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Management and outcomes following emergency surgery for traumatic brain injury – A multi-centre, international, prospective cohort study (the Global Neurotrauma Outcomes Study)

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ABSTRACT

Introduction: Traumatic brain injury (TBI) accounts for a significant amount of death and disability worldwide and the majority of this burden affects individuals in low-and-middle income countries. Despite this, considerable geographical differences have been reported in the care of TBI patients. On this background, we aim to provide a comprehensive international picture of the epidemiological

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characteristics, management and outcomes of patients undergoing emergency surgery for traumatic brain injury (TBI) worldwide.

Methods and analysis: The Global Neurotrauma Outcomes Study (GNOS) is a multi-centre, international, prospective observational cohort study. Any unit performing emergency surgery for TBI worldwide will be eligible to participate. All TBI patients who receive emergency surgery in any given consecutive 30-day period beginning between 1st of November 2018 and 31st of December 2019 in a given participating unit will be included. Data will be collected via a secure online platform in anonymised form. The primary outcome measures for the study will be 14-day mortality (or survival to hospital discharge, whichever comes first). Final day of data collection for the primary outcome measure is February 13th. Secondary outcome measures include return to theatre and surgical site infection.

Ethics and dissemination: This project will not affect clinical practice and has been classified as clinical audit following research ethics review. Access to source data will be made available to collaborators through national or international anonymised datasets on request and after review of the scientific validity of the proposed analysis by the central study team.

1. Background

The Global Burden of Disease study estimates that 27 million new cases of traumatic brain injury occur worldwide every year [1]. According to data from the US National Trauma Data Bank, almost 4% of these will require neurosurgical intervention [2]. Timely and adequate emergency surgery for TBI has long been known to dramatically improve outcome [3–6]. As such, multiple global health organisations recognise surgical procedures for neurotrauma, specifically the evacuation of traumatic intracranial haematomas and the elevation of depressed skull fractures, as essential to be available on an emergency basis to all worldwide [7,8]. However, although most injuries occur in LMICs [9], access to neurosurgical care in many LMICs is extremely limited – in sub-Saharan Africa, the average percentage of a country's population within 2 h of a neurosurgical service is estimated to be 25% [10].

For patients with neurosurgical pathology who do reach a centre that can provide the procedure they require, there is a paucity of data on their outcomes and the standard of management they receive [11]. To complicate matters, current best practise guidelines for the management of TBI typically advocate the use of expensive technologies (such as invasive intracranial pressure monitoring) which are often unavailable in low-resource settings [12,13] despite the fact that this is where the majority of serious injuries occur globally [9]. As such, context-specific research is urgently required to determine best practice for delivering effective surgical care for traumatic neurological injuries globally. The first step in this is to describe current practice and outcomes across varied settings and neurosurgical care is an extremely important aspect of the management of TBI patients.

We propose to conduct an international, multi-centre, prospective cohort study of outcomes following emergency surgery for traumatic brain injury. We believe such a project would provide valuable information to advance the care of patients with traumatic brain injuries globally and be feasible with the proposed methodology.

2. Methods and analysis

2.1. Primary aim

The primary aim of the study is to compare 14-day mortality (or in-hospital mortality if discharge occurs before 14 days) following emergency surgery for traumatic brain injury (TBI) across HDI settings.

2.2. Secondary aims

To describe and compare the following across HDI settings following emergency surgery for TBI:

- Perioperative complications
- Length of stay in hospital and length of stay in the intensive care unit
- Glasgow Coma Scale (GCS) on discharge and discharge destination
- Epidemiological characteristics (demographics, injury characteristics, baseline clinical characteristics and surgical case mix)
- Preoperative, perioperative and postoperative processes of care (including temporal delays to care)
- Resources available for the management of acute brain injury

2.3. Study design

This is a multicentre, international, prospective, observational cohort study of all patients receiving emergency surgery for TBI in any consecutive 30-day period. Local study teams may select any 30-day period from the 1st of November 2018 and the 31st of December 2019 to start their study. Patients operated on who meet the inclusion criteria between 00:01 on day 0 and 23:59 on day 30 of the selected study period will be included. The final study period will therefore begin on 31st December 2019 00:01 and end on 30th January 23:59. Teams must follow patients up for 14-days from the date of surgery or until they are discharged or die – whichever of these comes first. Final day of data collection for the primary outcome measure is therefore February 13th. Teams have 30 days after the end of their selected study period to complete the data validation exercise (see below) – all patient level data should therefore be submitted to the central study team by 29th February.

