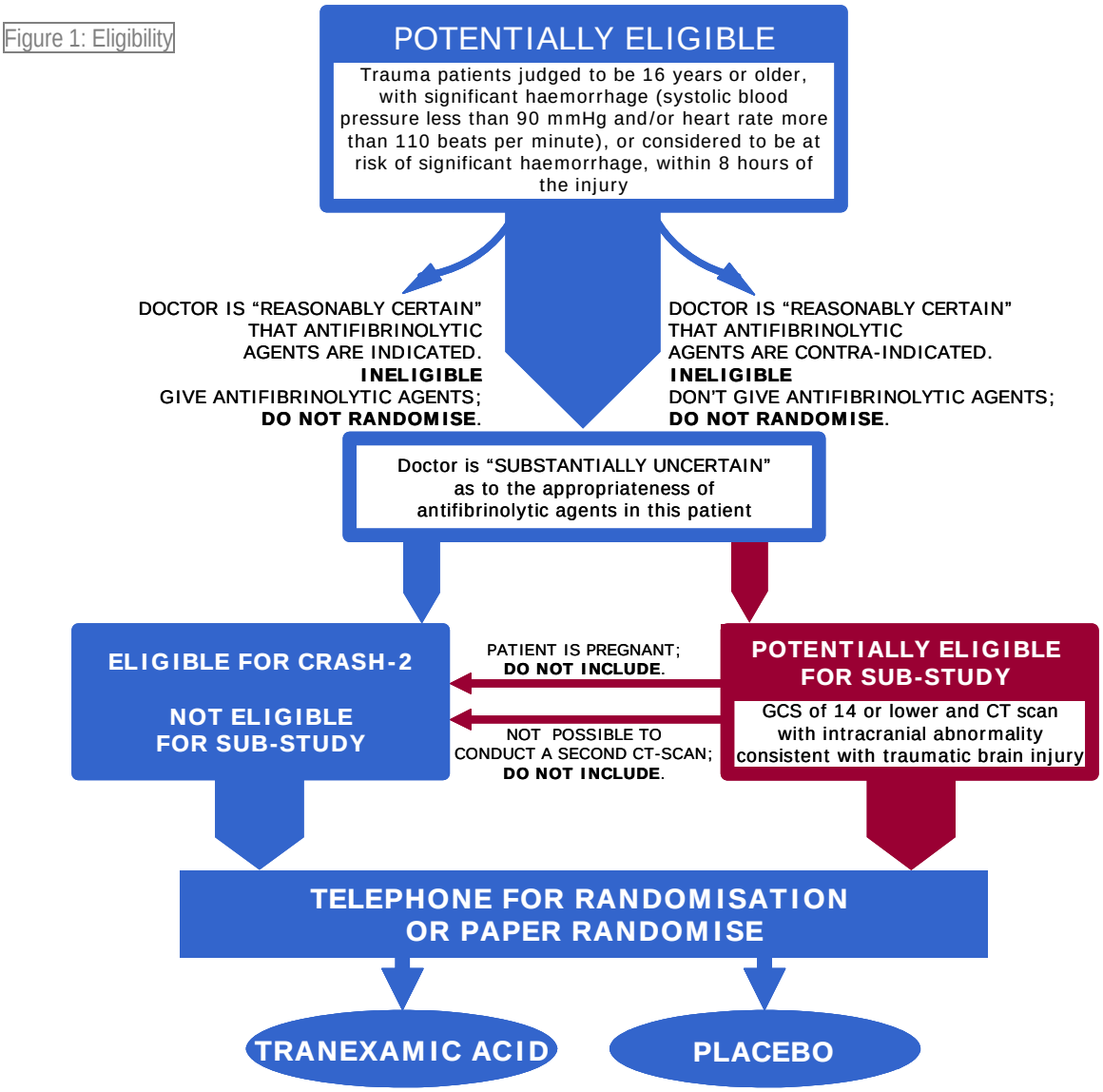
Methods

Participating hospitals: Participating hospitals have been selected based on level of interest by the principal investigator in the research question, the recruitment rate in the CRASH-2 trial and the ability of the hospital to collect and send the necessary CT scan data to the trial co-ordinating centre. This substudy will be conducted in the hospitals listed in Appendix 1.

