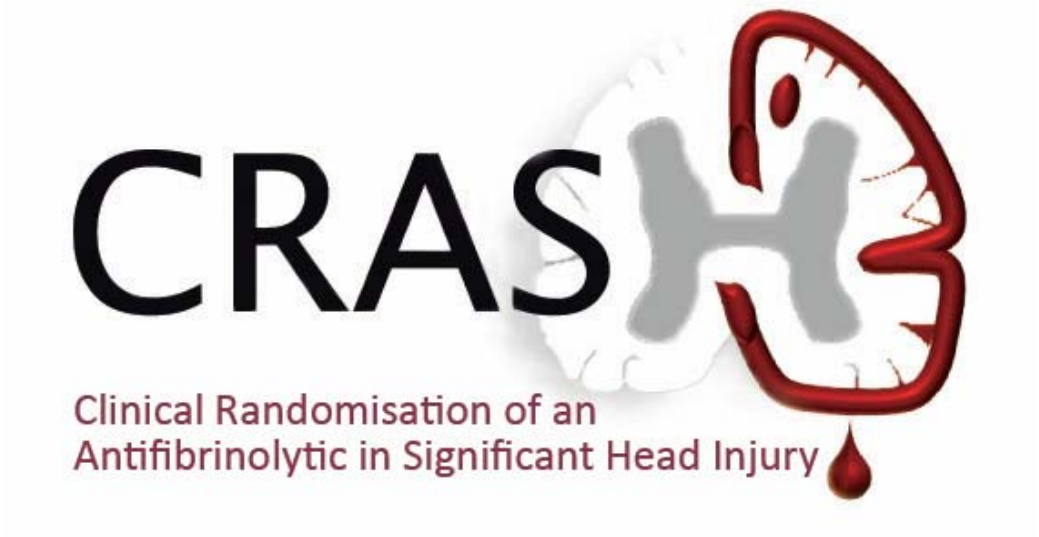


What to do if a patient develops an unexpected problem

Protocol Code: ISRCTN15088122
V 1.0 date 30 Jan 2012

If a patient develops an unexpected problem

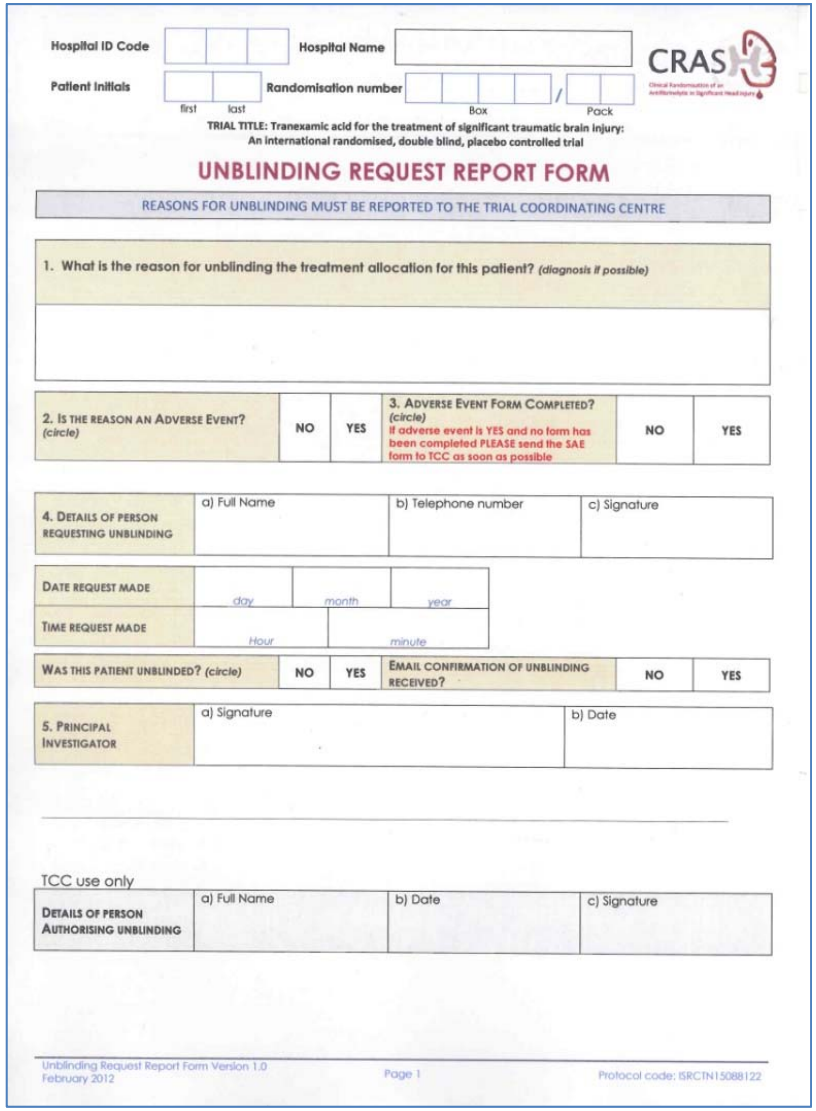
- If you have any concerns about a patient in the trial, you must contact the PI or his/her delegate at your hospital in the first instance