2.4. Study setting

Any hospital or clinic worldwide performing emergency surgery for traumatic brain injury is eligible to participate. In the majority of institutions, emergency surgery for TBI is provided by neurosurgeons – however, centres in which emergency surgery for TBI is provided by general surgeons, trauma surgeons, general medical doctors or even non-physician clinicians are also eligible to participate.

Table 1
Patient inclusion and exclusion criteria.

Patient inclusion criteria
All adult and paediatric patients admitted to the participating institution with a traumatic brain injury for which they receive emergency surgery during the selected 30-day inclusion period are eligible for inclusion in the study.
Patient exclusion criteria
• Patients who ONLY have an external ventricular drain or intraparenchymal wire (or other monitoring device) inserted for the diagnosis and/or management of intracranial hypertension.
• Patients who undergo procedures for chronic subdural haematoma(s), including burr holes or mini-craniotomies.
• Elective (planned admission) or semi-elective (where patient initially admitted as an emergency, then discharged from hospital, and re-admitted at later time for surgery) procedures.
• Patients who have previously had emergency cranial surgery for traumatic brain injury rendering them eligible for inclusion in this study (regardless of whether they were included)

2.5. Patient inclusion and exclusion criteria

Table 1 summarises the patient inclusion and exclusion criteria.

2.6. Outcome measures

The primary outcome measure will be 14-day mortality (or in-hospital mortality if discharge occurs before 14 days).

The secondary outcome measures will include:

1. Perioperative complications
   - o Return to operating theatre during follow up period
   - o Surgical site infection (SSI)
2. Length of stay (LOS)
   - o LOS in hospital (days)
   - o LOS in intensive care (days)
3. Glasgow Coma Score at discharge (GCS-D)
4. Discharge destination

2.7. Data points

A data set will be collected on all adult or paediatric patients receiving emergency surgery for TBI in the inclusion period (see Tables 2 through 5). The case report form is split into 3 subsections – injury/admission data, operative data and outcome data. The data fields were based on existing data sets and refined through iterative consultation with an interdisciplinary consortium of clinicians caring for TBI across a range of HDI settings.

Finally, each local study lead will complete a provider profiling questionnaire on resources available for the pre-hospital, emergency department, surgical, intensive care and rehabilitation management of patients with acute brain injuries at their institution. This questionnaire has been reviewed and endorsed by the WFNS Neurotraumatology Committee and British Neurotrauma Group.

2.8. Data capture

Collected data will be stored exclusively on a secure bespoke web-based system within the Outcome Registry Intervention and Operation Network (ORION) (https://orioncloud.org/). The platform enables secure data collection, validation and storage in a standard (SQL) format and is compliant with NHS security standards (including the NHS Information Governance toolkit). All patient data will be transmitted and held anonymously. An internal pilot has been conducted using the platform to assess feasibility prior to roll out of the full study. Prior to inputting data into the live platform, members of local study teams will be invited to practise entering 'dummy' data into an identical test platform with the aid of a comprehensive software guide.

2.9. Data quality

The protocol (including case report form and site questionnaire) has been translated, with the aid of global collaborators, into Arabic, Bengali, Chinese (traditional and simplified), French, Italian, Portuguese, Brazilian Portuguese, Spanish, Swahili and Urdu and to facilitate recruitment and participation from sites across the world. A comprehensive data dictionary is also available online.

2.10. Data validation

Data validation will occur by two mechanisms. Firstly, web-based forms in the online data capture platform will contain fixed options at the point of data entry to maximise the likelihood of accurate and complete data capture from the outset. Secondly, a local data validator independent of the local study team will be appointed at every participating site. After the study period has ended, each data validator will be asked to retrospectively identify all patients who received emergency surgery for TBI in their centre's study period (independent of the rest of the study team) to assess case ascertainment and collect data on 2 variables, namely the date and nature of the operation.

2.11. Sample size

As there is a paucity of data on emergency surgery for TBI globally, it was not possible to perform an accurate sample size calculation. However, we expect between 100 and 200 centres to participate and expect the majority of these centres to collect data on 5–10 patients in a given 30-day study period. This will result in a total of 500–2000 patients which we believe will be sufficient to analyse the study endpoints.

