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Towards a core outcome set for cranioplasty following traumatic brain injury and stroke 'A systematic review of reported outcomes'

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A R T I C L E I N F O

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A B S T R A C T

Background: There is wide-ranging published literature around cranioplasty following traumatic brain injury (TBI) and stroke, but the heterogeneity of outcomes limits the ability for meta-analysis. Consensus on appropriate outcome measures has not been reached, and given the clinical and research interest, a core outcome set (COS) would be beneficial.
Objectives: To collate outcomes currently reported across the cranioplasty literature which will subsequently be used in developing a cranioplasty COS.
Methods: This systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. All full-text English studies with more than ten patients (prospective) or more than 20 patients (retrospective) published after 1990 examining outcomes in CP were eligible for inclusion.
Results: The review included 205 studies from which 202 verbatim outcomes were extracted, grouped into 52 domains, and categorised into one or more of the OMERACT 2.0 framework core area(s). The total numbers of studies that reported outcomes in the core areas are 192 (94%) pathophysiological manifestations/ 114 (56%) resource use/economic impact/ 94 (46%) life impact/mortality 20 (10%). In addition, there are 61 outcome measures used in the 205 studies across all domains.
Conclusion: This study shows considerable heterogeneity in the types of outcomes used across the cranioplasty literature, demonstrating the importance and necessity of developing a COS to help standardise reporting across the literature.

1. Introduction

Several recent randomised trials (Hutchinson et al., 2016; Vahedi et al., 2007) have investigated the effectiveness of a decompressive craniectomy as the surgical management of raised intracranial pressure and/or brain swelling following a traumatic brain injury (TBI) or stroke. Patients who survive will usually have their skull reconstructed later via another operation, known as cranioplasty, with the annual numbers increasing. Cranioplasty aims to restore a degree of mechanical protection to the brain, improve craniofacial cosmesis and, in some cases, improve neurological symptoms and deficits. Although it is a well-established neurosurgical procedure, several essential but unanswered clinical questions remain, including the optimal material, timing, complications, and the effect a cranioplasty has on neurological recovery (Malcolm et al., 2018; Cola et al., 2018).

The exact mechanism of the sometimes-observed neurological Improvement is not entirely understood. It is likely secondary to the physiological effects that occur due to the reconstruction of the cranial vault on the brain (Nasi and Dobran, 2020). These include the stabilisation of the atmospheric pressure gradient and the re-establishment of

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the fixed volume of the cranium. In addition, the improved cerebrospinal fluid hydrodynamics (Shahid et al., 2018; Jiang et al., 2018; Yoshida et al., 1996) and improvements in cerebral blood flow that occur following reconstruction (Winkler et al., 2000)' (Chibbaro et al., 2013) give potential reasons to explain the sometimes-observed neurological Improvement. Given this, there are still no certainties of an enhancement in neurological outcomes following cranioplasty and further work is required to understand which patients would benefit most. Cranioplasty may have the greatest effect on neurological recovery in those patients who were neurologically improving independent of cranioplasty, with the cranioplasty helping to optimise the physiological state of the cranial vault as discussed, resulting in the most optimal state for neuroplasticity and neurological Improvement. Primarily subjectively observed in clinical practice, because the evidence is lacking, there are also more subtle areas of change post cranioplasty that can greatly impact a patient's rehabilitation potential, quality of life and overall outcome, including positioning, tone, and spasticity.

Given these interests, increasing necessary research is being undertaken, which results in a heterogeneity of outcomes. Without uniformity and standardisation difficulties arise with comparisons of studies, especially concerning systematic reviews, meta-analyses, and clinical guidelines. One way to overcome this is through the development of core outcome sets (COS), which aim to standardise outcomes and are defined as "an agreed standardised set of outcomes that should be measured and reported, as a minimum, in all clinical studies and trials in specific areas of health or health care." (Williamson et al., 2012). Different methodological approaches exist in the development of a COS. Therefore, it is necessary to predefine the framework from which to work. Broadly it is split into two main phases: Phase 1 involves identification of outcomes currently being reported for the specified disease or health condition and phase 2, using the outcomes from phase 1 to find consensus from which an agreed standardised set of outcomes, known as the "core outcome set", is finalised.

1.1. Objectives

The aims of this study were to classify and collate a comprehensive list of currently used outcomes across the cranioplasty TBI and stroke literature. Thus enabling an understanding of which measures are more commonly used, in what contexts, and identify common areas of inconsistencies in their reporting.

2. Methods

2.1. Protocol and registration

The preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines (Moher et al., 2009) have been followed and adhered to and the study was prospectively registered with the PROSPERO prospective register of systematic reviews (CRD42015027325). In addition, the COS project was registered with the Core Outcome Measures in Effectiveness Trials (COMET) initiative, and a detailed protocol of the study design and methods developed.

2.2. Search and eligibility criteria

We performed a specific search of English-language literature across 3 electronic databases: PubMed, Embase and Web of Science, to identify relevant studies from January 1990 to February 2021. We searched these databases using key words such as: decompressive craniectomy OR defect AND cranial OR calvarial OR skull AND replace OR repair OR implant OR reconstruct AND bone flap OR cranial OR skull OR cranioplasty AND English Language. (please supplement file 1 for complete search details). The broad nature of the search was chosen to be as inclusive as possible ensuring inclusion of potentially relevant studies.