Inclusion criteria: *All patients meeting the following criteria will be eligible for inclusion in the substudy:*

- *Fulfils the inclusion criteria for the CRASH-2 trial*
- *GCS of 14 or less*
- *Baseline clinical CT scan shows intracranial abnormality consistent with TBI*
- *Non pregnant*

Figure 1: Eligibility



Number of patients needed: Assuming a baseline intracranial bleeding volume of 20 ml, an average increase of 7 ml in the control group and a correlation of 0.6 between baseline and follow-up bleeding, we need to recruit 900 patients to have 80% power (with alpha=0.05) to detect a 20% reduction in the increase of intracranial bleeding volume in the control group. If 400 patients were recruited the trial could detect a 30% reduction in the primary outcome. A sample size of 200 patients could detect a 40% reduction in the primary outcome.

Procedures: Patients will follow all procedures as per CRASH-2 protocol; Additional procedures for the substudy are as follows:

Patients enrolled in the substudy will be identified by the completion of one form that will collect data on time since injury, time of initial (pre-randomisation) and follow-up CT scans and the file identifiers of the respective CT scan images. This form will also collect information on whether or not a decision to undertake neurosurgery was taken based on the CT scan result (see Appendix 2). This form will be sent to the trial co-ordinating centre in the same way as the CRASH-2 trial data.

CT scan protocol:

CT scan data acquisition: Two CT scans will be obtained for each participant, a clinical pre-randomisation scan and second scan 24-48 hours later. CT scans will be sent to the co-ordinating centre by uploading them onto the CRASH-2 trial server. Scans will be checked by the trial data manager to ensure that they are of the head, from the correct patient, performed on the correct date and of sufficient quality to be read. All study sites will be required to provide documentation as to the standard parameters used for each CT scanner. The specific scan protocol/parameters of the initial CT evaluation will be limited by the emergent nature at the time of admission. However, after a patient is enrolled, the follow-up scan must match the baseline CT scan with regard to section thickness, section spacing (overlap or no gap), matrix, field of view, and scan angulations. Consistency in these parameters across all CT evaluations for a patient allow comparable measurements because of identical spatial resolution. All name identifiers will be removed before loading the scans onto the CT reading system. The CT scans will be allocated to an expert CT scan reader for evaluation who will be blind to the treatment allocation.

CT scan data analysis: In both CT scans we will measure: type of bleeding (subdural, epidural, subarachnoid haemorrhage, parenchymal haematoma) volume of bleeding, ischaemic lesions and indirect signs of intracranial pressure. Volume of intracranial bleeding will be measured using validated methods; further details are described in the statistical analysis plan.

Consent

Because patients included in this substudy will have significant TBI, relatives or legal representatives would be asked to sign the informed consent in line with local legal requirements. To minimise the need for multiple information sheets and consent forms, one form which combines the CRASH-2 and substudy information will be used (Appendix 3).

Randomisation

As per CRASH-2 protocol

Treatment

As per CRASH-2 protocol

Serious unexpected suspected adverse events

As per CRASH-2 protocol

Expected side effects

As per CRASH-2 protocol

Potential risks associated with this substudy

It is standard care for all patients with a history of TBI and associated clinical signs to have a CT scan. Therefore, the initial scan will form part of standard care. The substudy requires one additional CT Scan to be done 24 to 48 hours after the first, which in many cases is likely to be clinically indicated. The effective radiation dose from a CT scan is about 2 mSv, which is about the amount received from background radiation in eight months.

Unblinding

As per CRASH-2 protocol

Analysis

Haemorrhage volume from CT scans will be analysed with use of generalised linear mixed models. The baseline bleeding volume and the time from injury to CT will be included as covariates. Because patients who undergo a neurosurgery based on the pre-randomisation CT scan would not have a baseline haematoma they would be excluded of this analysis.

We will express the effect of TXA on the occurrence of secondary endpoints using relative risks and 95% confidence intervals. All analysis will be based on the intention to treat principle. We will conduct subgroup analysis according to type of bleeding. No interim analysis is planned for the sub-study; the analysis

will be done at the end of the CRASH-2 Trial. Further details are described in the statistical analysis plan.