2.12. Statistical analysis

For the patient level data, an a priori statistical analysis plan has been developed with a statistician. The mean and standard deviation will be reported for normally distributed variables and the median and interquartile range for not normally distributed variables. Participating centres will be stratified based on their country into groups based on their Human Development Index (HDI) rank. The Human Development Index is calculated for each country based on its life expectancy at birth, years of schooling and gross national income (GNI) per capita (http://hdr.undp.org/en/composite/HDI). 14 day mortality (or survival to discharge, whichever comes first) will be reported for each HDI group and compared using the Pearson chi squared test. Univariable logistic regression analyses will be conducted between covariates and the primary outcome measure. Based on the results, covariates with a p value <0.20 will be included in the multivariable model. The final multivariable logistic model will be determined using stepwise back-

Table 2
Injury/admission data.

Gender	Male, Female
Age (in years at time of admission)	... (option for 'Unknown')
Mechanism of injury	- Road traffic collision (Pedestrian, Cyclist, Motorcyclist, Motorcyclist – passenger, Car – driver, Car – passenger, other type of vehicle – driver, other type of vehicle – passenger - Fall (standing height, from height) - Assault (without a weapon, blunt instrument, knife, firearm) - Other (Self Harm, Animal attack, Explosion, Sport/recreational activity, Industrial accident – that does not fit into the categories listed above, Other violence, Unknown, Other)
Date / time of injury	... (option for 'Unknown')
Date / time of admission to hospital where surgery is taking place	...
Was the patient directly transferred from the accident scene to the hospital where surgery is taking place?	Yes, No
Method of transport to the hospital where surgery is taking place	Helicopter - air ambulance, Land ambulance - staffed by paramedics, Land ambulance - not staffed by paramedics. Police, Private vehicle, By foot, Other - specify
American Society of Anaesthesiologists (ASA) Physical Status Classification	I, II, III, IV, V
Glasgow Coma Score on admission (or last documented GCS off sedation if sedated on admission)	Total and Eyes, Verbal ('T' if intubated/tracheostomy), Motor (option for 'Unknown')
	Left Right
Fixed and dilated pupil at any time point pre-operatively?	
Unreactive pupil at any point pre-operatively?	
Did the patient have an episode of hypoxia at any point prior to surgery?	Yes, No, Not measured prior to surgery
Did the patient have an episode of hypotension (systolic BP < 90 mmHg*) at any point prior to surgery?	Yes, No, Not measured prior to surgery
* Note that the lower limit of systolic BP differs for children with age according to the formula 90 + (2 × age in years)	
Major extra-cranial injury (defined as requiring hospital admission in its own right)?	Yes, No
Was a CT Head performed before the operation?	Yes, No

Table 3
CT data (if answered 'Yes' to 'Was a CT head performed before the operation?' in Table 2).

Date/time of first available CT head for review	...	
Midline shift in mm?	0–5 mm, 5–10 mm, >10 mm	
Basal cisterns	Open, Compressed/obliterated, Unknown	
Traumatic subarachnoid haemorrhage?	Yes, No	
Is there a depressed skull fracture?	Yes, No	
	If yes, are any of the fragments depressed > 1 cm relative to the rest of the skull on CT? Yes, No	
	If yes, is there any evidence of pneumocephalus on CT? Yes, No	
	If yes, is there evidence of a compound depressed skull fracture on examination of the patient? Yes, No	
	Left	*Right*
Supratentorial extradural haematoma?	No, 0–10 mm, 10–20 mm, >20 mm, Unknown	No, 0–10 mm, 10–20 mm, >20 mm, Unknown
Supratentorial subdural haematoma?	No, 0–10 mm, 10–20 mm, >20 mm, Unknown	No, 0–10 mm, 10–20 mm, >20 mm, Unknown
Supratentorial traumatic parenchymal lesion	No, Small, Large - >50 cm^3 volume, Unknown	No, Small, Large - >50 cm^3 volume, Unknown
Is there a traumatic posterior fossa haemorrhage?	Yes, No	

ward elimination. Pre-specified sub-group analyses will also be conducted for patients with severe TBI (GCS 3 to 8), and moderate and severe TBI (GCS 3 to 12). Individual surgeons and hospitals will not be identifiable from analyses (unless explicit consent to do so is given). Statistical analyses will be conducted using R (www.r-project.org). A p value of less than 0.05 will be considered statistically significant. The study and statistical analysis plan was pre-registered on Open Science Framework prior to commencement of data analysis: osf.io/ryjbs.

