NIHR Service Delivery and Organisation programme

NHS National Institute for Health Research

SDO Protocol - project ref: 09/1001/37
Version: 1
Date: 01/09/10

A Systematic Review of clinical outcome and cost effectiveness comparing a policy of triage and direct transfer to specialist care centres with delivery to the nearest local hospital

Chief investigator	Dr Alastair Pickering
Sponsor	University of Sheffield
Funder	SDO Programme
NIHR Portfolio number	n/a
ISRCTN registration (if applicable)	n/a

A Systematic Review of clinical outcome and cost effectiveness comparing a policy of triage and direct transfer to specialist care centres with delivery to the nearest local hospital

Research Question:
In pre-hospital patients, does triage to centralised specialist services result in a cost-effective improved clinical outcome compared with transfer to the local hospital for initial diagnosis, treatment and subsequent referral if appropriate?

Aim:
To enable evidence-based policy decisions about the reconfiguration of hospital and pre-hospital services specifically on the clinical and cost effectiveness of bypassing local hospitals to transfer emergency patients directly to specialist care centres.

Objectives:

- Perform a systematic review of the evidence for a policy of triage and direct transfer to specialist care centres in three clinical conditions. These are:
  - Multi-system trauma (classed as major/severe)
  - Stroke
  - Head injury
- Identify previous relevant reviews that compare directly the clinical effectiveness of different transfer strategies
- Identify current recommendations for best practice for acute management of the three clinical presentations specified.
- Develop evidence-based models for each decision-making strategy with assessment of both clinical and cost-effectiveness, including potential secondary effects of service reconfiguration.
- Provide recommendations for areas of primary research

Background:
The current status of Specialist Care centre development:
In the Department of Health report 'High Quality Care for All: NHS Next Stage Review' (1) Lord Darzi presents a compelling argument for saving lives by creating specialised centres for major trauma, heart attacks and strokes. The idea of centralisation is discussed in more detail by other public policy review groups with an increasing call for such reconfiguration of medical services (2-3)
The case for centralisation has been made on the grounds that:

- Institutional and individual competence needs to be maintained to achieve the improved outcomes in morbidity, mortality and error rates by treating higher volumes of complex cases;
- Financing specialist care can be expensive and pooling the limited resources (human and financial) available would allow for maintenance of equipment and safe levels of staff (24 hours a day, 7 days a week) with the required expertise for certain treatments, which may not be viable for all hospitals.
- The changing restrictions on junior medical staff working patterns and training have created opinion that alternate practices may be required to maintain the quality of care that the public expect from the NHS.

However, the Academy of Medical Royal Colleges produced a working party report on 'Acute Healthcare Services' (4) in which one of the key issues was that

> "Although there is evidence to suggest that the centralisation of services to deal with complex or specialised work provides better outcomes for patients, evidence for centralisation of non-complex and high volume cases does not exist."

The report highlights a number of specific issues about centralisation of services including the safety and reliability of pre-hospital triage systems, the quality of patient care during transfer and the impact of bypassing the nearest hospital to go straight to the facility most capable of providing definitive care for the patient. Concerns are raised about the recognition of the requirement for an appropriate increase in resources, not only for service capacity but also for training of staff.

In addition, variation in transfer times to a centralised resource depending on the geographical setting may have a variable effect on patient outcomes, with a potential for harm. Indeed evidence exists that increasing journey distance to hospital increases mortality rates for category 'A' patients. (5)

Existing Research:

Trauma services:

Centralisation of trauma services has been debated for some time after introduction of regional trauma systems in North America appeared wholly successful in improving mortality rates for major trauma patients (6-7) These two systematic reviews identified 47 papers evaluating the effectiveness of trauma systems based on specific methodological criteria from a combination of data sources (data registry, population based studies and panel reviews). The conclusions were similar in that those taken directly to a tertiary trauma centre had a lower mortality rate than those transferred from other hospitals.(8) However, the authors repeatedly comment on the moderate quality of the papers assessed and the need for outcome measures other than mortality. This work has led to the general belief that high volume centres have better outcomes for patients with more complex injuries or severe head injuries (9) although this has been disputed for general trauma patients.(10)

Superficially, evidence would suggest that such service reconfiguration would result in considerable patient care benefits (namely reduced morbidity and mortality) and the Royal College of Surgeons and British Orthopaedic Association's 2000 report "Better care for the severely injured"(11) argues for the implementation of a 'hub-and-spoke' 3-tiered trauma system in the UK for hospital services. Extrapolating from a retrospective study of avoidable deaths, they estimate that universal access to specialist trauma centres could save around 770 extra lives every year. This system would be inclusive of the current district general hospital (DGH) network and the majority of mild and moderately injured patients would still be managed locally at these DGH's. However, the severely injured would be fewer in number, estimated at 4 cases for every million inhabitants of the UK per week, and the specialist skills to care for these patients are best pooled in the 'trauma centres' to increase exposure and improve outcomes – based at the hub of the model. These hubs are then available to assist in the training of the regional trauma network developed around them. The concept of this kind of 'inclusive' trauma system as opposed to some US models of an 'exclusive' trauma centre, involving bypassing local non-designated hospitals, does demonstrate improved patient mortality rates. This is despite similar triage rates to the regional trauma centre for all trauma patients.(12)

Nevertheless, the applicability of US based trauma registry data to the NHS has been questioned. Nicholl reported on the effectiveness of a regional trauma system, in the

West Midlands, in reducing mortality and demonstrated little difference when compared with two UK control regions, during the first three years of implementation. (13) As this system has matured the overall mortality has reduced to somewhere near that of similar North American services (14) but this has not been compared with general improvements in trauma care in non-regionalised services. US studies often allow statistical adjustment for system maturity and it has been suggested that it can take up to ten years to stabilise through the transitional period. (15)

Stroke

In two reports for the Department of Health, a compelling argument is made for the development of specialist stroke units to which stroke patients are transferred directly by the ambulance service to receive their care.(1, 16) The background to this is the increasing body of evidence for early interventional therapy, namely thrombolysis,(17-19) and the coordinated care during rehabilitation that specialist units are able to provide.(20) Outcomes from such services are consistently better than those reported for conventional medical ward treatment. However the Sentinel audit for stroke (21) highlights a number of areas for improvement, in line with other countries, and there is a determination to improve the situation within the UK.

Current National Institute for Clinical Excellence (NICE) (22) and Royal College of Physicians (RCP) (23) guidelines on stroke management recommend CT and thrombolysis within three hours of symptom onset as the gold standard of treatment for most acute stroke patients. To achieve this target early recognition of symptoms and signs has become a focus strategy for development and triage tools have been validated for use in the pre-hospital setting. In the UK this is currently the Face Arm Speech Test (FAST) screening tool, which has been shown to have a positive predictive value (PPV) of 78% (95%CI 72-84%). A more accurate tool has been validated as an assessment tool for use in the emergency department, the Recognition of Stroke in the emergency room (ROSIER) scale, which resulted in much higher sensitivity (93%) and PPV of 90% (95%CI 85-95%).(22) These tools are being assessed for use by the ambulance service, within the stroke research network (ISRAS study), to facilitate appropriate transfer of patients directly to the regional stroke unit, bypassing the local hospital and emergency department.

In the NICE guidelines the benefits of early management on ‘acute’ stroke units was reviewed (when compared to standard medical wards) and the lack of high-quality evidence was noted although they identified 8 studies and a Cochrane review (sub-analysis performed). The expert panel reached a consensus opinion that ‘…there needed to be a very good reason not to generalise overall stroke unit results to those in the acute setting.’

With a final recommendation that all people with suspected stroke should be admitted directly to a specialist acute stroke unit following initial assessment either from the community or emergency department.

Regarding brain imaging in stroke patients, the same guidelines concluded that CT scans performed as early as possible provided the most cost effective management strategy. The evidence for thrombolysis repeatedly comments that “Time is Brain” and the outcomes for those thrombolysed within 90 minutes are better than for those beyond this time.(18) Coupling this with the cost-effectiveness of early scanning, enabling emergency department staff to manage the acute phase of this condition with subsequent transfer to the specialist unit following safe treatment could reduce the initial delays associated with direct transfer over greater distances, in particular in more rural areas of the UK.

Whilst the role and benefits of specialist stroke units are apparent from the evidence, the administration of thrombolysis need not be specific to such acute units and could easily be performed in the emergency department, prior to subsequent appropriate referral. The 2007 Cochrane review on thrombolysis (19) concludes that further trials are needed to identify which patients are most likely to benefit from treatment and the environment in which thrombolysis may best be given in routine practice.

Head Injury

The difficulty with this patient group lies in the fact that clinical assessment cannot be easily backed up with a simple pre-hospital test to confirm diagnosis, as is the case with STEMI. The NICE guidelines for head injured patients identify the figures of 8% suffering intracranial injury and 1% requiring neurosurgical intervention, based on CT findings, and these guidelines provide a clinical decision making framework within which to triage patients to CT scan. (24)

A modelling approach has been undertaken in the North Staffordshire region to assess the impact of different bypass strategies in patients with serious head injury. This was limited to mortality data rather than morbidity and costs, and whilst an improvement in service resulting in an extra 3.2-4.5 per 100 patients surviving if transferred direct from scene to the neurosurgical unit, the triage necessary in the pre-hospital phase was an artificial scale (Abbreviated Injury Scale (appendix 1) score of 3 or greater) and difficult to put in to practice in the reality.(25) Evidence for the time criticality of neurosurgical intervention is difficult to interpret, with the literature suggesting improved mortality figures when acute extra-dural and sub-dural haemorrhages are evacuated within 2-4 hours.(26-27) The difficulty in establishing a more accurate time frame for benefit is that often the more severely injured cases will be operated on earlier in the course of the bleed and can skew the mortality figures to being worse for earlier operation. It is generally agreed that the earlier decompression can be achieved the lesser the effects of secondary brain injury and the better the outcome for the patient.

An observational study on behalf of the UK Trauma Audit and Research Network (TARN) (28) looked at trends in head injury outcome and identified that patients suffering a severe head injury had better outcomes managed in a neurosurgical centre. Treatment in a non-neurosurgical centre was associated with a 26% increase in mortality and a 2.15-fold increase in the odds of death adjusted for case mix compared with neurosurgical centre treatment. The authors comment that despite this evidence, and current RCS England guidelines, there persists a reluctance to accept non-surgical severely head injured patients to specialist centres, which may be driven by the limited facilities and resources, resulting in surgical lesions taking priority. Only 53% of patients with severe head injury were transferred to receive neurosurgical or neurointensive care. This demonstrates the difficulties with pre-hospital triage to specialist centres that could develop as services become swamped with non-surgical patients to the potential detriment of those requiring urgent surgical intervention.

NHS need for proposed research:

Acute service reconfiguration is at the forefront of NHS strategic planning with an increasing call for the development of regional specialist centres. Three key clinical areas in which these changes have been proposed are major trauma, stroke and head injury.

The proposed research examines the evidence for such reconfiguration planning with respect to improving patient outcomes and aims to quantify the benefits of such strategies. The current system of treatment at the nearest local hospital may demonstrate unnecessary risks for patients who could be better treated in a regional centre. Modelling the clinical outcomes for each strategy will enable estimates of both healthcare improvement and cost effectiveness for the restructuring plans within a resource limited NHS.

The issues being addressed in this project are likely to remain highly relevant and important to service delivery in the NHS and will impact on future strategic planning for improving patient care with these common conditions. The project will inform future service development for the acute management of these key conditions.

Three key clinical areas that are focused upon in the aforementioned policy reports (1-4, 16) are major trauma, stroke, and ST elevation myocardial infarction (STEMI). Specialist services for head injury are partly encompassed by the trauma network.

Major trauma
Multi-system trauma victims will generally require two or more specialist opinions and interventions and the evidence from the United States would advocate transfer to level 1 trauma centres – with all specialities on site. However, the decision to bypass the local emergency department in preference of the centralised unit could result in adverse outcomes for patients. Would a period of stabilisation or 'primary resuscitation' with subsequent triage to inter-facility transfer for 'secondary treatment' actually result in better outcomes? What does the existing evidence demonstrate regarding these two different policies in terms of clinical and cost effectiveness? How do the pre-hospital decision-makers know which would be the better option?

Head injury
The gold standard for clinical identification of impending deterioration does not exist following head injury, with clinical decision rules directing the need for CT scan – a facility not applicable to pre-hospital services. As only a small proportion of all head injuries result in identifiable brain injury on CT scan (24) this would suggest that an advanced level of 'triage' including the CT scan would accurately identify only those requiring intervention and therefore not swamping the neurosurgical specialists with non-surgical head injury patients.

Stroke
A similar decision-making quandary exists in stroke patients. Whilst typical presentations of stroke to pre-hospital services makes the triage assessment easy allowing timely direct transfer for definitive treatment, patients with atypical features will suffer for the fact that they are dependent on local emergency department (ED) services which may not identify the cause of their presenting complaint in a timely fashion. The definitive investigation required is again a CT scan, which is only available to hospital-based services and should be performed as soon as possible after the onset of symptoms (22-23). Within the stroke care pathway would altering the acute management location improve mortality and morbidity outcomes?

ST elevation myocardial infarction (STEMI)
With regard to decision making in STEMI there exists an early, definitive triage tool already in clinical practice that is already utilised by pre-hospital staff. A typically abnormal ECG, in the clinical picture of cardiac sounding chest pain, is diagnostic for

STEMI and guidance is clear regarding the management of such patients. Decision-making in the three other important areas is not quite so clear-cut and presents an opportunity for review in order to add clarity and guidance based on existing evidence.

Summary
With a reconfiguration of specialist services becoming necessary for the future of the NHS, optimising the utilisation of these services for emergent patients must be a priority for policy makers to achieve the maximum benefit for the limited resources available. A thorough review of the current literature, regarding three key clinical conditions and the decision making processes involved in their management, is an essential starting point to direct policy decisions, identify any potential harmful effects and demonstrate the need for further primary research.

1. Systematic Review

This section will describe the systematic review methods that will be used. It will include a description of inclusion and exclusion criteria for selecting studies by defining the population, interventions, comparators, outcomes and study type. It will also describe the process of data extraction, assessment of methodological quality of included studies and data analysis

Inclusion and exclusion criteria

- Participants

Patients experiencing severe multi-system trauma (defined as ISS>15) or trauma requiring specialist multi-disciplinary surgical input (only available at tertiary centres)
Patients with a clinical presentation of stroke
Patients with isolated head injury
This will exclude the paediatric population (age under 16 years) unless included in general population studies

- Interventions

Interventions will include transfer to a specialist care unit, including specialist stroke units, neurosurgical centres, major trauma centres and level one trauma centres. The interventions will not include secondary transfer to a specialist unit but will focus on the effects of immediate transfer to the specialist centre, bypassing the local hospital facility. Areas that we shall focus on include:

Pre-hospital decision-making (or triage) tools;
Geographical variations in systems (in particular distance and times to travel to the nearest specialist centres/ focusing on the differentiation between urban and rural systems)
Time limitations for treatment options (optimal treatment windows for each clinical condition or recognised guidelines by the appropriate national body)
Estimation of the minimum number of patients required to maintain adequate specialist skills
Estimation of time from injury to definitive care

- Comparators

The comparison will include usual referral practices, such as transfer to a local hospital and subsequent selective referral to tertiary care. These will include:

Temporal comparisons with changes in system structure (before & after studies)

Geographical controls where transfer to local hospital services is substantial

Estimation of the additional time required for investigation/ stabilization in the local hospital

Estimation of the proportion of workload suitable for transfer to tertiary care

- Outcomes

The outcomes that will be considered will include:
Mortality measured at three time points: pre-hospital, 7 and 30 days post event
Morbidity measured using validated outcome measures including: Barthel Index, Glasgow Outcome Scale, Medical Outcomes Study Short Form (SF-36), and Nottingham Health Profile Index.
Length of stay in hospital
Time on intensive care
Patient satisfaction (using tools such as the Picker Patient Experience Questionnaire or Patient Satisfaction Questionnaire)
Impact on existing service provision (using previous health impact assessments and identification of any quantifiable data, secondary effects on local catchment area patients)
Cost and utilities data specific to identify incremental costs per QALY gained

- Study design

Randomised and non-randomised controlled studies will be included in this review. Whilst randomised controlled studies offer the most robust and reliable data to address question of effectiveness, non-randomised studies have value where randomised studies may not be available and may also usefully supplement any randomised trial evidence. Their design does however make them more vulnerable to bias that may exaggerate the effects of the intervention (29). This will be taken into account in the methods of the review. Non-randomised studies will be defined as an experimental study, in which the investigator has control over the allocation of participants to groups, but does not attempt randomisation (29).

Search Strategy

A comprehensive literature search of both published and unpublished 'grey literature' will be undertaken to identify relevant studies. This will include electronic searches of key databases, including MEDLINE, EMBASE, CINAHL, and the COCHRANE database, as well as hand searching of relevant journals (Journal of Trauma, Injury, Trauma, Journal of Neurology, Neurosurgery and Psychiatry, Brain Injury, Stroke, Pre-hospital Emergency Care). The search will limited by year (1988 to current date), after the publication of the working party report by the Royal College Of Surgeons of England in 1988 highlighted the serious deficiencies in the management of severely injured patients leading to considerable changes in the management of these patients. The review will also only include papers and abstracts published in English.

The core search strategy will include the following subject headings and MeSH headings will be expanded to include all relevant sub-headings;

i. Hospital adj bypass$; direct adj trans$; bypass adj protocol$; direct adj transfer
ii. Trauma system$; polytrauma; multi-system trauma; trauma cent$; prehospital adj trauma adj triage; tertiary adj trauma adj centres
iii. Stroke; cerebral infarct$; cerebrovascular accident; CVA
iv. Head injury; craniocerebral trauma; brain injury; intra-cranial haemorrhage/ bleed
v. Pre-hospital$; EMT; ambulance AND triage; Prehospital adj triage adj protocols; regionalisation; regionalization
vi. QALY$; utilities; costs; cost-effect$

An information specialist included in the proposal will, in collaboration with the review team, further develop the search strategy, undertake the electronic searches and create a database of citations using Reference Manager software.

In addition a bibliographic search of all the included studies will be carried out and citation search facilities used
Where systematic reviews and policy documents or reports already exist, these will be used both to identify relevant studies and inform subsequent analysis.

Two reviewers from our team will independently screen the titles and abstracts of papers identified through our search. Electronic or paper copies of all articles that are considered to potentially meet our inclusion criteria (by either one of the reviewers) will be retrieved. Papers will then be screened systematically and in duplicate using an in/out form. The assessment of study eligibility of this initial selection will not be blinded to publication details such as journal or author names.

Data collection
A data extraction form will be developed in consultation with systematic reviewers and clinical experts. Extraction forms will be trialled by two reviewers using a small sample of papers before proceeding with full data extraction. Data on study quality, baseline characteristics of patients and ambulance service provision, details of the intervention, details about the comparator and all relevant outcomes will be extracted. Two reviewers will independently extract data from all identified papers. A third reviewer will adjudicate if there is disagreement.