Definitions

Progressive haematoma will be defined as a growth of the haematoma larger than 25% from the initial to the follow-up CT scan.

Delayed haematoma will be defined as appearance of an haematoma in the follow-up CT scan where there was not one on the initial scan.

New focal ischaemic lesions will be defined as those ischaemic lesions which appear in the follow-up CT scan but not in the initial one.

3. Organisation

Data monitoring committee

The data monitoring committee members would be the same as CRASH-2.
Standard Operating Procedures: As per CRASH-2 protocol

Steering committee

The steering committee members would be the same as CRASH-2 plus Professor Peter Sandercock.
Standard Operating Procedures: As per CRASH-2 protocol

Substudy Protocol Committee

Rustam Al-Shahi Salman (UK), Yashbir Dewan (India), Anil P Lal (India), Carlos Morales (Colombia), Zoe Morris (UK), Pablo Perel (UK), P V Ramana (India), R R Ravi (India), Ian Roberts (UK), Peter Sandercock (UK), Haleema Shakur (UK), Joanna Wardlaw (UK)

Co-ordinating centre responsibilities

As per CRASH-2 protocol

Publication

The results of the trial will be reported first to trial collaborators. Dissemination of results to patients will take place via the media, trial website (www.crash2@Lshtm.ac.uk) and relevant patient organisations.

Indemnity

As per CRASH-2 protocol

Financial support: LSHTM

4. References

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2. MRC CRASH Trial Collaborators. Predicting outcome after traumatic brain injury: practical prognostic models based on large cohort of international patients. BMJ 2008;12:12.

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6. Yadav YR, Basoor A, Jain G, Nelson A. Expanding traumatic parenchymal contusion/hematoma. Neurol India. 2006;54:377-81.

7. Sullivan TP, Jarvik JG, cohen WA. Follow-up of conservatively managed epidural hematomas: implications for timing of repeat CT. AJNR Am J Neuroradiol 1999;20:107-13.

8. Henry DA, Moxey AJ, Carless PA, O'Connell D, McClelland B, Henderson KM, Sly K, Laupacis A, Fergusson D. Anti-fibrinolytic use for minimising perioperative allogeneic blood transfusion (Cochrane Review). In: The Cochrane Library, Issue 1, 2007. Chichester, UK: John Wiley & Sons, Ltd.

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Appendix 1

Hospitals that will participate in the substudy

1. Aditya Neuroscience Centre, Dibrugarh, India
2. GM Hospital (P) LTD, Dibrugarh, India
3. Sanjivani Hospital, Dibrugarh, India
4. Care Hospital, Visakhapatnam, India
5. Christian Medical College, Ludhiana , India
6. Medical Trust Hospital, Kochi, India
7. Hospital Universitario San Vicente de Paul, Medellín, Colombia

Other hospitals may be added if recruitment falls below predicted.

Appendix 2 - Investigator CT scan form

CRASH-2 Intracranial Bleeding Substudy
INVESTIGATOR CT SCAN FORM

A. Section to be completed after the **initial CT Scan**

1. Hospital ID					
2. Patient initials		**3.** Patient hospital identification number		**4.** Box / Pack	
5. CT scan compatible with head injury *(circle the correct answer)* **Yes No**	**6.** Time and date of injury Time ____ : ____ (24 hours) Date ____/____/____ (dd/mm/yy)		**7.** Time and date of initial CT scan Time ____ : ____ (24 hours) Date ____/____/____ (dd/mm/yy)		
8a. Haematoma evacuation decided based on initial CT results? *(circle the correct answer)* **Yes No**		**8b.** If yes, type of haematoma evacuated: *(tick all that apply)* ☐ Parenchymal ☐ Epidural ☐ Subdural			
9. CT scan Identifier: (OFFICE USE ONLY)	**10. CT scan parameters** Section thickness: Section spacing: Matrix: Field of view: Scan angulations :				
11. Name of the person completing the form			**12.** Date		