3. Ethics and dissemination

According to the United Kingdom National Health Service (NHS) Health Research Authority tool, this study is considered a clinical audit rather than research and, as such, does not require approval by a Research Ethics Committee. This has been confirmed formally by the South East Scotland NHS Research Ethics Committee in Edinburgh, Scotland as well as the NHS Research and Development Office at Cambridge University Hospitals. Local teams are expected to seek approval from the appropriate department (research or audit) at their institution prior to commencing the study. Where these departments do not exist, teams should follow the local procedure for obtaining approval for a study of this nature. Written confirmation of local approval and a signed data access and use agreement must be submitted electronically prior to local study teams being granted access to the online data capture platform and commencing data collection. The study has been registered on ClinicalTrials.gov (NCT04212754) and the Clinical Trials Registry – India (CTRI/2019/02/017479).

The study will be reported following the Strengthening the Reporting of Observational Studies in Epidemiology statement guidelines and checklists [14]. The results will be submitted for open access publication in a peer reviewed journal. Fully named authors on the byline of publications resulting from this study will be those that satisfy the International Committee of Medical Journal Editors (ICMJE) guidelines for authorship. In addition, 'on behalf of the Global Neurotrauma Outcomes Study Collaborators' will be listed on the byline. The local study lead,

Table 4
Operative data.

Grade of most senior surgeon present in the operating theatre	Fully qualified neurosurgeon, Neurosurgeon-in-training, Other qualified surgeon, Other surgeon in training, Medically qualified but not in a surgical training programme, Not medically qualified surgical provider
Grade of most senior anaesthesia provider present in the operating theatre	Fully qualified anaesthetist with medical qualification, Anaesthetist-in-training with medical qualification, Not medically qualified anaesthesia provider, Anaesthetic administered by the surgeon, Other (specify), No anaesthesia provided
Type of anaesthesia	General, Local, None
Date / time operation started?	. . .
Date / time operation finished?	. . .
Were pre-incision prophylactic antibiotics given?	Yes, No
Class of surgical wound	Clean, Clean-contaminated, Contaminated, Dirty-infected
Location of surgery	Left, Right, Bilateral, Midline
What was the main procedure undertaken? * if > 1 procedure undertaken, select the main one	- Exploratory burr holes *If selected 'Exploratory burr holes', what were the intraoperative findings?* Extradural haematoma, Acute subdural haematoma, Chronic subdural haematoma, ICH/contusion, No significant findings *If selected 'Exploratory burr holes', how did you proceed given the intraoperative findings?* No further operative steps, wounds closed, Proceeded to craniotomy, Proceeded to decompressive craniectomy- Supratentorial craniotomy/craniectomy for traumatic mass lesion (Evacuation of supratentorial EDH, Evacuation of supratentorial ASDH, Evacuation of supratentorial traumatic parenchymal haemorrhage) *If selected an option under 'supratentorial craniotomy for mass lesion', what was done with the bone flap at the end of the procedure?* Replaced and fixed, Replaced and left floating/hinged, Removed and placed in abdomen, Removed and stored, Removed and discarded- Infratentorial craniotomy/ craniectomy for traumatic mass lesion (Evacuation of posterior fossa EDH, Evacuation of posterior fossa ASDH, Evacuation of posterior fossa traumatic parenchyma haemorrhage)- Operations to decrease intracranial pressure (Decompressive craniectomy to control raised intracranial pressure - no significant haematoma evacuated, Posterior fossa decompression - no significant haematoma evacuated, Cisternostomy)- Other operation for cranial trauma (Elevation of depressed skull fracture/other operation for depressed skull fracture, Surgical debridement of penetrating injuries) *If selected 'Elevation of depressed skull fracture/other operation for depressed skull fracture' OR 'Surgical debridement of penetrating injuries', was there a dural tear?* Yes, No *If selected 'Elevation of depressed skull fracture/other operation for depressed skull fracture' OR 'Surgical debridement of penetrating injuries', was there an associated venous sinus injury?* Yes, No *If selected 'Elevation of depressed skull fracture/other operation for depressed skull fracture' OR 'Surgical debridement of penetrating injuries', were postoperative prophylactic antibiotics prescribed to prevent infection?* Yes, No
Did the patient have an episode of hypotension (systolic BP < 90 mmHg) at any point during their surgery? * Note that the lower limit of systolic BP differs for children with age, as above.	Yes, No, Unknown
Did you have to perform a lobectomy?	Yes, No *If yes, what was the anatomical location of the lobectomy? Tick all that apply.* Right frontal, Left frontal, Right temporal, Left temporal, Other anatomic region
Was a duraplasty performed?	- Yes, apposition of dural edges and watertight closure - Yes, rough approximation of dural edges with sutures but not watertight closure - Yes, autologous graft with watertight closure - Yes, autologous graft laid on top of dura with no watertight closure - Yes, non-autologous graft with watertight closure - Yes, non-autologous graft laid on top of dura with no watertight closure - No - Unknown
Did the patient have a wound drain placed?	Yes – subdural, Yes – extradural, Yes – subgaleal, No
Did the patient have an intracranial pressure (ICP) monitor in place for postoperative ICP monitoring?	Yes – intraparenchymal, Yes – ventricular, No
Further comments regarding the procedure	. . .
Intraoperative death	Yes, No

