

18th July 2022

Professor Andrew Farmer,
Director, NIHR Health Technology Assessment Programme
Nuffield Department of Primary Care
Radcliffe Primary Care Building,
Woodstock Road, Oxford. OX2 6GG.

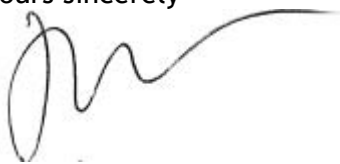
Dear Professor Farmer,

Re: The Jon Moulton Charity Trust support for the LSHTM programme of work on tranexamic acid.

The Jon Moulton Charity Trust has supported the LSHTM programme of clinical trial research on tranexamic acid (TXA) for acute severe bleeding since its inception in 2005. We first funded the pilot phase of the CRASH-2 trial that found that TXA reduces deaths in bleeding trauma patients. We then funded the pilot phase of the CRASH-3 trial that found TXA also reduces deaths in patients with isolated traumatic brain injury. Both trials showed that early treatment was most effective strongly suggesting the need for pre-hospital treatment. With this in mind, we funded the TRAUMA-INTACT trial, a clinical trial to determine the pharmacokinetics of intramuscular TXA. We were aware that intramuscular treatment would facilitate pre-hospital use and also that the UK Ministry of Defence are developing a TXA auto-injector for battlefield use. <https://www.gov.uk/government/news/life-saving-frontline-technology-given-5-million-boost>. Most recently, we funded the pilot phase of the CRASH-4 trial, that aims to evaluate the effects of pre-hospital intramuscular TXA for the prevention of death, disability and dementia in older adults with 'mild' traumatic brain injury.

The objective of the Jon Moulton Charity Trust is to fund non-commercial clinical trials that aim to make clinical advances and promote the relief of suffering. We consider that our investment in the LSHTM programme of work on TXA has been a success. TXA is now standard of care for trauma patients world-wide, saving many tens of thousands of lives each year. The CRASH-4 trial has the potential to extend the benefits of TXA into the prevention of disability and dementia in older adults with head injury. In view of the success of the pilot phase, we hope that the HTA programme will consider funding the CRASH-4 trial to its completion.

Yours sincerely



Jon Moulton
Trustee

Professor Andrew Farmer,
Director, NIHR Health Technology Assessment Programme
Nuffield Department of Primary Care
Radcliffe Primary Care Building,
Woodstock Road, Oxford. OX2 6GG.

19 July 2022

Dear Professor Farmer,

Re: BMGF funding for the LSHTM program of work on tranexamic acid in severe bleeding

At the request of Professor Ian Roberts and Professor Haleema Shakur-Still of the London School of Hygiene and Tropical Medicine, I am writing to share information related to clinical trial work funded by the Bill & Melinda Gates Foundation on the use of tranexamic acid (TXA) in severe obstetric bleeding. The WOMAN trial was a large, randomized trial of tranexamic acid for the treatment of post-partum hemorrhage. The trial was funded by our foundation, UK Department of Health and the Wellcome Trust. The trial, published in 2017, recruited 20 060 women with PPH and showed that intravenous (IV) TXA given soon after delivery reduces maternal bleeding deaths by about one third. Based on these results, in October 2017, the World Health Organization recommended early administration of IV TXA for all women with PPH. However, recognizing that IV treatment is not an option for the tens of thousands of women who give birth outside hospital, the WHO made 'the evaluation of benefits and potential harms of other routes of TXA administration' a research priority.

The WOMAN-2 trial is jointly funded by the Bill & Melinda Gates Foundation and Wellcome Trust and aims to evaluate the role of tranexamic acid in the prevention of PPH. The program also includes clinical trials to evaluate alternative routes of TXA administration including the intramuscular route. Because we believe the effects of TXA in obstetric and traumatic bleeding to be similar, results from the obstetric trials may be relevant to traumatic bleeding and vice versa.

We hope this information is useful to you in your deliberations.

