# A Review of Neurosurgical randomized controlled trials in the Cochrane Database of Systematic Reviews: Key Findings and Implications for Future Research

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■ OBJECTIVE: **Evidence available to clinicians and patients to inform treatment decisions is ideally produced by randomized controlled trials (RCTs). The objective of this study was to assess the extent to which neurosurgical practice is supported by RCT-level evidence.**

■ METHODS: **A search of the Cochrane Library was conducted to find reviews of the effectiveness of neurosurgical operative interventions. Data were extracted on the intervention, patient population, and outcome measures as well as the strength of evidence, as rated by the Cochrane authors. The extracted data were analyzed to identify the gaps and areas of (in)consistency across the RCTs included within the Cochrane Reviews.**

■ RESULTS: **A total of 52 Cochrane Reviews met the inclusion criteria, which covered 8 neurosurgical subspecialties. However, only 28 were published after 2015. There was limited coverage of multiple commonly performed neurosurgical interventions and 9 reviews found no RCTs related to their selected topic. In 28 reviews, results were synthesized from 5 or fewer trials. Primary outcomes also varied among trials examining similar interventions. The overall quality rating of the evidence for the different subspecialties varied, with the majority of reviews rating the evidence as being from very low to low.**

■ CONCLUSIONS: **The RCT-level evidence supporting neurosurgical practice is varied and the outcomes tested remain predominantly heterogeneous. There remain important neurosurgical conditions where treatment strategies are not underpinned by high-quality evidence. Pragmatic RCTs, well-designed observational studies as well as robust audit and registry processes may provide the real-world evidence for treatment decisions in neurosurgical care.**

## INTRODUCTION

Evidence-based medicine requires the integration of robust evidence from medical research with clinical expertise and the specific values and circumstances of a patient.[1] The gold standard for generating evidence on the comparative effectiveness of interventions is the randomized controlled trial (RCT) given the rigorous way in which the design can eliminate potential sources of bias, combined with well-conducted systematic reviews that synthesize the results from different trials.[2] The Cochrane Library of Reviews of therapeutic interventions has built up a comprehensive overview of the research evidence underpinning many areas of clinical practice. Its reviews are internationally recognized for being high-quality syntheses of RCT-level evidence because of their rigorous and transparent methods, and their focus on answering clearly formulated clinical questions.[3]

Neurosurgery is a relatively small surgical specialty with approximately 25,000 elective operations being performed in England each year.[4] It contains multiple subspecialties that require various models of coordinated care in order to treat different pathologies effectively and ensure good outcomes for patients. While many RCTs have been undertaken to evaluate the effectiveness of neurosurgical interventions, it is recognized that there are specific difficulties with conducting RCTs in

**Key words**
- Evidence-based medicine
- Outcomes
- Neurosurgery

**Abbreviations and Acronyms**
GRADE: Grading of RecommendationsAssessments Development and Evaluations
RCT: Randomized controlled trial

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neurosurgery and there remain many conditions for which there is not a consensus about the optimum strategy of care.[5] In a UK setting, groups have outlined variation in care delivery of cranial and spinal neurosurgical services.[6,7] The aim of this article was to evaluate the extent to which operative interventions in the different neurosurgical subspecialties are supported by high-quality evidence about their effectiveness within the Cochrane Database of Systematic Reviews. Following Howick et al., we defined high-quality evidence for an intervention as being supported by at least one primary outcome with a "high" Grading of Recommendations Assessments, Development and Evaluations (GRADE) rating, a statistically significant benefit, and the review authors concluding that the intervention to be effective or ineffective.[8,9] A lack of high-quality evidence to guide practice will explain variation in approach and galvanize efforts to increase the evidence base in neurosurgery.

## METHODS

### Information Sources and Eligibility Criteria

The study examined Cochrane Reviews that investigated questions related to the effectiveness of operative interventions for neurosurgical patients. Reviews were included that compared a neurosurgical operation that would take place in a neurosurgical theater of a known neurosurgical pathology against either another neurosurgical operation, another form of medical management or a placebo/sham. Reviews were not included if they pertained solely to the nonsurgical management of a neurosurgical pathology or were not related to the specialty of neurosurgery.

### Search Strategy

We designed a comprehensive search strategy of the Cochrane Review section of the Cochrane Library (Wiley). We utilized the "Advanced search" function with our key search terms initially and subsequently we searched each relevant Cochrane Group by hand for further studies. The search was run back to the inception of the Cochrane database. We excluded superseded, outdated versions of reviews or reviews that had been withdrawn. The search strategy is presented in **Supplementary Figure 1**.

### Data Items

A standard proforma was used to extract data from the eligible studies. Extracted details included neurosurgical pathology, interventions being compared, clinical question addressed, type of study (effectiveness/efficacy), quality of the evidence, primary and secondary outcomes, number of RCTs included in the review, number of study participants, and the year the review was published. The neurosurgical pathologies covered by the Cochrane literature were allocated to a neurosurgical subspecialty.

We utilized the Dodd classification of outcomes taxonomy to organize the outcomes tested within the reviews.[10] This organizes verbatim outcomes into 5 distinct areas that are qualitatively different in what they are measuring and was proposed to increase the reuse value of outcome data. The 5 areas are further subdivided into 38 specific outcome domains. We added one outcome domain "death or severe disability" that was not included in the original paper by Dodd et al. Outcomes were recorded as described in the "Methods" section of each review and these were divided into primary and secondary outcomes.