additional members of the local study team and independent data validator at each participating site will be listed as PubMed citable collaborator status authors on all publications resulting from this study.

After publication of the primary results, the pooled dataset will be available to all members of the GNOS collaboration for secondary analysis, after judgement and approval of each proposed analysis by the central study team.

4. Discussion

We present a study protocol for a multi-centre, international prospective cohort study to ascertain outcomes following emergency surgery for traumatic brain injury globally. We believe the planned 30-day data collection period for each site coupled with 14-day follow up for all patients will be feasible for clinicians even in low-resource settings where their time is at a premium. The collaborative methodology we propose to use in this study has already been employed successfully to obtain outcome data in national neurosurgical studies [15] as well as in international projects in surgery and intensive care [16–18]. Moreover, we have prospectively planned a data validation strategy to assess case ascertainment.

There is a scarcity of data on outcomes following neurosurgery globally in the literature. The African Surgical Outcomes Study (ASOS), a 7-day prospective observational cohort study of outcomes following all surgery (including neurosurgery, which made

Table 5
Outcomes data.

Was the patient admitted to intensive care after the operation at any point during the 14-day follow up period?	Yes, No *If yes, date of admission to ICU …* *If yes, was the patient discharged from ICU during the 14-day follow up period?* Yes, No *If yes, date of discharge from ICU …*
Surgical site infection	Yes, No *If yes, was it a superficial/deep incisional infection (i.e. scalp wound) or organ/space infection (i.e. bone flap osteitis, meningitis and/or empyema/ abscess)?* Superficial or deep incisional infection, Organ/space infection *If yes, how was it diagnosed? Tick all that apply.* Symptoms, Signs on examination, Blood tests, Imaging, Wound swab microscopy, Wound swab Gram stain, Wound swab culture, CSF microscopy, CSF Gram stain, CSF culture, Surgical diagnosis
Did the patient return to the operating theatre for cranial surgery during the current admission?	Yes, No *If yes, what was the re-operation?* Re-evacuation of ipsilateral haematoma, Infection - wound washout, Infection - removal of bone flap, Craniectomy, Cranioplasty, Evacuation of contralateral haematoma, Other neurosurgical procedure
Did the patient survive to the end of the follow up period (14 days post-operatively or until they were discharged from hospital, whichever came first)?	Yes, No *Was the patient still admitted to hospital on the 14th day post-operatively?* Yes, No
Date of death or discharge from your institution (as applicable)	…
Discharge destination (if applicable)	Transfer to another hospital, Transfer to rehabilitation unit, Usual place of residence, Absconded, Other (state)
Glasgow Coma Scale at discharge or at the end of the follow up period if not discharged at 14 days post-operatively (if applicable)	Total and Eyes, Verbal ('T' if intubated/tracheostomy), Motor (option for 'Unknown')

up 2.2% of the 11,393 procedures included) in a convenience sample of 25 African countries, found that mortality and postoperative complications were significantly higher in their population relative to high income countries [19]. Similarly, the GlobalSurg study found that mortality following abdominal surgery is significantly higher in countries with a low HDI [17]. Finally, the Corticosteroid Randomisation After Head Injury (CRASH) trial found that mortality following severe, but not mild or moderate TBI, was higher in LMICs than high-income countries [20]. However, no detailed data on the differences in the participating sites, epidemiological characteristics of the patients or processes of care between the 2 groups was presented in this post-hoc subgroup analysis.