Please feel free to contact me with any questions. (e-mail: jeffrey.smith@gatesfoundation.org; phone: +1 206 291-8367)

Sincerely,



Jeffrey Michael Smith, MD, MPH
Deputy Director,
Maternal, Newborn and Child Health

From: Jeremy Farrar <J.Farrar@wellcome.org>
Sent: Monday, July 25, 2022 4:06:07 PM
To: andrew.farmer@phc.ox.ac.uk <andrew.farmer@phc.ox.ac.uk>
Cc: Ian Roberts <ian.Roberts@lshtm.ac.uk>
Subject: Letter of support for the CRASH-4 trial.

*** This message originated outside LSHTM ***

Andrew Farmer
Chair of the NIHR HTA Programme

Dear Andrew

Re: Wellcome funding for the LSHTM programme of work on tranexamic acid in severe bleeding.

At the request of Professor Ian Roberts and Professor Haleema Shakur-Still, I am writing to let you know about the programme of clinical trial work on tranexamic acid in severe bleeding supported by the Wellcome Trust. The international CRASH-3 trial was co-funded by Wellcome as part of the Joint Global Health Trials funding initiative. It showed that timely tranexamic acid reduces head injury deaths. The WOMAN trial was a large randomized trial of tranexamic acid for the treatment of post-partum haemorrhage. The trial was funded by the UK Department of Health, Wellcome and the Bill & Melinda Gates Foundation. The trial recruited 20 060 women with PPH and showed that intravenous tranexamic acid given soon after delivery reduces maternal bleeding deaths by about one third. Based on these results, in 2017, WHO recommended IV TXA for all women with PPH. However, recognising that IV treatment is not an option for the tens of thousands of women who give birth outside hospital, the WHO made 'the evaluation of benefits and potential harms of other routes of TXA administration' a research priority.

The Woman-2 programme is jointly funded by Wellcome Trust and the Bill & Melinda Gates Foundation and aims to evaluate the role of tranexamic acid in the prevention of PPH. The programme also includes trials to evaluate alternative routes of TXA administration including the intramuscular route. Because the effects of tranexamic acid in obstetric and traumatic bleeding are similar, results from the obstetric trials may be relevant to traumatic bleeding and vice versa. The CRASH-4 trial extends this programme of work as the first trial of early pre-hospital intramuscular tranexamic acid in trauma patients (older adults with mild TBI).

I hope this is helpful, if I can provide any more help in your deliberations please let me know

Best wishes Jeremy

From: Keith Willett <keith.willett@ndorms.ox.ac.uk>
Sent: Friday, July 22, 2022 3:21:15 PM
To: Andrew Farmer <andrew.farmer@phc.ox.ac.uk>
Cc: Ian Roberts <Ian.Roberts@lshtm.ac.uk>
Subject: CRASH-4 trial for mild traumatic brain injury in older people

*** This message originated outside LSHTM ***

Professor Andrew Farmer,
Director, NIHR Health Technology Assessment Programme
Nuffield Department of Primary Care
Oxford. OX2 6GG.

Dear Andrew

Re: Support for the CRASH-4 trial of tranexamic acid in older adults with mild TBI in older people

I am now Chair of the Council of The Association of Ambulance Chief Executives (AACE) and Chair of the South Central Ambulance Service NHS Foundation Trust have stepped back from my national roles. I have been aware of the CRASH trials programme of work since the CRASH-2 trial showed that tranexamic acid (TXA) reduces deaths in bleeding trauma victims. When I was the National Clinical Director for Trauma Care I worked closely with the trial team on implementation of the CRASH-2 trial results within the NHS.

The CRASH-3 trial showed that TXA reduces deaths after traumatic brain injury and the CRASH-4 trial seems to be a natural extension of this programme of work, hopefully extending the benefits of TXA into the prevention of disability and dementia in older adults with mild traumatic brain injury.