2.3. Inclusion and exclusion criteria

We included articles that were (1) in English, (2) included adults (≥16 years), (3) published after 1990, (4) related to cranioplasty following decompressive craniectomy for either traumatic brain injury or stroke, (5) randomised control trials; prospective or retrospective cohort studies of at least 10 and 20 patients, respectively, (6) examining complications or other outcomes (clinical or radiological). We excluded studies of penetrating injuries, blast injuries and military populations.

2.4. Study selection and data extraction

After duplicates were removed, the initial search yielded 5084 potentially relevant studies. Titles and abstracts of 406 studies were screened for eligibility using the inclusion criteria, resulting in 205 articles for which full-text articles were retrieved (Fig. 1). Relevant data from included studies were collected independently by two authors via the software Rayyan. Any discrepancies were settled by consultation between the two authors with reference to the original article. Data extracted from each study included all types of outcomes which are referenced as verbatim in this review and then subsequently grouped into domains for analysis. Baseline data were also extracted, including the number of patients, study population demographics, indication for craniectomy, and follow up time frame.

Statistical analyses and graphics were performed using the computing environment R (R Core Team [2015], which is a language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria; http://www.R-project.org/) and using Atlas.ti (version 9.0).

2.5. Appraisal and synthesis of results

This study has adopted the framework developed by the Outcome Measures in Rheumatology (OMERACT) group, known as the OMERACT 2.0 filter (Kirwan et al., 2014), (Table 1) which is in its second iteration, and has been advocated for COS development by the COMET programme (Tugwell et al., 2007; Boers et al., 2014).

The verbatim outcomes extracted from studies have been grouped into outcome domains and subsequently categorised into at least one of the frameworks four core areas, namely: Life Impact; Resource Use/ Economical Impact; Pathophysiological Manifestations; Death. Life impact core area can include domains from both the International Classification of functioning (ICF) and the health-related quality of life (HRQoL) frameworks. The pathological manifestations core area is to assess whether the effect of the intervention targets the pathophysiology of the health condition explicitly. Resource use and economic impact should include domains describing the economic impact of the health condition for an individual and/or society and specific resource use.

3. Results

3.1. Study selection

The analysis included 205 studies comprising of 74996 patients with 64.5% male and 35.5% female, and a mean age of 43. Study types included: 148/205 (72%) retrospective, 37/205 (18%) prospective and 18/205 (9%) were a combination of both, with 2 (1%) randomised control trials (RCT's). Reflecting the known growing research interest in this field, the annual number of published studies in this review increased up to 2017 (Fig. 2), with a consistent number of publications since. USA was the country with the highest number of studies (27, 13.2%), followed by Germany (25, 12.2%), Korea (24, 11.7%) and China (18, 8.8%). Risk of bias tool was not applied to the included studies, as this is not a systematic review aiming to assess the effectiveness of a specific intervention, where formal assessment of risk of bias is essential rather an assessment of the full breadth of the cranioplasty literature in

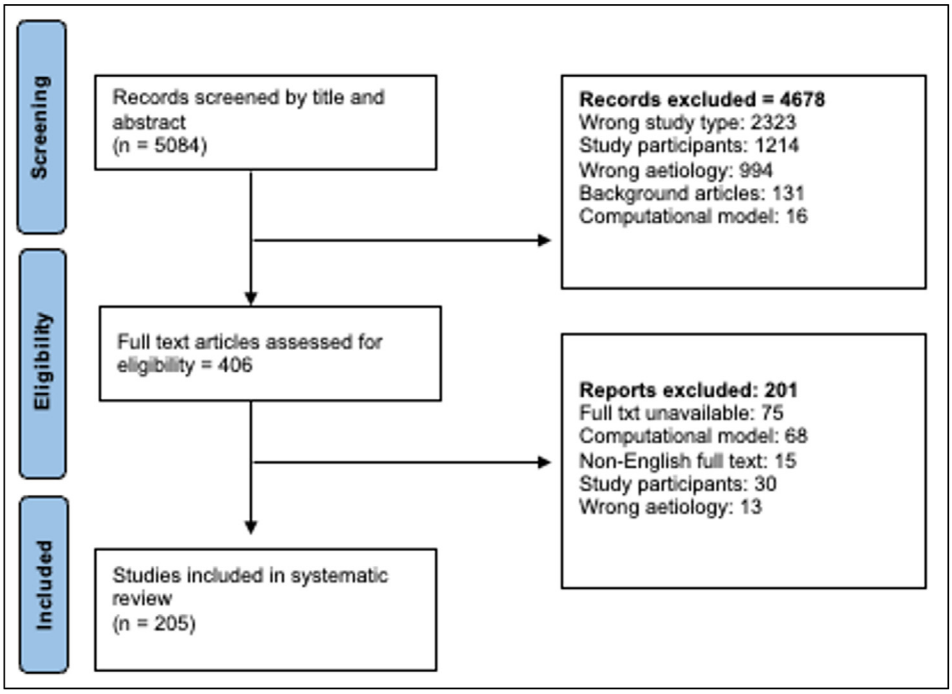
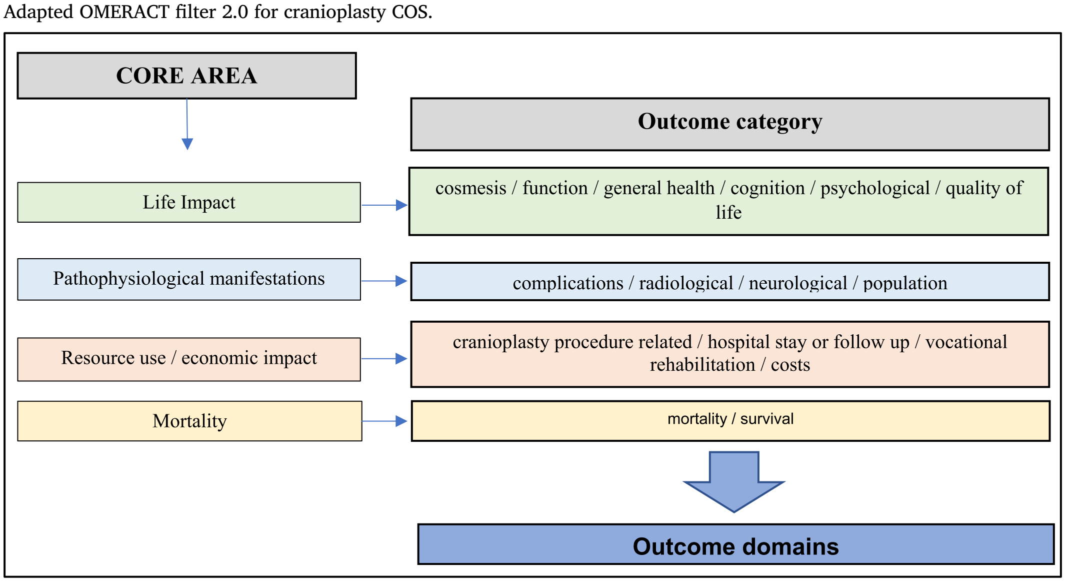


