

# Investigating the influence of intravenous and oral tranexamic acid on blood loss for patients undergoing primary hip and knee replacements

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<b>Registration date</b> 21/06/2016	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 10/07/2023	<b>Condition category</b> Musculoskeletal Diseases	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Patients having a hip or knee replacement lose almost a third of their blood during and after the operation. Many patients, especially those who are older will need a blood transfusion, suffer from anaemia (low levels of red cells in the blood) or have a slow recovery after the operation. Tranexamic acid is a medication used to treat or prevent excessive blood loss. It is used regularly in other areas of medicine, but only in patients who are likely to bleed a lot in routine hip or knee replacement surgery. In order to use this drug as in standard care for all patients, a study needs to be carried out to find out how well tranexamic acid works to reduce blood loss after the operation in a large group of patients having a hip or knee replacement, including those at risk of blood clots. This study also aims to find out how safe tranexamic acid treatment is to use in different patients and the best way to give tranexamic acid (in tablet form or through a drip), as well as how much to give and how long it should be given after an operation.

### Who can participate?

Adults awaiting hip or knee replacement surgery.

### What does the study involve?

Patients who are suitable and agree to take part are randomly placed in one of three treatment groups: no treatment (standard care), receiving treatment (tranexamic acid) during the hip or knee operation through a drip, or receiving treatment during the hip or knee operation through a drip plus taking a tablet every 8 hours (starting at 2 hours) for 24 hours after the operation. Patients are not evenly distributed among the three groups, as there will be a 1-in-5 chance of being in the no treatment group and a 2-in-5 chance of being in one of the treatment groups. For all patients, total blood loss is recorded 48 hours after surgery. A blood sample is also taken when the standard blood tests are done in order to measure how well the heart and blood clotting systems are working. For patients receiving treatment, if the routine kidney function tests taken before their operation show less than normal function, a lower dose of tranexamic acid is used.

What are the possible benefits and risks of participating?

It is expected that patients who receive the tranexamic acid will benefit from losing much less blood during and after their operation, and so be less likely to need a blood transfusion, have reduced stress on the heart and have an easier recovery. Tranexamic acid can cause side effects like other drugs. Mild nausea, vomiting, diarrhoea and allergic reactions are rare but possible. The drug literature mentions that patients with a history of clots are at a higher risk of another clot when taking tranexamic acid. However no studies on tranexamic acid have ever found this to be true. Depending on the diagnosis, patients who have had a previous clot will be included because we think that these patients will benefit the most from reduced blood loss. In addition, in this study, patients will only take tranexamic acid for one day. For other conditions, patients safely take tranexamic acid for a number of days or weeks.

Where is the study run from?

Primary Joint Unit, Musgrave Park Hospital (UK)

When is study starting and how long is it expected to run for?

January 2016 to June 2019

Who is funding the study?

Belfast Arthroplasty Research Trust (UK)

Who is the main contact?

Professor David Beverland

david.beverland@belfasttrust.hscni.net

## Contact information

### Type(s)

Scientific

### Contact name

Prof David Beverland

### Contact details

Primary Joint Unit  
Musgrave Park Hospital  
Stockman's Lane  
Belfast  
United Kingdom  
BT9 7JB

### Type(s)

Public

### Contact name

Dr Catherine Adams

### Contact details

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1st Floor Elliott Dynes  
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Grosvenor Road  
Belfast  
United Kingdom  
BT12 6BA

## Additional identifiers

### EudraCT/CTIS number

2015-002661-36

### IRAS number

### ClinicalTrials.gov number

### Secondary identifying numbers

15039DB-SW

## Study information

### Scientific Title

Single centre randomised controlled trial to assess the effect of the addition of twenty-four hours of oral tranexamic acid post-operatively to a single intra-operative intravenous dose of tranexamic acid on calculated blood loss following primary hip and knee arthroplasty

### Acronym

TRAC-24

### Study objectives

The use of oral TXA for 24 hours following a primary THA or TKA in addition to an intra-operative IV bolus of TXA will significantly reduce a patient's indirect blood loss at 48 hours as compared to intra-operative IV TXA in isolation.

### Ethics approval required

Old ethics approval format

### Ethics approval(s)

East of England- Cambridge East Research Ethics Committee, 10/03/2016, ref: 16/EE/0068

### Study design

Phase IV single-centre open label three-arm randomised controlled trial

### Primary study design

Interventional

### Secondary study design

Randomised controlled trial

### Study setting(s)

Hospital

## **Study type(s)**

Treatment

## **Participant information sheet**

Not available in web format, please use contact details to request a participant information sheet

## **Health condition(s) or problem(s) studied**

Elective primary hip or knee replacement

## **Interventions**

Current Interventions as of 28/03/2018

Randomisation of patients to Control Group 3 has stopped following the interim analysis and DMEC recommendation as outlined in section 13.4. Patients will be randomised to either Group 1 or Group 2 and treated as below.