Our South Central Ambulance Service has contributed importantly to the pilot phase of the trial and introduced the innovation of research cars to increase recruitment and reduce time to treatment. Recruitment to pre-hospital trials has grown considerably in recent years and CRASH-4 has the support of the National Ambulance Services Medical Directors (NASMeD). Given the success of the pilot phase, I am sure that the trial will be successfully recruit and complete if funded.

Yours sincerely

Prof Sir Keith Willett CBE

Chair of South Central Ambulance Service NHS Foundation Trust



London Ambulance Service
NHS Trust

Medical Directorate
Headquarters
220 Waterloo Road
London
SE1 8SD

Tel: 020 921 5100

www.londonambulance.nhs.uk

Professor Andrew Farmer
Programme Director
NIHR Health Technology Assessment (HTA)
National Institute for Health and Care Research

18th July 2022

Dear Professor Farmer,

RE: CRASH 4 STUDY

I am writing to you as Deputy Chief Executive and Chief Medical Officer for the London Ambulance NHS Trust, which is one of the pilot sites for the CRASH 4 trial, to confirm our support for the trial and its aims to provide reliable evidence about the effects of early intramuscular TXA on intracranial haemorrhage, disability, death, and dementia in older adults with symptomatic mild head injury.

As a key stakeholder, our Trust welcomes the opportunity for HTA funding to support the main phase of the study. This funding would allow the London Ambulance Service to continue to participate in this important trial and hopefully enable more ambulance services to become involved, widening research opportunities to pre-hospital patients across the country.

We have provided significant support to the pilot study to date, with nearly 150 of our clinicians trained to deliver the intervention, and almost 100 patients enrolled and counting. We would be keen to see the trial progress seamlessly to the main phase as we believe it has the potential to improve the outcomes of significant numbers of patients in the pre-hospital setting - something we are committed to achieving.

Kind regards

Dr Fenella Wrigley
Deputy Chief Executive and Chief Medical Officer





NHS

**South Central
Ambulance Service**
NHS Foundation Trust

Professor Andrew Farmer
NIHR Health Technology Assessment (HTA) Programme Director
National Institute for Health and Care Research

Southern House
Sparrowgrove
Otterbourne
Winchester
SO21 2RU
Tel: +44 (0) 1962 898044

18th July 2022

Dear Professor Farmer,

CRASH 4 STUDY

I understand that HTA funding may be available for the main phase of the CRASH4 study to enable it to transition seamlessly to the main phase from the initial pilot study.

As research lead for South Central Ambulance Service I am writing to let you know that as a main stakeholder, the Trust gives its full support to the study. We recognise that importance of providing reliable evidence about the effects of early intramuscular TXA on intracranial haemorrhage, disability, death, and dementia in older adults with symptomatic mild head injury and have provided significant support for the pilot study to date.

We would be keen to see the trial progresses seamlessly to the main phase because this is an important area of research that has the potential to improve the care and outcome of significant numbers of patients in the pre-hospital setting. With the necessary trial infrastructure in place, seamless transition would certainly facilitate trial recruitment as we would be able to avoid a break in patient recruitment.

This is an important trial that is likely to improve the immediate care of patients with traumatic brain injury. As such, South Central Ambulance Service fully support the trial and its progression to the main phase.

Kind regards

A handwritten signature in purple ink, appearing to read 'Charles D. Deakin', with a long, sweeping underline.