- Advice about the trial (not clinical care) is available from the TCC – see wall posters and Investigator Study File for contact information

Unblinding the treatment allocation

- In general there should be no need to unblind the allocated treatment. **If some contraindication to antifibrinolytic therapy develops after randomisation, the trial treatment should simply be stopped and all usual standard care given**.
- Unblinding should be done only in those rare cases when the clinician believes that clinical management depends importantly upon knowledge of whether the patient received tranexamic acid or placebo.
- In those few cases when urgent unblinding is considered necessary, a 24-hour telephone service is available and details provided in the Study File and wall posters.
- If unblinding is needed, the caller will be told whether the patient received TXA or placebo by email or fax; this is to ensure that the TCC staff remain blind to the study treatment

Unblinding the treatment allocation



Hospital ID Code | Hospital Name | CRASH

Patient Initials (first, last) | Randomisation number (Box / Pack)

TRIAL TITLE: Tranexamic acid for the treatment of significant traumatic brain injury: An international randomised, double blind, placebo controlled trial

UNBLINDING REQUEST REPORT FORM

REASONS FOR UNBLINDING MUST BE REPORTED TO THE TRIAL COORDINATING CENTRE

1. What is the reason for unblinding the treatment allocation for this patient? *(diagnosis if possible)*

2. Is the reason an Adverse Event? *(circle)* — NO / YES

3. Adverse Event Form Completed? *(circle)* If adverse event is YES and no form has been completed PLEASE send the SAE form to TCC as soon as possible — NO / YES

4. Details of person requesting unblinding — a) Full Name | b) Telephone number | c) Signature

Date request made — day / month / year

Time request made — Hour / minute

Was this patient unblinded? *(circle)* — NO / YES

Email confirmation of unblinding received? — NO / YES

5. Principal Investigator — a) Signature | b) Date

TCC use only

Details of person authorising unblinding — a) Full Name | b) Date | c) Signature

Unblinding Request Report Form Version 1.0 February 2012 — Page 1 — Protocol code: ISRCTN15088122

- An Unblinding Request Report form must be completed by the person who requested the unblinding
- TCC will send you a blank form immediately a request for unblinding has been granted
- If necessary, an Adverse Event Report must be completed

For further information see presentation titled 'Adverse Event reporting and completing the report form'

Complications – reported as outcomes

Mortality:

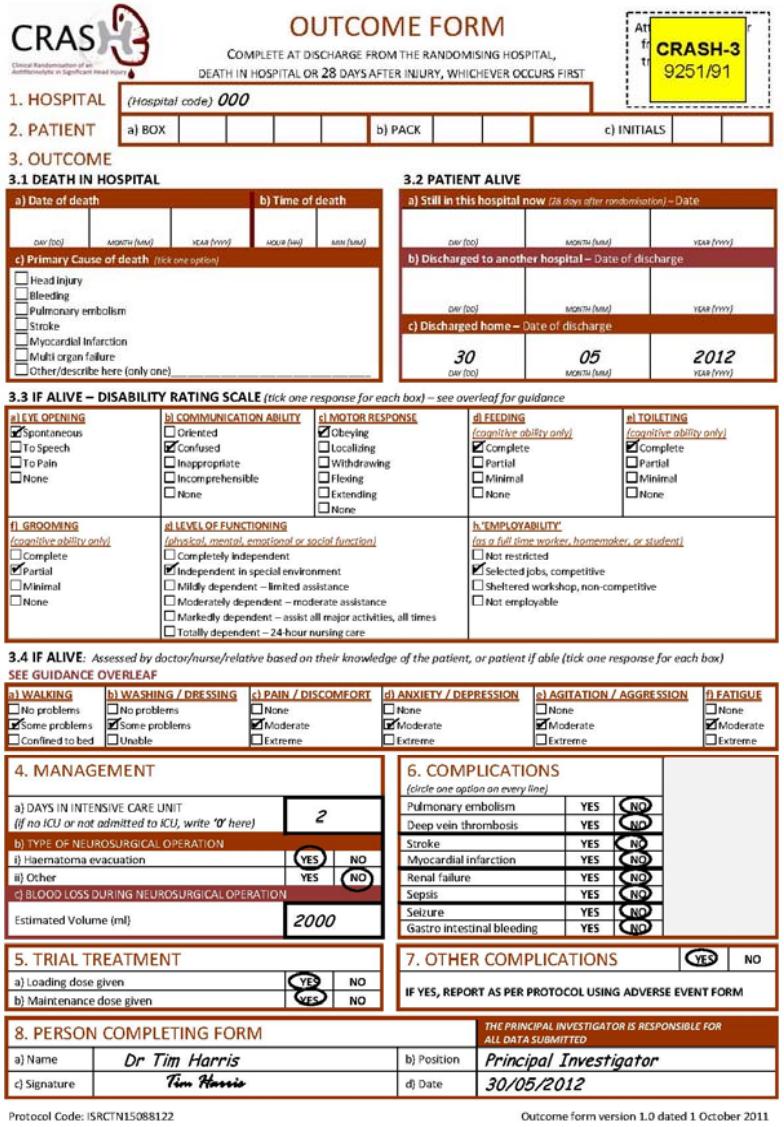
primary outcome routinely captured (including primary cause)

Other relevant medical events:

expected complications of TBI collected:

- neurosurgical interventions
- thromboembolic events
- renal failure
- stroke
- myocardial infarction
- sepsis
- seizure
- gastrointestinal bleeding

Outcomes routinely reported to the independent Data Monitoring Committee (DMC) for unblinded review



CRASH-3

OUTCOME FORM

COMPLETE AT DISCHARGE FROM THE RANDOMISING HOSPITAL, DEATH IN HOSPITAL OR 28 DAYS AFTER INJURY, WHICHEVER OCCURS FIRST

CRASH-3 9251/91

1. HOSPITAL (Hospital code) 000

2. PATIENT a) BOX b) PACK c) INITIALS

3. OUTCOME

3.1 DEATH IN HOSPITAL

a) Date of death b) Time of death

c) Primary Cause of death (tick one option)

- ☐ Head injury
- ☐ Bleeding
- ☐ Pulmonary embolism
- ☐ Stroke
- ☐ Myocardial infarction
- ☐ Multi organ failure
- ☐ Other/describe here (only one)

3.2 PATIENT ALIVE

a) Still in this hospital now (28 days after randomisation) – Date

b) Discharged to another hospital – Date of discharge

c) Discharged home – Date of discharge: 30 / 05 / 2012

3.3 IF ALIVE – DISABILITY RATING SCALE (tick one response for each box) – see overleaf for guidance

a) EYE OPENING	b) COMMUNICATION ABILITY	c) MOTOR RESPONSE	d) FEEDING (cognitive ability only)	e) TOILETING (cognitive ability only)
☑ Spontaneous	☐ Oriented	☑ Obeying	☑ Complete	☑ Complete
☐ To Speech	☑ Confused	☐ Localising	☐ Partial	☐ Partial
☐ To Pain	☐ Inappropriate	☐ Withdrawing	☐ Minimal	☐ Minimal
☐ None	☐ Incomprehensible	☐ Flexing	☐ None	☐ None
	☐ None	☐ Extending		
		☐ None		

f) GROOMING (cognitive ability only)	g) LEVEL OF FUNCTIONING (physical, mental, emotional or social function)	h) 'EMPLOYABILITY' (as a full time worker, homemaker, or student)
☐ Complete	☐ Completely independent	☐ Not restricted
☑ Partial	☑ Independent in special environment	☑ Selected jobs, competitive
☐ Minimal	☐ Mildly dependent – limited assistance	☐ Sheltered workshop, non-competitive
☐ None	☐ Moderately dependent – moderate assistance	☐ Not employable
	☐ Markedly dependent – assist all major activities, all times	
	☐ Totally dependent – 24-hour nursing care	