Fig. 1. Study Prisma flow chart.

Table 1
Adapted OMERACT filter 2.0 for cranioplasty COS.



order to understand which are the outcomes that are being currently reported and if only high-quality studies (ie RCTs and other prospective non-randomised studies) were included, we would end up with a very limited sample and risk missing some potentially novel outcomes.

3.2. Outcomes

202 verbatim outcomes were extracted from 205 studies and grouped into 56 outcome domains, which in turn have been grouped into core area(s). Total numbers of studies reporting outcomes in the core areas are: 192 (94%) pathophysiological manifestations/ 114 (56%) resource use/economic impact/ 94 (46%) life impact/ mortality 20 (10%). Within each core area, outcome domains have been grouped into categories based on type.

3.2.1. Outcome measures

61 outcome measures were used across all domains of which 55/61 (90%) were related to life impact outcomes.

3.3. Pathophysiological manifestations

192/205 (94%) studies have reported 113/202 (56%) verbatim outcomes. These have been grouped into 26 outcome domains across four categories (Table 2).

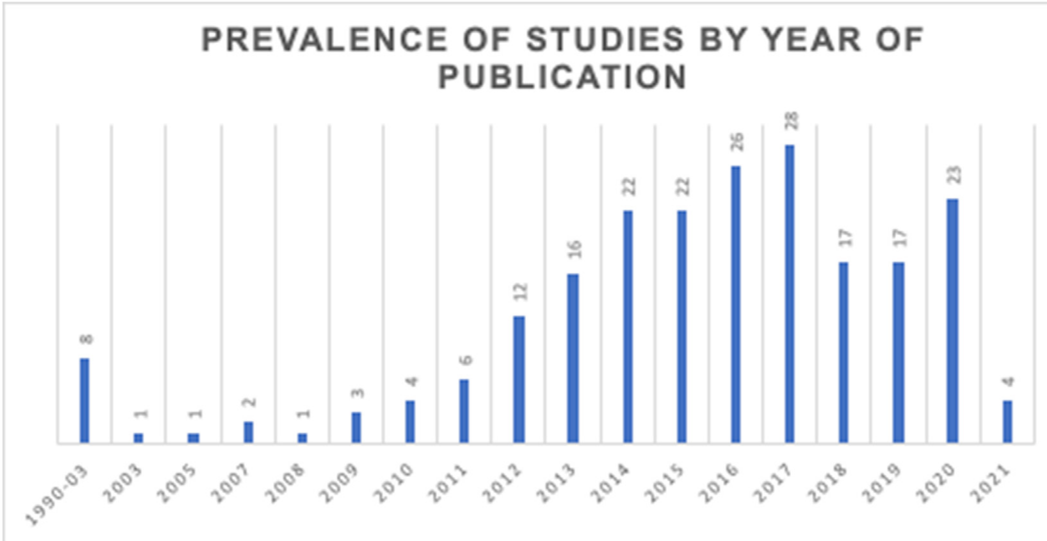


Fig. 2. Prevalence of reported studies by year.

3.3.1. Pathophysiological category 1: complications

Complications comprised of 83 verbatim outcomes categorised into 14 domains (Fig. 3). The three most common domains reported across all studies were infections (122/205 (60%)), overall complications (85/205 (41%)) and intracranial haematoma (76 (37%)).

3.3.2. Pathophysiological category 2: radiological

Radiological outcomes comprised of 9 verbatim outcomes categorised into five domains. Total number of occurrences of domains reported: bone resorption (42/205 (20%)), bone necrosis (3/205 (1%)), pneumocephalus (2/205 1%)), intracranial haematoma (7/205 (3%)) and cerebral blood flow (CBF) (7/205 (3%)). Perfusion CT-scan (4 studies), transcranial doppler (2 studies) and SPECT (1 study) were the different radiological methods of measuring CBF.

3.3.3. Pathophysiological category 3: neurological

Neurological outcomes comprised of 21 verbatim outcomes categorised into seven domains. The most widely reported in studies is level of consciousness (29/205 (14%)) (Fig. 4). The other six domains were each reported in only 1% of studies.

3.3.4. Pathophysiological category 4: patient co-morbidities

Co-morbiditiy outcomes comprise of three verbatim outcomes categorised into one domain: patient co-morbidites, which was reported in 8 studies (4%).