Original Interventions:

Patients will be randomised to to Intervention Group 1, Intervention Group 2 or Control Group 3 (standard care) with an allocation ratio of 2:2:1. The trial statistician will generate the randomisation sequence. A blocked randomisation process with randomly permuted block sizes will be used.

Intervention Group 1: Tranexamic acid (1 g) will be given via IV drip during the operation plus a tranexamic acid tablet (1 g) at 2 h, 10 h, 18 h and 26 h after the operation. Patients with impaired kidney function will be given a reduced dose dependent on creatinine levels measured before the operation.

Intervention Group 2: Tranexamic acid (1 g) will be given via IV drip during the operation. Patients with impaired kidney function will be given a reduced dose dependent on creatinine levels measured before the operation.

Control Group 3: Patients receive standard care (no tranexamic acid).

For up to 48 hours, extra blood for research purposes will be taken during routine blood tests on the day of surgery and after the operation. Any adverse events will be reported. At the 90 day follow up patients will be telephoned by a research nurse and asked questions about any complications and an oxford score questionnaire will be completed. Any complications and adverse events will be reported. Belfast Orthopaedic Information System and Death registry will be checked for outpatient mortality. At the 1 year follow up patients will be seen at a routine 1 year post-surgery clinic and oxford score date will be obtained. Belfast Orthopaedic Information System and Death registry will be checked for outpatient mortality. If a patient is discharged from hospital before their 48 hour blood sample has been taken, a research nurses will visit them in their home, if consent has been given, to take the sample at the 48 hour point.

## **Intervention Type**

Drug

## **Phase**

Phase IV

## **Drug/device/biological/vaccine name(s)**

Tranexamic acid

### **Primary outcome measure**

Indirectly calculated blood loss (ml) 48 hours post-surgery is calculated by using red cell counts before and after surgery in a mathematical formula.

### **Secondary outcome measures**

1. Incidence of post-operative haemoglobin (Hb) levels falling below the transfusion trigger (irrespective of transfusion) prior to discharge is measured from routine blood testing on day of surgery (Day 0) and post-operative Days 1-4
2. Effect of body mass index (BMI), pre-operative measure taken from the Belfast Orthopaedic Information System (BOIS), on the volume of indirect blood loss at 48 hours (Day 2) post-operative is found using statistical analysis by the Trial Statistician
3. C-reactive protein level is measured through blood testing at baseline and 48 hours post-surgery
4. Creatinine level is measured through blood testing at baseline and 48 hours post-surgery
5. 90 day mortality is measured using the BOIS and death registry at 90 days post-surgery
6. One year mortality is measured using BOIS and death registry at 1 year post-surgery

### **Overall study start date**

01/01/2016

### **Completion date**

06/07/2020

## **Eligibility**

### **Key inclusion criteria**

1. Awaiting primary elective hip or knee replacement
2. Both male & female
3. Aged between 18 and 100 years

### **Participant type(s)**

Patient

### **Age group**

Adult

### **Lower age limit**

18 Years

### **Upper age limit**

100 Years

### **Sex**

Both

### **Target number of participants**

1166 originally. Following the Interim Analysis a minimum of 932 patients is required.

## Total final enrolment

1056

### Key exclusion criteria

Current participant exclusion criteria as of 28/03/2018:

1. Patients who do not pass a pre-operative assessment for elective total hip or knee arthroplasty (THA/TKA)
  2. Fractured neck of femur
  3. Haemophilic or coagulation disorders that require TXA
  4. Allergy to tranexamic acid or any of its excipients
  5. Platelets <75,000/mm<sup>3</sup> at pre-operative assessment\*
  6. Patients on active treatment for venous thromboembolism (VTE) (deep vein thrombosis (DVT), pulmonary embolisms (PE)) within 6 months of surgery\*
  7. History of VTE within 6 months of surgery\*
  8. Patients who have had a myocardial infarction (MI) within 12 months\*
  9. Cardiac stent within 12 months of surgery\*
  10. Patients who have had a stroke (cerebrovascular accident (CVA)) or transient ischemic attack (TIA) within 9 months of surgery\*
  11. Use of antiplatelet medication within 7 days of surgery\* (Does not include aspirin if dose <300mg). Anticoagulant use within 7 days of surgery (thienopyridines, clopidogrel etc.)\*
  12. Direct thrombin inhibitors within 2 days of surgery\*
  13. Factor Xa inhibitors within 2 days of surgery\* Xa inhibitors within 2 weeks of surgery\*
  14. The INR level is greater than or equal to 1.5 in a patient who has stopped warfarin in preparation for surgery Patients who have stopped Warfarin in preparation for surgery but have an INR level greater than or equal to 1.5\*
  15. Hepatic failure\*
  16. Patients with epilepsy
  17. Patients requiring therapeutic anticoagulation post-operatively eg. metallic heart valves.
  18. Pregnant women, women who have not yet reached the menopause (no menses for  $\geq$  12 months without an alternative medical cause) who test positive for pregnancy, are unwilling to take a pregnancy test prior to trial entry
  19. Patients who have been using combined hormonal contraception (which includes combined oral contraception (COC), combined contraceptive transdermal patch and vaginal ring) within 4 weeks of surgery\*. Patients who have taken the combined oral contraceptive pill within 4 weeks of surgery\*
  20. Female patients who are breastfeeding
  21. Treated with any other investigational medication or device within 60 days
  22. Patients unable to provide informed consent
  23. Patients who are unable or unwilling to commit to the study schedule of events
  24. Patients unwilling to provide informed consent
  25. Patients who present for simultaneous bilateral THA or TKA
  26. Patients who are on renal dialysis and have an AV fistula
  27. Patients who previously have been enrolled in this study
- \*These are patients with contra-indications to primary hip or knee replacement.