Following Howick et al., we defined high-quality evidence for an intervention as being supported by at least one primary outcome with a "high" GRADE rating, a statistically significant benefit, and the review authors concluding the intervention to be effective or ineffective.[8] For those reviews that did not use the GRADE rating system, we defined the rating system used for quality analysis. Those reviews that were unable to find any RCTs describing their interventions were excluded from this part of the analysis.

### Data Synthesis and Analysis

Microsoft Excel for Mac Version 16.72 used for collection and analysis of data.

## RESULTS

### Literature Search Results

Of the 9251 Cochrane Reviews published at the time of the review (May 1, 2024), there were 1452 reviews related to Neurosurg* or Spine. 1403 of these reviews were related to an "intervention" and the title and abstract of these were assessed for relevance. Forty-four full Cochrane Reviews were retrieved. Relevant "Cochrane Groups" as indicated by the retrieved papers and others that were considered to overlap with neurosurgical care were then searched by hand. These groups are described in the **Supplementary Material** "search strategy." A further 16 Cochrane Reviews were retrieved. The examination of the full text of these 60 reviews subsequently led to 8 being excluded because they did not evaluate a surgical intervention, had been withdrawn or applied to a non-neurosurgical pathology. This left 52 reviews meeting the inclusion criteria.

The 52 reviews addressed a range of neurosurgical interventions (see **Supplementary Table 1**) and covered 8 neurosurgical subspecialties. The number of reviews was largest in the spinal surgery subspecialty (n = 15), followed by neuro-oncology (n = 10) and neurovascular surgery (n = 7). The other reviews covered: cranial trauma (n = 3), epilepsy (n = 4), functional/pain neurosurgery (n = 4), hydrocephalus (n = 4), and skull base (n = 2). There were no reviews on interventions in pediatric neurosurgery. In most subspecialties, at least half of the reviews had been published since January 2015; the exception was spinal surgery, with 11 of the 15 being published between 2005 and 2014 (**Supplementary Table 1** & **Supplementary Figure 2**).

**Table 1** summarizes the pathologies covered by the review in each subspecialty, and the number of RCTs and patients that were included in the review. In 9 reviews, the review authors found no RCTs met their eligibility criteria. In 28 other reviews, the results were synthesized from 5 or fewer trials. Another feature of the evidence base was the small number of participants included in many trials. The mean number of participants per trial exceeded 150 for just 12 reviews, with only the neurovascular subspecialty having an average trial size above this in the greatest proportion of its reviews.

**Table 1.** Summary of the 52 Cochrane Reviews on Neurosurgical Interventions

| Subspecialty | No. of Reviews Total/Post 2015 | Pathology (No. of Reviews) | No of RCTs (Patients) in Each Review |
|---|---|---|---|
| Cranial trauma | 3/3 | Chronic subdural hematoma (1) | 9 (968) |
| | | Coma (1) | 1 (324) |
| | | Traumatic brain injury (1) | 3 (590) |
| Epilepsy | 4/4 | Seizures (4) | 9 (621), 5 (439), 0 (0), 12 (374) |
| Functional/Pain | 6/4 | Dystonia (1) | 2 (102) |
| Neurosurgery | | Trigeminal neuralgia (1) | 11 (496) |
| | | Low back pain (1) | 13 (699) |
| | | Chronic critical limb ischemia (1) | 6 (450) |
| | | Cancer-related pain (1) | 0 (0) |
| | | Chronic pain (1) | 15 (908) |
| Hydrocephalus | 4/2 | Normal pressure hydrocephalus (3) | 0 (0), 1 (42), 0 (0) |
| | | Hydrocephalus (1) | 6 (962) |
| Neuro-oncology | 10/6 | Glioblastoma multiforme (3) | 1 (30), 12 (1818), 34 (5236) |
| | | Low-grade gliomas (1) | 0 (0) |
| | | Brain metastases (4) | 3 (195), 0 (0), 5 (663), 2 (85) |
| | | Brain tumors (2) | 4 (663), 4 (439) |
| Neurovascular | 8/4 | Subarachnoid hemorrhage (1) | 1 (216) |
| | | Intracranial aneurysms (2) | 4 (2458), 2 (216) |
| | | Arteriovenous malformations (1) | 3 (134), |
| | | Stroke (3) | 10 (2059), 3 (134), 9 (513) |
| | | Carotid artery disease (1) | 2 (1573) |
| Skull base | 2/1 | Vestibular schwannoma (1) | 0 (0) |
| | | GHS pituitary adenoma (1) | 8 (445) |
| Spinal surgery | 15/4 | Cervical degenerative disc disease (2) | 2 (149), 33 (2267), |
| | | Lumbar degenerative disc disease (4) | 31 (2884), 40 (5197), 7 (1474), 11 (1172) |
| | | Lumbar spine stenosis (3) | 10 (733), 5 (643), 24 (2352) |
| | | Spinal cord compression: Met. (1) | 7 (876) |
| | | Spinal cord injury (1) | 0 (0) |
| | | Spinal fractures (4) | 2 (84), 2 (79), 5 (448), 0 (0) |

GHS, growth hormone secreting; RCTs, randomized controlled trials.

### Quality of Evidence

Among the 52 reviews included in the study, the quality of evidence was not rated in 9 reviews because they did not contain RCT-level evidence. Of the remaining 43, 30 reviews had rated the quality of evidence using the GRADE system. The other reviews were typically performed before Cochrane had adopted the GRADE approach, and had rated the quality of the evidence using the "risk of bias" tool in the Cochrane handbook (n = 4) or another set of criteria (n = 6). Three reviews, all of which were neurovascular surgery, used an unknown tool to rate individual studies and one did not provide an overall rating of the evidence.[11]

The quality of the evidence is summarized in Table 2. In 16 of the 30 reviews that used the GRADE system, the overall rating of the available evidence was either very low or low quality. A very low or low rating had been awarded in 6 of the 12 reviews that had produced a rating using a non-GRADE tool. Only 5 of the subspecialties had any review awarded a "high"-quality rating (GRADE or non-GRADE tool); these subspecialties also had 5 reviews given a "moderate" rating. The highest quality of evidence for "cranial trauma" was "moderate" (all 3 reviews), but for the subspecialties "functional/pain," "hydrocephalus," and "skull base," the highest quality rating was "low" (See Supplementary Table 3 for more detail).

**Table 2.** Quality of Evidence in Each Cochrane Review, as Rated by Review Authors, Stratified by Neurosurgical Subspecialty, and Method of Rating

| | | | Rating Using GRADE | | | | |
|---|---|---|---|---|---|---|---|
| **Subspecialty** | **Unrated: No RCTs** | **Reviews Not Using GRADE (Rating Given)** | **Very Low** | **Low** | **Moderate** | **High** | **Total** |
| Cranial trauma | 0 | 1 (M) | 0 | 0 | 2 | 0 | 3 |
| Epilepsy | 1 | 0 | 0 | 0 | 2 | 1 | 4 |
| Functional/Pain | 1 | 2 (VL,H) | 0 | 3 | 0 | 0 | 6 |
| Hydrocephalus | 2 | 0 | 1 | 1 | 0 | 0 | 4 |
| Neuro-oncology | 2 | 2 (L,M) | 0 | 4 | 1 | 1 | 10 |
| Neurovascular | 0 | 4 (L,M,M,?) | 1 | 0 | 1 | 2 | 8 |
| Spinal surgery | 2 | 4 (L,L,L,M) | 1 | 4 | 3 | 1 | 15 |
| Skull base | 1 | 0 | 0 | 1 | 0 | 0 | 2 |
| Total | 9 | 13 | 3 | 13 | 9 | 5 | 52 |

Some reviews had no rating because no RCTs were identified as eligible for the review.
VL, very low; L, low; M, moderate; H, high.

Three of the 6 high-quality reviews contained over 2000 participants. The average (mean) number of study participants in a review deemed high quality (n = 6) was 1897, for moderate quality reviews (n = 14) there were 1228 participants on average, for low quality reviews (n = 18) there were 629 on average and for very low quality reviews (n = 4) the average fell to 210.

### Outcomes

Table 3 demonstrates the outcomes from each study containing at least one RCT using the taxonomy as defined by Dodd et al. Supplementary Table 2 shows the verbatim outcomes that were used by the reviewers and categorized by their core areas to demonstrate the spread of outcomes. Two spinal reviews did not differentiate between primary and secondary outcomes, which has led to an inflated number of primary outcomes for the spinal subspecialty.[12,13] Each neurosurgical subspecialty was found to favor particular outcome core areas. Neurovascular surgery, neuro-oncology, and cranial trauma contained primary outcomes particularly focused upon capturing mortality (17/29 primary outcomes). For hydrocephalus, over 50% of the primary outcomes were focused on adverse events and mortality (6/9 primary outcomes). Whereas spinal surgery, epilepsy surgery, and functional neurosurgery contained many more primary outcomes within the core areas of "life impact" and "physiological/clinical" (60/75 primary outcomes). With respect to the core areas themselves, it is of note that resource use was only used as a primary outcome in "lumbar degenerative disc disease" Cochrane Reviews.

Table 4 describes the range of primary outcomes that were used across the reviews within each subspecialty. The different reviews in cranial trauma and epilepsy surgery generally selected the same verbatim primary outcomes. More heterogeneity was found within the other subspecialties and within spinal surgery, there was an especially low concordance between reviews.

## DISCUSSION

### Coverage of Evidence

The spread of Cochrane Reviews of operative interventions across neurosurgical subspecialties is limited in its breadth and quality. Pediatric neurosurgery did not have any review of RCT-generated evidence, while skull base, epilepsy, and hydrocephalus had 3 or fewer reviews. Across the other subspecialties, only spinal surgery had reviews that gave a reasonable coverage of the major pathologies treated by the subspecialty. There are multiple neurosurgical pathologies that are the cause of large numbers of admissions to English neurosurgical centers that are not found in the Cochrane Library such as Chiari 1 malformation, meningioma, and Parkinson's disease. This may reflect the process of selecting topics for review, but it may also reflect the small numbers of RCTs compared with other specialties as well as issues with quality and a failure of design to meet the stated study objectives.[2]

### Quality of Evidence and Outcomes

The majority of Cochrane Reviewers now use the GRADE system for rating the quality of evidence.[9] The system begins by rating RCTs as generating high-quality evidence and but the rating can be downgraded if there is felt to be bias, inconsistency, indirectness, imprecision or publication bias contained within the trials reviewed by a study. Furthermore, the rating can be upgraded if there is a large effect demonstrated, a dose response, and all plausible confounding is dealt with. Only 5 of the 30 reviews that utilized the GRADE approach rated the evidence as high quality. The issues with RCTs were predominantly related to blinding, allocation concealment as well as the small number of participants in many studies.