3.4. Life impact

94/205 (46%) studies reported outcomes categorised in this core area 63/202 verbatim outcomes (31%) were grouped into 20 domains and six categories (Table 3).

The six categories are displayed in Fig. 5, with function 56/205 (27%), cosmesis 44/205 (21%) and cognition 14/205 (7%) being the most reported.

3.4.1. Life impact category 1: function

49/205 (24%) studies reported 'global functional outcome' domain, which includes the verbatim outcomes: activities of daily living, functional capacity, functional outcome and transfers.

8/61(13%) outcome measures were used for measuring function. The most used measure was the GOS, reported in 29/205 (14%) studies. Fig. 6 shows the relationship between function domains and outcome measures, with total study numbers reported.

3.4.2. Life impact category 2: cosmesis

The cosmetic appearance was assessed in 44 (21%) studies with 9 (20%) of these using either a validated or non validated outcome measure: Cosmesis satisfaction survey, cosmetic satisfaction score, outcome after cervical spine surgery (ODOM) criteria, Rostock Functional and Cosmetic Cranioplasty Score and Visual Analog Scale for cosmesis as well as several self-designed questionnaires.

3.4.3. Life impact category 3: cognition

Given the wide definitions of cognition, the 25 verbatim outcomes have been grouped into six domains, of which 14 (7%) studies reported on. There are 28 different outcome measures, some grouped into cognitive batteries. 5/14 (36%) reported using the Mini-Mental State Examination (MMSE) with the COGNISTAT cognitive assessment, frontal assessment battery and Rey Auditory Verbal Learning test being other commonly used measures.

3.4.4. Life impact category 4: quality of life

Health-related quality of life evaluation was included in 4 studies (2%). The Short Form-36 Health Survey (SF-36) was performed in 2 studies, both with longitudinal evaluation. The 5-level European Quality of Life-5 Dimensions (EQ-5D-5L) and Glasgow Benefit Inventory (GBI) were used in one study each.

3.5. Resource use/economic impact

114/205 (56%) studies reported outcomes categorised in the core area 'resource use/economic impact'. In total 24/202 verbatum outcomes (12%) were grouped into 8 domains and 4 categories. Reported domains include: Implant failure (5 (2%) studies)/ repeat intervention (33 (16%) studies)/ cranioplasty costs (11 (5%) studies)/ health economic evaluation (11 (5%) studies)/ length of hospitalisation (8 (4%) studies)/ return to work (2 (1%) studies).

3.6. Mortality

34/205 studies reported overall mortality, which, for this study, due to the variability of reporting and study design, has been categorised as 'reported or not reported.

3.7. Follow up

Length of follow-up was stated in 118 studies (58%) as a mean value

Table 2
Pathophysiological manifestations outcomes (Table 2)
192/205 (94%) studies reported on 113/202 (56%) outcomes and subsequently categorised into 26 outcome domains and 4 outcome categories.

Outcome category	Outcome domain (Delphi outcome)	Outcome verbatim	Outcome measure
Complications	**Overall complications**	Minor complications	
		Overall complications	
	Infection	Brain abscess	
		Intra-cranial infection	
		Major infection	Complication score
		Phlebitis	Landriel ibanez classification
		Sub dural empyema	
		Wound infection	
		Deep surgical site infection	
		Superficial surgical site infection	
		Surgical site infection	
		Osteomyelitis	
	Wound/ soft tissue related issues	Scalp necrosis	
		Skin tissue necrosis	
		Tissue necrosis	
		Wound dehiscence	
		Wound healing disturbance	
		Wound healing rate	
		Pressure ulcer on scalp	
		Soft tissue injury	
		Swelling around cranioplasty site	
		Scar retraction	
	Intra cranial haematoma Inc re-operation or not	Bleeding	
		Blood loss	
		Epidural haematoma	
		Epidural haemorrhage	
		Extra dural haematoma	
		Haematoma	
		Haematoma not requiring evacuation	
		Haematoma requiring evacuation	
		Haemorrhage	
		Intra cranial haemorrhage	
		Intracerebral haematoma	
		Sub dural drain	
		Sub dural haematoma	
		Subgalea collection	
	Extra cranial haematoma collections	Collections	
		Effusion	
		Extra axial fluid collection	
		Hygroma	
		Pseudomeningocoele	
		Seroma	
		Sub dural fluid collection	
	Seizure	Seizure	
	Hydrocephalus	Hydrocephalus	
		Shunt dependant hydrocephalus	
	Graft specific	Cranioplasty to bone shift	
		Cranioplasty dislocation	
		Fractures	
		Fracture of MMA	
		Graft displacement	
		Graft fracture	
		Graft removal secondary to infection	
		Implant failure	
		Loosening of CP	
		Mesh broken	
		Sunken bone plate	
	Temporal muscle	Jaw movement	Jaw function limitation scale
		Mouth opening	
		Post operative hypertrophy of temporal muscle	
		Temporal hallowing	
		Temporal muscle atrophy	
		Temporal wasting	
	Medical - systemic complications post operative	DVT	
		Abdominal wall pressure	
		Cardiac arrest	
		Coagulation disorder	
		Haematoma (non-surgical)	
		Meningitis	
		Myocardial infarction	
		Pneumonia	
		Pneumonitis	
		Pseudomembranous colitis	
		Pulmonary thromboembolism	
		Sepsis	
		Urinary tract infection	
	Cerebrovascular event	Ischaemic stroke	
		Stroke	
	Pain - scalp	Local discomfort	
		Pain	
		Paresis	
	Headache	Headache	
Radiological	**Bone resorption**	Bone resorption	
	Bone necrosis	Aseptic bone necrosis	
		Bone necrosis	
	Pneumocephalus	Pneumocephalus	
	Intra cranial haematoma	Cerebral contusions	
		Brain herniation	
	Cerebral blood flow	Cerebral blood flow	
		CT perfusion	
		Cerebral blood volume	
	Osseointegration	Osseointegration	
Neurological	**Level of consciousness**	Consciousness	Coma Recovery Scale (CRS)
		Level of consciousness	Glasgow coma scale
		EEG results	AVPU
	Muscle function	Muscle power	
		Worsening of standing	
	Swallow and communicate	Dysphasia	
	Scalp sensory disturbance	Temperature sensitivity	
		Neuropathy	
		Skin irritation	
	Sleep	Insomnia	
		Tiredness	
	Physical symptoms of neurological nature	Blurry vision	
		Buzzing	
		Dizziness	
		Irritability	
		Salivation	
		Tiredness	
		Vibration intolerance	
Patient's co-morbidities	**Co-morbidities**	Age	
		Co-morbidities	

(*continued on next page*)

Table 2 (*continued*)

Outcome category	Outcome domain (Delphi outcome)	Outcome verbatim	Outcome measure
		Medical co-morbidities	

or range of days. Among those studies that described the meantime of follow-up, we found an overall meantime of 652 ± 556 days, range 7–2916 days. We did not detect a significant difference in the meantime of follow-up between prospective and retrospective studies.

4. Discussion

One of the challenges in developing a core outcome set for cranioplasty is defining outcomes specific to the cranioplasty procedure. Overlap with outcomes relating to the trajectory of recovery from the underlying brain injury is expected but the outcomes in this review relate to the cranioplasty procedure itself, and the impact cranioplasty may have on patient outcome. This standardisation of outcomes relating to cranioplasty, and subsequent COS development will not only help with the future standardisation of outcomes but will also help in the development of an outcome measure, specific to cranioplasty. This outcome measure will be particularly important as the currently utilised functional outcome measures, such as the GOSE or quality of life measures, such as

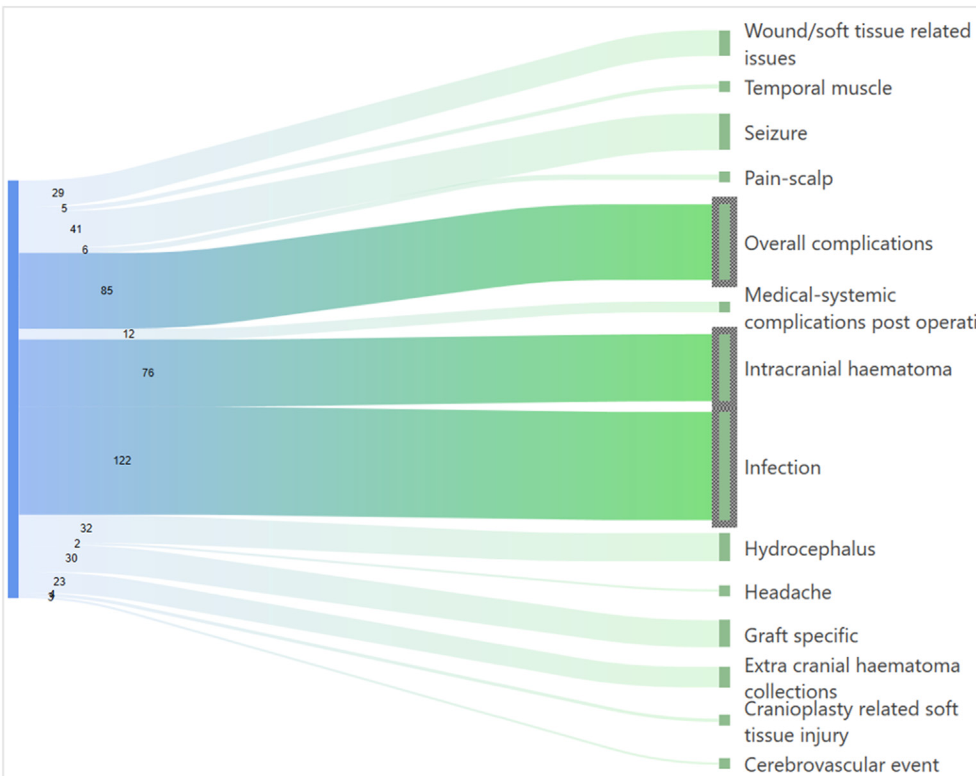


Fig. 3. Pathophysiological core area – Outcome domains in complications category.

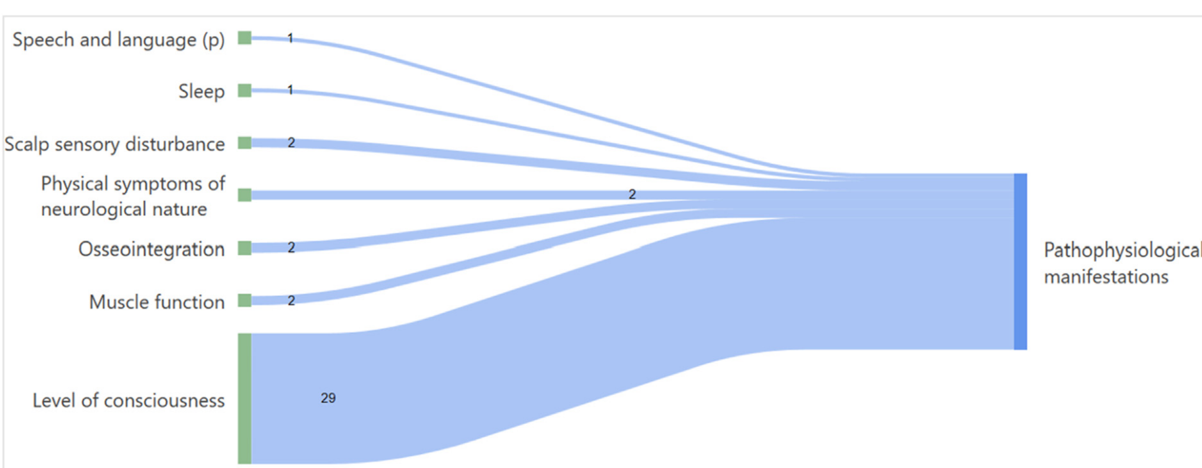


Fig. 4. Pathophysiological core area – Outcome domains in neurological category.

Table 3
Life Impact outcomes (Table 3)
94/205 (46%) studies reported on 63/202 (31%) outcomes and subsequently categorised into 20 outcome domains and 6 outcome categories.

Outcome category	Outcome domain (Delphi outcome)	Outcome verbatim	Outcome measure
Cosmesis	**Overall cosmetic outcome**	Cosmesis	Cosmesis satisfaction survey
		Symmetry	Cosmetic satisfaction score
	Patient satisfaction of cosmetic outcome	Overall satisfaction	Outcome after cervical spine surgery (ODOM) criteria
		Patient satisfaction	Rostock functional and cosmetic cranioplasty score
		Clinician satisfaction	Self-designed questionnaire for cosmesis
			Visual analogue scale for cosmesis
Function	**Global Functional outcome**	Activities of daily living	GOS
		Functional capacity	GOSE
		Functional outcome	Barthel Index
		Transfers	Korean modified Barthel index
			Karnofsky performance scale
			mRS
			Modified Glasgow outcome scale
			National Institutes of Health Stroke Scale (NIHSS)
	Functional independence	Independence	FIM
		Living situation	FIM (Motor)
		Self-care	FIM (Cognition)
	Motor function	Mobility	Muscle power
		Motor function	
		Muscle power	
		Physical status	
		Transfers	
	Pain	Pain	Visual analogue scale for pain intensity
			Visual analogue scale
General health	**Physical health**	General health	American Society of Anaesthesiologist (ASA) outcome
		Physical aspects	
		Physical health	
	Bladder control	Bladder control	
		Sphincter control	
	Bowel control	Bowel control	
	Well-being	Vitality	
		Well-being	
Cognition	**Cognition (global)**	Cognition (general)	Digit symbol substitution test
			COGNISTAT cognitive assessment
			Cognitive performance index
			Community mental state examination
			Korean MMSE
			Levels of cognitive functioning
			MMSE
			Luria-Nebraska Neuropsychological battery screening test short form (LNNBS)
			Rancho Los Amigo Scale (RLS)
			Rey Auditory Verbal Learning Test (RAVLT)
	Executive functioning	Abstract thinking	Digit span
		Calculations	Frontal assessment battery
		Categorisation	Modified Wisconsin Card Sorting Test
		Cognitive flexibility	Ravens coloured progressive matrices
		Construction	Semantic fluency test
		Construction	Simplified Tower of London Test
		Executive function	Trail making test
		Judgement	Trail making test A + B
		Psychomotor speed	
		Reasoning	
		Spatial logic thinking	
		Task switching	
	Memory	Memory	Rivermead behavioural memory test
			The Rey-Osterrieth Complex figure test
	Attention	Attention	Test of Attentional Performance
		Awareness	
		Visual attention	
	Orientation	Orientation	
	Communication and language	Comprehension	Category verbal fluency
		Expression	Computerized naming and reading
		Language	Controlled oral word association test
		Phonemic fluency	Letter fluency
		Repetition	Sentence construction test
		Sentence understanding	Story recall test
		Verbal learning	Token Test
Psychological	**Depression and anxiety**	Anxiety	Hamilton Rating Scale: anxiety
		Depression	Hamilton Rating Scale: depression
		Insecurity	Centre for epidemiological studies - depression
	Mental health	Emotional aspects	
		Mental health	
	Social outcome	Social aspects	
		Social cognition	
		Social support	
Quality of life	**Quality of life**	Quality of life	EQ5D-5L
		Patient satisfaction	Short form health questionnaire (SF-36)
		Vitality	Glasgow benefit inventory
		Well-being	

the EQ5D-5L, are not specific enough to capture changes in outcomes related to cranioplasty, rather the overall brain injury recovery. The enhancement of data collection using an outcome measure specific to cranioplasty will help maximise the opportunities in capturing changes in outcomes related specifically to cranioplasty in addition to the probable changes in outcomes from the underlying brain injury.

We have identified significant heterogeneity in both outcomes and outcome measures used in clinical studies assessing cranioplasty following TBI or stroke. Most of the studies had not explicitly defined a primary outcome and often no specific definitions of the outcomes that

Table 4
Resource use/economic impact (Table 4)
114/205 (56%) studies reported on 24/202 (12%) outcomes and subsequently categorised into 8 outcome domains and 4 outcome categories.

