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Complex trauma research in the UK

A rapid review of the funding landscape

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Prepared for the Department of Health (England)
The research described in this report was prepared for the Department of Health (England).
Preface

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Acknowledgements

The authors would like to thank Samuel Drabble for some of the initial research he did identifying potential funders of research. We would also like to thank Laura Staetsky for support in identifying important research centres and the background political context in the Israeli setting. Finally, we would like to thank Stephanie Diepeveen and Alexandra Pollitt for their quality assurance review of the research and final report.

This is an independent report commissioned and funded by the Policy Research Programme in the Department of Health. The views expressed are not necessarily those of the Department.
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Executive summary

RAND Europe was asked by the England Department of Health (DH) in December 2010 to provide a strategic, rapid review of the funding landscape for complex trauma research in the UK and, where possible, internationally. Part of the motivation behind the study was the perception that National Health Service (NHS) and Ministry of Defence (MoD) clinicians and researchers working in the area of complex trauma could do more to learn from each other. The findings of the review will be used to inform ongoing, strategic discussions between the DH and the MoD.

In reviewing complex trauma research, we were asked to focus on those areas of research which target the early phase of injury and can improve the effectiveness of therapies and interventions at the pre-hospital and early in-hospital phase. In addition, we were asked to review research which had a focus on the infective challenges faced by injured patients and to exclude basic research from the review, such as that looking at underlying cellular and biological mechanisms associated with major injury.

For the purposes of this review we adopted an understanding of complex trauma research as one akin to ‘major trauma’ and based on a description provided by the National Audit Office (NAO): “major trauma describes serious and often multiple injuries where there is a strong possibility of death or disability” (NAO, 2010a, p. 4). We found early on that there are different terms used in the area of ‘trauma’ research, and although terms sometimes are used interchangeably, they do not always mean the same thing. These definitional issues are not insignificant to analysis of the funding landscape and we comment on the implications of this throughout the report.

In this review we map the UK funding landscape for current research in the five priority areas of complex trauma at the pre-hospital and early in-hospital phase; assess the nature and quality of research being conducted; and identify gaps in the UK research landscape and make recommendations about priorities, opportunities and future directions. We took a multi-staged approach to the research, including a review of public and private sector research and development (R&D) statistics, a review of expenditure in UK public and private sector organisations, interviews with selected experts and a review of international in civilian and military trauma research in Israel and the USA.

Our findings indicate that within the UK, funding for complex trauma research is in the order of £15m across public and private funders. Approximately £10m of this is from public R&D funding, most of which is provided through the National Institute for Health Research (NIHR) or the MoD. A further £5m is provided by private charities and companies. Investment by pharmaceutical companies was difficult to estimate and remains unknown. Therefore, overall research expenditure on complex trauma is fewer than 1% of total UK public expenditure on health research, which has been previously estimated by RAND Europe to be in the order of £1.7 billion. Of the complex trauma research we identified as being funded within the UK, the majority is being done in the area of ‘acute injury’, although there is also significant activity in the area of regenerative medicine.
Due to the definitional issues around complex trauma research, we did not include research focused solely on ‘trauma’ or ‘injury’, as this is not the same as complex trauma research. The context of complex trauma in a clinical setting means that the application of techniques developed elsewhere, for example in orthopaedic research, may need to be adapted when applied to complex trauma patients. Thus, although research findings can be ‘exported’ or ‘imported’ across health research fields, this translational space needs to be strengthened and closely monitored if a long-term funding strategy is to be developed.

Our review suggests that there are fewer than five centres capable of handling large-scale complex trauma clinical research studies in the UK. This has knock-on effects for the translation of clinical research into the marketplace. Additional challenges in clinical translation include patient enrolment under critical care circumstances, difficulties in obtaining informed consent, the ‘24/7’ nature of patient arrival, and lack of researcher capacity and capability. Moreover, although pockets of good research do exist, strategic thinking is a problem and there is a research gap between military and civilian contexts. Our analysis of research in Israel and the USA suggests that internationally, complex trauma is also a niche area of research, but civilian and military sectors seem better integrated in Israel and the USA than in the UK.

Our findings have led us to draw the following conclusions and recommendations.

- Complex trauma is an ‘orphan’ and niche area of research that is disproportionately resourced in comparison to the burden of the disease.
- If a comprehensive research strategy or programme is established, ‘complex trauma’ needs to be clearly defined and protected against mission creep.
- Findings from other health and biomedical research fields are relevant to complex trauma, but this translational space needs to be strengthened and monitored.
- There is a lack of strategic coordination among researchers and funders, resulting in missed opportunities for joint learning and, ultimately, patient impact.
- There are barriers to clinical trials and translation of research findings, mainly due to institutional and infrastructure issues within the field.
- There is significant potential for integrating the civilian and military health research sectors, but relationships between them will take time to build.
- Identification of short, medium and long-term goals will aid integration between the military and civilian research sectors. In the short term there is a need to identify existing research gaps, maximise synergies and understand the state of each others’ (and joint) markets. In the medium to long term we recommend establishing mechanisms to translate research from the one context to the other, for example, joint research and training programmes at major trauma centres around the country.
- A research strategy for complex trauma will have to address two key issues: (1) capacity and capability building; and (2) incentivising collaboration across the military and civilian sectors so that joint working does actually occur.
- Future mapping research can inform the development of strategy in this area. More in-depth mapping should review the state of the field, and compare this
against clinical needs and strategic priorities. In particular, a detailed bibliometric analysis could help to characterise, define and evaluate performance of the field.
List of abbreviations

BBSRC – Biotechnology and Biological Sciences Research Council
DfID – Department for International Development
DfT – Department for Transport
DH – Department of Health
EPSRC – Engineering and Physical Sciences Research Council
HEFCE – Higher Education Funding Council for England
MRC – Medical Research Council
MRMC – Medical Research and Materiel Command
MoD – Ministry of Defence
NHS – National Health Service
NICE – National Institute of Health and Clinical Excellence
NIH – National Institutes of Health
NIHR – National Institute for Health Research
US AISR – United States Army Institute of Surgical Research
This documented briefing provides an overview of the funding landscape for complex trauma research in the UK. RAND Europe was asked by the England Department of Health (DH) in December 2010 to conduct a rapid review of research in the field of complex trauma in the UK. The outputs of the review will be used to feed into ongoing, strategic discussions with the UK Ministry of Defence (MoD) and the DH. The documented briefing begins with a statement of the research problem and the approach taken to the rapid review. It then provides a baseline overview of funding for health research in the UK by both public and private funding bodies, including the charitable sector. Chapter 2 provides a detailed analysis of each of the main funders active in the area of complex trauma research, and a summary of projects for each funding body is given. Chapter 3 takes a broader look at the international landscape for complex trauma research, focusing on the experiences of Israel and the USA, to test the hypotheses about complex trauma research developed from the analysis in Chapter 2. Finally, Chapter 4 summarises the findings and offers recommendations about how to proceed with strategic funding and strengthening of complex trauma research in the UK.
Estimates of costs to the NHS for complex trauma treatment and care are in the order of £0.3m to £0.4m per annum, however long-term costs to the economy of someone affected by major trauma are much more difficult to estimate but could be upwards of £3.5 billion (National Audit Office (NAO), 2010a). Thus, there is both a medical and economic interest in ensuring that complex trauma is effectively and efficiently administered within the UK health system.

One of the first steps in our review was to specify what is meant by the term ‘complex trauma research’. There are different terms used in the area of ‘trauma’ research, including ‘complex trauma’, but also ‘major trauma’ and ‘multiple injury’ research. Sometimes these terms are used interchangeably, but they do not always mean the same thing, neither are they always referring to research that is relevant to our review of complex trauma research. Similarly, we found instances where research not labelled as complex trauma per se might still be relevant to the wider field.

Therefore we adopted a general understanding of what could be considered complex trauma research for this report, rather than a strict definition, so that we could be more flexible in our interpretation of the relevance of different types of health research to the field. Our understanding is based on a description of major trauma provided by the NAO in its 2010 report on major trauma care in England: “major trauma describes serious and often multiple injuries where there is a strong possibility of death or disability” (NAO, 2010a, p. 4). This leads to a situation where multiple injuries compound each other and there is a unique and urgent need for treatment. Many experts explained to us that complex trauma is a ‘disease’ where the body’s own immune system response becomes a major factor in an individual’s ability to cope with the stress and trauma associated with the injuries. Therefore, complex trauma requires a different approach to the treatment,
care and therapeutic interventions offered to the individual. The following quote from a publication by the Royal College of Surgeons in England is helpful in understanding this point:

*For a unit to be defined as a major trauma centre it must provide, 24 hours a day, a fully staffed emergency department, a consultant-led resuscitative trauma team, dedicated trauma theatres and operating lists, the presence of all major surgical specialties on site (orthopaedic trauma, general and vascular surgery, neurosurgery, plastic surgery, cardiothoracic surgery, head and neck surgery, urology), interventional radiology (which uses radiological techniques to place wires, tubes or other instruments inside a patient to diagnose and treat various conditions) and anaesthesia with appropriate intensive care facilities.* (Royal College of Surgeons in England, 2007, p. 2)

A final point which helped us to scope the extent of our review was the perception that the National Health Service (NHS) and MoD clinicians and researchers working in the area of complex trauma could do more to learn from each other. For example, it was thought the NHS was not doing enough to benefit from advances and experience in the field of military medicine, while the MoD could do more in taking clinical problems identified on the battlefield into the research laboratory for further investigation and translation into clinical solutions applicable in civilian and military contexts. The research questions which arose from this included verifying whether this observation was the case and, if so, how the situation could be improved. This issue is a central focus of the analysis of the international landscape and final recommendations.
Areas of critical focus

- Applied and clinical research addressing the early phases of injury and pre-hospital/early in-hospital care
- Identification of market failure
- Five priority areas were defined by the DH:
  - Acute injury
  - Wound infection and microbiology
  - Regenerative medicine
  - Rehabilitation
  - Medical training

For this report we were asked to focus on several research areas, particularly research which targeted the early phase of injury in order to improve the effectiveness of therapies and interventions at the pre-hospital and early in-hospital phase. An explicit focus on the infective challenges faced by injured patients was also important, while basic research such as the underlying cellular and biological mechanisms associated with major injury were to be excluded. Finally, in identifying planned, pipeline and completed clinical research, a specific focus on areas of market failure was requested.

To further help focus our review, the DH provided five priority areas in complex trauma research on which our review should focus.

1. **Acute injury** – covering research into resuscitation, perfusion, haemostasis, wound care, spinal cord injury, patient transport care, trauma casualty care, surgical care, peripheral nerve injury, monitoring and imaging, decision support and bone injury.
2. **Wound infection and microbiology** – including wound treatment and management, wound irrigation, nosocomial transmission of bacteria, assessment of combination therapy and dentistry.
3. **Regenerative medicine** – including strategies to improve surgical reconstruction outcomes and material science.
4. **Rehabilitation** – with a specific focus on how early-stage treatment can help to improve the success of new prosthetics and techniques, or on the detection and treatment of brain injuries.
5. **Medical training** – including strategies to improve surgical and teamworking skills using simulation.
Study overview: aims and approach

- To map the funding landscape for current research in the priority areas of complex trauma at the pre-hospital and early in-hospital stage in the UK, including identification of centres of excellence
- To assess the nature and quality of research being conducted based on expert opinion and in comparison to the international landscape
- To identify gaps in the UK research landscape and make recommendations about priorities, opportunities and future directions

This slide outlines the approach employed in order to map the UK funding landscape for current research in the five priority areas of complex trauma at the pre-hospital and early in-hospital phase, to assess the nature and quality of research being conducted and identify gaps in the UK research landscape, and to make recommendations about priorities, opportunities and future directions. As a key motivation in this study was to identify strategic opportunities between the MoD and the DH, particular attention was paid to understanding the nature of relationships between military and civilian research and treatment contexts in the UK, as well as internationally. Figure 1 above gives an overview of the methodology, and each stage is described in detail below.

