The Head Injury Transportation Straight to Neurosurgery (HITS-NS) randomised trial: a feasibility study

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Scientific summary

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Background

The National Institute for Health and Care Excellence (NICE) 2007 Head Injury Guideline revision suggested that all patients with 'severe head injury' [abnormal computed tomography brain scan (CT) suggesting traumatic brain injury (TBI) and arriving at the first hospital intubated or with a Glasgow Coma Scale (GCS) score of < 9] should be treated at, or transferred to, a neuroscience centre (NC). Consequently, the current NHS England reconfiguration of trauma services – with direct transportation of patients with TBI to specialist neuroscience centres (SNCs), bypassing nearer non-specialist acute hospitals (NSAHs) – could potentially improve outcomes by expediting earlier neurosurgical intervention.

However, delays in stabilisation of airway, breathing and circulation (ABC) and the difficulties in reliably identifying TBI at the scene of injury may make this practice deleterious compared with later selective secondary transfer from nearest NSAH to SNC. Delays in correcting hypoxia and hypovolaemia associated with longer journeys to hospital for unconscious patients could worsen outcomes through secondary brain injury. The occult nature of TBI in the ageing population could also mean that large numbers of patients are taken significant distances past their nearest hospital for no benefit (overtriage).

National Institute for Health and Care Excellence guidance and systematic reviews suggested equipoise and highlighted poor-quality evidence with regard to the clinical effectiveness and cost-effectiveness of early neurosurgery through bypass in this cohort. We sought to address this by establishing the feasibility of a cluster randomised trial to establish the benefit of early neurosurgery in patients with suspected TBI who are injured nearest a NSAH.

Methods

The study had eight objectives, which were to:

- determine the feasibility of conducting a cluster randomised trial of early neurosurgery in patients with TBI
- determine the acceptability of the intervention (early neurosurgery) and control (usual care) pathways to patients, families and staff
- estimate the 'magnitude of effect' of early neurosurgery and other parameters required for sample size estimation, thereby enabling costing of a full study (given successful recruitment)
- determine the accuracy with which paramedics identify isolated TBI at the incident scene (given successful recruitment)
- estimate the cost per quality-adjusted life-year (QALY) of early neurosurgery, compared with usual care, based on currently available data (including data from this pilot) and the degree of uncertainty surrounding this estimate
- determine the expected value of sample information (EVSI) from a fully powered cluster randomised trial of early neurosurgery in patients with TBI
- identify the major barriers to conducting a cluster randomised trial of early neurosurgery in patients with TBI and the strategies to overcome them
- contribute to the existing evidence on conducting randomised trials in pre-hospital care through identifying barriers and facilitators of successful strategies that are generic to pre-hospital trials.

The study had two work streams: A and B. Stream A consisted of a pilot cluster randomised controlled trial of bypass to SNC for early neurosurgery – conducted in two ambulance services (ASs) with the ambulance station ($n = 74$) as unit of cluster [Lancashire/Cumbria in the North West Ambulance service (NWAS) and the North East Ambulance Service (NEAS)]. Adult patients with signs of isolated TBI (GCS score of < 13 in NWAS, GCS score of < 14 in NEAS) and stable ABC, injured nearest to a NSAH, were transported either to that closest hospital (control clusters) or bypassed to the nearest SNC (intervention clusters). The study was conducted between January 2012 and September 2013, with the vast majority of recruitment occurring from April 2012 to March 2013. A nested qualitative cohort study of patients who had consented to 6-month follow-up and a paramedic focus group study were conducted in October and November 2013.

The primary feasibility outcomes were the recruitment rate, protocol compliance, selection bias as a result of non-compliance, accuracy of paramedic TBI identification (overtriage as a result of study inclusion criteria) and pathway acceptability to patients, families and staff.

The secondary outcomes of stream A were those that would form the primary outcomes of a fully powered trial: 30-day mortality, 6-month Extended Glasgow Outcome Scale and the European Quality of Life-5 Dimensions.

As an adaptation to the unexpected case mix in the study cohort, an interrogation of the Trauma Audit and Research Network (TARN = National Trauma Registry) database from the relevant hospitals was conducted in May 2013 after recruitment had ceased. This enabled a check on the robustness of study screening and an estimate of the numbers of patients with TBI and on-scene GCS scores that were too high for study inclusion (undertriage).

Stream B consisted of an economic evaluation using decision analysis modelling to examine alternative management pathways for adult patients with suspected significant TBI injured closest to a NSAH. Four interventions applicable to NHS practice were compared: pre-hospital triage and bypass, and secondary transfer management strategies defined according to the treatment of patients with TBI requiring critical care (selective, routine and no transfer). Detailed literature searches and formal systematic reviews were conducted to guide model structuring and inform model parameterisation. The elicitation of expert opinion was necessary to characterise relative effectiveness and specific inpatient and long-term costs. Incremental costs between bypass and selective transfer strategies were estimated from Head Injury Transportation Straight to Neurosurgery (HITS-NS) pilot data.

A hybrid decision tree state transition model was implemented to estimate the cost-effectiveness of competing strategies in terms of expected net monetary benefit and incremental cost per QALY. The base-case model followed NICE reference case recommendations and was evaluated probabilistically to account for parameter uncertainty. The impact of parameter and structural uncertainty was further examined in a series of scenario, threshold and one-way sensitivity analyses. Decision uncertainty was also presented using a cost-effectiveness acceptability curve and frontier. Expected value of perfect information (EVPI) and expected value of partial perfect information (EVPPI) techniques were then calculated to inform future research priorities. The EVSI and the expected net benefit of sampling (ENBS) from conducting a definitive trial of bypass were also examined, identifying the optimal sample size for a future study under a range of assumptions for disease incidence and study characteristics.