Professor Charles D. Deakin MA MD FRCP FRCA FFICM
Divisional Medical Director

crash4

From: Natalie Teich <nreich@virginmedia.com>
Sent: 25 July 2022 15:20
To: crash4
Subject: Evaluation of TXA Project

*** This message originated outside LSHTM ***

For the attention of Professor Andrew Farmer, Director of NIHR Health Technology Assessment Programme

Dear Professor Farmer,

I was first invited to be a patient and public involvement member of the CRASH-4 Trial team about two years ago. Since that time the team has been very successful in recruiting patients and staff to the pilot project. The aim is to determine whether early tranexamic acid (TXA) treatment of older adults with mild traumatic brain injury can reduce disability, dementia and death and allow people to return to live at home. This is a difficult project on many levels. In the first instance, the responding ambulance team members must make their definitive diagnosis very quickly in the course of their evaluation of the patient so that the TXA treatment can be initiated very quickly – within minutes of the injury - to gain maximum effect. Second, it is often difficult to get buy-in from a large number of the front-line staff involved. Third is the difficulty to manage committed followup to the outcome of the treatment (involving secondary care records to be investigated). Fourth, this is a long-term project to assess final outcomes and one would hope to be able to follow a large number of patients through to their important final outcomes.

I have been involved in evaluating projects by the London Ambulance Service and I have been impressed that suitable numbers of patients have been recruited by the CRASH-4 team so far. From the pilot phase, 480 patients were recruited and randomised, and patients treated soon after injury with intramuscular TXA show high tolerance. The more long-term goals of assessing the effects of this innovative treatment on avoiding admission to hospital, and early discharge back home where admission to hospital is unavoidable, are of extreme value and require continuation of this project.

Yours sincerely,

Natalie M. Teich, PhD, MBE

Lay member, London Ambulance Service Clinical Audit and Research Steering Group

20 July 2022

Dear Dr Farmer

I was a patient enrolled in the CRASH-3 trial. I hit my head after falling off my bicycle in 2014 and was enrolled into the CRASH-3 trial several hours later after a CT scan done in the hospital showed some bleeding inside my skull. I have since learned that this kind of bleeding happens very soon after a head injury and that tranexamic acid has to be given as soon as possible in order to prevent it. The CRASH-4 trial will evaluate the safety and effectiveness of early intramuscular tranexamic acid in mild traumatic brain injury and I am pleased to represent patients and the public on this trial. An intramuscular injection of tranexamic acid given by the ambulance crew should greatly reduce time to treatment and reduce the chance of dangerous intracranial bleeding.

After the end of the CRASH-3 trial, I found out from the trial team that I had received tranexamic acid and there is a good chance that this contributed to my full recovery. Timely intramuscular treatment of patients with so called 'mild' traumatic brain injuries has huge potential to improve health and well-being in the UK and for this reason I hope that NIHR will continue to support the CRASH-4 trial.

Yours sincerely

*Pam Foley
Oxford*

RoadPeace

The national charity for road crash victims



Dr Andrew Farmer
National Institute for Health and Care Research

3rd Floor
245a Coldharbour Lane
London
SW9 8RR
020 7733 1603
Helpline 0845 4500 355
www.roadpeace.org

25th July 2022

Dear Dr Farmer

I am the Director of Operations and Deputy CEO of RoadPeace, the national charity for road crash victims in the UK. RoadPeace are proud to have been involved in the CRASH trials for many years, including acting as patient and public representatives on the Trial Steering Committees for both the CRASH-3 and CRASH-4 trials.

Traumatic brain injuries are often caused by road crashes, and I am therefore pleased to write in support of the CRASH-4 trial which will evaluate the safety and effectiveness of early intramuscular tranexamic acid in older adults with mild traumatic brain injury.

The results of this trial have the potential to improve the outcomes of older road crash victims suffering mild traumatic brain injury by offering an injection of tranexamic acid that can be administered at the roadside to reduce the chance of intracranial bleeding.

I hope that the NIHR can see the potential benefit the CRASH-4 trial could bring, not only to older road crash victims but to all older adults with so called 'mild' traumatic brain injuries, and that they continue to support the trial.

Yours sincerely

Sara Dowling
Director of Operations, Deputy CEO
RoadPeace

Professor Andrew Farmer,
Director, NIHR Health Technology Assessment Programme
Nuffield Department of Primary Care
Radcliffe Primary Care Building,
Woodstock Road, Oxford. OX2 6GG.