Review of public and private sector R&D statistics
We used figures provided by the Office for National Statistics on public R&D expenditure by government bodies. The most recent figures available are planned figures from 2008/09. We then reviewed national data on private and charitable R&D expenditure published in the ‘R&D Scorecard’ by the Department for Business, Innovation and Skills, and in annual reports from the medical charity sector.

Review of public expenditure on complex trauma research
We focused our review on those government bodies\(^1\) with an obvious or potential interest in complex trauma research (and a high R&D expenditure). We also analysed the funding

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\(^1\) As will be shown in slides to follow, these include the DH, Medical Research Council, Biotechnology and Biological Sciences Research Council, Engineering and Physical Sciences Research Council, the MoD, the Department for International Development and Department for Transport.
portfolios of the Welsh Assembly Government, the Scottish Government and the devolved authority of Northern Ireland.

In order to identify relevant projects and potential strategic interests in complex trauma research, annual reports and strategy documents from the respective funder websites were reviewed. When available, we conducted searches of research project databases on the funders’ websites. We searched these databases by different subject areas and with combinations of keywords from the priority areas, such as ‘trauma’, ‘injury’, ‘resuscitation’, ‘coagulopathy’, etc. The findings from these searches were cross-referenced against the projects identified using the UK PubMed grant look-up search tool, rapid bibliometric analysis (see below) and expert interviews, in order to mitigate against omissions or double-counting.

**Review of private and charitable sector expenditure on complex trauma research**

Identification of private and charitable funders was more complicated, as there was no one source of information to begin our search. We used a combination of approaches to identify private sources of funding, including the use of the UK PubMed grant search tool which allowed us to search charitable funding from The Wellcome Trust, Arthritis Research UK and the British Heart Foundation. We also used inputs from the rapid bibliometric analysis and interviews with experts (see below) in order to identify major funders. Identification of specific projects was done in a similar manner to that described above for public funders.

**Rapid bibliometric analysis**

A rapid bibliometric analysis using the Web of Science database was used to identify top journals in which UK trauma researchers published articles, guide our analysis of UK centres of excellence and identify private funders, as discussed above. Due to constraints of time and resources it was not a comprehensive bibliometric analysis where datasets are cleaned, systematic use of keywords is employed and detailed quantitative analysis of publication statistics is conducted. Instead, we used a sampling of relevant keywords and subject headings to provide initial indications of funders and centres of high publication output.

**Telephone interviews with key experts**

Alongside the expenditure reviews and bibliometric analyses, we conducted 10 interviews with leading experts in complex trauma research. The experts were clinicians and researchers spanning a range of biomedical and health disciplines, and working in the UK in either the military, civilian health (NHS) or academic health research sectors. A list of the interviewees’ areas of expertise are provided in Annex A, along with an interview protocol. The main subject areas discussed were:

- the expert’s research in relation to the five priority areas, particularly focusing on sources of research funding and clinical applications;
- the state of complex trauma research in the UK, including centres of excellence;

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2 See: http://ukpmc.ac.uk/GrantLookup/. Grant information is provided for the eight UK PubMed Central funders: Arthritis Research UK, Biotechnology and Biological Sciences Research Council, British Heart Foundation, Cancer Research UK, Chief Scientist’s Office (Scottish Government), National Institute for Health Research, Medical Research Council and The Wellcome Trust. Associate funders include Australian Science FWF, Health Research Board, Science Foundation Ireland and Telethon Italy.
• the position of the UK relative to other international efforts; and
• UK strategy and research priorities in the field of complex trauma.

Mapping of national and international research landscape
This component involved using the outputs of the rapid bibliometric analysis to try and identify major funders and centres or researchers of excellence in the UK, as well as mapping the projects identified in the earlier stages against the five priority areas. In order to map the international landscape, we conducted some rough bibliometric analyses using Web of Science database to identify areas of publication in different countries. However, because we were limited in our ability to conduct a full and comprehensive bibliometric analysis, we relied more heavily on guidance from our interviews to identify sources of information about leading centres and research programmes. These leads were followed up through more detailed web-based searches and information retrieval.

Reporting and briefing
An interim report was delivered to the DH in mid-January 2011. This documented briefing is based on that interim report and is the final report for this study.
With the aims and methodological approach of the study set out, we will now move to mapping the research landscape. First we will provide an overview of this landscape by summarising public and private sector R&D spending across the UK. Second, we will look at individual government body, private and charitable sector expenditure on complex trauma.

Figure 2 above shows the planned UK public R&D expenditure\(^3\) for 2008/09 (Office for National Statistics (ONS), 2009). As described above in the methodological approach, figures are shown for those government bodies with a demonstrated or potential strategic interest in complex trauma research and a high R&D budget (greater than £50m). Not all departments meeting these criteria were found to have a research portfolio relevant to complex trauma, but this is not to say that there may not be strategic interest in complex trauma research, and so they were included in the initial analysis.

\(^3\) For ease of comparison, figures are based on planned 2008/09 R&D expenditure, as actual figures were not available for all government bodies. Subsequent slides may show actual expenditure figures for 2008/09 or 2009/10, where available.
Overall we can see that the DH, including NHS R&D spending (administered through the National Institute for Health Research; NIHR) has one of the highest expenditures of any UK government body on R&D. The MoD has a combined R&D budget which nears £2 billion, but the ‘research’ component of this budget is significantly smaller, totalling just under £600m.

Total public funding for health R&D is in the order of £1.7 billion, a figure largely composed of the DH budget, but also contributed to by other government departmental expenditure, including that of the research councils. Analysis presented later in this report estimates the proportion of this total health R&D figure that is related to complex trauma research (see summary on p. 33).

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4 Figure based on estimates from the Medicines and Healthcare Strategy 2009–2011 (Technology Strategy Board, 2009) and confirmed by analysis previously developed by RAND Europe for a report to the Bill and Melinda Gates Foundation (Wamae et al., 2010).
Private and charitable sector expenditure on health R&D

- £8.9 billion was invested in medical and health R&D in 2009 by industry
- In 2009-10, the 120 members of the Association of Medical Research Charities (AMRC) spent more than £1 billion on medical research in the UK
- It is estimated that the Wellcome Trust, Cancer Research UK and the British Heart Foundation fund 80% of all charitable, health-related research in the UK (UKCRC, 2006)
- Bottom line: UK private industry and charitable sector health and medical R&D investments approach £10 billion

While all of UK public expenditure on R&D in 2008/09 was £8.7 billion, private industry invested £8.9 billion in medical and health-related R&D alone in 2009. This figure comprises the total investments made by the 129 pharmaceutical and biotechnology companies which fall into the category of the top 1,000 UK firms investing most heavily in R&D (in any sector; Department for Business, Innovation and Skills, 2010).

In the charitable research sector, the 120 members of the Association of Medical Research Charities spent a combined total of more than £1 billion on medical research in the UK. Of this, previous analysis in 2006 estimated that the Wellcome Trust, Cancer Research UK and British Heart Foundation funded up to 80% of all charitable health-related research in the UK (UK Clinical Research Collaboration, 2006). Looking at the most recent figures for annual expenditure for each of these three charities, it is likely that they spend more than 80% today. Figures published in 2010 for 2009 expenditure showed the following breakdown:

- Wellcome Trust: £720m (Wellcome Trust, 2010)
- Cancer Research UK: £308m (Cancer Research UK, 2010)
- British Heart Foundation: £78.8m (British Heart Foundation, 2010)

These annual expenditures are total figures for all investments, so depending on how research expenditure figures are interpreted (as opposed to capital expenditure), the proportional contributions may be smaller. Nevertheless, the investment of both private and charitable sectors is significant, and overall we can conclude that UK private industry and charitable sector health and medical R&D investments approach £10 billion.
Mapping the research landscape: individual funder information

- Information and data come from several sources:
  - Reviews of annual reports
  - Funder strategy documents
  - Reviews of existing grants databases (funder websites and UK PubMed grant tool)
  - Interviewee input (10 interviews conducted with trauma researchers with a range of disciplinary specialties)

Before moving to the individual funder summaries and discussion of the research portfolio\(^5\) of the main UK bodies actively funding complex trauma research, we will briefly introduce the content and structure of the information.

In the slides that follow, we provide a summary of the main activities and research projects relevant to complex trauma (where they were identifiable) for each research funding body. The majority of projects are ongoing, although a few were completed within the past two years. In some cases we also highlight strategic aims which might be related to complex trauma in order to identify opportunities for leveraging.

The projects italicised in the summary tables are those where there was uncertainty as to the full relevance to complex trauma. This uncertainty was due to the definitional problems associated with complex trauma research highlighted earlier in Chapter 1.

The information and data presented in the following slides comes from several sources including: annual reports; funder strategy documents; existing grant databases found on funder websites and through UK PubMed; and interviewee input from trauma researchers around the country. Estimates of annual expenditure are derived by averaging the project total across the years of the project and then summing this across all relevant projects for a given funder.

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\(^5\) Although every effort was made to cross-reference research portfolios from numerous sources, we cannot guarantee that the lists are either comprehensive or are free from double-counting projects or expenditure. They are provided here as best estimates.
The goal of the National Institutes of Health Research (NIHR) is to establish a health research system in which the NHS supports outstanding researchers who are conducting cutting-edge research. The NIHR funding portfolio includes all funding for NHS research in England, as well as funding to support clinical research and academics. Therefore, it spans a wide range of health research fields. The total budget for the NIHR in 2009/10 was £919.5m,\(^6\) and it is projected to be £992m in 2010/11 (NIHR, 2010). Out of this, we estimate funding specific to complex trauma research to be in the order of £3.5m to £4m, or less than 0.5% of total NIHR funding. (A full list of projects relevant to complex trauma is summarised in Table 1 below.)

The majority of the research conducted in the area of complex trauma and funded by NIHR is focused on acute injury, in particular coagulopathy, resuscitation and surgical care. Most of the NIHR projects in complex trauma are funded through the Health Technology Assessment (HTA)\(^7\) programme. The total funding for the HTA programme was £40.7m in 2009/10. If we assume that the majority of NIHR funding for complex trauma comes from the budget of this programme, the field still receives less than 10% of overall funding in a given area.

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\(^6\) Some readers may note this figure is much higher than that given for the R&D budget of the DH on p. 8 above. This is because the earlier figure is one which breaks down total expenditure by specific R&D costs, whereas this data is not available for 2009/10 or 2010/11, therefore the total budget for the NIHR is given.

\(^7\) The HTA programme produces independent research information about the effectiveness, costs and broader impact of healthcare treatments and tests. Projects are funded in the following areas: response-mode clinical trials, primary research and technology assessment reviews for the National Institute of Clinical Excellence (NICE).
However, not all projects are funded through the HTA programme. One project identified in Table 1 below (Traumatic Coagulopathy and Massive Transfusion) is funded through the Programme Grants for Applied Research (PIGR) stream, which had a total expenditure in 2009/10 of about £20m. These are very prestigious awards given to individual researchers, with values of up to £2m for three to five years. Other projects were identified through additional sources, such as the UK Clinical Research Network Study Portfolio database, but specific funding streams in the NIHR were not specified. It is worth noting that a keyword search for ‘trauma’ on the clinical research database only showed three active clinical research trials relevant to the area of complex trauma.

There is also a dedicated stream of funding relevant to complex trauma research through NHS Blood and Transplant. Total R&D funding awarded to NHS Blood and Transplant from NIHR was £11.9m in 2009/10 for a five-year research programme into cellular engineering, platelet biology, clinical use of stem cells and erythropoiesis (NHS Blood and Transplant, 2010). Of the total £11.9m, it is estimated that 10%, or about £250,000 per annum, will be spent on complex trauma (Personal communication, 2010).

Finally, expert feedback from our interviews reinforced the important role that NIHR funding plays in this field. All the UK researchers interviewed cited the NIHR (or in one case, the DH) as their main source of funding. Therefore, it seems that under any set of future funding scenarios, the NIHR can and should play an important coordinating and catalysing role.
<table>
<thead>
<tr>
<th>Project title</th>
<th>NIHR programme</th>
<th>Amount</th>
<th>Years</th>
<th>Institution</th>
<th>Trauma area</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRASH2 (Clinical Randomisation of an Antifibrinolytic in Significant Haemorrhage) trial</td>
<td>HTA</td>
<td>£2,513,781</td>
<td>2007–12</td>
<td>London School of Hygiene and Tropical Medicine</td>
<td>Acute injury: coagulopathy</td>
</tr>
<tr>
<td>CRASH-2 IBS (Intracranial Bleeding Study): the effect of tranexamic acid on intracranial bleeding among CRASH-2 trial participants</td>
<td>HTA</td>
<td>£102,814</td>
<td>2009–12</td>
<td>London School of Hygiene and Tropical Medicine</td>
<td>Acute injury: coagulopathy</td>
</tr>
<tr>
<td>Development and validation of a risk score for trauma patients with haemorrhage: the CRASH-2 score</td>
<td>HTA</td>
<td>£121,025</td>
<td>2010–12</td>
<td>London School of Hygiene and Tropical Medicine</td>
<td>Acute injury: coagulopathy</td>
</tr>
<tr>
<td>Can emergency endovascular aneurysm repair (eEVAR) improve the survival from ruptured abdominal aortic aneurysm?</td>
<td>HTA</td>
<td>£1,044,106</td>
<td>2009–13</td>
<td>Imperial College London</td>
<td>Acute injury: resuscitation</td>
</tr>
<tr>
<td>Multi-centre randomised controlled trial of the cost-effectiveness of infra-inguinal percutaneous transluminal angioplasty (PTA) versus reconstructive surgery for severe limb ischaemia (BASIL)</td>
<td>HTA</td>
<td>£1,012,736</td>
<td>1999–2010</td>
<td>Solihull Hospital</td>
<td>Acute injury: surgical care and bone injury</td>
</tr>
<tr>
<td>Surgical trial in traumatic intracerebral haemorrhage (STITCH)</td>
<td>HTA</td>
<td>£2,328,920</td>
<td>2009–15</td>
<td>University of Newcastle-upon-Tyne</td>
<td>Acute injury: brain injury and surgical care</td>
</tr>
<tr>
<td>Risk Adjustment In Neurocritical care (RAIN): prospective validation of risk prediction models for adult patients with acute traumatic brain injury to evaluate the optimum location and comparative costs of neurocritical care</td>
<td>HTA</td>
<td>£617,028</td>
<td>2009–13</td>
<td>Intensive Care National Audit and Research Centre</td>
<td>Acute injury: decision support; medical training</td>
</tr>
<tr>
<td>Head Injury Transportation Straight to Neurosurgery (HITS-NS) trial: a feasibility study</td>
<td>HTA</td>
<td>£539,573</td>
<td>2010–14</td>
<td>University of Manchester</td>
<td>Acute injury: decision support</td>
</tr>
<tr>
<td>Comparison of close contact cast (CCC) technique to open surgical reduction and internal fixation (ORIF) in the treatment of unstable ankle fractures</td>
<td>HTA</td>
<td>£2,408,961</td>
<td>2008–13</td>
<td>University of Oxford</td>
<td>Acute injury: surgical care and bone injury</td>
</tr>
<tr>
<td>A randomised controlled trial of the LUCAS (Lund University Cardiopulmonary Assistance System) mechanical compression/decompression device for out of hospital cardiac arrest</td>
<td>HTA</td>
<td>£2,176,422</td>
<td>2009–14</td>
<td>Warwick Medical School, University of Warwick</td>
<td>Acute injury: resuscitation</td>
</tr>
</tbody>
</table>
Medical Research Council

- Annual funding for complex trauma is estimated at just over £1m
- Most research is basic and in the area of acute injury, although some translational research is funded
  - Recent grant award to MoD researchers of £300,000 to fund translational research in complex trauma
- Expert feedback:
  - Funding for complex trauma is limited
  - The MRC needs a greater focus and understanding of what constitutes complex trauma work
  - The MRC needs to provide greater support for translational research
- Possible opportunities for leveraging funding under priority area of ageing research (e.g., complex fractures, cellular response to traumatic injuries)

The UK Medical Research Council (MRC) supports research across the biomedical spectrum, from fundamental research to clinical trials. In 2008/09, the MRC spent £704.2m on research across all areas of biomedical research and disease (MRC, 2009). We estimate that of this total, £1m per annum is spent on research related to complex trauma. (Relevant projects are summarised in Table 2 below.)

Our findings suggest that there might be many more projects relevant to complex trauma funded by the MRC than those summarised below. However, the project descriptions led us to conclude that many of these were basic research projects which were outside the scope of our review. This was confirmed to some extent by the experts we spoke with, who commented that the distribution of research within the MRC was skewed towards basic research. One interviewee referred to the MRC as the "molecular research council", emphasising his view that funding was skewed towards basic science, focusing on the molecular underpinnings rather than the clinical aspects of disease. However, when we look at the funding and stakeholder engagement model of the MRC, it is clear that the MRC sees itself as taking a lead role in discovery and exploratory research, while other stakeholders and partners, notably NIHR, lead in the application and delivery research areas (see Figure 1 in MRC, 2009, p. 9). This suggests that the breakdown in the translational pipeline is in the implementation and translation of research across the ‘discovery-to-delivery’ gap (Cooksey, 2006). Thus there may be scope for improvement in the way that the NIHR and MRC address this aspect of translation for complex trauma.

Like the NIHR projects, most complex trauma research projects currently funded by the MRC fall under the category of acute injury. Some research which is cross-council-funded may not be captured because it is reflected in another research council’s project database. This is particularly the case for work in the field of regenerative medicine, but may be relevant in other areas.
Table 2: MRC projects in the area of complex trauma research

<table>
<thead>
<tr>
<th>Project title</th>
<th>Amount</th>
<th>Years</th>
<th>Institution</th>
<th>Trauma area</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuro-inflammation following human traumatic brain injury</td>
<td>£205,220</td>
<td>2009–12</td>
<td>University of Cambridge</td>
<td>Acute injury</td>
</tr>
<tr>
<td>Novel non-invasive optical methods to characterise cerebral oxygen delivery</td>
<td>£295,297</td>
<td>2009–11</td>
<td>University College London</td>
<td>Acute injury</td>
</tr>
<tr>
<td>and utilisation after traumatic brain injury</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RESCUEicp decompressive craniectomy study</td>
<td>£877,384</td>
<td>2008–13</td>
<td>University of Cambridge</td>
<td>Acute injury</td>
</tr>
<tr>
<td>Overcoming the limitations of allograft in impaction bone grafting for</td>
<td>£462,159</td>
<td>2010–12</td>
<td>University of Southampton</td>
<td>Regenerative medicine</td>
</tr>
<tr>
<td>revision arthroplasty</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mechanisms of interleukin-1 action in neuronal injury</td>
<td>£754,131</td>
<td>2009–12</td>
<td>University of Manchester</td>
<td>Acute injury</td>
</tr>
<tr>
<td>Novel bio-synthetic matrix for ocular surface reconstruction</td>
<td>£91,311</td>
<td>2008–09</td>
<td>University of Nottingham</td>
<td>Acute injury: peripheral nerve injury</td>
</tr>
<tr>
<td>Promoting plasticity and repair after spinal cord injury</td>
<td>£619,462</td>
<td>2003–11</td>
<td>King’s College London</td>
<td>Regenerative medicine: plastic and reconstructive surgery</td>
</tr>
<tr>
<td>DAVROS: development and validation of risk-adjusted outcomes for systems of emergency medical care</td>
<td>£951,517</td>
<td>2007–11</td>
<td>University of Sheffield</td>
<td>Medical training: simulation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Acute injury: decision support</td>
</tr>
</tbody>
</table>
The Biotechnology and Biological Sciences Research Council (BBSRC) supports research related to the understanding and exploitation of biological systems across a range of sectors, including agriculture, bioprocessing, chemical, food, healthcare, pharmaceutical and other biotechnological related industries. In 2008/09, BBSRC gross expenditure on research was approximately £418m (Biotechnology and Biological Sciences Research Council, 2009).

We estimate that the BBSRC funds around £1m to £1.5m per annum of research related to complex trauma, and that most of this is in the area of regenerative medicine and is co-funded with the Engineering and Physical Sciences Research Council (EPSRC). An estimated range is provided due to uncertainty over how to classify some research that is basic in nature. For example, most regenerative medicine research is basic and clinical trials are a long way off; nevertheless, UK researchers at the University of Sheffield told us about their involvement with regenerative bone research that is about to begin clinical trials in the USA. Such ‘injectable bone’ can be used to accelerate wound care, and has been developed from regenerative medicine research into bone stem cells and material engineering. Therefore, some regenerative medicine research may be closer to clinical application than others. The projects funded by the BBSRC which we identified as potentially relevant to complex trauma are listed in Table 3 below.

Looking to future work and partnering opportunities, the priority research areas of the BBSRC are:

- ageing research
- bioenergy
• global security
• living with environmental change
• nanoscience and bionanotechnology
• systems approaches to biological research
• synthetic biology
• technology development for bioscience
• animal health
• crop science (food security).

Of these, research related to complex trauma might be fostered in the areas of nanoscience, systems approaches, ageing research and technology development for bioscience. From a strategic perspective, then, research in these priority areas can be leveraged. In addition, there is an emphasis on ageing research in BBSRC strategy documents, and significant cross-research council work is done in this area. There could be opportunities for leveraging funding here, as many areas of complex trauma research overlap with trauma affecting an ageing population (stroke, complex fractures, etc). There is also scope for some crossover funding in the priority area of ‘technology development for bioscience’. Here, proposals are being sought in the areas which may be related to complex trauma: functional analysis and bioimaging, and predictive modelling. Both of these are listed as specific priority areas of work for the DH, and so there could be real scope for engagement.
<table>
<thead>
<tr>
<th>Project Title</th>
<th>Amount</th>
<th>Years</th>
<th>Institution</th>
<th>Trauma area</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimisation of perfusion bioreactor for bone tissue growth</td>
<td>£509,341</td>
<td>2008–12</td>
<td>University of Manchester</td>
<td>Regenerative medicine: plastic and reconstructive surgery</td>
</tr>
<tr>
<td>Combining stem cell science and tissue engineering to study the development and repair of human skeletal tissues</td>
<td>£625,309</td>
<td>2010–15</td>
<td>Keele University</td>
<td>Regenerative medicine: plastic and reconstructive surgery</td>
</tr>
<tr>
<td>Combining stem cell science and tissue engineering to study the development and repair of human skeletal tissue</td>
<td>£1,600,799</td>
<td>2009–14</td>
<td>University of Southampton</td>
<td>Regenerative medicine: plastic and reconstructive surgery</td>
</tr>
<tr>
<td>Combining stem cell science and tissue engineering to study the development and repair of human skeletal tissue</td>
<td>£198,362</td>
<td>2009–14</td>
<td>Imperial College London</td>
<td>Regenerative medicine: plastic and reconstructive surgery</td>
</tr>
<tr>
<td>Combining stem cell science and tissue engineering to study the development and repair of human skeletal tissues</td>
<td>£1,076,543</td>
<td>2009–14</td>
<td>University of Nottingham</td>
<td>Regenerative medicine: plastic and reconstructive surgery</td>
</tr>
<tr>
<td>Growth, form and function: the mathematics of 3D tissue morphogenesis and regenerative medicine</td>
<td>£1,184,107</td>
<td>2006–11</td>
<td>University of Nottingham</td>
<td>Regenerative medicine: plastic and reconstructive surgery</td>
</tr>
<tr>
<td><strong>Immune regulation at epithelial barrier sites</strong></td>
<td><strong>£138,997</strong></td>
<td><strong>2010–15</strong></td>
<td><strong>Unlisted institution</strong></td>
<td><strong>Acute injury: resuscitation</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Infection: wound treatment and management</strong></td>
</tr>
</tbody>
</table>
**Engineering and Physical Sciences Research Council**

- Expenditure on complex trauma related research is estimated at £500,000 per annum
- Expenditure is centred around wound management and regenerative medicine (medical engineering)
- Contributions to cross-research council initiatives through Biotechnology and Biological Sciences Research Council or Medical Research Council are difficult to capture
- EPSRC’s cross-disciplinary programmes have some relevance to complex trauma and existing research can be more efficiently leveraged
- Opportunities for strengthening work exist in the area of complex trauma response modelling

The Engineering and Physical Sciences Research Council (EPSRC) supports research into mathematics, engineering, physics, chemistry, materials science, information and communication technologies. In 2008/09, EPSRC spent £790m on research (EPSRC, 2009). If we assume a similar annual spend over the past few years, we estimate that less than 1%, or about £500,000 per annum, is direct expenditure on complex trauma-related research. The majority of this expenditure is around wound management and regenerative medicine, in particular medical engineering. Table 4 below shows identified projects in the area of complex trauma. Although current funding for complex trauma seems to be limited, there appears to be significant scope for leveraging funding from other, more general, research programmes across the council, as well as through other research council priority areas, such as regenerative medicine funding by the BBSRC and MRC.

