

CRASH2 Trial, a large randomised placebo-controlled trial among trauma patients with significant haemorrhage of the effects of an antifibrinolytic treatment on death and transfusion requirement

Submission date 13/07/2004	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 10/09/2004	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 09/07/2014	Condition category Signs and Symptoms	<input type="checkbox"/> Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT00375258

Protocol serial number

HTA 06/303/20; HTA 09/102/01; SLCTR/2007/008

Study information

Scientific Title**Acronym**

CRASH2

Study objectives

Because the coagulation abnormalities that occur after injury are similar to those after surgery, it is possible that antifibrinolytic agents might also reduce blood loss, the need for transfusion and mortality following trauma. However, to date there has been only one small randomised controlled trial (70 randomised patients, drug versus placebo: 0 versus 3 deaths) of the effect of antifibrinolytic agents in major trauma. As a result, there is insufficient evidence to either support or refute a clinically important treatment effect. Systemic antifibrinolytic agents have been used in the management of eye injuries where there is some evidence that they reduce the rate of secondary haemorrhage.

CRASH2 aims to determine the effect of the early administration of the antifibrinolytic agent tranexamic acid (TXA) on death and transfusion requirement in adult trauma patients with ongoing significant haemorrhage, or who are considered to be at risk of significant haemorrhage. In addition, the effect on the risk of non-fatal vascular events (either haemorrhagic or occlusive) will be assessed.

The initial stages of the trial was funded by the London School of Hygiene, the Bupa Foundation and the Moulton Charitable Trust. In 2007, this trial obtained main funding from the NIHR Health Technology Assessment Programme, which will fund this trial from April 2007 to September 2010.

More information on the CRASH2 trial can be found at: <http://www.nets.nihr.ac.uk/projects/hta/0630320>

As of 16/06/2008, the CRASH2 trial will conduct sub-group analyses "CRASH-2 Intracranial Bleeding Study (IBS)" (start date: October 2009) to study the effect of TXA in participants who also have traumatic brain injury (TBI). About 40% of participants out of 9,000 enrolled so far have TBI. Details of this sub-study can be found at: <http://www.nets.nihr.ac.uk/projects/hta/0910201>

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

On 21/08/2009 the anticipated start and end dates of this trial were changed from 01/05/2005 and 30/04/2010 to 01/04/2007 and 30/09/2010, respectively.

This trial completed follow-up on the 02/03/2010, and the record was updated to reflect this on 09/07/2010.

Ethics approval required

Old ethics approval format

Ethics approval(s)

All trial centres will seek ethics approval before recruiting participants. As of 10/06/2008, over 275 approvals have been received.

Study design

Randomised placebo-controlled trial

Primary study design

Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Trauma

Interventions

Tranexamic acid 2 g intravenously over 8 hours versus placebo.

Please note that as of 24/03/10 this trial has completed recruitment, analysis is ongoing.

Intervention Type

Drug

Phase

Not Applicable

Drug/device/biological/vaccine name(s)

Tranexamic acid

Primary outcome(s)

The primary outcome measure is death in hospital within 4 weeks of injury (causes of death will be classified).

An additional outcome measure for the sub-group analyses (added as of 18/06/2008):

1. Increase in volume of intracranial bleeding. A repeat CT scan will be carried out 24-48 hours after injury and compared to a clinical baseline CT scan.

Key secondary outcome(s)

Secondary outcome measures will be receipt of a blood transfusion, volume of blood transfused, surgical intervention and the occurrence of vascular events (haemorrhagic stroke, occlusive stroke, myocardial infarction, pulmonary embolism, clinically diagnosed deep vein thrombosis). Data will be recorded on a single sided outcome form which can be completed entirely from the hospital notes. There will be no additional tests.

Additional outcome measures for the sub-group analyses (added as of 18/06/2008):

A repeat CT scan will be carried out 24 - 48 hours after injury and compared to a clinical baseline CT scan to assess the following:

1. Frequency of progressive haematomas

2. Frequency of delayed haematomas
3. New focal ischaemic lesions

Completion date

02/03/2010

Eligibility

Key inclusion criteria

All adult trauma patients who are considered to be at risk of significant haemorrhage and are within 8 hours of the injury, are eligible for trial entry if they appear to be at least 16 years old. There are no other pre-specified exclusion criteria, as the fundamental eligibility criterion is the responsible doctor's 'uncertainty' whether or not to use tranexamic acid (TXA) in a particular adult with traumatic haemorrhage. Patients for whom there is considered by the responsible doctor to be a clear indication for TXA should not be randomised. Likewise, any for whom there is considered to be a clear contraindication to TXA (such as, perhaps, those who have clinical evidence of a thrombotic disseminated intravascular coagulation) should not be randomised. All those for whom the responsible doctor is substantially uncertain as to whether or not to use an anti-fibrinolytic agent are eligible for randomisation, and as many such patients as possible should be considered for the trial.

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Sex

All

Key exclusion criteria

The fundamental eligibility criterion is the responsible doctor's 'uncertainty' as to whether or not to use an antifibrinolytic agent in a particular adult with traumatic haemorrhage. Patients for whom the responsible doctor considers there is a clear indication for antifibrinolytic therapy should not be randomised. Likewise, patients for whom there is considered to be a clear contraindication to antifibrinolytic therapy (such as, perhaps, those who have clinical evidence of a thrombotic disseminated intravascular coagulation) should not be randomised. Where the responsible doctor is substantially uncertain as to whether or not to use an antifibrinolytic, all these patients are eligible for randomisation and should be considered for the trial. There are no other pre-specified exclusion criteria.

Date of first enrolment

01/04/2007

Date of final enrolment

02/03/2010

Locations

Countries of recruitment

United Kingdom

England

Albania

Argentina

Australia

Austria

Bangladesh

Belgium

Cameroon

Canada

China

Colombia

Cuba

Czech Republic

Ecuador

Egypt

El Salvador

Georgia

Ghana

India

Indonesia

Iran

Iraq

Italy

Jamaica

Japan

Kenya

Malaysia

Mexico

Montenegro

Nigeria

Peru

Poland

Saudi Arabia

Serbia

Singapore

Slovakia

South Africa

Spain

Sri Lanka

Tanzania

Thailand

Tunisia

Zambia

Study participating centre

London School of Hygiene and Tropical Medicine

London

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Sponsor information

Organisation

London School of Hygiene and Tropical Medicine (UK)

ROR

<https://ror.org/00a0jsq62>

Funder(s)**Funder type**

Research organisation

Funder Name

NIHR Health Technology Assessment Programme - HTA (UK)

Funder Name

Bupa Foundation (UK)

Alternative Name(s)**Funding Body Type**

Private sector organisation

Funding Body Subtype

Trusts, charities, foundations (both public and private)

Location

United Kingdom

Funder Name

Moulton Charitable trust (UK)

Funder Name

London School of Hygiene and Tropical Medicine (UK)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	initial progress results	27/10/2006		Yes	No
Results article	effects of tranexamic acid results	03/07/2010		Yes	No
Results article	tranexamic acid results	01/12/2010		Yes	No
Results article	early treatment results	26/03/2011		Yes	No
Results article	cost-effectiveness analysis results	03/05/2011		Yes	No
Results article	tranexamic acid results	01/07/2011		Yes	No
Results article	tranexamic acid results	01/07/2012		Yes	No
Results article	tranexamic acid mortality results	11/09/2012		Yes	No
Results article	results	01/03/2013		Yes	No
Results article	results	01/06/2014		Yes	No
Other publications	Letter to the Editor	21/06/2006		Yes	No
Other publications	reduced environmental impact of trials	03/02/2011		Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes