

Institution: Queen Mary University of London		
Unit of Assessment: 1		
Title of case study: Novel Resuscitation Protocols for Patients with Severe Trauma: Optimising Treatment and Reducing Mortality from Major Bleeding		
Period when the underpinning research was undertaken: 2008 - 2020		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	Role(s) (e.g. job title):	Period(s) employed by submitting HEI:
1) Karim Brohi 2) Ross Davenport 3) Elaine Cole	1) Chair of Trauma Sciences 2) Senior Lecturer 3) Senior Lecturer	1) 08/2008 - present 2) 05/2012 - present 3) 11/2015 - present
Period when the claimed impact occurred: 2014 – present		
Is this case study continued from a case study submitted in 2014? N		
<p>1. Summary of the impact (indicative maximum 100 words)</p> <p>Tens of thousands of young people in the UK die each year due to severe bleeding following traumatic injury. To optimise trauma care, Prof. Brohi's team at Queen Mary developed a damage control resuscitation (DCR) strategy and a massive haemorrhage protocol (MHP, or 'Code Red'). DCR was accepted by NHS England in 2014, and the MHP is now an essential criterion for accreditation of all 23 major trauma centres (MTCs) in England. After the DCR and MHP strategies were adopted by the NHS in 2014, mortality rates for patients with major bleeding after trauma fell by 29.4% at the Royal London Hospital (2014–2020). The team have shown that viscoelastic haemostatic assays (VHA) can identify patients for activation of DCR and MHP within five minutes of arrival in the Emergency Department. They have also showed that a single dose of the drug, Tranexamic acid (TXA), is effective for the MHP, thus reducing unnecessary exposure to TXA. These findings resulted in a change in national and international clinical guidelines in 2016.</p>		
<p>2. Underpinning research (indicative maximum 500 words)</p> <p>Trauma is a major cause of death and disability worldwide. The increasing burden of trauma is highest in young adults and children, with 90,000 people under 30 dying each year in Europe, and half of these deaths are due to bleeding. The UK mortality rates for trauma patients with massive haemorrhage is almost 50%, with one of the main reasons for this high mortality rate being abnormal blood clotting after injury.</p> <p>Prior to the work of Queen Mary's Prof. Brohi, loss of clotting function (coagulopathy) in severe bleeding was thought to be a late phenomenon caused by the loss or dilution of blood coagulation factors. Brohi retrospectively analysed blood samples from trauma patients brought by the Helicopter Emergency Medical Service to the Royal London Hospital, and identified that 1 in 4 patients already had established coagulopathy on arrival — and that this 'Acute Traumatic Coagulopathy' (ATC) was associated with a four-fold increase in mortality [3.1].</p> <p>Brohi's group has since focused on understanding the biological mechanisms underlying this condition, specifically:</p> <ul style="list-style-type: none"> • <i>The emergence of Trauma-Induced Coagulopathy (TIC) due to suboptimal transfusion protocols during resuscitation.</i> Suboptimal transfusion causes blood coagulation factors to be diluted, and results in clots that are poorly formed and rapidly broken down. Brohi's team has refined blood transfusion strategies for treating TIC, creating a 'balanced' resuscitation regimen — involving transfusion of blood and coagulation products in equal ratios [3.2] — that promotes blood clotting and targets early clotting changes post-injury. The group has also shown that a single dose of tranexamic acid (TXA; a drug used to reduce bleeding risk) is effective for this regimen, thus reducing unnecessary exposure to TXA [3.3]. • <i>The utility of near-patient diagnostics for goal-directed therapy.</i> ATC is an issue predominantly relating to clot strength and breakdown, and standard laboratory clotting assays are insensitive to its presence. Brohi's team has determined a diagnostic 		

threshold for the condition, and was one of the first research groups to show that viscoelastic haemostatic assays (VHA) can identify patients with ATC within five minutes of arrival at the Emergency Department [3.4, 3.5].