In its most recent delivery plan, the EPSRC has set out several ‘global challenge’ themes in which it will focus its resources, in addition to continued support for cross-council themes (such as ageing research, discussed above). Of the four ‘global challenge’ themes, the healthcare technologies theme is directly relevant to complex trauma in that there is a specific focus on “advancing the engineering and physical sciences knowledge and techniques essential to pull-through biology” (EPSRC, 2010, p. 13). Work in this theme also contributes to the cross-council initiative of lifelong health and well-being referred to earlier. There is likely to be scope and opportunity for leveraging across these initiatives, particularly in being aware of research which can be ‘imported’ into complex trauma and supported in the pull-through and translational stages.

In addition to the global challenges themes, EPSRC’s cross-disciplinary programmes may have relevance to complex trauma. The Materials, Mechanical and Medical Engineering
Programme has a broad remit and a focus on medical instrumentation and devices, including imaging, biomaterials, tissue engineering, biomechanics and rehabilitation. Medical modelling activities also fall under this programme. Materials and medical bioengineering programmes have overall relevance to complex trauma, and projects on tissue and bone engineering in relation to dental repair, corneal repair, ceramic lattices for bone repair and teleplanning for liver transplant have all been conducted. Overall, grants across the programme total £109m, or 24% of the overall EPSRC programme, so it is a significant funding stream within which to be aware of potentially relevant projects.

Another programme to be aware of in terms of complex trauma relevance is the Cross-Disciplinary Interface Programme. It accounts for 11.4% of the total EPSRC budget, or approximately £90m per annum (EPSRC, 2009). The vision of the programme is to enable UK researchers to work at the interfaces of existing and emerging cross-disciplinary fields. In this sense, there seems to be a high potential for work in complex trauma to occur within this programme, particularly in the cross-disciplinary sub-themes of human health, technologies of the life sciences and biological systems. For example, the budget for the human health sub-theme is £50m per annum and includes research into disease and treatment, drug formation and delivery, tissue engineering and biocompatibility. Leading institutes receiving funding under this programme are at the Loughborough Innovative Manufacturing Research Centre in Regenerative Medicine (£4m grant) and the Leeds Innovation and Knowledge Centre in Regenerative Device and Therapies (£5m grant). Collaborations with users of the research include AstraZeneca, Medipex Ltd, De Puy, TWI Ltd and Yorkshire Forward (EPSRC, 2009). While not all users may have an interest in complex trauma, it does seem to be a fruitful area in which to consider future links.

Finally, given the remit of EPSRC, there may be unrealised opportunities for developing a cross-council programme in the area of complex trauma response modelling – a priority area that our review has found to be significantly under-researched. In addition, the current delivery plan has a focus on next-generation healthcare. This is another area where much of the cross-research council funding is coming from, again suggesting there could be good opportunities for leveraging funding for complex trauma research across many research council funding streams and fields of health and medical research.
<table>
<thead>
<tr>
<th>Project title</th>
<th>Amount</th>
<th>Years</th>
<th>Institution</th>
<th>Trauma area</th>
</tr>
</thead>
<tbody>
<tr>
<td>Robotic reduction of complex fractures using 3D puzzle-solving algorithm</td>
<td>£98,864</td>
<td>2010–12</td>
<td>University of the West of England</td>
<td>Infection: wound care</td>
</tr>
<tr>
<td>Inkjet printing of cellular sheets and gelation mechanisms</td>
<td>£253,566</td>
<td>2009–12</td>
<td>University of Manchester</td>
<td>Regenerative medicine</td>
</tr>
<tr>
<td>Improving chronic wound healing with intelligent dressings</td>
<td>£438,989</td>
<td>2006–09</td>
<td>Imperial College London</td>
<td>Infection: wound treatment and management</td>
</tr>
<tr>
<td>DIADEM: data information and analysis for clinical decision making</td>
<td>£161,383</td>
<td>2008–09</td>
<td>Queen Mary, University of London</td>
<td>Acute injury: decision support</td>
</tr>
</tbody>
</table>
The Ministry of Defence (MoD) research budget for science, innovation and technology was £500m in 2009–10 (Ministry of Defence, 2010). This budget is separate from the ‘development’ budget, which includes military technology and equipment development such as planes, ships, army vehicles, etc. Military expenditure on complex trauma research is estimated at £3m to £3.5m per annum (Personal communication, 2011), and overall programme summaries are captured in Table 5 below. It is worth noting that this amount is roughly equivalent to that spent by the NIHR on complex trauma.

The Defence Science and Technology Laboratory (DSTL) is an agency of the MoD that is responsible for leading the defence science and technology research programme. DSTL also “transfers knowledge to defence industries, spins off knowledge for civil application and undertakes collaborative research with other institutions” (MoD, 2006, p. 22). Most funding for complex trauma research within the MoD comes from DSTL and/or from central MoD research funds. Currently, DSTL provides £2.3m over three years for a combat casualty care programme, which includes research into resuscitation, wound patterns, trauma timelines and blood transfusion. In addition to this, the MoD provides £250,000 per annum for general health research (although this year this amount has been supplemented by an additional £1.1m). However, this total of £1.4m of funding is part of a wider medical research strategy pursued by the MoD, and so not all of it is supporting research relevant to complex trauma. Funding for any MoD research programme, complex trauma or otherwise, is obtained by bidding into various funding streams within DSTL or the MoD.

One example of how MoD work in other areas of medical research might be imported into the field of complex trauma is in protection against the threat or use of Chemical,
Biological, Radiological or Nuclear weapons. Within this area, there is significant health-related research on medical countermeasures (MoD, 2006). The strategy for the development of CBRN medical countermeasures is to explore approaches from academia and small and medium-sized enterprises, adapt them at DSTL and then seek to share the burden of clinical trials and licensing with international and industrial partners. The priority areas for medical counter-measures in which capabilities relevant to complex trauma are being developed are as follows.

- Pharmacology, immunology, microbiology and pathology – with expertise in understanding CBRN agents in order to develop medical countermeasures, and in the identification, development and licensing of medical products (eg vaccines, antibiotics, chemical agent therapies), including efficacy testing in a range of in vitro and in vivo models.
- Clinical science – in order to conduct experiments and clinical trials in human volunteer subjects for the licensing of medical products.
- Biotechnology – for the application of genetic and protein engineering techniques to the identification and development of medical countermeasures (including vaccines and generic post-exposure therapies), as well as in the design and development of drug delivery methods and technologies.

In addition to MoD-specific research programmes, projects in complex trauma are part-funded by other organisations in the UK and abroad. A major trauma centre has been established in Birmingham with matched funding of £1m each from the DH (through NIHR) and the MoD, as well as contributions (of unknown value) from University Hospitals Birmingham NHS Foundation Trust and University of Birmingham. The centre also has a start-up grant of £300,000 from the MRC to support translational research.

We heard from some of the interviewees we spoke with (who work outside the military) that they felt there was difficulty in conducting research with the military, particularly at a clinical level. Cultural and ethical barriers were cited as reasons which contributed to this difficulty. For example, there are historical issues associated with conducting research with soldiers which make clinical trial work particularly challenging. However, conversations with military medical staff revealed that there are joint research efforts at some UK universities and with the US military. The Birmingham centre discussed above is a new initiative, but there has been ongoing research on evaluating critical care patient outcome data at Birmingham. At Imperial College London there is a fully integrated, jointly sponsored research laboratory looking at blast effects on bone and soft tissue. There is also a military clinician seconded to the neurotrauma unit at Hammersmith Hospital who is conducting research on neuroimaging and brain markers.

Links with the US military seem fairly strong. There is a shared field hospital in Afghanistan (NAO, 2010b), and there are formal research links with the US AISR. In this arrangement, the UK military sends researchers to the USA for periods of six months to one year to conduct research in areas of joint interest. Recent projects have focused on vascular and body trauma.

Overall, the evidence from the interviewees suggests that the UK military has the capacity to conduct good clinical studies because of the high volume of eligible patients, but historically it has been less well placed for academic research due, perhaps in part, to weak
links with universities. The interviewees also suggested the military was more focused on basic research, for example into blast injuries, but less on developing a more holistic understanding of complex trauma as a ‘disease’. However, military researchers do publish in journals, and are increasingly attending and being invited to conferences to share research findings. Therefore, there are indications that links and collaborative efforts are improving, but dedicated attention and initiatives may be needed to ensure that full potential is reached.
## Table 5: MoD research projects in complex trauma

<table>
<thead>
<tr>
<th>Programme area</th>
<th>Funder</th>
<th>Amount</th>
<th>Years</th>
<th>Institution</th>
<th>Trauma area</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combat casualty care programme</td>
<td>MoD</td>
<td>£2,300,000</td>
<td>3 years</td>
<td>DSTL</td>
<td>Acute injury: wound patterns; resuscitation; coagulopathy; blast effects on soft tissue and bone; critical care outcome data</td>
</tr>
<tr>
<td>Research centre to be established at Birmingham</td>
<td>DH (through NIHR), MoD, University of Birmingham, University Hospitals Birmingham NHS Foundation Trust</td>
<td>Upwards of £2,000,000</td>
<td>Unknown</td>
<td>Selly Oak Hospital</td>
<td>Multiple</td>
</tr>
<tr>
<td>Supporting translational research at the new centre</td>
<td>MRC</td>
<td>£300,000</td>
<td>2010–15</td>
<td>Selly Oak Hospital</td>
<td>Start-up funding to support collaborations and move basic science to clinical trials</td>
</tr>
<tr>
<td>Collaborative research with the US military</td>
<td>MoD/US AISR</td>
<td>Travel and subsistence costs of researchers</td>
<td>Ongoing</td>
<td>US AISR</td>
<td>Acute injury: vascular trauma and body trauma</td>
</tr>
</tbody>
</table>
The following summaries are provided for those government departments and devolved administration governments which have a high annual R&D expenditure and a potential strategic interest in complex trauma research, but for which no information about existing research projects in complex trauma could be found.

The Department for Transport aims to deliver a transport system which balances the needs of the economy, environment and society. The department’s evidence and research needs are structured around its five strategic objectives, of which at least one, “contributing to better safety, security, health and life-expectancy” (Department for Transport, 2009, p. 126), discusses research and evidence needs that in principle could address issues relevant to complex trauma research. Previous work conducted by RAND Europe (Wamae et al., 2010) estimated that 5% to 10% of the department’s £48m research budget was spent on health-related research, so we can assume that an even smaller percentage might be related to complex trauma.