Data analysis
Quality assessment
Two reviewers will independently assess the quality of each included study and a third reviewer will adjudicate if there is disagreement. Quality assessment will be undertaken using the Cochrane Collaboration's tool for assessing risk of bias (30). This assesses six key methodological domains; sequence generation, allocation concealment, baseline comparability, intention to treat analysis, loss to follow-up and selective outcome reporting. Blinding of participants and treatment providers would not be possible, however, blinding of the outcome assessor and analysis would be possible and will be assessed. It is also anticipated that the review may include cluster-randomised trials. Particular biases that will be considered with this type of study design include; recruitment bias, baseline imbalance, loss of clusters, incorrect analysis and comparability with individually randomised trials.

The objective of the quality assessment is to identify the subset of studies from which potentially reliable conclusions can be drawn. We will deal with variation in methodological quality in the included studies with a sensitivity analysis exploring the effects of major sources of bias or variability upon study outcomes.

Data Synthesis

Where possible and if appropriate, the results of eligible studies will be statistically synthesised in a meta-analysis. Where data is missing one attempt will be made to contact the investigator to obtain the required information. If data remains missing, this will, where possible be imputed. Meta-analysis will be undertaken using Cochrane Collaboration Review Manager (RevMan) 5.0 software (The Cochrane Collaboration, 2008). If cluster randomised trials are included the generic inverse-variance method in RevMan will be used. Appropriate statistical support will be sought to support the meta-analysis. For outcomes where a meta-analysis is not appropriate the trial results will be presented in a narrative analysis.

For continuous outcomes where different scales have been employed to measure outcomes, a standardised mean difference will be used in the meta-analysis.

Statistical heterogeneity will be assessed using the $chi^{2,}$ its corresponding P-value and the I^2 test. As a guide it has been suggested that I^2 values of up to 40% might be unimportant, 30 to 50% might be moderate, 50 to 90% may be substantial and 75% to 100% considerable (30). Some of the potential sources of heterogeneity will be explored in subgroup and sensitivity analysis.

Where there is a sufficient number of studies intended subgroup analysis will explore the impact of injury severity, Glasgow Coma Score in head injury, patients age, pre-hospital protocols, predictive accuracy of triage tools, geographical variations (rural vs. urban), transfer times/distances upon study outcomes. A sensitivity analysis will explore the effects of study design and potential bias on outcomes.

2. Decision Analysis Modelling

The over-arching focus of the decision analytical model is to identify strategies that are both clinically and cost effective for each of the clinical conditions under review. To fulfil this objective the following steps would be required.

a. To generate from published literature a time dependent outcome relationship for each clinical condition in question. Where appropriate data cannot be identified elicitation sessions with clinical experts would be undertaken.(31) The relationship, which would incorporate covariates, such as the severity of injury or presence of multiple trauma sites would enable comparisons of strategies for the variable distances required to travel to local and specialist hospitals.

b. Predictive outcome models for each condition would be generated to compare different pre-hospital strategies. The core comparisons would be:
    i. Transfer all to specialist centre
    ii. Transfer none to specialist centre
    iii. Inclusion of triage tools to transfer patients with specified characteristics to specialist centre care.

3. Cost effectiveness Analysis

Having generated an appropriate statistical model relating clinical outcome to patient characteristics the cost effectiveness of the pre-hospital strategies would be compared in relation to a theoretical cohort of pre-hospital patients.

A *de novo* economic evaluation of the cost effectiveness of comparing a policy of triage and direct transfer to specialist care centres with delivery to the nearest local hospital will be conducted. A model will be developed to identify whether hypothesised improvements to the current practice would result in more cost effective treatment. Cost effectiveness modelling will take account of potential benefits and harms of altered treatment, and (if data allow) will identify any subgroup of patients where amendments to the current practice are most likely to be cost effective.

The primary outcome from the model will be an estimate of the incremental cost per additional quality-adjusted life year (QALY) gained. A lifetime time horizon will be used in order to reflect the potential mortality associated with alternative routing strategies. The perspective used will be that of the National Health Services and Personal Social Services. Costs and QALYS will be discounted at 3.5% as recommended in current guidelines (32) Modelling assumptions will be taken from the literature, supplemented by clinical expert opinion where required.

The ScHARR modelling team have published papers using different modelling techniques (such as discrete event simulation (33-35), transition state modelling (36) and meta-modelling (37) and different software packages, such as Microsoft Excel ® and Simul8 ®. The model structure and software used to construct the model will be determined following data collection in order that the most appropriate technique is used for this particular assessment. Clinical experts will be consulted at the conceptual stage to ensure that the structure of the model is appropriate to clinical practice. The model will include estimates of the effects of alternative routing strategies on the management of patients, as well as costs of intervention and subsequent downstream costs associated with appropriate and inappropriate care. If data allow, this approach will enable an analysis of whether the cost effectiveness of alternative routing strategies differs between patient groups.

Ideally, health related quality of life evidence will be available directly from the review literature. In the absence of such evidence, the mathematical model may use indirect evidence on quality of life from alternative sources. Quality of life data will be reviewed and used to generate the quality adjustment weights required for the model. In addition to the reviewed literature, national sources (eg. NHS reference costs (38)), national unit costs (39), British National Formulary (http://bnf.org)) will be used to estimate resource use and costs for use in the economic model.