B. Section to be completed after the **follow-up CT Scan**

13. Patient initials		**14.** Patient hospital identification number		**15.** Box / Pack	
16. Time and date of follow-up CT scan Time ____ : ____ (24 hours) Date ____/____/____ (dd/mm/yy)					
17a. Haematoma evacuation decided based on follow-up CT results? *(circle the correct answer)* **Yes No**		**17b.** If yes, type of haematoma evacuated: *(tick all that apply)* ☐ Parenchymal ☐ Epidural ☐ Subdural			
18. CT scan identifier: (OFFICE USE ONLY)	**19. CT scan parameters** Section thickness: Section spacing: Matrix: Field of view: Scan angulations:				
20. Name of the person completing the form			**21.** Date		

Appendix 3a – Information for relatives and representatives

PI & Hospital name
Address
Tel, Email

INFORMATION FOR RELATIVES AND REPRESENTATIVES

INTERNATIONAL STUDY OF BLEEDING AFTER INJURY AND INTRACRANIAL BLEEDING SUBSTUDY

This hospital is taking part in a research study to find ways to reduce severe bleeding after serious injury. We would like to include (name of patient) in this study.

WHAT YOU SHOULD KNOW ABOUT RESEARCH STUDIES:

This form gives information about the study including the aims, risks and benefits of taking part.

In this hospital, patients with severe bleeding and injury to the head are given the usual emergency treatment. The aim of this research study is to find a better treatment. We hope that the study treatment (tranexamic acid) will help clotting and so lessen the amount of blood lost and reduce the need for a blood transfusion and bleeding into the brain. But the study treatment may cause clots where they are not needed. We hope to find that the treatment will do a little more good than harm but we don't yet know this. Please read the information below carefully and ask the responsible doctor for any questions you have.

1) Why is this research being done?
Severe bleeding is a common cause of death after injury and it is important to find better ways of reducing the amount of blood lost.

2) What is the purpose of this study?
Tranexamic acid is often used to reduce bleeding after major surgery such as heart operations. This study is being done to see if it can also reduce bleeding after major injury. Tranexamic acid is not a new drug and is an approved treatment for many common conditions that involve bleeding.

3) Who is doing the study?
Dr (name) is in charge of this study at this hospital. The study is co-ordinated by doctors at the University of London.

4) A patient cannot be in this study if:

- he/she is known not to be legally adult
- he/she was injured more than 8 hours before arriving in hospital
- the doctor thinks there is a particular reason why tranexamic acid definitely **should not** be given
- the doctor thinks there is a particular reason why tranexamic acid definitely **should** be given
- she is pregnant
- the brain scan is normal

5) What will happen to the patient after he/she is included in this study?
The patient will be given all the usual emergency treatments for bleeding, including fluids to replace the blood that he/she lost. The patient will also be given a dose of either the active tranexamic acid or an inactive dummy medicine called saline. The dose will be given over a period of eight hours. The choice of what to give (active treatment or dummy treatment) will be made randomly by a computer at the University of Oxford, UK. The doctors looking after (patient name) will not know whether he/she gets the active or the dummy medicine. This information is kept on a confidential list in another hospital. It is routine practice to do a CT scan after a traumatic brain injury; this study involves doing a second CT scan within 24-48 hours of the injury. Doctor (doctor's name) will send brief details about how the patient is doing to the Co-ordinating Centre in London. This information will be used in strict confidence by the people working on the study and will not be released under any circumstance.

6) What are the possible risks of being in the study?
Tranexamic acid is widely used and at the moment there is no conclusive evidence of serious side effects with short term use. Tranexamic acid is NOT a new drug. A patient would normally be exposed to at least one CT scan; during this study an extra CT scan (within 24-48 hours) would be done. Level of exposure to X-ray radiation is about the same as (patient name) would receive naturally from the environment over eight months.

7) What are the possible benefits of being in the study?
We hope that tranexamic acid may help reduce blood loss and bleeding into the brain. The knowledge that we gain from this study will help people with similar injuries in the future.