The Department for International Development (DfID) may have a potential interest in complex trauma research because of its strategic importance in the developing world. In a working paper on better health (developed in preparation for the 2008 DfID Research Strategy), it was stated that respondents to a survey about causes of death claimed that:

\[
\begin{align*}
\text{trauma is second only to HIV and AIDS as a cause of death ... [regarding] injury control and trauma most of the current research is not conducted in developing countries, yet this is where most of the burden occurs. (DfID, 2008, p. 7)}
\end{align*}
\]

Thus, DfID may have a strategic interest in supporting research in complex trauma that is applicable to traumatic events involving road injuries, landmine injuries, healthcare system
effectiveness and natural disaster response. However, conversations with research staff at DfID revealed that they were unaware of any DfID-supported research in the area of complex trauma.

The Scottish Government has a Chief Scientist Office which is responsible for allocating health research funds. Annual funding is approximately £9m and is allocated in four priority areas: cancer, cardiovascular disease and stroke, mental health and public health. Although there is potential for funding of complex trauma research under the broader heading of ‘public health’, there were no complex trauma projects in Scotland identified through the UK PubMed grant look-up tool. Additional searches of the projects funded through the Chief Scientist Office revealed that there are some pockets of work in different areas which might be related to complex trauma, such as in trials for new methods of appendectomy surgery, and a project on the development of a safe and effective method for ultrasound-guided pain relief for patients with a broken hip, but overall these did not fit within our classification of complex trauma research, which deals with multiple injuries and bodily response in this context. There is the Aberdeen Centre for Trauma Research, but the work there focuses on the psychopathology of trauma and post-intervention evaluations of trauma care. Thus, none of these projects seem to be fully relevant to addressing complex trauma in the manner defined for this review.

In Wales, under the Welsh Assembly Government, the National Institute for Health and Social Care Research funds most health research work in this area. Our search did not reveal any research projects related to complex trauma, although there is one thematic research network around emergency care. However, there may be future opportunities for strengthening research efforts related to complex trauma through the new biomedical research centres. The Biomedical Research Centre and Units Strategy document was published in November 2010 and states that the main aim of the centres will be to:

- drive innovation in the prevention, diagnosis and treatment of ill health; translate advances in biomedical research into benefits for patients; [and] provide a key component of the NHS contribution to Wales’ international competitiveness by making the best centre(s) even better. (Welsh Assembly Government, 2010)

In Northern Ireland, there is a Northern Ireland Centre for Trauma and Transformation which is funded by the private charity, the Northern Ireland Community Relations Council, but it is focused on psychological trauma and treatment. In 2009, it was announced that a regional major trauma centre would be developed at the Royal Victoria Hospital, Belfast, with £300,000 being allocated to support the centre in its role. However, no further information about R&D funding related to complex trauma treatment and care could be obtained through our internet searches.

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**Medical charities**

- **The Healing Foundation**
  - £10m (over 25 years) at Manchester funding regenerative medicine research
  - Funding available for three new burns research centres (£1.5m each over five years)

- **The Wellcome Trust**
  - Funding in the order of more than £2m, most through technology transfer awards or for regenerative medicine

- **Other foundations identified, but there is little information on research funding:**
  - BUPA Foundation (CRASH-2 trial)
  - British Skin Foundation (Bradford)
  - Dunhill Medical Trust (rehabilitation work)
  - Resuscitation Council UK
  - Royal College of Surgeons of England
  - Arthritis Research UK (though more of a chronic focus)
  - JP Moulton Charitable Foundation
  - Brain Injury Foundation
  - Trauma Foundation

The next two slides summarise the complex trauma research funded by UK medical charities and private companies which was identified through our review. Although the overall annual health and medical R&D spending by these sectors approaches £10 billion, the amount of this that is relevant to complex trauma research is comparatively very small. A summary of the projects funded by the main private and charitable sector funders is provided in Table 6 below.

The Healing Foundation was established in 1999 and champions the cause of those who have visible loss of function and disfigurement due to traumatic injury. It funds research into “pioneering” surgical and psychological healing techniques, and is the only charity with such a dedicated cause in the UK and Ireland (The Healing Foundation, 2010). The foundation currently supports The Healing Foundation Centre (for Tissue Regeneration) at the University of Manchester with a 25-year £10m grant. However, work at the centre is still in the early stages, and is focused mostly on basic research in regenerative medicine. The foundation does have a call out to fund up to three new burns research centres in the UK (£1.5m for five years). These centres will have formal links to the US Army Regenerative Medicine Institute, as well as close links with the MRC, NIHR and UK armed forces through The Healing Foundation’s strategic partnerships. The outcome of the funding call will be announced in June 2011, but it is likely that these centres will present an opportunity for joined-up research and strategic thinking across multiple partners.

The Wellcome Trust is a global charity supporting biomedical research to improve health. The current strategic plan for the Wellcome Trust identifies five major challenges looking forward, three of which seem to have relevance to complex trauma: maximising the health benefits of genetics and genomics (e.g., regenerative medicine and stem cell therapy); understanding the brain (e.g., neurotrauma); and investigating development, ageing and
chronic disease (eg traumatic injury in older people may have relevance to bone injury, rehabilitation, etc). We estimate that the Wellcome Trust spends at least £2m per annum on research relevant to complex trauma, although this figure could be significantly higher, depending on how much of the work in regenerative medicine and stem cells is considered to be relevant. For example, a recent £3m project awarded to the University of Edinburgh will investigate the potential of generating red blood cells from stem cells. The clinical applications of this research may be several years away, but this would be relevant to complex trauma research in the area of coagulopathy. Other complex trauma research funded by the Wellcome Trust falls under its technology transfer programme, which is focused on supporting research that is near-market.

While these are two of the largest foundations supporting work in complex trauma, the experts that we interviewed, and additional desk research conducted, helped us to identify charities which have funded research in this area in the past or are doing so currently. Unfortunately, there was very little information available on specific research projects, but where some was identified, it is noted in the list below.

- BUPA Foundation – the BUPA Foundation was a partial sponsor of the CRASH-2 trial (see Table 1); however, a review of its annual reports from the last three years showed that no projects related to complex trauma research, treatment and care were funded.

- British Skin Foundation – this charity was mentioned by an expert interviewee who works at the Centre for Skin Sciences at the University of Bradford. The foundation has supported research at the centre in recent years.

- Dunhill Medical Trust – this trust supports rehabilitation work and was mentioned by a trauma rehabilitation expert during an interview.

- Resuscitation Council UK – the Council supports many kinds of research into the science, practice and teaching of resuscitation techniques. Currently it is supporting one of the NIHR projects using the LUCAS device for simulated cardiopulmonary resuscitation (see Table 1). Research grants are provided for up to £20,000.

- Royal College of Surgeons of England – one interviewee had three research fellowships in his laboratory which were supported by the College.

- Arthritis Research UK – this charity was mentioned as relevant to complex trauma research by one interviewee, although it was emphasised that it focuses more on chronic injury research as opposed to complex trauma.

- JP Moulton Charitable Foundation – this charity was involved in the CRASH-2 trial and, along with the BUPA Foundation, provided funding for the run-in stage of the trial.

- Brain Injury Foundation – one interviewee suggested that this foundation spends in the tens to low hundreds of thousand pounds on research, although not all may be related to complex trauma.

- Trauma Foundation – this foundation is based in San Francisco, but funds research around the world in injury prevention, policy development and dissemination. One interviewee estimated that it may spend in the low hundreds of thousand pounds each year on trauma research.
Private companies

- Private company expenditure is difficult to estimate, but the following companies have been mentioned by experts or identified through literature searches:
  - Novo Nordisk
  - Pfizer
  - AstraZeneca
  - Unilever
  - Small university spin-outs

- Most private company investment identified by interviewees was in the area of regenerative medicine

- Expert feedback suggests that investment by pharmaceutical companies is limited, in some cases due to the difficulties associated with clinical trials.

In the summary of private health research funding above (see p. 10), we stated that approximately £9 billion is spent on medical and health R&D in the UK. We found very little funding information about the amounts spent on complex trauma research of this total, although we suspect that it is probably very limited, based on the feedback from the expert interviews. The following companies were identified by the experts we interviewed as funding or supporting some research or trial work, but they were never able to give us specific figures.

- Pfizer and AstraZeneca support work in regenerative medicine once the research begins to approach clinical trial stage.
- Pfizer also supported some of the CRASH-2 trials by providing a grant-in-aid for purchasing the tranexamic acid (the main drug used in the trial to try and control bleeding) and placebo used in the trial.
- Unilever supports work done at the Centre for Skin Sciences at Bradford.
- Novo Nordisk was mentioned by one interviewee as active in complex trauma research, but we were unable to determine the specific areas that it was funding.
- Small university spin-outs play a role in funding research, particularly when they were formed because of research originally carried out at the university.

Expert feedback stressed that investment by pharmaceutical companies is limited, and in some cases this was due to the difficulties associated with clinical trials in complex trauma. This issue is addressed in further detail below, but is important to bear in mind when thinking about issues around market failure for complex trauma.
### Table 6: Private sector and charitable projects in complex trauma

<table>
<thead>
<tr>
<th>Project title</th>
<th>Funder</th>
<th>Amount</th>
<th>Years</th>
<th>Institution</th>
<th>Trauma area</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tissue engineering of teeth II</td>
<td>Wellcome Trust</td>
<td>£1,350,000</td>
<td>2006–09</td>
<td>King’s College London</td>
<td>Regenerative medicine, Infection: dentistry</td>
</tr>
<tr>
<td>Development of PeproStat, a new class of topical haemostat for the control of bleeding</td>
<td>Wellcome Trust</td>
<td>£409,894</td>
<td>2010–11</td>
<td>Haemostatix Ltd</td>
<td>Acute injury: coagulopathy</td>
</tr>
<tr>
<td>Automated rapid manufacture of facial soft tissue prostheses</td>
<td>Wellcome Trust</td>
<td>£498,979</td>
<td>2009–12</td>
<td>University of Sheffield</td>
<td>Infection: dentistry</td>
</tr>
<tr>
<td>Identification of retinoic acid receptor beta agonists for the treatment of spinal cord injury</td>
<td>Wellcome Trust</td>
<td>£1,400,577</td>
<td>2010–13</td>
<td>King’s College London</td>
<td>Acute injury: spinal cord injury</td>
</tr>
<tr>
<td>Proof of principle: human embryonic stem cell derived red cell concentrates for clinical transfusion</td>
<td>Wellcome Trust</td>
<td>£2,909,332</td>
<td>2009–12</td>
<td>NHS Lothian</td>
<td>Acute injury: coagulopathy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Programme area</th>
<th>Funder</th>
<th>Amount</th>
<th>Years</th>
<th>Institution</th>
<th>Trauma area</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regenerative medicine: The Healing Foundation Centre at the University of Manchester</td>
<td>The Healing Foundation</td>
<td>£10,000,000</td>
<td>2006–31</td>
<td>University of Manchester</td>
<td>Regenerative medicine</td>
</tr>
<tr>
<td>Burns Research Strategy: funding for up to three UK centres for burns research</td>
<td>The Healing Foundation</td>
<td>£4,500,000</td>
<td>2011–16</td>
<td>To be decided</td>
<td>Regenerative medicine</td>
</tr>
</tbody>
</table>
### Summary of funding

<table>
<thead>
<tr>
<th>Funder</th>
<th>Funding for complex trauma (annual estimates)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DH (including NIHR and NHS)</td>
<td>£3.5m-£4m</td>
</tr>
<tr>
<td>National Health Service Blood and Transplant</td>
<td>£250,000</td>
</tr>
<tr>
<td>MRC</td>
<td>£1m</td>
</tr>
<tr>
<td>BBSRC</td>
<td>£1m-£1.5m</td>
</tr>
<tr>
<td>EPSRC</td>
<td>£500,000</td>
</tr>
<tr>
<td>MoD</td>
<td>£3.5m</td>
</tr>
<tr>
<td>Wellcome Trust</td>
<td>£2.5m+</td>
</tr>
<tr>
<td>The Healing Foundation</td>
<td>£1m</td>
</tr>
<tr>
<td>Private sector</td>
<td>£2m</td>
</tr>
<tr>
<td>Total</td>
<td>~£15m</td>
</tr>
</tbody>
</table>

This chapter has discussed the funding and strategic portfolios of the main public, private, and charitable funders active in complex trauma research. The table in the slide above summarises the main funding figures that we identified through our rapid review. This total amounts to an approximate expenditure on complex trauma research of £15m. However, as stated previously, this estimate is only a rough indication based on a very rapidly conducted review. A more comprehensive picture of the funding landscape can be completed, but it would take more time and resource. Further comments on how this would be done and through what research review mechanisms are made in the final conclusions (see pp. 45–53).