**Table 3.** Outcomes Classified by the Dodd Criteria Stratified by Neurosurgical Subspecialty and Pathology

| Subspecialty | Pathology (No. of Reviews) | Primary Outcome per Review (No. of Outcomes) | Secondary Outcomes Used in a Review |
|---|---|---|---|
| Cranial trauma[14-16] | Chronic subdural hematoma (1) | P(1) | M _ L A _ |
| | Coma (1) | M(1), L(1) | _ _ _ A _ |
| | Traumatic brain injury (1) | M(1), L(1) | _ P _ A _ |
| Epilepsy[17-20] | Seizures (4) | P(4) | _ P L A _ |
| Functional/Pain | Dystonia (1) | P(1), A(1) | _ P L A _ |
| Neurosurgery[21-26] | Trigeminal neuralgia (1) | P(1) | _ _L A _ |
| | Low back pain (1) | P(1), L(3), A(3) | _ P L A R |
| | Chronic critical limb ischemia (1) | P(1) | _ P L A R |
| | Cancer-related pain (1) | | |
| | Chronic pain (1) | P(1), A(1) | _ P L _ R |
| Hydrocephalus[27-30] | Normal pressure hydrocephalus (3) | M(1), P(2), L(1), A(2) | M P _ A R |
| | Hydrocephalus (1) | M(1), A(2) | _ P L _ _ |
| Neuro-oncology[31-40] | Glioblastoma multiforme (3) | M(3), L(1) | M P L A R |
| | Low-grade gliomas (1) | | |
| | Brain metastases (4) | M(3), A(1) | M P L A _ |
| | Brain tumors (2) | P(2), A(2) | M _ L _ _ |
| Neurovascular[11,41-47] | Subarachnoid hemorrhage (1) | M(1), L(2) | _ _ L A R |
| | Intracranial aneurysms (2) | M(1) | M _ L A R |
| | Arteriovenous malformations (1) | M(1) | _ _ L A _ |
| | Stroke (3) | M(4) | M _ L A _ |
| | Carotid artery disease (1) | M(2), P(1) | M P _ A _ |
| Skull base[48,49] | Vestibular schwannoma (1) | | |
| | GHS pituitary adenoma (1) | P(1), A(2) | M P L A _ |
| Spinal surgery[12,13,50-62] | Cervical degenerative disc disease (2) | P(2), L(3), A(1), | _ P L A _ |
| | Lumbar degenerative disc disease (4) | P(9), R(2), L(15), A(4) | M P L A R |
| | Lumbar spine stenosis (3) | P(3), L(8) | M P L A R |
| | Spinal cord compression: Met. (1) | L(1) | M P L A _ |
| | Spinal cord injury (1) | | |
| | Spinal fractures (4) | M(1), P(1), L(6), A(2) | _ P L A _ |

GHS, growth hormone secreting; Met., metastatic; Outcome labels, M (mortality), P (physiological), R (resource use), L (life impact), A (adverse events).

The synthesis of research and the ability to generalize results requires studies to use meaningful, standardized outcomes. Across the Cochrane Reviews, there was significant heterogeneity in the reported outcomes. Primary outcomes did not have good coverage of all the different core areas of outcomes for any subspecialty. Neuro-oncology, neurovascular, and cranial trauma prioritized mortality, whereas spinal surgery and functional/pain neurosurgery focused on physiological and life impact-related measures. This may mean that outcomes that are of greater importance to patients are ignored by multiple studies.

It is also clear from assessing the literature that certain core areas currently appear to be under-represented. "Resource use" could be given greater attention because dealing with pathologies of the central and peripheral nervous system often involves efforts to prevent disability, which have huge implications for people's ability to function in society and the welfare burden.[63,64] Further work is needed to ensure studies of treatment effectiveness use a consistent set of outcome measures across the various subspecialties. One option is for this work to be undertaken as part of the Core Outcome Measures in Effectiveness Trials initiative.[65]

**Table 4.** Homogeneity of Primary Outcomes Used by Cochrane Reviewers, by Subspecialty

| Subspecialty (No. of Reviews) | % Verbatim Primary Outcomes Used Found in Over Half of Reviews |
|---|---|
| Cranial trauma (3) | 80% (4/5 primary outcomes) |
| Epilepsy (4) | 100% (4/4 primary outcomes) |
| Functional/Pain neurosurgery (6) | 31% (3/11 primary outcomes) |
| Hydrocephalus (4) | 56% (5/9 primary outcomes) |
| Neuro-oncology (10) | 50% (6/12 primary outcomes) |
| Neurovascular (8) | 69% (8/12 primary outcomes) |
| Skull base (2) | N/A |
| Spinal surgery (15) | 16% (9/58 primary outcomes) |

### Difficulties with Randomized Controlled Trials in Neurosurgery

High-quality evidence on treatment effectiveness is invaluable for any surgical specialty. However, conducting RCTs in surgery and specifically neurosurgery can be a difficult and time-consuming process. Multiple papers have demonstrated issues such as the lack of blinding outcome measurements, small sample sizes, and failures to implement protocols correctly.[2,66,67] The treatment algorithms are often complex and individual equipoise can disrupt the clinical equipoise being tested.[68] Even once an RCT is commenced, randomizing based upon individual equipoise can introduce subjectivity and vary between surgeons.[69,70] Indeed, neurosurgical pathologies themselves have nuances meaning that trials often end up being run with very tightly defined inclusion criteria, which can be at the expense of the external validity of the conclusions.[71] While RCT-generated evidence on treatment effectiveness should still be the aim for neurosurgery, there is a growing recognition that questions of treatment effectiveness can be well answered using robust real-world evidence.[2,72] This can also lead to huge potential savings in both time and cost. The neurosurgical community as a whole must address these concerns and adopt other robust research methods, including well-designed observational studies, to help bolster its evidence base.[73]

### Strategies to Increase the Neurosurgical Evidence Base in the United Kingdom

Large, collaborative research projects within neurosurgery are essential to increasing the evidence base. The recent Randomised Evaluation of Surgery with Craniectomy for patients Undergoing Evacuation of Acute Subdural Haematoma trial that enrolled 462 patients from 40 centers in 11 countries adopted a pragmatic, randomized trial model.[74] It demonstrated that outcomes were similar between craniotomy and craniectomy groups in surgical treatment for acute subdural hematoma at 12 months. Trainee collaborations in the United Kingdom through the British Neurosurgical Trainee Research Collaborative have also produced effective research. The recent British Neurosurgical Trainee Research Collaborative run multicenter, randomized trial conducted across the United Kingdom investigating the use of dexamethasone for treatment of chronic subdural hematoma demonstrated worse outcomes using dexamethasone in a trial consisting of 748 patients.[75] Prior to this finding, low-dose steroids had been widely prescribed for patients with chronic subdural hematomas surgeons believed could be treated nonsurgically.

As well as these collaborative projects, we also require a strong audit and registry practice in order to ensure safety and improve the quality of neurosurgical care. There are currently 13 audit and registry programs covering neurosurgical practice in the United Kingdom, from small groups such as the vestibular schwannoma registry to larger programs such as the British Spinal Registry and the National Neurosurgical Audit Programme.[76]

Furthermore, observational studies using administrative datasets possess huge potential for increasing the evidence base in the field of neurosurgery.[72,77] Extracts of routine hospital administrative data are an increasingly accurate reflection of the patient journey in hospital.[78,79] This means that sophisticated observational studies that emulate target trials can be developed to make use of this increasingly robust source of data.[80] Even with strict inclusion criteria mirroring that of an RCT, these data still allow for larger samples than most RCTs and at far lower costs. Modern, advanced epidemiological tools such as instrumental variable analysis means that we possess means for dealing with known and unknown confounding that has previously plagued observational studies and are stronger tests of causality.[81-83] It is important that we have neurosurgeons trained in using this data in order to maximize the potential of this evidence stream.

### Limitations

There are several limitations to this study. This review only covers RCT-level evidence included within the Cochrane Database of Systematic Reviews and therefore, although this is one of the most acclaimed databases for publishing systematic reviews, there may be high-quality RCT evidence in neurosurgery not captured within this study. Furthermore, we rely upon the reviewers and their appropriate use of the GRADE criteria in order to effectively rate the studies. There is evidence to suggest that GRADE is used reliably among trained reviewers.[84] The use of the GRADE criteria may also be too stringent and therefore mean that very few interventions meet it. Another limitation is that older studies, such as those predominantly found in spinal surgery, did not have the option to use the GRADE criteria and therefore the assessment of quality may be more variable.

## CONCLUSION

This review of neurosurgical intervention in the Cochrane Database of Systematic Reviews suggests the quality of the RCT-level evidence underpinning neurosurgical practice is variable. It also suggests that there is a lack of coverage of multiple commonly performed neurosurgical interventions and outcomes remain predominantly heterogeneous. There remain important neurosurgical conditions where treatment strategies are not underpinned by high-quality evidence. Pragmatic RCTs, real-world evidence observational studies as well as robust audit and registry processes may provide the key for justifying treatment decisions in United Kingdom neurosurgical care going forward.

## CRediT AUTHORSHIP CONTRIBUTION STATEMENT

**Daniel Thompson:** Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Adam Williams:** Writing – review & editing, Validation, Supervision, Methodology, Conceptualization. **Peter Hutchinson:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision. **Adel Helmy:** Writing – review & editing, Writing – original draft, Validation, Supervision, Project administration, Methodology, Conceptualization. **David Cromwell:** Writing – review & editing, Writing – original draft, Validation, Supervision, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

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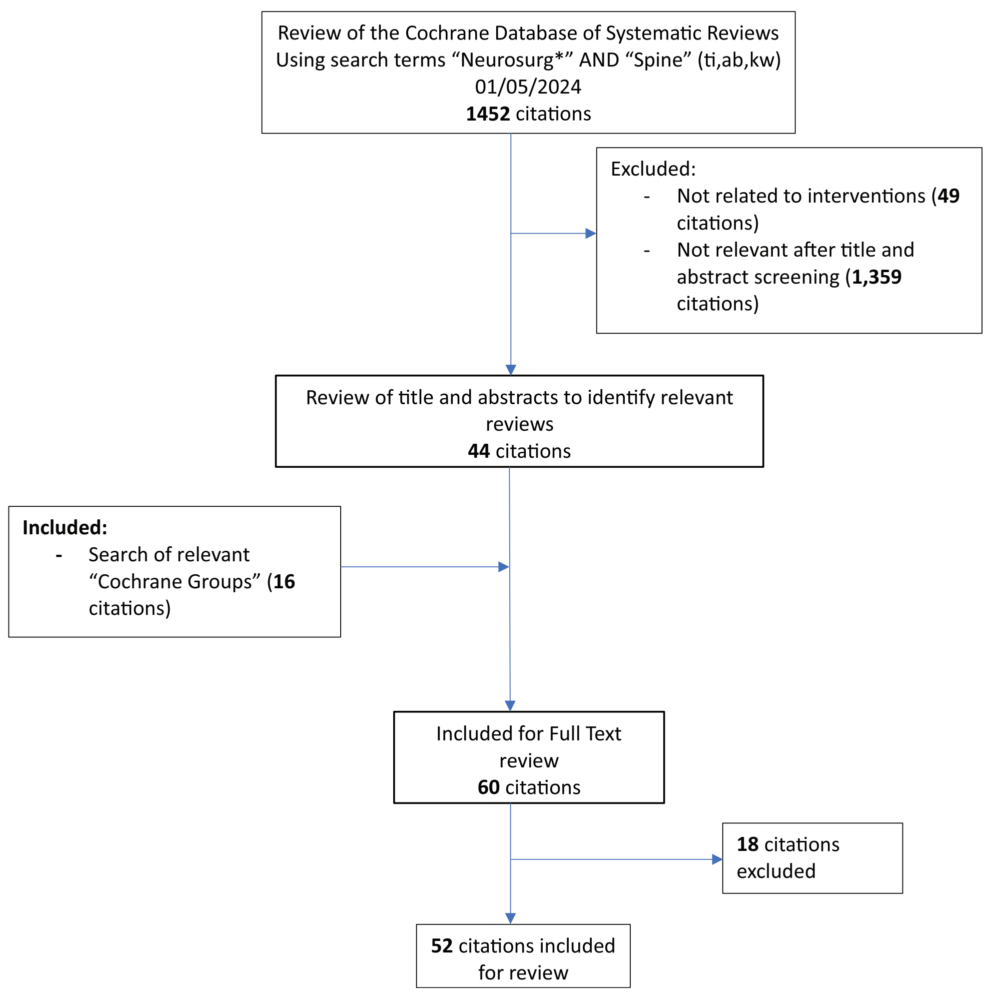
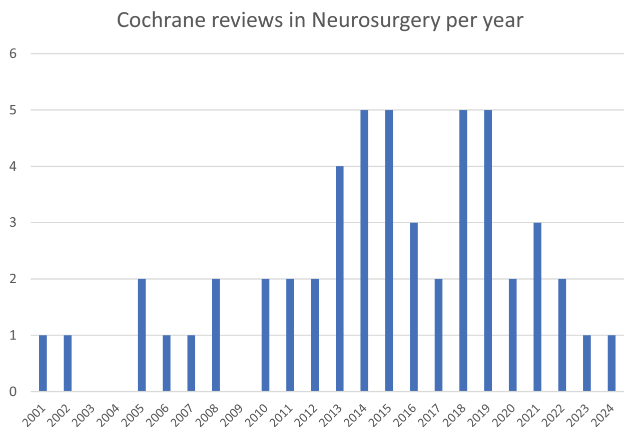
## SUPPLEMENTARY DATA