3.4 IF ALIVE: Assessed by doctor/nurse/relative based on their knowledge of the patient, or patient if able (tick one response for each box)

SEE GUIDANCE OVERLEAF

a) WALKING	b) WASHING / DRESSING	c) PAIN / DISCOMFORT	d) ANXIETY / DEPRESSION	e) AGITATION / AGGRESSION	f) FATIGUE
☐ No problems	☐ No problems	☐ None	☐ None	☐ None	☐ None
☑ Some problems	☑ Some problems	☑ Moderate	☑ Moderate	☑ Moderate	☑ Moderate
☐ Confined to bed	☐ Unable	☐ Extreme	☐ Extreme	☐ Extreme	☐ Extreme

4. MANAGEMENT

a) DAYS IN INTENSIVE CARE UNIT (if no ICU or not admitted to ICU, write '0' here): 2

b) TYPE OF NEUROSURGICAL OPERATION

- i) Haematoma evacuation: (YES) NO
- ii) Other: YES (NO)

c) BLOOD LOSS DURING NEUROSURGICAL OPERATION

Estimated Volume (ml): 2000

6. COMPLICATIONS (circle one option on every line)

Pulmonary embolism	YES	(NO)
Deep vein thrombosis	YES	(NO)
Stroke	YES	(NO)
Myocardial infarction	YES	(NO)
Renal failure	YES	(NO)
Sepsis	YES	(NO)
Seizure	YES	(NO)
Gastro intestinal bleeding	YES	(NO)

5. TRIAL TREATMENT

- a) Loading dose given: (YES) NO
- b) Maintenance dose given: (YES) NO

7. OTHER COMPLICATIONS (YES) NO

IF YES, REPORT AS PER PROTOCOL USING ADVERSE EVENT FORM

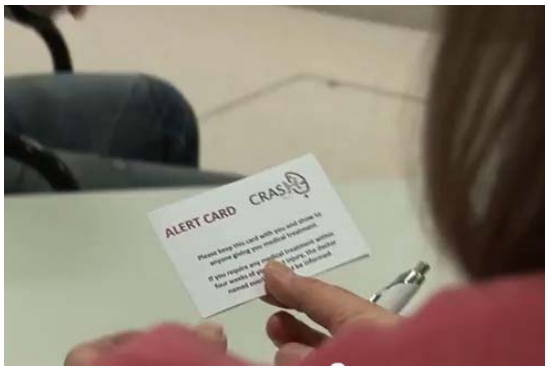
8. PERSON COMPLETING FORM (THE PRINCIPAL INVESTIGATOR IS RESPONSIBLE FOR ALL DATA SUBMITTED)

a) Name	Dr Tim Harris	b) Position	Principal Investigator
c) Signature	Tim Harris	d) Date	30/05/2012

Protocol Code: ISRCTN15088122 Outcome form version 1.0 dated 1 October 2011

What should be reported as AE or SAE?

- Any untoward medical occurrence NOT collected on the outcome form, up to 28 days after randomisation, should be reported
- If a patient is discharged or transferred to another hospital, they should be given an ALERT CARD which should contain information on who to contact if they develop any problems



- Report untoward medical occurrence:
  - not on the outcome form during hospitalisation
  - any event which develops after discharge and up to 28 days after randomisation
  - for each event, an Adverse Event Report form must be completed
  - for further information see presentation titled 'Adverse Event reporting and completing the report form'

CRASH-3

Clinical Randomisation of an Antifibrinolytic in Significant Head Injury

Trial Coordinating Centre
London School of Hygiene & Tropical Medicine
Room 180, Keppel Street, London WC1E 7HT
Tel +44(0)20 7299 4684 | Fax +44(0)20 7299 4663
crash@Lshtm.ac.uk

crash3.Lshtm.ac.uk

UKCRC Registered Clinical Trials Units