Compared to other areas of medical research such as cancer research, which in 2006 was estimated to receive more than 25% of all health expenditure in the UK across public and private sources, the amount of funding received by complex trauma is very small. This leads us to conclude that complex trauma is a niche, and possibly ‘orphan’, area of research where the majority of public funding comes from the MoD and the DH. Therefore, greater coordination between these two funders could ensure that the small amount of available funding is spent most efficiently. In addition, our analysis shows that there is enough strategic interest in areas of biomedical research relevant to complex trauma among potential public and private funders for there to be opportunities for leveraging funding and strengthening translational pathways for importing research findings from other areas of health and biomedicine into the field of complex trauma.
CHAPTER 3  
Strategic analysis of international efforts in complex trauma

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**International benchmarking**

- Getting detailed information about funding and centres of excellence internationally is difficult at any level of depth
- However, we can test hypotheses based on the analysis of complex trauma research in the UK
  - Hypothesis: trauma research is a niche area of research and integration between civilian and military sectors can be strengthened
- This hypothesis was tested in Israel and the USA, two countries viewed to be strong in complex trauma treatment and research

The first part of this study required us to look at the funding landscape in the UK for complex trauma research. The second part involved looking at the international landscape to see if there were any parallels or lessons that could be learned from the experiences and expertise of other countries. However, as mentioned previously, obtaining detailed information about funding mechanisms and identifying specific research programmes and centres of excellences in other countries was difficult due to the limited resources available for this rapid review.

Given this, we adopted a hypothesis-driven approach to understanding the international context which was based upon our analysis of the UK funding landscape. We proposed that complex trauma research was a niche area of research in other countries, and that integration between military and civilian sectors could be strengthened. We tested this hypothesis in Israel and the USA, two countries which were frequently mentioned by expert interviewees as strong in complex trauma treatment and research. Due to the original aims of the DH to inform strategic discussions with the MoD, we focused our review largely on research in the military context.
Complex trauma research in the USA (military)

- US Army Medical Department: Medical Research and Materiel Command (MRMC)
  - Manages a large intramural and extramural research programme with six medical research laboratories
- The US Army Institute of Surgical Research
  - A medical research laboratory of the MRMC, runs a research programme in combat casualty care
- US Army Institute of Regenerative Medicine
- The Naval Medical Research Unit
- US Air Force C-STARS programme
  - Air Force medical personnel routinely report to civilian trauma centres for further training
- US military funding and collaboration is relevant to UK research
  - Shared hospital sites in Afghanistan (NAO, 2010b)
  - Seconded researcher programmes

The US Army Medical Department has a Medical Research and Materiel Command (MRMC), which manages a large intramural and extramural research programme with six medical research laboratories covering the areas of military infectious diseases, combat casualty care, military operational medicine, medical chemical and biological defence and clinical and rehabilitative medicine. The Command also manages a large extramural research programme composed of joint contracts, grants and cooperative R&D programmes funded across the civilian sector, including academia, private industry and other government organisations. Based on this, it seems that there are many examples where state-of-the-art research between civilian and military sectors has been successfully leveraged.

One of the research programmes managed by the MRMC has a specific focus on combat casualty care. The Combat Casualty Care Research Programme (CCCRP) focuses on leveraging cutting-edge research and knowledge from government and civilian research programmes to fill existing and emerging gaps in combat casualty care. There are 10 major areas of emphasis within the programme, including:

- damage control resuscitation
- extremity trauma and regenerative medicine
- pain control
- advanced capabilities for emergency medical monitoring
- critical care engineering (including medical knowledge engineering)

Further detail about each of these areas can be found at: https://mrmc-www.army.mil/index.cfm?pageid=medical_r_and_d.ccc.overview.
- clinical trials
- craniomaxillofacial injury
- blood products
- neuroprotection
- neurological effects of blast.

All clinical trial work managed by the MRMC is done at the US Army Institute of Surgical Research (US AISR), and the nature of the work is unique in that medical professionals, patients and research scientists are all present within the institute. This provides opportunities to directly observe current combat casualties and identify emergent challenges and opportunities for improving care. It also presents an environment in which pre-clinical research science can be directly translated into the clinical setting for validation. Such a strategy of co-location seems to be important to the US AISR, as it is emphasised in their programme descriptions and is one that might be pursued by the DH and MoD.

The CCCRP also works closely with other US military and civilian research sectors, including the Office of Naval Research’s Casualty Care and Management Group and the US Air Force. These research efforts are coordinated through the Biomedical Initiative Steering Committee, the Tactical Combat Casualty Care Committee and Joint Program Committee 6. The links may be facilitated by the fact that much military combat casualty care and research seems to happen out of units based around the San Antonio Military Medical Centre. More broadly, the CCCRP also works with the US National Institutes of Health, the Defense Advanced Research Projects Agency and other organisations interested in improvements in the care of combat casualties.10

As mentioned above, the US AISR is a sub-command of the MRMC and seems to be responsible for at least some, if not all, components of the CCCRP. There are also several trauma-related research programmes run out of the US AISR, which may or may not be a part of the overarching CCCRP.11 These programmes include a joint theatre trauma system, a burns centre and a dental and trauma research detachment. The CCCRP funds external as well as internal research, and its scope includes an orthopaedic trauma research programme which funds intramural and extramural research. The topics of interest for which grant applications across basic (b), translational (t), and clinical (c) research are requested include:12

- improved healing of segmental bone defects\(^{(b,c)}\);
- reduction in wound infection\(^{(t)}\);
- prevention of heteroptic ossification\(^{(b,t,c)}\);
- improved healing of massive soft tissue defects\(^{(t,c)}\);
- tissue viability and wound irrigation/debridement technologies\(^{(t,c)}\); and
- translating research into practice\(^{(c)}\).

10 For more information see: https://ccc.amedd.army.mil/about.jspx.
11 This level of detail could not be determined through our review.
12 For further information see: http://www.usaisr.amedd.army.mil/default.html. The designations of ‘b’, ‘t’ and ‘c’ correspond to whether ‘basic’, ‘translational’ or ‘clinical’ research, respectively, is sought.
Other specific areas of research within the CCCRP at the US AISR include:

- bone regeneration and soft tissue;
- clinical trauma (following up basic and pre-clinical research with clinical studies) – including studies in haemoglobin-based oxygen-carrying capacity resuscitation fluid, antimicrobial polymer dressing for superficial wounds, coagulation dynamics, monitoring devices and pain management techniques;
- damage control resuscitation;
- pain management; and
- trauma informatics.

Research at the US Armed Forces Institute of Regenerative Medicine focuses on developing advanced treatment options, using regenerative medicine techniques for severely wounded soldiers. It is concerned with increasing the speed of delivering the promise of regenerative medicine, and its active research areas include bone repair, craniofacial reconstruction, limb and digit salvage, scarless wound healing and compartment syndrome. The main funding partners include the MRMC, Office of Naval Research, US Air Force, Office of the Surgeon General, National Institutes of Health, Office of the Director, Department of Veterans Affairs, and Department of Defense, Health Affairs. Of these, the National Institutes of Health and Department of Veterans Affairs are the only two civilian partners. However, the US Armed Forces Institute of Regenerative Medicine is also made up of two civilian research consortia that work with US AISR. One consortium is led by Wake Forest University and the McGowan Institute for Regenerative Medicine in Pittsburgh, and the other consortium is led by Rutgers University and the Cleveland Clinic.

The US Army is not the only military group active in complex trauma research. The Naval Medical Research Unit conducts combat casualty care research, along with dental and biomedical research. The three main research areas for this unit include resuscitative medicine, trauma medicine and expeditionary medicine. Examples of joint funding and research between the navy and the MRMC were identified above, and it is likely that other pockets exist. In addition, army, navy and air force medical personnel routinely report to civilian trauma centres for further training. The US Air Force runs the Centre for Sustainment of Trauma Readiness Skills (C-STARS), a programme developed after the events of September 2001 to give air force medics hands-on clinical experience throughout the entire spectrum of civilian acute trauma care. The programme began at the Baltimore Shock and Trauma Centre, and now two other programmes are active at Saint Louis University and another at the University Hospital of Cincinatti.13

Finally, US military funding and collaboration plays a role in the UK research landscape. The USA and the UK share hospital sites in Afghanistan (NAO, 2010b), and UK military medics are seconded to US AISR in areas of UK strategic interest (currently, vascular trauma and body trauma). These relationships present multiple opportunities for joint learning. One example we discussed with an interviewee included comparative research into patient outcomes based on different treatment guidelines on the battlefield. This and

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13 More information can be found at: http://www.sg.af.mil/history/section11.asp.
other areas of collaboration could provide invaluable insight for both UK and US researchers. More importantly, though, the US military seems to have strong and well-developed links with civilian researchers, and throughout the US military apparatus (across army, naval, air force, etc). Thus, there are many different models and opportunities for the UK to learn from the US experience in integrating complex trauma research across the military and civilian sectors.
## Complex trauma research in the USA (civilian)

Select list of some leading civilian research centres (not exhaustive)

- R Adams Cowley Shock Trauma Center at the University of Maryland Medical Center
  - Previous research includes extra corporeal lung support, hyperbaric therapy and soft tissue infections
- University of California San Francisco and San Francisco General Hospital Trauma Center
  - Home to the Orthopaedic Trauma Institute (and the Traumatic Brain Injury Program)
- Massachusetts General Hospital
  - The Trauma Research Laboratory conducts basic research into major trauma
- Center for Integration of Medicine and Innovative Technology (CIMIT)
  - Has a significant Trauma & Casualty Care programme, in addition to a Traumatic Brain Injury and Neurotrauma programme
  - UK sister institution at the University of Manchester (MIMIT)

The previous slide addressed leading US military research programmes relevant to complex trauma. This slide considers a select list of some of the leading civilian research centres in the USA. An initial list for consideration was generated through discussion with UK experts during the interviews, and further web-based searches helped to complete the review. We are conscious that this list is not exhaustive, and so we present it as indicative of the geographic range and disciplinary scope of complex trauma research in the USA. Moreover, we are conscious of the differing nature of complex trauma injuries in a civilian context in the USA where, for example, gun injuries are much more common than in the UK. Inevitably this will have an impact on the type of research conducted and, although resource constraints prevented us from exploring this issue in detail, it is worth bearing in mind when drawing comparisons between the UK and USA.

The R Adams Cowley Shock Trauma Center at the University of Maryland Medical Center was mentioned frequently by interviewees as a leading trauma center for patient care. The affiliated research programme is the Shock, Trauma and Anesthesiology Research Organised Research Centre (STAR-ORC). It serves as an umbrella research organisation for the Department of Anaesthesiology and the Program in Trauma at the Maryland Medical School. STAR-ORC is dedicated exclusively to the study of trauma, its complications and prevention. Research work focuses on brain injuries, critical care and organ support, resuscitation, surgical outcomes, patient safety and injury prevention. It is also home to the National Study Center for Trauma and Emergency Medical Systems, which is focused on improving the delivery of trauma care. Other areas of active research at STAR-ORC which are relevant to DH interests in complex trauma include:

- decompressive craniectomy trials;
- injury epidemiology, with a focus on motor vehicle accidents;
- molecular mechanisms underlying ischemic and traumatic brain injury;
- study of real-time vital signs data to predict life-saving interventions;
- field collection of vital signs and imaging for trauma and mass casualty care; and
- neural cell death and other neurological implications of trauma.