It is anticipated that there may be limited evidence for some of the parameters that will be included in the economic model. Therefore, the uncertainty around the parameter estimates will be modelled to take this into account. The uncertainty in the central value for each required parameter will be represented by a distribution, enabling probabilistic sensitivity analysis to be undertaken (40), the expected value of perfect information (41) and the expected value of partial perfect information (42). This will allow an assessment of the uncertainty to be made. If resources allow, the cost effectiveness of collecting further information will be explicitly explored using

Expected Value of Sample Information techniques (43). The research team have had experience in these techniques (44-45)

4. Future Research Questions:

This review will identify the current evidence for triage and direct transfer to specialist treatment centres when compared to present, local hospital transfer policies, from both a clinical and cost-effectiveness perspective. It is anticipated that areas of data will be missing or of insufficient quality to be included, which will provide a starting point for suggestions for future primary research. The inclusion criteria for this project include patient satisfaction outcomes and impact on existing service provision, both of which are likely to provide limited information, as few models currently exist for centralised emergency care. Most data from the US are registry based and in the UK cardiology service for primary PCI are only recently developed which would suggest that these areas of qualitative research, impact on patients and relatives and on the current models of service, are likely to require further investigation. Separate research in to the effect on staff morale and training is also expected to be lacking.
Direct comparison of local ED and stroke unit thrombolysis outcomes has not been performed in depth, particularly regarding onset or door to needle times.

Plan of Investigation & timeline:
Commencing date estimated at June 2010 with expected end date by June 2011

Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Searches & retrieval	*	*	*	*	*							
Evidence Review			*	*	*	*	*					
Data analysis				*	*	*	*	*				
Modelling						*	*	*	*	*		
Report										*	*	*
Interim Report						*						
Peer review & Revisions											*	*

Output:

i. Systematic review and meta-analysis of current evidence on the clinical effectiveness of direct transfer or bypass policies
ii. Cost-effectiveness analysis of different transfer and transport strategies
iii. Model generation for optimal patient pathways in each of three clinical conditions
iv. Recommendations for future primary research with the generation of specific research questions
v. Peer reviewed publications and conference presentations
vi. Report for NETSCC SDO programme

Dissemination:
Publication of the systematic review would be expected in a high impact peer-reviewed journal such as the Journal of Trauma, Health Services Research Journal

or the British Medical Journal. In conjunction with this oral and poster presentations would be expected at national and international conferences. A priority would be for a published report being demonstrated to local policy makers within the Strategic Health Authority for feedback and comments. Any significant findings would be highlighted to the Department of Health as potential strategy alterations for the future of the NHS changes.

Appendix 1

Definitions

Severe/ Major Trauma

The Injury Severity Score (ISS) is an anatomical scoring system that provides an overall score for patients with multiple injuries. Each injury is assigned an Abbreviated Injury Scale (AIS) score, allocated to one of six body regions (Head, Face, Chest, Abdomen, Extremities (including Pelvis), External). Only the highest AIS score in each body region is used. The 3 most severely injured body regions have their score squared and added together to produce the ISS score. An ISS of 16 or greater is commonly accepted as severe, or major, trauma. As injuries are not always evident in the early stages of patient management the ISS is not a suitable triage tool.

Abbreviated Injury Scale:
A six-point scale that identifies the severity of the injury in the context of a threat to the patient's life:

1 Minor
2 Moderate
3 Serious
4 Severe
5 Critical
6 Unsurvivable

Stroke

Stroke is a serious medical condition in which the blood supply to the brain is disrupted, potentially resulting in disability and mortality. The World Health Organisation defined stroke as a 'neurological deficit of cerebrovascular cause that persists beyond 24 hours or is interrupted by death within 24 hours'(46) This definition was supposed to reflect the reversibility of tissue damage and was devised for the purpose, with the time frame of 24 hours being chosen arbitrarily. The 24-hour limit divides stroke from transient ischemic attack, which is a related syndrome of stroke symptoms that resolve completely within 24 hours. The term 'Brain attack' is increasingly being used to emphasise the urgency with which this problem should be treated.

Head Injury

Head injury is not to be confused with brain injury. Head injury has been defined by Wade as '…any blow to the head which leads to a diagnosis of head injury being made.'(47) Within this definition should be encompassed any traumatic brain injury (TBI) but not all head injuries result in underlying damage to the brain. Head injury could be classed as a sign and TBI a diagnosis. Unfortunately, prior to imaging investigations, the small proportion of head injury patients with underlying TBI cannot be easily identified but they have been the focus of considerable research and guideline development (24, 48-50). For this reason this review will focus its search on those patients with identified brain injury but will include all 'head injury' patient data in the modelling calculations (estimated to be 90% of head injuries with no brain injury).