3. References to the research (indicative maximum of six references)

- [3.1] Davenport, R., Manson, J., De'Ath, H., Platton, S., Coates, A., Allard, S., Hart, D., Pearse, R., Pasi, K. J., MacCallum, P., Stanworth, S. & Brohi, K. (2011). Functional definition and characterization of acute traumatic coagulopathy. *Critical Care Medicine*, 39 (12), 2652-2658. <https://doi.org/10.1097/CCM.0b013e3182281af5>
- [3.2] Khan, S., Davenport, R., Raza, I., Glasgow, S., De'Ath, H. D., Johansson, P. I., Curry, N., Stanworth, S., Gaarder, C., & Brohi, K. (2015). Damage control resuscitation using blood component therapy in standard doses has a limited effect on coagulopathy during trauma hemorrhage. *Intensive Care Medicine*, 41 (2), 239-247. <https://doi.org/10.1007/s00134-014-3584-1>
- [3.3] Khan, S., Allard, S., Weaver, A., Barber, C., Davenport, R., & Brohi, K. (2013). A major haemorrhage protocol improves the delivery of blood component therapy and reduces waste in trauma massive transfusion. *Injury*, 44 (5), 587-592. <https://doi.org/10.1016/j.injury.2012.09.029>
- [3.4] Raza, I., Davenport, R., Rourke, C., Platton, S., Manson, J., Spoons, C., Khan, S., De'Ath, H. D., Allard, S., Hart, D. P., Pasi, K. J., Hunt, B. J., Stanworth, S., MacCallum, P. & K., Brohi, K. (2013). The incidence and magnitude of fibrinolytic activation in trauma patients. *Journal of Thrombosis and Haemostasis*, 11 (2), 307-314. <https://doi.org/10.1111/jth.12078>
- [3.5] Gall, L. S., Vulliamy, P., Gillespie, S., Jones, T. F., Pierre, R. S. J., Breukers, S. E., Gaarder, C., Juffermans, N. P., Maegele, M., Stensballe, J., Johansson, P. I., Davenport, R. A., Brohi, K. & The Targeted Action for Curing Trauma-Induced Coagulopathy (TACTIC) partners. (2018). The S100A10 Pathway Mediates an Occult Hyperfibrinolytic Subtype in Trauma Patients. *Annals of Surgery*, 269 (6), 1184-1191. <https://doi.org/10.1097/SLA.0000000000002733>

Evidence of the quality of the research

- [EQR. 1] Brohi, K. (2008-2013). Trauma Coagulopathy: Improving outcomes and saving blood [5637]. *National Institute for Health Research*. Programme Grant for Applied Research. GBP1,999,950.
- [EQR. 2] Brohi, K. (2013-2018). Targeted Action for Curing Trauma Induced Coagulopathy (TACTIC) [602771]. *European Commission*. FP7 Health. EUR1,400,000.
- [EQR. 3] Brohi, K. (2016). Lifetime Achievement Award for Trauma Resuscitation Research. *The American Heart Association*. The awards honour scientists for their outstanding contributions in resuscitation science and this was the first time the award had been given to a researcher based outside of the United States. <https://www.qmul.ac.uk/media/news/2016/smd/lifetime-achievement-award-for-trauma-research.html>
- [EQR. 4] Brohi, K. (2018-2020). An evaluation of leucocyte depleted red cells and plasma transfusion for major traumatic haemorrhage [MGU0431/32]. *London Air Ambulance and Barts and the London Charity*. Research Grant. GBP200,000.
- [EQR. 5] Brohi, K. (2019-2021). Defining and predicting the innate immune response to critical injury [MR/S009574/1]. *MRC*. Research Grant. GBP860,547.
- [EQR.6] Brohi, K. (2018-2019). The Progress 1000. *Evening Standard*. Brohi was named as one of London's 1,000 most influential people in the Evening Standard's (print circulation: 787,447; print readership: 1,200,000; monthly unique online browsers: 18,880,050) Progress Awards in both [2018](#) and [2019](#).

4. Details of the impact (indicative maximum 750 words)

Queen Mary's damage control resuscitation (DCR) strategy and massive haemorrhage protocol (MHP) have been adopted or recommended both nationally and internationally. As a result, Queen Mary's trauma team has:

Drastically reduced mortality

As a result of Queen Mary's MHP and DCR strategies, mortality rates from bleeding reduced by 29.4% between 2014 and 2020 at Europe's biggest trauma centre, the Royal London Hospital. The average number of red blood cell transfusions required by each patient in the first 24 hours also dropped from 12 (2008) to just 4 (2020), and the number of patients requiring a massive transfusion (10 or more units, essentially replacing their entire blood volume) dropped by over half (from 68% to 17% from 2008–2020, and so a fourfold reduction from 2008).