The description of its research into trauma care provided by the National Study Centre highlights the military and civilian benefits of the research, suggesting that there is potential for spillover benefits from integration.

The University of California at San Francisco, the San Francisco General Hospital Trauma Center, Massachusetts General Hospital and the Rocky Mountain Regional Trauma Center in Denver, Colorado were all mentioned by multiple experts as having expertise in complex trauma research. The University of California at San Francisco and the San Francisco General Hospital Trauma Center are home to the Orthopaedic Trauma Institute and the Traumatic Brain Injury Program. The Institute is one of 12 core clinical centres in a Department of Defense-sponsored Extremity Trauma Clinical Research Consortium and the Traumatic Brain Injury Program, providing further evidence of integration between civilian and military-funded complex trauma research. Massachusetts General Hospital has a trauma research laboratory at the hospital which conducts basic research into major trauma, including control of bleeding, improved resuscitation strategies, treatment of central nervous system injuries, tissue preservation strategies, treatments for septic shock, and the development and testing of blood products. Research at the Rocky Mountain Regional Trauma Center at the Denver Health Medical Center has focused on topics such as coagulopathy and indications for prophylactic or therapeutic interventions in a clinical setting.

Finally, the Center for Integration of Medicine and Innovative Technology (CIMIT) is a consortium of Boston teaching hospitals and schools fostering interdisciplinary collaboration among experts in medicine, science and engineering. Importantly, there is an explicit focus on translation of research from pre-clinical to clinical and on new technologies for addressing medical challenges, especially those addressing soldier care and disaster response, which makes it of interest for the DH. It has a significant Trauma & Casualty Care programme, in addition to a Traumatic Brain Injury and Neurotrauma programme. There is a UK counterpart of CIMIT based at the University of Manchester. Manchester: Integrating Medicine and Innovative Technology (MIMIT), is a collaboration between the university and Greater Manchester NHS and Primary Care Trusts and is the first international affiliate of CIMIT. Although there are some projects that seem to have relevance to complex trauma research, for example one study entitled ‘Peripheral Nerve Repair Using a Novel Fabricated Polymer Conduit’ and another entitled ‘The Development of a Blood Transfusion Trigger Using Near Infrared Spectroscopy (NIRS)’, there is no dedicated programme in complex trauma research at MIMIT. This suggests that there may be scope for strategic engagement with MIMIT and leveraging of the CIMIT relationship to have a more targeted focus on complex trauma research in the future.

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Complex trauma research in Israel

- Trauma care is fairly politicised in Israel, with debates about the levels and nature of investment in hospital trauma centres.
- Currently there are six hospitals which handle major trauma cases: Rambam, Beilinson-Schneider, Sheba, Tel Aviv Sourasky, Hadassah-Ein Kerem and Soroka.
- Research institutions publishing most frequently in major trauma include Tel Aviv Hospital and Medical Centre, Hadassah University Hospital, Rambam Medical Centre, Hebrew University Jerusalem.
- A national trauma registry is maintained by the Israel National Center for Trauma & Emergency Medicine Research.
  - The Israeli military medical corps maintains its own trauma database.
- There is a permanent medical corps in the Israeli Defense Forces, but civilian medical professionals do rotate into the Forces for active duty.

Israel was mentioned by some of our interviewees as having an international reputation in trauma research, care and treatment. They suggested that complex trauma research in Israel is advanced in areas including wound management, and blast and ballistics management. However, detailed information about specific research programmes was difficult to identify, both from expert interviews and from the rapid review of Israeli funding bodies, research centres and publications. Therefore, our approach to the review of complex trauma research in Israel took a slightly different track than that for the USA, in that we relied more on rough bibliometric analysis and published literature and review articles for insights into the nature of complex trauma research, treatment and care in Israel.

Our review suggests that trauma care is a fairly politicised topic in Israel, with debates about the type of care that should be provided across the country, the level and nature of investment in hospital trauma centres and (it is likely) associated research programmes. Israel, like most developed countries in the world, has adopted an Anglo-American system of emergency care (where the patient is brought to the hospital for their treatment, as opposed to on-site treatment at point of injury). However, emergency medicine was only established as an independent area of medical specialisation in 1999, which is a very recent development (Halpern et al., 2004), especially in contrast with the UK and USA.15

The debate regarding trauma care in Israel revolves around whether there should be trauma care teams in every hospital, or whether there should be investment into selected highly specialised hospitals. In a review by Stein (2006), the first position is summarised as

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15 In the UK the first consultants in accident and emergency medicine were accredited in 1972, and the first formal emergency medicine residency training programmes began in the USA in the late 1970s.
deriving from the conviction (held by at least some in the Israeli Ministry of Health) that all Israeli hospitals should be able to cope with complex trauma due to the country’s political and military volatility. The second position argues that major outbreaks of war are relatively rare, but small-scale terrorism is frequent: thus it would be more sensible to orientate the system towards investment into designated, specialised trauma centres in specific high-risk areas (Stein, 2006). Despite the politics, the reality is that the trauma system operates in a manner similar to the second position, where investment goes into highly specialised hospitals and patients are transported to these designated centres (Stein, 2006, p. 136). Interestingly, the evidence shows that trauma cases related to terrorism are not a frequent occurrence. Terror and combatant activity constitute fewer than 4% of all trauma cases, while falls and road accidents constitute the majority of trauma cases (but not necessarily major trauma).

Currently there are six hospitals which can handle major trauma cases: Rambam, Beilinson-Schneider, Sheba, Tel Aviv Sourasky, Hadassah-Ein Kerem and Soroka. Rough bibliometric analysis shows that most publications in major trauma are from the following institutions, all of which have affiliations with at least one of the major trauma hospitals, including Tel Aviv Hospital and Medical Centre, Hadassah University Hospital, Rambam Medical Centre and Hebrew University Jerusalem. A similar analysis of publications in the last three years under a subject heading search of ‘major trauma’ have been in the area of coagulopathy, acute injury topics, medical simulation and trauma response modelling.

A trauma registry was established in Israel in 1995 and is maintained by the Israel National Center for Trauma & Emergency Medicine Research. The Center works closely with all the level 1 trauma hospitals in the country to maintain the database. Areas of complex trauma research at the Center include terror-related injuries, road traffic injuries, burn injuries and management of mass casualty events. The Israeli military medical corps maintains its own trauma database and we could not identify any information about the type of data held on this system.

Although there is a permanent medical corps in the Israeli Defense Forces, civilian medical professionals continually rotate into the Forces for active duty. This would suggest that military and civilian medical skills capabilities are being exchanged to some extent, but we cannot fully verify this. However, some have argued this is not the case, as the mere presence of rotating medical staff does not necessarily translate into improved major trauma treatment and care, and there is a need for dedicated specialty training in emergency medicine within the Forces (Gutman, 2006). Historically, there have been issues about medics’ ability to practise major trauma skills when not serving (Ben-Abraham et al., 1999; Gutman, 2006). Despite this, there are examples of close integration and opportunities for learning, even when medical personnel are not on active duty. The provision of air transport services for complex trauma care is done solely by the military. Tel Aviv University Hospital provides a resuscitation and emergency medicine training and education programme for medical and non-medical professionals, and the Israel Center for Medical Simulation, based at the Sheba Medical Center, trains Forces personnel for mass casualty scenarios. Overall, then, the situation in Israel seems mixed, with less readily available evidence than in the USA for the effectiveness of integration between civilian and military complex trauma research.
Our hypothesis for the international review was that complex trauma research was a niche area of research in Israel and the USA, and that integration between military and civilian sectors could be strengthened. While we were not able to conduct a detailed enough review to determine whether complex trauma truly is a niche or ‘orphan’ area of research in Israel and the USA, the entirety of the evidence found in this rapid review does seem to suggest that due to the specialty skills needed for complex trauma research and treatment, it is a niche area of research on this basis. While it does not seem to be an ‘orphan’ area in the USA due to the strong military role in funding intramural and extramural research programmes, the evidence for this in the Israeli context was not forthcoming. In addition, while we can conclude that civilian and military integration is strong in the USA, mixed messages emerged from the Israeli context, and therefore no definitive conclusions could be made.

Our analysis of military and civilian complex trauma research and infrastructure in the USA suggests that trauma research is probably a niche area, but overall research capability and capacity in both civilian and military contexts seems higher than in the UK. This may be due in part to a larger and better funded medical research sector overall, but also to a wider array of trauma cases presenting themselves in the USA where, for example, gun wounds are more prevalent. In addition, US civilian and military sector researchers and healthcare specialists seem to be well integrated. There are multiple research and training programmes across military and civilian contexts, and across a range of disciplines and medical areas in complex trauma treatment and care. In addition, the US military plays an active role in funding and managing civilian and military research programmes.

Detailed information on specific complex trauma research programmes in Israel was difficult to find, but bibliometric analysis suggests that most research is centred on the level
1 trauma hospitals and affiliated university research centres. Expert opinion suggested that researchers in Israel held particular expertise in blast injury and wound management, although we could not verify this with additional evidence. We might tentatively say, based on the research identified, that expertise is particularly strong in some areas, but not as wide-ranging as seen in the USA. In principle, civilian and military medical professionals are integrated as a result of the nature of military service in Israel, however some evidence suggests that dedicated attention is needed to maintain medical capabilities in complex trauma when civilians are not on active duty.
This final chapter summarises the findings presented in the earlier chapters, and makes recommendations on where improvements might be made, strategic engagements sought and opportunities realised within the area of complex trauma. First it summarises UK centres of excellence which were identified over the course of our review. Second, it goes on to discuss the nature of complex trauma research, including main funders and funding activities, the types of research which are ongoing and issues which seem to be facing the field. Third, it relates specific gaps, barriers and opportunities in the area of complex trauma research in the UK. Finally, it makes recommendations on the basis of these conclusions as to how the DH and MoD might strengthen their engagement and support the field moving forward. In drawing these final conclusions and recommendations, we stress again the rapid nature of this review and the constraints on the breadth and depth of research that we were able to undertake in the four-week period during which the research was undertaken. Therefore, the conclusions should be interpreted with caution and a more thorough mapping process and review is needed to assure full robustness.
We have found that centres of excellence and researchers dedicated to major trauma are limited and exist in pockets. This conclusion is based on interview data and supported by rough bibliometric analysis looking at the main institutional addresses of academics with high publication counts relative to other institutions within the search. The institutions and areas of field-specific expertise we identified through this process include:

- The Royal London Hospital (major trauma)
- University of Oxford (trauma and orthopaedic trauma)
- University of Manchester (research and innovation programme through MIMIT)
- Imperial College London (expertise on blast effects on bone and soft tissue)
- Selly Oak Hospital and University Hospitals Birmingham NHS Foundation Trust hospitals have good clinical work
- Universities of Leeds, Sheffield and Bradford (regenerative medicine)

Experts told us that there were fewer than five, and possibly no more than two, centres in the UK capable of handling major trauma cases. This limits the extent to which clinical and academic work can coexist, but we do not know the extent to which this also might be impacted by a lack of complex trauma patients in the UK (although the interview data suggest that this may be the case). In addition, many experts stated that they would go to different places for different types of expertise, but there were few places that they would go to for expertise in everything. Many felt that improvements could be made by drawing on researcher strengths and knowledge across a range of disciplines. It was also suggested...
that the capacity within the military for complex trauma research may be lower than that seen in academic and clinical research conducted in universities and hospitals, due in part to limited researcher time and willingness. Moreover, the sustainability of clinical patient populations in the military was raised as a concern, and so any future strategic integration between the two sectors should keep this in mind.
We have looked across the majority of funders of complex trauma-related research in the UK and found that complex trauma research seems to be an ‘orphan’ area of medical research, with approximately £15m in funding per annum. This is less than 1% of all public funding on health R&D, and far less than 1% of all private and public funding on health and medical R&D in the UK.

