SUPPLEMENTAL MATERIAL (APPENDICES)

APPENDIX 1:

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APPENDIX 2: BASELINE GCS-ADJUSTED GOSE (SLIDING-DICHOTOMY ANALYSIS)

Methods

In addition to the extended Glasgow Outcome Scale (GOSE) fixed dichotomy analysis described in the main paper, a further GOSE sliding dichotomy analysis was undertaken, in which the favourable/unfavourable categorisation was defined as follows: if GCS (Glasgow Coma Scale) at randomisation was between 3 and 8 (patient comatosed) (1), a favourable outcome was defined as upper severe disability or better but if GCS at randomisation was between 9 and 15 (responsive patient), a favourable outcome was defined as lower moderate disability or better. The cost-effectiveness analysis using this sliding dichotomy, replicated that described in the main paper for the fixed dichotomy, with a view to estimating the cost per additional favourable outcome.

Results and conclusions

For the craniotomy group compared with the DC group, the mean difference in cost was -£6,091 (95% CI -£18,857 to £6,675) with an odds ratio of favourable outcome on the GOSE score of 1.741 (95% CI 1.019 to 2.977). Craniotomy therefore dominated DC.

APPENDIX 3: FURTHER SENSITIVITY ANALYSES

Methods

In addition to the two sensitivity analyses described in the main paper, a further four were defined in the Health Economic Analysis Plan (HEAP) and analysed. The consequence of excluding patient self-reported resource use data (more missing data was expected from this source), and using only hospital-recorded costs was assessed as a sensitivity analysis (SA hospital-recorded post-discharge operations only). Another sensitivity analysis (SA patient-reported post-discharge operations only) included only patient-reported post-discharge skull/brain operations (with associated length of stay) instead of hospital-reported post-discharge cranioplasties and shunts. A further sensitivity analysis (SA per protocol) re-analysed the data on a per protocol basis, excluding patients whose primary treatment was not as allocated, e.g. allocated to DC but received craniotomy and vice versa. A complete case analysis based on the base-case was also undertaken (SA complete case analysis), where participants were only included if they have complete hospital records, participant self-report and QALY data, with no imputation undertaken. These sensitivity analyses were undertaken for both the cost-utility analysis and cost-effectiveness analysis.

Results and Conclusions

The results of the four sensitivity analyses described are presented in Table A1. In all sensitivity analyses, craniotomy was found to dominate DC. This is in keeping with the base-case cost-utility and cost-effectiveness analyses and other sensitivity analyses presented in this paper.

Supplemental Table A1 | Estimates of the mean incremental cost, incremental effect (QALY gain or odds ratio), and cost effectiveness of craniotomy compared with DC for additional sensitivity analyses.

Analysis (N craniotomy,N DC)	Incremental cost (95% CI)	QALY gain (95% CI)	ICER	CEAC*
SA hospital-recorded post-discharge operations only: (126,122) MI	-£6,252 (-£12,180 to -£325)	0.092 (0.031 to 0.153)	Dominant	99%
SA patient-reported post-discharge operations only: (126,122) MI	-£6,328 (-19,389 to £6,733)	0.093 (0.032 to 0.154)	Dominant	89%
SA per protocol: (113,114) MI	-£10,711 (-£23,361 to £1,939)	0.121 (0.056 to 0.185)	Dominant	98%
SA complete case analysis: (60,44)	-£1,917 (-£15,564 to £11,729)	0.071 (-0.0106 to 0.153)	Dominant	68%
Analysis (N craniotomy,N DC)	**Incremental cost (95% CI)**	**Odds ratio (95% CI) ‡**	**ICER**	
SA hospital-recorded post-discharge operations only: (126,122)	-£5,709 (-£11,783 to £365)	1.704 (1.010 to 2.888)	Dominant	-
SA patient-reported post-discharge operations only: (126,122)	-£5,374 (-£18,782 to £8,033)	1.687 (0.999 to 2.849	Dominant	-
SA per protocol: (113,114)	-£10,567 (-£23,434 to £2,299)	2.189 (1.252 to 3.827)	Dominant	-
SA complete case analysis: (83,67)	-£4,335 (-£18,545 to £9,876)	1.360 (0.698 to 2.649)	Dominant	-

DC= decompressive craniectomy; 95% CI=95% confidence interval; ICER =incremental cost-effectiveness ratio; Dominant = lower mean costs and higher mean effect; N craniotomy (N DC) = number Randomized to craniotomy/decompressive craniectomy who were included in the analysis; SA:sensitivity analysis, described in the Methods; QALY=Quality Adjusted Life Years; ICER =incremental cost-effectiveness ratio, described in the Methods; *Probability of being cost-effective on the CEAC at a threshold of £20,000 per QALY;‡ for a favourable outcome for craniotomy compared with DC, based on the GOSE (Extended Glasgow Outcome Scale), as described in the Methods.

APPENDIX 4: DEVIATION FROM THE HEAP IN “SA WIDER COST PERSPECTIVE”

Within the Health Economic Analysis Plan (HEAP) it was stated that lost productivity costs would be estimated. Below we explain why this was not undertaken.

The following was stated within the ‘Costs’ section for the HEAP:

“…Participants were asked to report a) whether they were currently working (paid or unpaid), with the following additional questions (if applicable); b) how many hours per week they work (paid or unpaid); c) whether the number of hours was the same as before their brain injury; d) whether they currently work fewer or more hours per week than before your brain injury; e) when they returned to work following the brain injury; f) whether they have taken any days off due to sickness since returning; g) if they have had to leave work / change job since their brain injury and why. In order to estimate lost productivity, in line with the opportunity cost method (2), the mean lost work time over the 12 month follow-up period (regardless of whether a payment was made) will be estimated and valued at the 2019 UK mean hourly gross wage (£17.25) (3)…“

Within the ‘Analysis’ section for the HEAP we stated that the base-case analysis would be from the cost perspective of the NHS and PSS. However, it was stated that the first sensitivity analysis (SA) (“SA wider cost perspective” in this paper) would take a more societal perspective and include lost productivity costs, as well as care home and carer costs.

We attempted to include lost productivity costs at the analysis stage but found that we did not have information as to the number of hours participants were working before their brain injury, as intended. The main reason for this was that if a participant reported that they were *not* currently working in response to the above question a) they were not asked to complete questions b-f. In hindsight, this was an error in how the questionnaire was formulated, and they should have been asked to complete questions c and d as well. Considering this error in the framing of the questionnaire we chose to deviate from the HEAP and not estimate lost productivity costs. Consequently, as detailed in the paper, in “SA wider cost perspective” only the care home and carer costs were added to the (base-case) NHS and PSS costs.

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