The proposed study has several important limitations. Firstly, there is a considerable risk of sampling bias due to our convenience sampling methodology which may limit our ability to extrapolate our findings. We plan to partially address this limitation by having each site fill out a detailed provider profile questionnaire (including questions such as whether each participating hospital is urban or rural, private or government funded and average annual total neurosurgical case volume) and reporting the findings to contextualise the patient level data. Moreover, we will not be collecting a true measure of functional outcome in this study. Studies in traumatic brain injury patients often utilise a rudimentary assessment of functional outcome, such as the Extended Glasgow Outcome Score (GOS-E). However, we believe this would be too onerous for all low resource centres to reliably collect in this study – in addition to the extra work involved in interviewing patients, it would likely be necessary for many centres to translate and possibly culturally validate the GOS-E questionnaire (or similar outcome assessment tool) prior to study commencement. As such, we have opted to include basic surrogate measures of functional outcome such as Glasgow Coma Scale at discharge and discharge destination.

4.1. Conclusions

The Global Neurotrauma Outcomes Study seeks to describe the differences in the epidemiological characteristics, management and outcome of emergency surgery for TBI across different Human Development Index settings. The results of GNOS could help identify practices that may best explain differences in outcomes, and will help inform the design of future local, national and international quality improvement programmes and clinical trials for this patient population globally. Moreover, we intend for this study and the international collaboration of clinicians involved in it to inform the development and facilitate the rollout of an international, prospective, hospital-based traumatic brain injury registry, supported by the World Federation of Neurosurgical Societies.

Ethical approval

Confirmation of audit/service evaluation status by the South East Scotland Research Ethics Service in Edinburgh.

Author contribution

DC conceived the idea for the study, wrote the study protocol, designed the case report form and site questionnaire and revised the study design/data capture tools following feedback. PH, DC, AJ and AK are the Principal Investigators of the study. DC, AJ, AHB, TB, HB, KB, TF, DKG, MJ, TK, TL, VM, AR, HS, MT, MyT, MaT, RT, IDB, FS, DM, AK, PH contributed to the funding application. AJ, OIA, AOA, AHB, TB, HB, KB, RFM, TF, DKG, MJ, TK, TL, VM, KP, AR, HS, KS, MT, AT, MyT, MaT, RT, SV, IDB, FS, DM, AK, PH, NB, IC, CI, GR, BS contributed input and revisions to the study design and study protocol. SV, DC and RFM created the statistical analysis plan. AB, AI, YS and KB were involved with the revision of the case report form and data capture platform, including assessing their feasibility. DC, PH, AJ and AK made critical revisions to the manuscript. All authors contributed to the manuscript and agreed to submission.

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Research registration number

The study has been registered on ClinicalTrials.gov (NCT04212754) and the Clinical Trials Registry – India (CTRI/2019/02/017479).

Guarantor

David Clark and Peter Hutchinson are the guarantors for the study.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

[1] GBD collaborators, Global, regional, and national burden of traumatic brain injury and spinal cord injury, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016, Lancet Neurol. 18 (1) (2019) 56–87, https://doi.org/10.1016/S1474-4422(18)30415-0 [published Online First: 2018/11/26].

[2] T.J. Esposito, R.L. Reed, R.L. Gamelli, et al., Neurosurgical coverage: essential, desired, or irrelevant for good patient care and trauma center status, Ann. Surg. 242 (3) (2005) 364–370, discussion 70–4.

[3] J.M. Seelig, D.P. Becker, J.D. Miller, et al., Traumatic acute subdural hematoma: major mortality reduction in comatose patients treated within four hours, N. Engl. J. Med. 304 (25) (1981) 1511–1518, https://doi.org/10.1056/NEJM198106183042503.

[4] K. Haselsberger, R. Pucher, L.M. Auer, Prognosis after acute subdural or epidural haemorrhage, Acta Neurochir. (Wien) 90 (3–4) (1988) 111–116.

[5] J.E. Cohen, A. Montero, Z.H. Israel, Prognosis and clinical relevance of anisocoria-craniotomy latency for epidural hematoma in comatose patients, J. Trauma 41 (1) (1996) 120–122.