Dear Professor Farmer

Re: The CRASH-4 trial of tranexamic acid in older adults with mild TBI.

I am a consultant in Emergency Medicine, clinical lead for the Devon Air Ambulance and Honorary Professor of Prehospital Critical Care at the University of Plymouth. I also serve on the data monitoring committee of the CRASH-4 trial. It is my view that the CRASH-4 trial will answer an important clinical question and has the potential to improve the care of the many thousands of older adults who sustain mild traumatic brain injury each year in the UK.

I recently published an analysis of UK Trauma Audit data that showed that women are much less likely than men to be treated with TXA. The sex differential got worse with increasing age. Because older women are more often injured in falls at home and take longer to reach hospital, it is often too late to treat them with TXA. By treating older patients with mild TBI in their homes or immediately after arriving in the emergency department, prior to scan, we might improve patient care and reduce inequalities. There is a national need for the data that this trial will provide. The pilot phase was a success and I am confident that should NIHR fund the trial it will be successfully completed.

Yours sincerely



Tim Nutbeam
Lead Consultant

20 July 2022

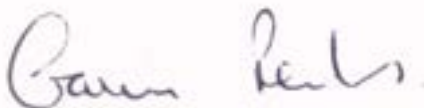
Professor Andrew Farmer,
Director, NIHR Health Technology Assessment Programme
Oxford
OX2 6GG

Dear Andrew

Re Clinical Randomisation of Antifibrinolytic in Symptomatic mild Head injury in older adults (CRASH-4)

I am writing to you in my role as an independent member of the CRASH-4 Trial Steering Committee. As a practicing critical care consultant and pre-hospital care (ambulance) consultant, I am only too aware that in acute life threatening emergencies such as acute traumatic brain injury, reducing time to treatment is critically important to improve patient outcomes. The CRASH-4 trial is evaluating the use of early intramuscular tranexamic acid to prevent or reduce intracranial bleeding in older adults with mild traumatic brain injury. The pilot phase has shown that the trial can recruit well and that paramedics are willing and able to give the intramuscular injection at the scene of the injury. On the basis of the success of the pilot phase and the track record of the CRASH team I am confident that the main phase will be a success.

Yours sincerely



Prof Gavin Perkins MD FRCP FMedSci
Director of Warwick Clinical Trials Unit

Professor Andrew Farmer,
Director, NIHR Health Technology Assessment Programme
Nuffield Department of Primary Care
Radcliffe Primary Care Building,
Woodstock Road, Oxford. OX2 6GG.

Dr Adrian Boyle,
President-Elect
Royal College of Emergency Medicine
Octavia House
54 Ayres Street
London
SE1 1EU

Dear Professor Farmer

I am pleased to write in support of the CRASH-4 trial which is recruiting older adults with mild traumatic brain injury from Ambulance Trusts and NHS Emergency Departments throughout the UK. The evidence that this trial will provide has the potential to significantly improve the care of older adults with traumatic brain injury. The epidemiology of trauma in the UK has changed and the typical trauma patient is an older patient who presents to hospital after a fall. Indeed, of the one million people that attend emergency departments in the UK with a minor head injury, a third are over 65 years old. By preventing intracranial bleeding, urgent pre-hospital treatment with tranexamic acid could reduce the risks of death, disability and dementia. We know from the CRASH-2 and CRASH-3 trials that the effects of tranexamic acid in traumatic bleeding are strongly time dependent and that the drug must be given as soon as possible after injury. If intramuscular tranexamic acid is shown to be safe and effective in this trial, it will facilitate timely pre-hospital use and greatly reduce time to treatment especially in vulnerable older patients.

Yours sincerely

A handwritten signature in blue ink that reads "A Boyle". The signature is written in a cursive style with a long horizontal stroke extending to the right.