**Supplementary Figure 1.** Flow diagram of Neurosurgical literature review of Cochrane Database of Systematic Reviews (Wiley).




**Supplementary Figure 2.** Bar chart showing the number of neurosurgical Cochrane Reviews per year.

## Search strategy

The Cochrane Library search terms:

1. "neuro*" ti,ab,kw.
2. "spine" ti,ab,kw.
3. "spinal" ti,ab,kw.
4. 1 and 2 and 3.

Cochrane Groups reviewed by hand:

| |
|---|
| Back and Neck |
| Bone, joint, and muscle trauma |
| Child health |
| Childhood cancer |
| Dementia and cognitive improvement |
| Emergency and critical care |
| Ear, nose & throat |
| Epilepsy |
| Gynecological, neuro-oncology, and orphan cancer |
| Infectious diseases |
| Injuries |
| Metabolic and endocrine disorders |
| Movement disorders |
| Neonatal |
| Neuromuscular |
| Pain, palliative, and supportive care |
| Stroke |
| Wounds |

**Supplementary Table 1.** Table Consolidating the Key Aspects of the Cochrane Reviews

| First Author | Year | Pathology | Interventions | Quality of Evidence | RCTs in Review | Study Participants | Rating Tool |
|---|---|---|---|---|---|---|---|
| Cranial trauma | | | | | | | |
| Peng, D | 2016 | Chronic subdural hematoma | Burrhole drainage of CSDH | Moderate | 9 | 968 | Grade |
| Forsyth, R | 2015 | Coma | ICP monitor insertion | Moderate* | 1 | 324 | Cochrane's 'Risk of bias' tool (Higgins 2011a). |
| Sahuquillo, J | 2019 | Traumatic brain injury | Decompressive craniectomy | Moderate | 3 | 590 | Grade |
| Epilepsy | | | | | | | |
| West, S | 2019 | Seizures | Anterior temporal lobectomy, corpus callosotomy, selective amygdalohippocampectomy, parahippocampectomy, stereotactic radiosurgery | Moderate | 9 | 621 | Grade |
| Panebianco, M | 2022 | Seizures | Vagal nerve stimulator insertion | Moderate | 5 | 439 | Grade |
| Krishnaiah, B | 2018 | Seizures | Subpial transection | No RCT evidence | 0 | 0 | n/a |
| Sprengers, M | 2017 | Seizures | Deep brain stimulation, Cortical stimulation | High | 12 | 374 | Grade |
| Functional/Pain neurosurgery | | | | | | | |
| Rodrigues, F | 2019 | Dystonia | Deep brain stimulation | Low | 2 | 102 | Grade |
| Zakrzewska, J | 2011 | Trigeminal neuralgia | Stereotactic radiosurgery, microvascular decompression, radiofrequency thermocoagulation | Very low* | 11 | 496 | Cochrane 'Risk of bias' traits (Higgins 2008) |
| Traeger, A | 2023 | Low back pain | Spinal cord stimulation, placebo, medical management | Low | 13 | 699 | Grade |
| Ubbink, D | 2013 | Chronic critical limb ischemia | Spinal cord stimulation, medical management | High* | 6 | 450 | Dutch CC |
| Peng, L | 2015 | Cancer-related pain | Spinal cord stimulation, medical management | No RCT evidence | 0 | 0 | Strobe |
| O'Connell, N | 2021 | Chronic pain | Spinal cord stimulation, sham, placebo, medical management | Low | 15 | 908 | Grade |
| Hydrocephalus | | | | | | | |
| Esmonde, T | 2002 | Normal pressure hydrocephalus | Ventriculoperitoneal shunt insertion | No RCT evidence | 0 | 0 | n/a |
| Tudor, K | 2015 | Normal pressure hydrocephalus | Endoscopic third ventriculostomy, ventriculoperitoneal shunt insertion | Very low | 1 | 42 | Grade |
| Ziebell, M | 2013 | Normal pressure hydrocephalus | Ventriculoperitoneal shunt: flow controlled shunt valve, differential pressure shunt valve | No RCT evidence | 0 | 0 | n/a |
| Garegnani, L | 2020 | Hydrocephalus | Ventriculoperitoneal shunt insertion | Low | 6 | 962 | Grade |
| Neuro-oncology | | | | | | | |
| Hart, M | 2019 | Glioblastoma multiforme | Craniotomy and resection of tumor, biopsy of tumor | Low* | 1 | 30 | Fowkes 1991 and CRD 2009. |