8) If you have any questions or problems, who can you call?
If you have any questions you can contact Dr (name) by telephoning (tel)

9) What information do we keep private?
All information about (patient name) and his/her injury will be kept private. The only people allowed to look at the information will be the doctors who are running the study, the staff at the Co-ordinating Centre and the regulatory authorities who check that the study is being carried out correctly. We will publish the results of the study in a medical journal so that other doctors can benefit from the knowledge, but (patient name)'s personal information will not be included and there will be no way that he/she can be identified.

10) Can the study end early for the participant?
We hope that you will let us use information about how the patient got on, but if you do not want us to use it then please tell the doctor who is looking after the patient.

11) What else do you need to know?

- The study is funded by the University of London and the World Health Organisation, not the makers of tranexamic acid.
- The London School of Hygiene & Tropical Medicine (University of London) as the Co-ordinating Centre for the study accepts responsibility attached to its sponsorship of the study and, as such, would be responsible for claims for any non-negligent harm suffered by anyone as a result of participating in this study.
- We will ask you to sign a separate consent form and give you a copy to keep.

STUDY CO-ORDINATING CENTRE:
International Study of Bleeding After Injury, Room 180
London School of Hygiene & Tropical Medicine, Keppel Street, London WC1E 7HT
Tel +44 20 7299 4684
WWW.CRASH2.LSHTM.AC.UK

INTRACRANIAL BLEEDING SUBSTUDY – LEGAL REPRESENTATIVE INFORMATION SHEET & CONSENT, (HOSPITAL NAME)

PI & Hospital name
Address
Tel, Email

Hospital Name:	
Patient Hospital ID:	
Randomisation Number:	
Name of Principal Investigator:	

RELATIVE AND REPRESENTATIVE CONSENT FORM

INTERNATIONAL STUDY OF BLEEDING AFTER INJURY and Intracranial Injury Substudy

PLEASE INITIAL BOX

1. I confirm that I have read and understood the information sheet Version 1, dated 6 June 2008, for the above study and have had the opportunity to ask questions. ☐
2. I understand that the patient participation is voluntary and that he/she is free to withdraw at any time, without giving any reason, without his/her medical care or legal rights being affected. ☐
3. I understand that sections of any of the patient's medical notes may be looked at by responsible individuals from The London School of Hygiene & Tropical Medicine or from regulatory authorities where it is relevant to his/her taking part in research. I give permission for these individuals to have access to the patient records. ☐
4. I agree for (patient name) to take part in the above study / for (patient name)'s information to be used in this trial. ☐
5. I understand that I can withdraw my consent at any time and the patient's medical care will not be affected in anyway by my withdrawal. ☐

_____	_____	_____
Name of relative or representative	Date	Signature
_____	_____	_____
Name of Person taking consent (if different from researcher)	Date	Signature
_____	_____	_____
Researcher	Date	Signature

Appendix 3b – Information for patients

PI & Hospital name
Address
Tel, Email

INFORMATION FOR PATIENTS

INTERNATIONAL STUDY OF BLEEDING AFTER INJURY AND INTRACRANIAL INJURY SUBSTUDY

This hospital is taking part in a research study to find ways to reduce severe bleeding after serious injury. You have been included in this study.

WHAT YOU SHOULD KNOW ABOUT RESEARCH STUDIES:

This form gives information about the study including the aims, risks and benefits of taking part.

In this hospital, patients with severe bleeding and injury to the head are given the usual emergency treatment. The aim of this research study is to find a better treatment. We hope that the study treatment (tranexamic acid) will help clotting and so lessen the amount of blood lost and reduce the need for a blood transfusion and bleeding into the brain. But the study treatment may cause clots where they are not needed. We hope to find that the treatment will do a little more good than harm but we don't yet know this. Please read the information below carefully and ask the doctor looking after you any questions you have.

1) Why is this research being done?
Severe bleeding is a common cause of death after injury and it is important to find better ways of reducing the amount of blood lost.

2) What is the purpose of this study?
Tranexamic acid is often used to reduce bleeding after major surgery such as heart operations. This study is being done to see if it can also reduce bleeding after major injury. Tranexamic acid is not a new drug and is an approved treatment for many common conditions that involve bleeding.