Driven a change in clinical management and cost savings in the NHS

DCR was adopted by the NHS Commissioning Board (now NHS England) in April 2014, and became the primary resuscitation and clinical management strategy for patients suffering from major traumatic bleeding. MHP, or 'Code Red', has been adopted as an essential criterion for the accreditation of all 23 major trauma centres (MTCs) in England [5.1], with Prof. Brohi acting as a steering group member of the Clinical Advisory Group. Approximately 8,600 severely injured patients per year are admitted to MTCs in the UK, of which ~10% activate the local MHP.

The introduction of 'Code Red' is estimated to save the NHS GBP6,600,000 a year, with wider social cost savings estimated over a five year period being GBP3,600,000,000 in 2010 prices [5.2]. Furthermore, the Department of Health and Social Care submitted the team's work to Treasury as one of only two examples of NIHR-funded work [EQR.1] having impactful research with regards to spending [5.2].

Influenced national and international clinical guidelines

Both DCR and MHP are now used internationally [5.3, 5.4]. Based on Brohi's work on DCR and MHP, and findings that a single dose of TXA is effective for their regimen, the 2016 guidelines from the UK's National Institute for Health and Care Excellence (NICE) for Major Trauma [5.5] recommend that all 11 ambulance trusts, 23 MTCs and 105 trauma units in England should have: a specific MHP for adults and children; a fixed-ratio protocol for blood components (blood and plasma); and early use of TXA. This coagulation-centric approach has also been incorporated into:

- UK national transfusion guidelines for all major bleeding [5.6]
- European guidelines on the management of trauma haemorrhage [5.4]
- The global Advanced Trauma Life Support Manual (ATLS), which was updated in June 2018 (10th ed.) to include TIC-targeted therapy in its protocols [5.7]
- The international Viscoelastic Testing in Trauma Consensus Panel, of which Brohi and Dr. Davenport were members [5.8], and guidelines from the British Society for Haematology [5.9].

Improved public awareness and understanding of trauma science

Queen Mary's work on TIC has been featured in national television programmes and is part of the Barts Charity 'Transform Trauma Appeal', which has been the subject of seven feature articles in the Sunday Mirror (readership approximately 1,600,000). In December 2017, the first Transform Trauma Appeal video had 4,200,000 views; Brohi's 2017 appearance on ITV's This Morning had around 2,000,000 live viewers; and the online video has been watched more than 34,000 times [5.10].

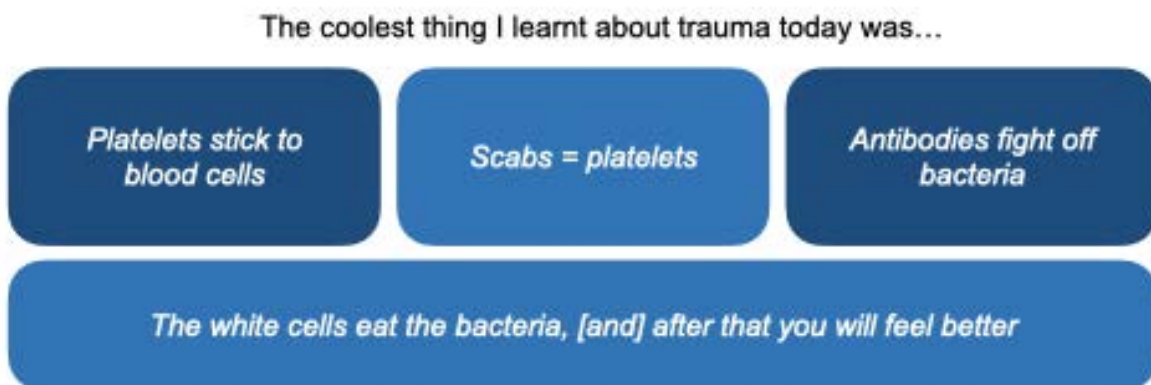
The team has showcased its work to the public [5.11] at:

- The British Science Festival (2014): 50-80,000 attendees each year
- International Clinical Trials Day (2014 and 2019)
- A sold-out ‘Pint of Science’ talk by Brohi (May 2017, ‘Bloody hell!’): Pint of Science festival events reached roughly 120,000 attendees in Europe in 2018, 24,000 of which were in the UK)
- Big Bang Fair South East (2014, 2015 and 2018): approximately 9,000 children and teachers
- Big Bang Eastbourne (2018): approximately 100 children and teachers
- Big Bang Newham (2018): approximately 2,500 attendees
- Queen Mary’s Festival of Communities (2018 and 2019): approximately 3,000 local residents

When surveyed, 100% of the visitors to these events agreed that they had “learnt something new about trauma today,” with many demonstrating a change in their perception of what trauma is: over 90% of children initially referred to psychological trauma, after which the team was able to introduce the notion of trauma as bodily injury.