RCT, randomized controlled trial; CSDH, chronic subdural haematoma; ICP, intracranial pressure; EC/IC, extracranial/intracranial.
*Quality of evidence not defined using GRADE approach.

Continues

**Supplementary Table 1.** Continued

| First Author | Year | Pathology | Interventions | Quality of Evidence | RCTs in Review | Study Participants | Rating Tool |
|---|---|---|---|---|---|---|---|
| Hanna, C | 2020 | Glioblastoma multiforme | Routine medical management, chemotherapy, radiotherapy, craniotomy and resection of tumor | Moderate | 12 | 1818 | Grade |
| McBain, C | 2021 | Glioblastoma multiforme | Chemotherapy, reoperation, radiotherapy | High | 34 | 5236 | Grade |
| Jiang, B | 2017 | Low-grade gliomas | Routine medical management, chemotherapy, radiotherapy, craniotomy, and resection of tumor | No RCT evidence | 0 | 0 | n/a |
| Hart, M | 2005 | Brain metastases | Craniotomy and resection of tumor, whole brain radiotherapy | Moderate* | 3 | 195 | Fowkes 1991 and CRD 2009. |
| Fuentes, R | 2006 | Brain metastases | Craniotomy and resection of tumor, stereotactic radiosurgery | No RCT evidence | 0 | 0 | n/a |
| Soon, Y | 2014 | Brain metastases | Craniotomy and resection of tumor, stereotactic radiosurgery, whole brain radiotherapy | Low | 5 | 663 | Grade |
| Fuentes, R | 2018 | Brain metastases | Craniotomy and resection of tumor, stereotactic radiosurgery | Low | 2 | 85 | Grade |
| Barone, D | 2014 | Brain tumors | Craniotomy and resection of tumor | Low | 4 | 663 | Grade |
| Jenkinson, M | 2018 | Brain tumors | Craniotomy and resection of tumor | Low | 4 | 439 | Grade |
| Neurovascular | | | | | | | |
| Whitfield, P | 2001 | Subarachnoid hemorrhage | Clipping or wrapping of intracranial aneurysm | Low* | 1 | 216 | Unclear |
| Lindgren, A | 2018 | Intracranial aneurysms | Endovascular coiling, microsurgical clipping | High | 4 | 2458 | Grade |
| Pontes, F | 2021 | Intracranial aneurysms | Endovascular coiling, microsurgical clipping, conservative management | Very low | 2 | 216 | Grade |
| Zuurbier, S | 2019 | Arteriovenous malformations | Routine medical management, endovascular embolization, microsurgical extirpation | Moderate | 1 | 226 | Grade |
| Prasad, K | 2008 | Stroke | Routine medical management, craniotomy and evacuation of clot, endoscopic clot evacuation, stereotactic evacuation of clot | Moderate* | 10 | 2059 | Unclear |
| Cruz-Flores, S | 2012 | Stroke | Decompressive craniectomy | Moderate* | 3 | 134 | Fowkes 1991 |
| Dower, A | 2022 | Stroke | Decompressive craniectomy | High | 9 | 513 | Grade |
| Fluri, F | 2010 | Occlusive carotid artery disease | EC/IC bypass + medical management, medical management alone | Not stated* | 2 | 1573 | Unclear |
| Skull base | | | | | | | |
| Muzevic, D | 2014 | Vestibular schwannoma | Microsurgical resection, stereotactic radiosurgery, observation | No RCT evidence | 0 | 0 | n/a |
| Caulley, L | 2024 | Growth hormone secreting pituitary adenoma | Surgical resection, pharmacological therapy, radiation therapy, combination therapy | Low | 8 | 445 | Grade |
| Spinal surgery | | | | | | | |
| Bagnall, A-M | 2008 | Spinal cord injury | Spinal fixation, conservative management | No RCT evidence | 0 | 0 | n/a |