### Original participant exclusion criteria

1. Patients who do not pass a pre-operative assessment for elective total hip or knee arthroplasty (THA/TKA)
2. Fractured neck of femur
3. Haemophilic or coagulation disorders that require TXA
4. Allergy to tranexamic acid or any of its excipients

5. Platelets less than 75,000/mm<sup>3</sup> at pre-operative assessment\*
6. Patients on active treatment for venous thromboembolism (VTE) (deep vein thrombosis (DVT), pulmonary embolisms (PE)) within 6 months of surgery\*
7. History of VTE within 6 months of surgery\*
8. Patients who have had a myocardial infarction (MI) within 12 months\*
9. Cardiac stent within 12 months of surgery\*
10. Patients who have had a stroke (cerebrovascular accident (CVA)) or transient ischemic attack (TIA) within 9 months of surgery\*
11. Anticoagulant use within 7 days of surgery (thienopyridines, clopidogrel etc.)\*
12. Direct thrombin inhibitors within 2 days of surgery\*
13. Xa inhibitors within 2 weeks of surgery\*
14. Patients who have stopped Warfarin in preparation for surgery but have an INR level greater than or equal to 1.5\*
15. Hepatic failure\*
16. Patients with epilepsy
17. Patients requiring therapeutic anticoagulation post-operatively eg. metallic heart valves.
18. Pregnant women, women who have not yet reached the menopause (no menses for  $\geq 12$  months without an alternative medical cause) who test positive for pregnancy, are unwilling to take a pregnancy test prior to trial entry
19. Patients who have taken the combined oral contraceptive pill within 4 weeks of surgery\*
20. Female patients who are breastfeeding
21. Treated with any other investigational medication or device within 60 days
22. Patients unable to provide informed consent
23. Patients who are unable or unwilling to commit to the study schedule of events

**Date of first enrolment**

01/07/2016

**Date of final enrolment**

06/07/2018

## Locations

**Countries of recruitment**

Northern Ireland

United Kingdom

**Study participating centre****Musgrave Park Hospital**

Primary Joint Unit

Stockman's Lane

Belfast

United Kingdom

BT9 7JB

## Sponsor information

**Organisation**

The Belfast and Health Social Care Trust (BHSCT)

**Sponsor details**

Research Governance  
King Edward Building  
Belfast Health and Social Care Trust  
Royal Victoria Hospital Site  
Grosvenor Road  
Belfast  
Northern Ireland  
United Kingdom  
BT12 6BA

**Sponsor type**

Hospital/treatment centre

**ROR**

<https://ror.org/02tdmfk69>

**Funder(s)****Funder type**

Charity

**Funder Name**

Belfast Arthroplasty Research Trust (BART)

**Results and Publications****Publication and dissemination plan**

It is hoped to publish study findings in peer review journals and present findings at appropriate conferences and patient group meetings. Publication of the trial protocol is expected in June 2018.

**Intention to publish date**

06/07/2021

**Individual participant data (IPD) sharing plan**

The datasets generated during and/or analysed during the current study are/will be available upon request made to Sponsor who will decide based on information provided. The point of contact for requests is Professor David Beverland, Principal Investigator (david.beverland@belfasttrust.hscni.net, +44 (0)7736679869) or Alison Murphy, Research and Development Office (ResearchSponsor@belfasttrust.hscni.net, +44 (0)28 9615 6057). Data



collected as per published Protocol cannot be personally identified and will be kept by the Sponsor for five years. Informed consent was obtained from all participants and as part of this agreed to the data being used in an anonymised format in publications and at conferences. It is an ethically approved trial and the responsibility of the sponsor to ensure that all the conditions are complied with.

## IPD sharing plan summary

Available on request

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Protocol article</a>	protocol	31/07/2018		Yes	No
<a href="#">Results article</a>	results for total hip arthroplasty	01/07/2021	20/01/2022	Yes	No
<a href="#">Results article</a>	results for total knee arthroplasty	30/09/2021	20/01/2022	Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Other publications</a>	Cost analysis	01/07/2022	10/07/2023	Yes	No