Children gained a good understanding of why blood samples are taken from trauma patients — 100% learnt that blood samples are studied to understand Multiple Organ Dysfunction Syndrome (MODS), and also understood the differing roles of a) the immune system and b) the cells making a blood clot. When asked to identify the “coolest thing [they had] learnt about trauma [at the event]” (Figure 1), children showed knowledge of information that is not taught to their age group in the school syllabus, reflecting the central role of Queen Mary’s engagement work in increasing children’s awareness and understanding of trauma. This work is reinforced by the team’s educational programme TSCIPP, which produced the educational resource on trauma *Billy and His Blood Cells* [5.12]. Brohi’s team distributed the document to medical professionals across the Emergency Department at the Royal London Hospital, who in turn use it to educate children about trauma.

Figure 1:



5. Sources to corroborate the impact (indicative maximum of 10 references)

[5.1] NHS England. (2013). *NHS Standard Contract for Major Trauma Service (D15/S/a)*. <https://www.england.nhs.uk/wp-content/uploads/2014/04/d15-major-trauma-0414.pdf>

[5.2] NIHR. (2020). *Committee member update*. <https://mailchi.mp/bb3b4d6cbd4e/pqfar-committee-member-update?e=0514e3d9cd>. Accessed 19 February 2021.

[5.3] The Joint United Kingdom Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee. (2014). *Transfusion Handbook: Transfusion management of major haemorrhage*. <https://www.transfusionguidelines.org/transfusion-handbook/7->

[effective-transfusion-in-surgery-and-critical-care/7-3-transfusion-management-of-major-haemorrhage](#)

[5.4] Rossaint, R., Bouillon, B., Cerny, V., Coats, T. J., Duranteau, J., Fernández-Mondéjar, E., Filipescu, D., Hunt, B. J., Komadina, R., Nardi, G., Neugebauer, E. A. M., Ozier, Y., Riddez, L., Schultz, A., Vincent, J. & Spahn, D. R. (2016). The European guideline on management of major bleeding and coagulopathy following trauma: fourth edition. *Critical Care*, 20, 100. <https://doi.org/10.1186/s13054-016-1265-x>

[5.5] NICE. (2016). *NICE Guidance (NG39) Major Trauma: assessment and initial management*. <https://www.nice.org.uk/guidance/ng39>

[5.6] Hunt, B. J., Allard, S., Keeling, D., Norfolk, D., Stanworth, S. J. & Pendry, K. on behalf of The British Committee for Standards in Haematology. (2015). A practical guideline for the haematological management of major haemorrhage. *British Journal of Haematology*, 170 (6), 788-803. <https://doi.org/10.1111/bjh.13580>

[5.7] American College of Surgeons. *The Advanced Trauma Life Support (ATLS) program*. <https://www.facs.org/quality-programs/trauma/atls>

[5.8] Inaba, K., Rizoli, S., Veigas, P. V., Callum, J., Davenport, R., Hess, J. & Maegele, M. the Viscoelastic Testing in Trauma Consensus Panel. (2015). 2014 Consensus conference on viscoelastic test-based transfusion guidelines for early trauma resuscitation: Report of the panel. *The Journal of Trauma and Acute Care Surgery*, 78 (6), 1220-1229. <https://doi.org/10.1097/TA.0000000000000657>

[5.9] Curry, N. S., Davenport, R., Pavord, S., Mallett, S. V., Kitchen, D., Klein, A. A., Maybury, H., Collins, P. W. & Laffan, M. (2018) The use of viscoelastic haemostatic assays in the management of major bleeding: A British Society for Haematology Guideline. *British Journal of Haematology*, 182 (6), 789-806. <https://doi.org/10.1111/bjh.15524>

[5.10] Centre for Trauma Sciences. *Latest News*. <http://www.c4ts.qmul.ac.uk/main/latest-news/post/48-c4ts-in-the-news>. Accessed 10 December 2020.

[5.11] Centre for Trauma Sciences. *Education*. <http://www.c4ts.qmul.ac.uk/education-outreach/outreach-programmes-and-events>. Accessed 10 December 2020.

[5.12] Centre for Trauma Sciences. (2020). *Explaining Trauma to Children – Billy and His Blood Cells*. <https://www.c4ts.qmul.ac.uk/education-outreach/public-engagement-for-children-billy-and-his-blood-cells->. Accessed 23 January 2021.