Adrian Boyle



Dept of Research and Clinical Innovation

Lieutenant Colonel Harvey Pynn FRCEM MA FIMC DMM DMCC
DTM&H RAMC
Defence Consultant Advisor in Pre-Hospital Emergency Care
Consultant in Emergency Medicine
Emergency Department, Bristol Royal Infirmary, Upper Maudlin
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SG DMed MedD DCA PHEM
harvey.pynn@nhs.net

Reference: PHEC/HJP/IR/22/01

Date: 25 JUL 2022

Dear Professor Farmer

CRASH 4 - APPLICABILITY TO MILITARY OPERATIONAL CAPABILITY

1. 90% of Military Operational deaths occur before a patient reaches a medical facility - 80% of these deaths are due to haemorrhage.
2. Approximately 55% of the deaths due to haemorrhage are non-compressible in nature.
3. TXA delivered intravenously in a Military Operational setting (MATTERS study 2012) showed a NNT of less than 10. However, intravenous access requires a semi-permissive environment and trained medical provision.
4. Patients in an Operational setting may not receive care from specialist medical providers for over an hour after injury has occurred.
5. The efficacy of TXA wanes with time post injury.
6. All service personnel are trained to treat catastrophic bleeding at point of injury. As yet, there is no effective first aid measure for limiting non-compressible haemorrhage in the chest or abdomen.
7. The development of a TXA auto injector (strongly supported by Surgeon General [Major General Tim Hodgetts]) will lead to lives being saved in a Military Operational environment as the auto injector will be added to the suite of first aid measures that all service personnel are trained in resulting in casualties receiving TXA at point of injury.
8. The research evidence provided by Professor Roberts and his team at the London School of Hygiene and Tropical Medicine has been valuable to the ongoing development of the autoinjector and the additional evidence on the effectiveness and safety of intramuscular TXA that will be provided by the CRASH-4 trial will be valuable.

In my opinion, from a Military pre-hospital emergency care perspective, the development of a safe and effective TXA auto injector will have the greatest impact on addressing potentially avoidable pre-hospital deaths due to haemorrhage in an Operational setting and therefore research pertaining to intramuscular delivery of TXA is crucial and very welcome.

With kind regards

A handwritten signature in black ink, consisting of a stylized 'B' followed by a horizontal line that curves upwards at the end.

HJ PYNN
Lt Col
DCA PHEC

Major Trauma Service
The Royal London
Ward 12D
Whitechapel Road
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Email: bhnt.vasctraumasecretary@nhs.net
Tel: 0203 594 0725

Professor Andrew Farmer,
Director, NIHR Health Technology Assessment
Programme
Nuffield Department of Primary Care
Radcliffe Primary Care Building,
Woodstock Road, Oxford. OX2 6GG.

Dear Professor Farmer,

Re CRASH 4.

Helped by the evidence obtained from the CRASH-2 and CRASH-3 clinical studies, the use of Tranexamic Acid (TXA) is well established in both civilian and military trauma patients. The relationship between early administration of TXA and subsequent scale of beneficial effect, gleaned by Professor Ian Roberts and others has hastened research in to TXA auto-injectors designed to deliver TXA intra-muscularly. The prospect is that by packaging the drug in to a pre-filled auto-injector, injured civilians and soldiers can be rapidly treated with TXA prior to the arrival of formal medical help.

I have previously worked with Professor Roberts in this area, as have other colleagues from the Centre for Trauma Sciences at Queen Mary University London. I have no role in CRASH 4 but as a Trauma and Military surgeon, I fully support his team's research proposal and commend the continued research in to understanding the influence of TXA on patient outcomes in major trauma.

Yours sincerely,



Colonel Nigel Tai CBE MS FRCS
Consultant Vascular and Trauma Surgeon Barts Health NHS Trust
Honorary Professor of Trauma Surgery & Innovation, QMUL



20th July 2022

Professor Andrew Farmer
Chair NIHR HTA programme

Re: Support for funding of the CRASH-4 trial

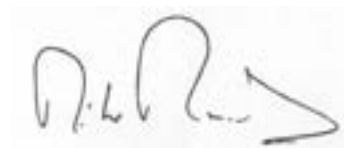
Dear Professor Farmer,

This is a letter of support of support for the funding of the main phase of the CRASH-4 trial of intramuscular tranexamic acid for the treatment of mild traumatic brain injury in older adults.