In addition, we have found that there are definitional problems with classifying complex trauma research. Much of the research in the broader fields of trauma or injury can be ‘re-badged’ as complex trauma research, when in fact they may be only related to an aspect of trauma research, for example bone injury. In this case, while orthopaedic research may be highly relevant to complex trauma treatment, the context of major trauma means that the nature of research and, in particular, the clinical translation and application, is different. However, this is not to say that learning cannot be both exported and imported across trauma and injury research areas. For example, one rehabilitation researcher regularly applies techniques from areas such as geriatric care to complex trauma rehabilitation. Similarly, regenerative medicine is not conducted with the context of complex trauma in mind, but the interventions developed will be relevant. Therefore, although funding streams and expertise in complex trauma research are limited, there is scope to grow the field through careful attention to these areas of intersection. Both the dangers of ‘re-badging’ and the awareness of synergies are critical to bear in mind when developing a long-term funding strategy in this area.

Finally, of the complex trauma research that is done in the UK, there is an uneven distribution of research in the priority areas. The majority of the research is in the areas of acute injury, while little work is done in the area of medical simulation, disaster response modelling and infection and wound management. While we did not get a sense of
distribution across basic and clinical research (due to the scope of the review), there does seem to be a need to look afresh at the balance across the DH priority areas. Many interviewees commented on the need for a better and more integrated approach to research in the field, in particular one that adopted a systems-level approach to complex trauma research. One interviewee said that the real challenge in this was developing systematic understanding in a way that encouraged people to cross disciplines to foster understanding and learning. Such an initiative could be achieved through taking the opportunity to develop an overarching strategy for the field, a topic addressed in the next slide.
Our findings have led us to identify a set of gaps, barriers and opportunities in the field of complex trauma research. First, there is a lack of capacity and infrastructure to support complex trauma research and clinical trials on a large scale. In particular, although clinical trials and clinical intervention studies are occurring, there are significant barriers including lack of funding for the translational stages of research leading to clinical trials, inherent difficulties in patient recruitment, and inadequate infrastructure to support large-scale clinical trials of the kind needed for complex trauma clinical research.

The latter of these points relates strongly to the one made previously about the lack of centres of excellence in the UK which are capable of conducting all aspects of complex trauma care and research. The lack of capacity seems to stem in part from the fact that there are fewer than five centres capable of supporting a large-scale clinical trial in complex trauma. One expert talked us through the difficulties in setting up a clinical trial, from training ambulance staff to all the nurses who might be on duty, to ensuring that all doctors in the needed specialities are trained in the trial as well. These issues of infrastructure, patient enrolment and funding were all singled out by the interviewees as significant barriers to commercialisation, and given as possible reasons for market failure and lack of pull-through of research findings into new medical technologies and applications. In addition to this, at least one interviewee mentioned the regulatory burdens in the UK on clinical trial research as a barrier to international competitiveness.

This underscores the need for strategic thinking so that limited resources and research capabilities are utilised in the most efficient way. Currently, it appears there is a lack of strategic focus on the direction of complex trauma research in the UK and there is sub-optimal utilisation of the limited resources, both monetary and human-based, that exist.
Therefore, there is an urgent need for coordination among funders and researchers. We were told during the interviews that the establishment of regional trauma networks and the appointment of a national director of trauma were steps in the right direction, but these efforts need to be scaled up and better coordinated to be effective. Many experts we spoke with felt that efforts had stalled.

Second, there is a missed opportunity for learning between military and civilian researchers and care providers in this field – a view also supported by the Healthcare Commission (2009). Our review of the situation in Israel and the USA suggests that integration between the military and civilian sectors has the potential to yield a stronger research sector that delivers real clinical benefits for both military and civilian patients across the country. However, like any strategic endeavour, this must be managed carefully to ensure that an appropriate balance of research in priority areas for both sectors is obtained. Gabrielle Giffords, the US congresswomen shot in Arizona in January 2010, was the beneficiary of life-saving brain surgery techniques developed on the military battlefield. A recent article in Science also highlighted the spillover benefits from medical research in the military, going back to the First World War (Bohannon, 2011). Thus, although the situation may be improving in the UK, with the recent opening of a joint hospital and research centre in Birmingham, there are still important lessons to take on board, including management of patient populations, geographic distribution of researchers and awareness of different healthcare contexts for the translation of research findings. Moreover, more strategic and coordinated international research collaborations could help these efforts, as well as those directed at improving the niche and 'orphan' status of complex trauma research in the UK.
We were asked to conduct a rapid review of the funding landscape for complex trauma research in the UK. Our findings would feed into ongoing strategic discussions between the DH and the MoD. Based on this, we offer the following recommendations for consideration and future decision-making.

Trauma research is an ‘orphan’ field of research which is disproportionately funded relative to the monetary burden of the disease. Therefore, a compelling case can be made that the field is under-resourced.

If a research programme in complex trauma is established, definitions need to be agreed and protection against mission creep put in place. Definitional issues are important and blurring at the boundaries of ‘major trauma’ and ‘trauma’ research will need to be managed.

The research community is small. Improved coordination and strategic thinking among researchers and funders could lead to significant steps forward in the research landscape. We recommend that a workshop bringing together researchers across all priority areas in complex trauma should be held as soon as possible, in order to identify where research gaps exist, where synergies can be exploited, and where and how a strategy for the field might be articulated.

There are significant and deep-seated institutional and infrastructure barriers to bringing new research and medical technologies to market in the field of complex trauma. Funding and patient enrolment is an important part of this storyline.

We recommend that these issues be critically explored and engagement with the private sector strengthened in order to understand where the biggest gaps in translation exist, and how to overcome them.
There are cultural and regulatory barriers between civilian and military researchers. This has led to significant unrealised potential in learning between each sector.

*We recommend that in the short term, researchers and practitioners should identify gaps and opportunities and seek to understand each other’s markets. In the medium to long term, joint research and training programmes should be established to facilitate learning and integration, especially in light of the declining numbers of patients expected at Selly Oak Hospital.*

A research strategy will have to address two key issues: (1) capacity and capability building; and (2) incentivising collaboration between different research fields, sectors and internationally.

*We recommend that a ‘sandpit’ approach might be employed, where researchers are asked to develop funding proposal(s) based on a set amount of research funds.*

Future mapping research, of the kind undertaken for this rapid review, can help to inform the development of a long-term strategy.

*We recommend that future mapping work is undertaken in the following areas:*  
  
  - a detailed review of ‘market’ and ‘clinical’ gaps and an assessment of whether current research is addressing these gaps;  
  - a more thorough and systematic review of the international landscape and identification of opportunities for collaboration across countries, where appropriate;  
  - a comparison with other areas of ‘orphan’ research and identification of lessons that can be learned across sectors; and  
  - an assessment of specific examples and areas where research can and is being imported into the field of complex trauma, with analysis of areas to build on going forward.

*In addition, a detailed bibliometric analysis can provide valuable insight into the nature of the field and its subject area and disciplinary composition, as well as allow for benchmarking of research performance and centres of excellence within the UK against other international groups.*
References


Annex A: Interview protocol

Interviewees

<table>
<thead>
<tr>
<th>Name</th>
<th>Speciality</th>
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<tbody>
<tr>
<td>Expert 1</td>
<td>Tissue and bone banking; coagulopathy</td>
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<tr>
<td>Expert 2</td>
<td>Anaesthesia and medical modelling</td>
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<tr>
<td>Expert 3</td>
<td>Pharmaceutical and regenerative medicine (biofilms)</td>
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<tr>
<td>Expert 4</td>
<td>Trauma care and orthopaedic research</td>
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<tr>
<td>Expert 5</td>
<td>Emergency medicine</td>
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<td>Expert 6</td>
<td>Rehabilitation</td>
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<tr>
<td>Expert 7</td>
<td>Plastic and reconstructive surgery</td>
</tr>
<tr>
<td>Expert 8</td>
<td>Military and defence medicine</td>
</tr>
<tr>
<td>Expert 9</td>
<td>Trauma sciences and coagulopathy</td>
</tr>
<tr>
<td>Expert 10</td>
<td>Skin and wound healing</td>
</tr>
</tbody>
</table>

Topics

The interview will cover four main subject areas:

1. research description of the interviewee, focusing on sources of funding, clinical applications and research priorities
2. the state of research in the UK in the priority areas (strengths, weaknesses, centres of excellence, nurturing next generation of academic consultants, researchers, etc)
3. the position of the UK relative to other international efforts
4. future UK strategy and research priorities.

Questions

1. Description of interviewee’s research in relation to the five priority areas, particularly focusing on sources of research funding, clinical application(s) and research priorities
   - Nature of research:
     - What is your primary area of expertise? What is your secondary area of expertise?
     - What proportion of what you do is basic versus applied or clinical research?
○ How much of your research is collaborative and/or multidisciplinary?
Who are your collaborators?
○ What is the primary institutional setting for your research?

• Funders:
○ Who are your main funders? Is most of your funding core or soft? Public or private? Charity? Industry partnerships? Average length of a grant?
○ Do big pharmaceutical companies fund any of your research? Are you aware of any colleagues who have pharmaceutical company funding?
○ How do you identify sources of funding? Is it a proactive or reactive process?
○ Is collaboration necessary for funding?

• Military interactions:
○ What, if any, interactions with the military/defence establishment/emergency medicine do you have in your research activities?

• Clinical applications:
○ Are you involved in any pre-clinical or clinical trials at the moment? What stages? Where is the investigation occurring? What is the likelihood of approval? Was it your research which led to the investigation or someone else’s? Do you know when the original research began?
○ Was there ever any research that should have reached clinical trial stage and didn’t? Why did this happen?
○ What are the main barriers in the clinical application pipeline? Are these different, in your view, from other areas of biomedical research and clinical medicine?
○ Generally speaking, what is your sense of the level of market failure in this area? Why does it happen?

• Research priorities:
○ How do you identify research priorities?
○ Do you have a sense of how funders identify research priorities?
• Can you provide technical background or illustrative examples of your research where relevant?

2. State of research in the UK in the priority areas (areas of strength, weakness, centres of excellence, etc)

• Centres/researchers of excellence:
○ Who or where are the research leaders in the UK in this area, in your opinion?
○ Is there significant regional disparity? If so, what factors cause this?
What is the infrastructure for research in this field like? Does this differ from care/treatment?

- **Dissemination:**
  - Apart from publications, what efforts do you make to disseminate the results of your research? Who do you work with to do this?

- **Impact:**
  - Are you aware of your research improving delivery of services and thereby patient outcomes in any major way at the national or international level?

### 3. Position of the UK relative to other international efforts

- What is the state of your field of research in the UK relative to other countries?
- Do you coordinate on international research initiatives? Can you describe them?
- Are there particular centres that you would want to collaborate or coordinate with on their initiatives?

### 4. Perception of UK strategy and research priorities in the field of complex trauma treatment and care

- **Strategic vision:**
  - What is your perception of UK strategy for complex trauma treatment and care and the relative research priorities? How easy is it to get funding here? What is the relative position of the UK to other countries?
  - What needs to be done that currently isn’t being done in your field and why? What barriers are there to getting this research done?

- **Challenges:**
  - What are the biggest challenges facing complex trauma research in the UK? Does this differ at the international level?

- **Future priorities – big picture funding:**
  - Roughly how much do you estimate is spent on complex trauma research per annum? If that was to be reduced by 75% across the board, how would you refocus your priorities? If funding was increased by 150%, what else would you do?