[6] D.E. Sakas, M.R. Bullock, G.M. Teasdale, One-year outcome following craniotomy for traumatic hematoma in patients with fixed dilated pupils, J. Neurosurg. 82 (6) (1995) 961–965, https://doi.org/10.3171/jns.1995.82.6.0961.

[7] M. Botman, R.J. Meester, R. Voorhoeve, et al., The Amsterdam declaration on essential surgical care, World J. Surg. 39 (6) (2015) 1335–1340, https://doi.org/10.1007/s00268-015-3057-x.

[8] C.N. Mock, P. Donkor, A. Gawande, et al., Essential surgery: key messages from Disease Control Priorities, 3rd edition, Lancet 385 (9983) (2015) 2209–2219, https://doi.org/10.1016/S0140-6736(15)60091-5 [published Online First: 2015/02/05].

[9] WHO. Cause-specific mortality: estimates for 2015 http://www.who.int/healthinfo/global_burden_disease/estimates/en/index1.html: World Health Organisation; 2015 [accessed 24th of July 2017.

[10] M. Punchak, S. Mukhopadhyay, S. Sachdev, et al., Neurosurgical care: availability and access in low-income and middle-income countries, World Neurosurg. 112 (2018) e240–e254, https://doi.org/10.1016/j.wneu.2018.01.029 [published Online First: 2018/01/08].

[11] J.S. Hauptman, D.S. Chow, N.A. Martin, et al., Research productivity in neurosurgery: trends in globalization, scientific focus, and funding, J. Neurosurg. 115 (6) (2011) 1262–1272, https://doi.org/10.3171/2011.8.JNS11857 [published Online First: 2011/08/26].

[12] A. Patel, M.M. Vieira, J. Abraham, et al., Quality of the development of traumatic brain injury clinical practice guidelines: a systematic review, PLoS One 11 (9) (2016), https://doi.org/10.1371/journal.pone.0161554 [published Online First: 2016/09/01] e0161554.

[13] Foundation BT, Surgeons AAoN, Surgeons CoN, Guidelines for the management of severe traumatic brain injury, J. Neurotrauma 24 (Suppl 1) (2007) S1–106, https://doi.org/10.1089/neu.2007.9999.

[14] E. von Elm, D.G. Altman, M. Egger, et al., The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies, Int. J. Surg. 12 (12) (2014) 1495–1499, https://doi.org/10.1016/j.ijsu.2014.07.013 [published Online First: 2014/07/18].

[15] P.M. Brennan, A.G. Kolias, A.J. Joannides, et al., The management and outcome for patients with chronic subdural hematoma: a prospective, multicenter, observational cohort study in the United Kingdom, J. Neurosurg. (2017) 1–8, https://doi.org/10.3171/2016.8.JNS16134.test [published Online First: 2017/03/17].

[16] G. Collaborative, Surgical site infection after gastrointestinal surgery in high-income, middle-income, and low-income countries: a prospective, international, multicentre cohort study, Lancet Infect. Dis. (2018), https://doi.org/10.1016/S1473-3099(18)30101-4 [published Online First: 2018/02/13].

[17] G. Collaborative, Mortality of emergency abdominal surgery in high-, middle- and low-income countries, Br. J. Surg. 103 (8) (2016) 971–988, https://doi.org/10.1002/bjs.10151.

[18] J.L. Vincent, J.C. Marshall, S.A. Namendys-Silva, et al., Assessment of the worldwide burden of critical illness: the intensive care over nations (ICON) audit, LancetRespir. Med. 2 (5) (2014) 380–386, https://doi.org/10.1016/S2213-2600(14)70061-X [published Online First: 2014/04/14].

[19] B.M. Biccard, T.E. Madiba, H.L. Kluyts, et al., Perioperative patient outcomes in the African Surgical Outcomes Study: a 7-day prospective observational cohort study, Lancet 391 (10130) (2018) 1589–1598, https://doi.org/10.1016/S0140-6736(18)30001-1 [published Online First: 2018/01/03].

[20] M.J. De Silva, I. Roberts, P. Perel, et al., Patient outcome after traumatic brain injury in high-, middle- and low-income countries: analysis of data on 8927 patients in 46 countries, Int. J. Epidemiol. 38 (2) (2009) 452–458, https://doi.org/10.1093/ije/dyn189 [published Online First: 2008/09/09].