Reference List

1. Darzi L. High Quality Care for All: NHS Next Stage Review. In: Health Do, editor. London: Department of Health; 2008.
2. IPPR. Hospital Reconfiguration. Briefing. Southampton: Institute for Public Policy Research2006 September 2006.
3. Farrington-Douglas J, Brooks R. The Future Hospital - the progressive case for change. London: Institute for Public Policy Research2007.
4. AOMRC. Acute health care sevices: Report of a working party. London: Academy of Medical Royal Colleges 2007 September 2007.
5. Nicholl J, West J, Goodacre S, Turner J. The reltionship between distance to hospital and patient mortality in emergencies: an observational study. Emergency Medicine Journal. 2007;24:665-8.
6. Mann CN, Mullins RJ, MacKenzie EJ, Jurkovich GJ, Mock CN. Systematic Review of Published evidence regarding trauma system effectiveness. J Trauma. 1999 Sept 1999;47(3 Suppl):S25-S33.
7. Celso B, Tepas J, Langland-Orben B, Pracht E, Papa l, Lottenberg L, et al. A Systematic Review and Meta-analysis comparing outcome of severely injured patients treated in trauma centers following the establishment of trauma systems. J Trauma. 2006;60(2):371-8.
8. Sampalis JS, Denis R, Frechette P, Brown R, Fleiszer D, Mulder D. Direct transport to tertiary trauma centers versus transfer from lower level facilities: Impact on mortality and morbidity among patients with major trauma. J Trauma. 1997 Aug 1997;43(2):288-96.
9. Hartl R, Gerber LM, Iacono L, Ni Q, Lyons K, Ghajar J. Direct transport within an organized state trauma system reduces mortality in patients with severe traumatic brain injury. J Trauma. 2006 June 2006;60(6):1250-6.
10. Glance LG, Osler TM, Dick A, Mukamel D. The relation between trauma center outcome and volume in the National trauma databank. J Trauma. 2004 March 2004;56(3):682-90.
11. Phillips H, Carney C, Catterall A, Court Brown C, Day V, Dow A, et al. Better Care for the Severely Injured: Joint Report from the Royal College of Surgeons of England and the British Orthopaedic Association2000.
12. Utter GH, Maier RV, Rivara FP, Mock CN, Jurkovich GJ, Nathens AB. Inclusive trauma systems: Do they improve triage or outcomes of the severely injured? J Trauma. 2006 March 2006;60(3):529-37.
13. Nicholl J, Turner J. Effectiveness of a regional trauma system in reducing mortality from major trauma: before and after study. BMJ. 1997 Nov 22 1997;315:1349-54.
14. Oakley PA, Kirby RM, Redmond AD, Templeton J. Effectiveness of regional trauma systems (response letter). BMJ. 1998 May 2 1998;316:1383.
15. Mann CN, Cahn RM, Mullins RJ, Brand DM, Jurkovich GA. Survival among Injured Geriatric Patients during Construction of a Statewide Trauma System. J Trauma: Injury, Infection and critical care. 2001;50(6):1111-6.
16. Boyle R. Mending Hearts and Brains
Clinical case for change. London: Department of Health2006 December 2006.
17. Hacke W, Kaste M, Bluhmki E, Brozman M, Davalos A, Guidetti D, et al. Thrombolysis with Alteplase 3 to 4.5 Hours after Acute Ischemic Stroke. N Engl J Med. 2008 September 25, 2008;359(13):1317-29.
18. Association of outcome with early stroke treatment: pooled analysis of ATLANTIS, ECASS, and NINDS rt-PA stroke trials. The Lancet. 2004;363(9411):768-74.
19. Wardlaw JM, Murray V, Berge E, del Zoppo GJ. Thrombolysis for acute ischaemic stroke.: The Cochrane Collaboration.2009. Report No.: CD000213.