Outcome category (Delphi outcome)	Outcome domain	Outcome verbatim
Cranioplasty procedure related	**Timing of procedure**	Timing
	Repeat intervention	Re-intervention Removal of implant Repeat operation Revision
	Implant failure	Implant failure
Hospital stay/ follow up	**Length of hospitalisation**	Hospital stay Hospital ward stay Length of hospitalisation Interval of hospital visits
	Length of intensive care stay	ICU stay
Vocational rehabilitation	**Return to work/study**	Working with limitations Working without limitations Return to work Incapable of working
Costs	**Cranioplasty costs**	Cost of implant Cost of operation Operating room and surgical costs Total costs Cost of implant
	Health economic evaluation	Cost effectiveness Re-intervention Total costs Re-operation before cranioplasty

Table 5
Mortality (Table 5)
34/205 (17%) studies reported either mortality or survival.

Outcome domain	Outcome verbatim
Mortality	Mortality
Survival	Mean survival

	Traumatic brain injury	Stroke
Reason for DC (primary)	171	34
Patients per study		
<100	101	34
>100	70	0
Type of study		
Observational	170	34
RCT	1	0
Studies by Country (Top 4)	USA 27 Germany 25 Korea 24 China 18	
Age (mean)	42	48
Material	191 studies (93%) reported material 122 studies (60%) included autologous 94 studies (46%) evaluated 1 material type	
Timing of cranioplasty	Mean time to cranioplasty 202 days (40–2555 days) 135 studies reported as a mean range 42 studies (21%) had pre-defined cut off for early and late 8 studies (3.9%) divided time into 3 categories Significant heterogenity in the timeframe definitions 50% of studies that reported time frames used <90 and >90 days	

were being measured. The findings from this study are not surprising, and similar patterns have been demonstrated in other neurosurgical conditions such as Chronic Subdural Haematoma (CSDH) (Chari et al., 2016) and Subarachnoid Haemorrhage (SAH) (Andersen et al., 2019) and in other specialities such as vascular surgery and ENT (Machin et al., 2021; Metryka et al., 2019) in which a lack of consistency in outcomes was also demonstrated. From this, there is a clear case for the development of a core outcome set (COS) that would homogenise outcome domains and help standardise what should be measured as a minimum for future cranioplasty studies.

The most widely reported core area was pathophysiological manifestations, with 192/205 (94%) of studies reporting 116/202 (57%) verbatim outcomes. This is no surprise given that the cranioplasty is a type of implant, and so the pathophysiological consequences of such are critically important in better understanding its safe application, and although the cranioplasty is typically an elective procedure following resolution of the original pathology, the historical concerns for clinicians around earlier cranioplasty increasing the risk of infection (Coulter et al., 2014; Hill et al., 2012) are echoed in this study, with complication category comprising of 83 verbatim outcomes grouped into 14 domains, with infections being directly reported in 60% of studies (60%).

There are multiple case series demonstrating neurological enhancement in functional, physical and cognitive recovery following cranial reconstruction (Kim et al., 2017; Archavlis and Nievas, 2012; Stefano et al., 2015) both dependent and independent of time frames. A 2018 systematic review explored the motor and cognitive changes following cranioplasty and showed procedures performed within 90 days improved motor function but not cognition (Cola et al., 2018) and a further systematic review comparing 'early and late' cohorts showed significantly improved outcomes in the early cohort (Malcolm et al., 2018). In this review, only 24% (49/205) of studies reported on global functional outcomes. The Glasgow outcome scale (GOS), a global assessment tool developed for evaluating functional outcome post-TBI (Jennett and Bond, 1975) was only used in 14% (29/205) studies. Although other measures of functional outcome were utilised, including the FIM, karnofsky performance scale and mRS, less than half the studies reporting on global functional outcome had an associated functional outcome scale. In addition, quality of life was only measured in 4 studies (2%) and with the potential impact a cranioplasty may have on a patients recovery, this is unexpected. This can be explained partly by 185 (87%) of studies being retrospective reviews, which demonstrates the likely complexities of research study design of prospective studies in this area. A core outcome set, with outcome domains crossing all core areas, would help close these weighted discrepancies of what is deemed important to report on and ensure a wide range of outcomes are consistently reported on.

As discussed earlier, a COS is defined as an agreed standardised set of outcomes that should be measured and reported (Williamson et al., 2012), but it is important to remember that the COS defines 'what to measure' and not 'how to measure'. These two terms are particularily important to separate for cranioplasty because of the different baseline and rehabilitation trajectories of brain injury survivors. In addition, the heterogeneity of neurological baselines from patients in a prolonged disorder of consciousness through to being independent at time of cranioplasty needs to be addressed when answering the 'how to measure' question.

4.1. Limitations

Limitations of this study include limiting our search to English papers only and the exclusion of studies pre 1990, which may have resulted in missing additional outcomes. In relation to the search strategy as we predefined some inclusion criteria and excluded case series, small cohort studies and some specific populations.