As you know, CRASH-4 follows previous highly successful CRASH trials in trauma and traumatic brain injury demonstrating that early treatment reduces mortality. CRASH-4 will evaluate the effect of early pre-hospital intramuscular tranexamic acid for older adults with mild traumatic brain injury. The pilot phase has tested the trial procedures and established the procedures for recruitment and data collection for the main trial.

Please do not hesitate to contact me if you would like further information.

Yours sincerely,



Michael F Murphy
Professor of Blood Transfusion Medicine, University of Oxford
Consultant Haematologist, NHS Blood and Transplant and the Oxford University Hospitals NHS
Foundation Trust

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Thursday, July 21, 2022

Professor Andrew Farmer,
Director, NIHR Health Technology Assessment Programme
Nuffield Department of Primary Care
Oxford. OX2 6GG.

Dear Dr Farmer,

Re: Support for the CRASH-4 trial of tranexamic acid in older adults with mild TBI

Owen Mumford is a privately-owned Oxford-based medical device company with 70-years' experience in diagnostics and drug delivery systems. We have been pioneering medical device development by hearing and understanding the challenges of hospital and home health treatments for people all over the world and then translating these requirements into new real-world innovations.

We are currently working with a diverse national and international group of healthcare stakeholders to develop a tranexamic acid autoinjector suitable for military and civilian use. We are well aware of the results of the CRASH-2 and CRASH-3 clinical trials and the lifesaving effects of timely tranexamic acid treatment. Indeed, these results have motivated our current efforts to develop an easy to use autoinjector.

We are also aware of the on-going CRASH-4 trial and believe that this trial answers an important clinical question. If early intramuscular tranexamic acid is shown to improve patient outcome in this vulnerable group, it would be a major medical advance. There is certainly a demand for the information that this trial will provide. We understand that the pilot phase has reached its recruitment target and we hope that NIHR will continue to fund the trial to completion.

Yours sincerely,



Andy Wertheim

Group Head of Portfolio Development



EMERGENCY DEPARTMENT
QUEENS HOSPITAL
Rom Valley Way, Romford, Essex RM7
Tel: 01708 435 000

Dear Professor Farmer

I am pleased to write in support of the CRASH-4 trial which potentially offers elderly patients who suffer a traumatic brain injury a treatment option that may reduce mortality. The study is currently recruiting older adults with mild traumatic brain injury from Ambulance Trusts and NHS Emergency Departments throughout the UK. The evidence that this trial will provide has the potential to significantly improve the care of older adults with traumatic brain injury. The epidemiology of trauma in the UK has changed and the typical trauma patient is an older patient who presents to hospital after a fall. Indeed, of the one million people that attend emergency departments in the UK with a minor head injury, a third are over 65 years old. By preventing intracranial bleeding, urgent pre-hospital treatment with tranexamic acid could reduce the risks of death, disability and dementia. We know from the CRASH-2 and CRASH-3 trials that the effects of tranexamic acid in traumatic bleeding are strongly time dependent and that the drug must be given as soon as possible after injury. If intramuscular tranexamic acid is shown to be safe and effective in this trial, it will facilitate timely pre-hospital use and greatly reduce time to treatment especially in vulnerable older patients. Elderly trauma is fast becoming a national epidemic and trials such as Crash-4 will go a long way to provide treatment options to this vulnerable population group.

Yours sincerely

Darryl Wood
NIHR:CRN Trauma and Emergency Care Specialty Lead North Thames
PhD, MBBCh, FCEM (SA), aFCEM (UK), M.Phil (EM), DipPEC (SA), DA(SA), B.Pharm