20. Collaboration SUT. Organised inpatient (stroke unit) care for stroke.: The Cochrane Collaboration.2007. Report No.: CD000197.
21. Hoffman A, Down C, Grant R, Wurie F, Lowe D, Rudd A. National Sentinel Stroke Audit: Royal College of Physicians2007.
22. Conditions NCCfC. Stroke: national clinical guideline for diagnosis and initial management of acute stroke and transient ischaemic attack (TIA). London: Royal College of Physicians2008.
23. Party ISW. National Clinical Guideline for stroke. London: Royal College of Physicians2008.
24. N.I.C.E. Head Injury: Triage, assessment, investigation and early management of head injury in infants, children and adults. London: National Institute for Clinical Excellence2007 September 2007.
25. Stevenson MD, Oakley PA, Beard SM, Brennan A, Cook AL. Triaging strategies with serious head injury: results of a simulation evaluating strategies to bypass hospitals without neurosurgical facilities. Injury. 2001 2001;32:267-74.
26. Wilberger JE, Harris M, Diamond DL. Acute Subdural Hematoma: Morbidity and mortality related to timing of operative intervention. J Trauma. 1990 June 1990;30(6):733-6.
27. Haselsberger K, Pucher R, Auer LM. Prognosis after acute subdural or epidural haemorrhage. Acta Neurochir. 1988;90:111-6.
28. Patel HC, Bouamra O, Woodford M, King AT, Lecky FE. Trends in head injury outcome from 1989 to 2003 and the effect of neurosurgical care: an observational study. Lancet. 2005 Oct 29 2005;366:1538-44.
29. Deeks JJ, Dinnes J, D'Amico R, Sowden AJ, Sakarovitch C, Song F ea. Evaluating non-randomised intervention studies.2003 Contract No.: 27.
30. Higgins JPT, DG A. Chapter 8: Assessing risk of bias in included studies. In: Higgins JPT GS, editor. Cochrane handbook for systematic reviews of interventions version 500 (updated February 2008): The Cochrane Collaboration; 2008.
31. O'Hagan A, CE B, A D, JE E, PH G, DJ J, et al. Uncertain judgements: eliciting experts' probabilities. 1st ed. Chichester: John Wiley and Sons.; 2006.
32. N.I.C.E. Guide to the methods of technology appraisals. London, UK: National Institute for Health and Clinical Excellence2008.
33. Stevenson MD, Macdonald FC, Langley J, Hunsche E, RL. A. The cost-effectiveness of bosentan in the UK for patients with pulmonary arterial hypertension of WHO functional class III. Value in Health. 2009a;12(8):1100-5.
34. Stevenson MD, Simpson EL, Rawdin AC, . PD. A review of discrete event simulation in National Coordinating Centre for Health Technology Assessment funded work and a case study exploring the cost-effectiveness of testing for thrombophilia in patients presenting with an initial idiopathic venous thromboembolism Journal of Simulation (In Press a).
35. Michaels J, Campbell W, King B, Palfreyman S, Shackley P, Stevenson M. A Randomised Controlled Trial and Cost-effectiveness Analysis of Antimicrobial silver Antimicrobial Dressings for Venous Leg Ulcers: The VULCAN Trial. British Journal of Surgery. 2009;96(10):1147-56.
36. Wardlaw JM, Stevenson M, Chappell F, Rothwell PM, Gillard J, Young G, et al. Carotid artery imaging for secondary stroke prevention: both imaging modality and rapid access to imaging are important. Stroke. 2009;40(11):3511-7.
37. Stevenson MD, Oakley J, JB C. Gaussian process modelling in conjunction with individual patient simulation modelling. A case study describing the calculation of cost-effectiveness ratios for the treatment of osteoporosis. Med Decis Making. 2004;24 89-100.
38. D.o.H. NHS reference costs 2007-08. London UK: Department of Health2009.
39. Curtis L. Unit costs of health and social care. 2008.

40. Doubilet P, Begg C, Weinstein M, Braun P, McNeill B. Probabilistic sensitivity analysis using Monte Carlo simulation: a practical approach. Med Decis Making. 1985;5:157-77.
41. Claxton K, Posnett J. An economic approach to clinical trial design and research priority-setting. Health Econ. 1996;5:513-24.
42. Felli J, Hazen G. Sensitivity analysis and the expected value of perfect information. Med Decis Making. 1998;18:95-109.
43. Ades A, Lu G, Claxton K. Expected values of sample information calculation in medical decision making. Med Decis Making. 2004;24:207-27.
44. Stevenson MD, Oakley JE, Lloyd Jones M, Brennan A, Compston JE, McCloskey EV, et al. The cost-effectiveness of an RCT to establish whether 5 or 10 years of bisphosphonate treatment is the better duration for women with a prior fracture. Medical Decision Making. 2009b;29(6):678-89.
45. Stevenson MD, M. LJ. The cost effectiveness of an RCT comparing alendronate with Vitamin K1. Medical Decision Making (In Press b).
46. World Health O. Cerebrovascular disorders : a clinical and research classification. Geneva; Albany, N.Y.: World Health Organization ; obtainable from the WHO Publications Centre]; 1978.
47. Wade DT, Crawford S, Wenden FJ, King NS, Moss NE. Does routine follow up after head injury help? A randomised controlled trial. J Neurol Neurosurg Psychiatry. 1997 May 1, 1997;62(5):478-84.
48. N.I.C.E. Head Injury. Triage, assessment, investigation and early management of head injury in infants, children and young adults. London: National Institute for Clinical Excellence2003 June 2003.
49. Stiell I, Wells G, Vandemheen K, Clement C, Lesiuk H, Laupacis A, et al. The Canadian CT Head Rule for patients with minor head injury. Lancet. 2001 May 5, 2001;357:1391-6.
50. Haydel MJ, Preston CA, Mills TJ, Luber S. Indications for computed tomography in patients with minor head injury. NEJM. 2000;343(2).

This protocol refers to independent research commissioned by the National Institute for Health Research (NIHR). Any views and opinions expressed therein are those of the authors and do not necessarily reflect those of the NHS, the NIHR, the SDO programme or the Department of Health.