Results

In total, 56 clusters recruited 293 patients in 12 months, demonstrating cluster randomised pre-hospital trials as viable for heath service evaluations. Overall, compliance from the paramedics in terms of taking patients to the hospital in their cluster was randomised to 62% but achieved 90% in the control arm when face-to-face paramedic training was possible. Non-compliance appeared to be driven by proximity of the nearest hospital and perceptions of injury severity, and so occurred more frequently in the intervention arm, for which the perceived time to the SNC was greater and severity of injury was lower; there were no other differences between the populations with which the allocation was/was not complied.

Fewer than 25% of recruited patients had TBI on CT scan ($n = 70$), with 7% ($n = 20$) requiring neurosurgery (craniotomy, elevation of bone flap or intracranial pressure monitoring with or without subsequent surgery) but a further 6% ($n = 18$) required admission to an intensive care unit. An intention-to-treat analysis revealed the control and intervention groups to be equivalent in terms of median age, GCS and severity of injury. No significant 30-day mortality differences were found (8.8% vs. 9.1/%; $p > 0.05$) in the 273 patients with data available. There were no apparent differences in staff and patient preferences for either pathway, with satisfaction rated as high with both. Very low response rates to invitations to consent for follow-up in the large number of mild head injury-enrolled patients meant that only 20% of patients had 6-month outcomes or satisfaction data. The rates of recruitment, compliance and, most importantly, of traumatic brain injury were below that of the prespecified feasibility outcomes for proceeding to a full trial of 'early neurosurgery' facilitated by bypass in this cohort. It was not possible to generate an 'effect estimate' of early neurosurgery from the trial data because of the small numbers of patients who required neurosurgery at any time.

The search of the TARN database for the NEAS trial NSAHs found that a further 62 patients with TBI had a scene GCS score of 14–15 and were, therefore, ineligible for bypass or study inclusion during the recruitment period. Only five eligible patients with TBI were missed by study screening of > 65,000 patients.

Stream B inevitably has evaluated bypass of patients with suspected TBI – which rarely results in neurosurgery – rather than early neurosurgery, which was the original intention. Base-case probabilistic analysis suggested that routine transfer (transport to the local non-specialist hospital and routine secondary transfer of all patients with acute expanding intracranial haematomas or TBI requiring critical care to regional NCs) may provide the optimal management strategy at a willingness-to-pay threshold of £20,000 [mean incremental cost-effectiveness ratio (ICER) £2260]. At a higher threshold of £30,000, pre-hospital triage and bypass was the most cost-effective option (mean ICER £27,158). At both thresholds there was considerable decision uncertainty, with a high probability of erroneously adopting a suboptimal strategy (54% and 52%, respectively). Sensitivity analyses demonstrated that this result was critically dependent on the parameterisation of costs and effects for routine transfer and bypass strategies. Furthermore, alternative assumptions about life expectancy following injury, utility weights assigned to Glasgow Outcome Score health states, neurosurgery costs, and discounting rates all resulted in reversal of the adoption decision at $\lambda = £20,000$ and indicated that bypass is the optimal strategy.

The considerable decision uncertainty and important public health burden of TBI was reflected in a large population EVPI result. Further research up to a value of £36M may be indicated to eliminate parameter uncertainty and opportunity costs from making the wrong adoption decision at a cost-effectiveness threshold of £20,000. EVPPI analyses demonstrate that future research would have high value in comparing costs and relative effectiveness between bypass and selective secondary transfer: that is, a definitive trial-based economic evaluation of bypass rather than early neurosurgery as a health technology in the HITS-NS cohort. EVSI results suggested that, if feasible, a definitive bypass trial examining comparative effectiveness is potentially cost-effective. Maximal ENBS (£11M) would be achieved with a trial of 520 patients per arm, randomised across eight ASs and taking 3 years. Expected value of information results varied substantially in sensitivity analyses examining alternative estimates for the population that may benefit from future research and assumptions on trial characteristics.

Conclusions

The HITS-NS trial has demonstrated that pre-hospital cluster randomised trials can be used for health technology assessments of complex interventions. The important new finding of the low rate of TBI and requirement for neurosurgery in the population eligible for trauma bypass means that the potential effect of the intervention (early neurosurgery) is diluted and therefore small. An unfeasibly large trial would be required to reliably detect its impact in this cohort.

Current NHS England practice of bypassing suspected patients with TBI to NCs gives an overtriage ratio of 13 : 1 for neurosurgery and 4 : 1 for TBI, with uncertain cost-effectiveness. There also is significant undertriage for patients with TBI presenting with a higher GCS score, some of whom later require neurosurgery through selective secondary transfer. These findings – alongside those of the health-economic modelling of pathways from the scene of injury – call into question the clinical effectiveness and cost-effectiveness of bypass for this study cohort group within the current NHS England trauma systems. Further evaluations of 'trauma bypass' – as opposed to early neurosurgical intervention the technology evaluated in this feasibility study – would probably be cost-effective for the NHS. However, a trial of trauma bypass may be difficult to achieve in recently reconfigured services and there would be a need to consider the challenges of meaningful follow-up and whether or not the other trauma patients currently eligible for bypass should be included.

It may now be possible to conduct a further evaluation of 'early neurosurgery through bypass' on early mortality in patients with TBI using registry (TARN) data and a comparative effectiveness or case–control design, which was not possible in the pre-'trauma system' climate in which HITS-NS was conceived and no land ambulance bypass was occurring. In the interim, secondary transfer will remain a necessary pathway for patients with TBI injured nearest a NSAH with a high level of consciousness (GCS score of > 13) at the scene.

Trial registration

This trial is registered as ISRCTN68087745.

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