3) Who is doing the study?
Dr (name) is in charge of this study at this hospital. The study is co-ordinated by doctors at the University of London.

4) A patient cannot be in this study if:

- he/she is known not to be legally adult
- he/she was injured more than 8 hours before arriving in hospital
- the doctor thinks there is a particular reason why tranexamic acid definitely **should not** be given
- the doctor thinks there is a particular reason why tranexamic acid definitely **should** be given
- she is pregnant
- the brain scan is normal

5) What has happened to you after you were included in this study?
You were given all the usual emergency treatments for bleeding, including fluids to replace the blood that you lost. You were also given a dose of either the active tranexamic acid or an inactive dummy medicine called saline. The dose was given over a period of eight hours. The choice of what to give (active treatment or dummy treatment) was made randomly by a computer at the University of Oxford, UK. The doctors looking after you do not know whether you got the active or the dummy medicine. This information is kept on a confidential list in another hospital. It is routine practice to do a CT scan after a traumatic brain injury; this study involves doing a second CT scan within 24-48 hours of the injury. Your doctor will send brief details about how you have been to the Co-ordinating Centre in London. This information will be used in strict confidence by the people working on the study and will not be released under any circumstance.

6) What are the possible risks of being in the study?
Tranexamic acid is widely used and at the moment there is no conclusive evidence of serious side effects with short term use. Tranexamic acid is NOT a new drug. You would normally be exposed to at least one CT scan; during this study an extra CT scan (within 24-48 hours) would be done. Level of exposure to X-ray radiation is about the same as you would receive naturally from the environment over eight months.

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We hope that tranexamic acid may help reduce blood loss and bleeding into the brain. The knowledge that we gain from this study will help people with similar injuries in the future.

8) If you have any questions or problems, who can you call?
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9) What information do we keep private?
All information about you and your injury will be kept private. The only people allowed to look at the information will be the doctors who are running the study, the staff at the Co-ordinating Centre and the regulatory authorities who check that the study is being carried out correctly. We will publish the results of the study in a medical journal so that other doctors can benefit from the knowledge, but your personal information will not be included and there will be no way that you can be identified.

10) Can the study end early for the participant?
The study treatment was given in the emergency situation. We hope that you will let us use information about how you got on, but if you do not want us to use it then please tell your doctor.

11) What else do you need to know?

- The study is funded by the University of London and the World Health Organisation, not the makers of tranexamic acid.
- The London School of Hygiene & Tropical Medicine (University of London) as the Co-ordinating Centre for the study accepts responsibility attached to its sponsorship of the study and, as such, would be responsible for claims for any non-negligent harm suffered by anyone as a result of participating in this study.
- We will ask you to sign a separate consent form and give you a copy to keep.

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Tel +44 20 7299 4684
WWW.CRASH2.LSHTM.AC.UK

PI & Hospital name
Address
Tel, Email

Hospital Name:	
Patient Hospital ID:	
Randomisation Number:	
Name of Principal Investigator:	

PATIENT CONSENT FORM

INTERNATIONAL STUDY OF BLEEDING AFTER INJURY and Intracranial Injury Substudy

PLEASE INITIAL BOX

1. I confirm that I have read and understood the information sheet Version 1, dated 6 June 2008, for the above study and have had the opportunity to ask questions. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐
3. I understand that sections of any of my medical notes may be looked at by responsible individuals from The London School of Hygiene & Tropical Medicine or from regulatory authorities where it is relevant to my taking part in research. I give permission for these individuals to have access to my records. ☐
4. I agree to take part in the above study / for my information to be used in this trial. ☐
5. I understand that I can withdraw my consent at any time and my medical care will not be affected in anyway by my withdrawal. ☐

_____	_____	_____
Name of Patient	Date	Signature
_____	_____	_____
Name of Person taking consent (if different from researcher)	Date	Signature
_____	_____	_____
Researcher	Date	Signature

CRASH TRIALS CO-ORDINATING CENTRE
London School of Hygiene & Tropical Medicine
Keppel Street, London WC1E 7HT
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Fax +44(0)20 7299 4663
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WWW.CRASH2.LSHTM.AC.UK

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