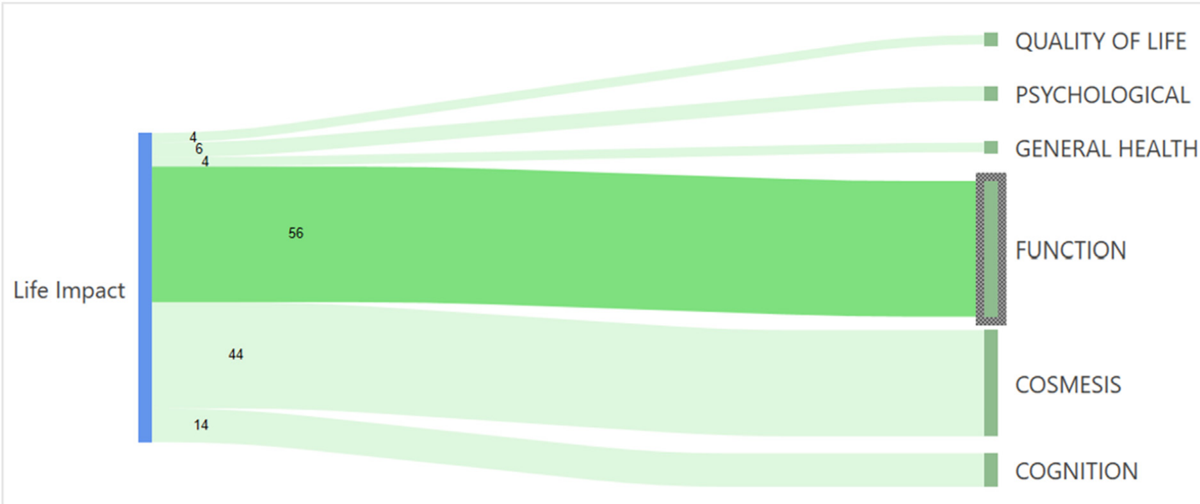


Fig. 5. Life impact core area – category overview.

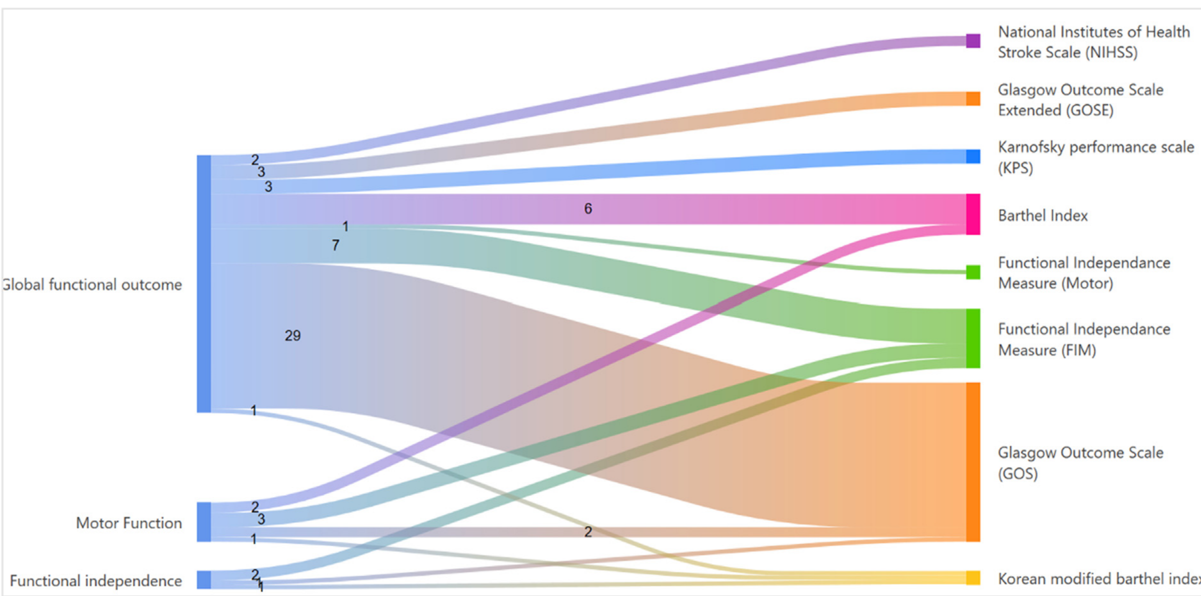


Fig. 6. Relationship between functional outcome domains and outcome measures.

4.2. Future directions

This systematic review is the first step in the development of a COS for cranioplasty following TBI or stroke. The outcome domains from this study will be used in part to formulate a Delphi questionnaire that will be scored by key stakeholder groups with a subsequent consensus meeting resulting in a consensus-driven COS. In addition, a common data element (CDE) set is being developed for cranioplasty studies, which would standardise the data elements to be collected by future cranioplasty TBI and stroke studies, ensuring homogenous and consistent reporting of demographic data, pre-operative status and intra-operative details. When both the COS and CDE are complete, we will have clearly defined, methodologically driven, consensus-based reporting sets that will allow for cross-study comparisons and hopefully resulting in a higher level of evidence in the future.

Development a cranioplasty specific outcome measure underpinned by the COS would help answer the 'how to measure' question. There is complexity here, given the variations in pathophysiological disease types, neurological baselines, and heterogeneity of outcomes but a cranioplasty outcome measure would be beneficial both for clinical and research purposes and could be integrated into registries (Kolias et al., 2014) to help standardise long term outcomes following cranioplasty.

5. Conclusions

A robust methodology and application of the OMERACT filter 2.0 as a conceptual framework has helped develop this comprehensive systematic review of currently used outcomes for cranioplasty following TBI or stroke. This review has demonstrated substantial heterogeneity in outcomes and outcome measures across the cranioplasty literature however classifying outcomes within a conceptual health framework, such as the OMERACT 2.0 filter, provides a platform for clinicians and researchers to ensure outcomes are used that are both relvant, patient focused, but that also cover the core areas of any given study or clinical service. Using this study and continuing adherence to the COS development protocol and with a consensus-driven approach, we are one step closer to the development of a COS and the standardisation of outcomes, which in turn will help improve clinical care.

Statement of authorship

HM and ACL wrote the manuscript.

FA, KG NO, CT, GW, EV IT, AH, AK and PH reviewed, gave expert guidance, and edited the manuscript.

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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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