Continues

**Supplementary Table 1.** Continued

| First Author | Year | Pathology | Interventions | Quality of Evidence | RCTs in Review | Study Participants | Rating Tool |
|---|---|---|---|---|---|---|---|
| Nikolaidis, I | 2010 | Cervical degenerative disc disease | Anterior cervical decompression ± fusion, posterior cervical decompression ± fusion | Low | 2 | 149 | Grade |
| Jacobs, W | 2011 | Cervical degenerative disc disease | Single-level anterior discectomy + interbody fusion, two-level anterior discectomy + interbody fusion | Moderate | 33 | 2267 | Grade |
| Del Curto, D | 2014 | Cervical spine facet fracture | Anterior cervical fixation, posterior cervical fixation | Very low | 2 | 84 | Grade |
| Abudou, M | 2013 | Thoracolumbar fracture | Open reduction and anterior fixation, open reduction and posterior fixation, conservative management ± thoracolumbar brace | Low* | 2 | 79 | Cochrane 'Risk of bias' tool (Higgins 2011) |
| Cheng, L | 2013 | Thoracolumbar fracture | Short-segment pedicle screw instrumentation, long-segment pedicle screw instrumentation, monosegmental pedicle screw instrumentation | Low* | 5 | 448 | Cochrane 'Risk of bias' tool (Higgins 2011) |
| Overdevest, G | 2015 | Lumbar spine stenosis | Laminectomy, unilateral laminotomy, bilateral laminotomy, split spinous process laminotomy | Low | 10 | 733 | Grade |
| Zaina, F | 2016 | Lumbar spine stenosis | Decompression of spine, decompression of spine + fusion, routine medical management | Low | 5 | 643 | Grade |
| Machado, G | 2016 | Lumbar spine stenosis | Decompression of lumbar spine, placebo, sham, conservative management | High | 24 | 2352 | Grade |
| Gibson, JN | 2005 | Lumbar degenerative disc disease | Lumbar laminectomy, lumbar laminotomy, lumbar disc arthroplasty, intradiscal electrotherapy | Low* | 31 | 2884 | Schulz 1995 |
| Gibson, JN | 2007 | Lumbar degenerative disc disease | Lumbar discectomy, lumbar microdiscectomy, nucleoplasty, others | Moderate* | 40 | 5197 | Schulz 1995 |
| Jacobs, W | 2012 | Lumbar degenerative disc disease | Lumbar disc arthroplasty, lumbar fusion | Moderate | 7 | 1474 | Grade |
| Rasouli, R | 2014 | Lumbar degenerative disc disease | Lumbar microdiscectomy, lumbar open discectomy, minimally invasive lumbar discectomy | Low | 11 | 1172 | Grade |
| George, R | 2015 | Metastatic spinal cord compression | Radiotherapy, laminectomy, corticosteroids | Moderate | 7 | 876 | Grade |
| Shears, E | 2008 | Odontoid fractures | Surgical management, conservative management | No RCT evidence | 0 | 0 | n/a |

RCT, randomized controlled trial; CSDH, chronic subdural haematoma; ICP, intracranial pressure; EC/IC, extracranial/intracranial.
*Quality of evidence not defined using GRADE approach.

**Supplementary Table 2.** Verbatim Outcomes from Reviews Classified by the Dodd criteria

| Core Area | Outcome Domain | |
|---|---|---|
| Mortality | Mortality/Survival | Mortality $\leq$ 30 days + > 30 days |
| | | Perioperative mortality rates |
| | | Death at 6 and 12 months |
| | | Death at the end of follow-up |
| | | Overall survival |
| | | Mortality |
| | | All-cause mortality |
| | | Progression-free survival |
| | | Time to deterioration |
| | | Functionally independent survival |
| | Death or severe disability | Death or mrs>4 at 6 to 12 months |
| | | Death or dependence |
| | | Death or dependence at 12 months |
| | | Death or dependence at the end of follow-up |
| | | Death or mrs>3 at 6 to 12 months |
| **Core area** | **Outcome domain** | |
| Physiological/ Clinical | Nervous system outcomes | Postop changes in clinical signs and symptoms using validated assessment tools—up to and including 6 months, >6 months |
| | | Proportion free from seizures at 1 year |
| | | 50% reduction in seizure frequency |
| | | Seizure freedom |
| | | Responder rate |
| | | Symptomatic recurrence |
| | | Dystonia-specific symptoms |
| | | Seizure |
| | | Seizure frequency reduction |
| | | Symptom control |
| | | Local/distant intracranial disease progression |
| | | Significant reduction in ICP |
| | | Local recurrence |

Continues

**Supplementary Table 2.** Continued

| Core area | Outcome domain | |
|---|---|---|
| | | Fusion rate |
| | | Ventricular size reduction |
| | | Head circumference |
| | | Changes in measurements of diagnostic tests |
| | | Hydrocephalus |
| | | Urinary continence |
| | | Surgically induced spinal stability |
| | | Paraspinal atrophy |
| | | Muscle cell injury |
| | | Radiographical outcomes (fusion, sagittal alignment) |
| | | Sagittal alignment |
| | | Degree of spinal canal compromise |
| | | Radiological evaluation |
| | | Motion segment mobility |
| | | Extent of resection |
| | | Radiological outcome measures |
| | | Sciatica-specific outcome measure |
| | | Biochemical remission |
| | | Change in absolute tumor size |
| | | Nonsurgical therapy for recurrent or persistent disease |
| | | Normalization of cerebral hemodynamics |
| | Vascular outcomes | Limb salvage |
| | Skin outcomes | Wound healing |
| | Infection | Infection rate |
| | | Surgical site infection |
| | | Other infection |
| | Pain | Complete pain relief without medication at one year after randomization |
| | | Pain intensity |
| | | Leg pain |
| | | Pain |
| | | Symptoms—pain/analgesia use |
| | | Arm pain |

Continues

**Supplementary Table 2.** Continued

| Core area | Outcome domain | |
|---|---|---|
| | | Neck pain |
| | | Pain intensity |
| | | Reduction in analgesia/ narcotic use |
| | | Back pain |
| | | Postoperative use of analgesics |
| | | Medication use |
| **Core area** | **Outcome domain** | |
| Life impact | QoL | QoL |
| | | QoL at 1 year |
| | | HRQoL |
| | Psychosocial | Neuropsychological outcome |
| | | Cognitive impairment |
| | Compliance with treatment | Withdrawals |
| | Satisfaction | Perceived recovery |
| | | Proportion of patients who recovered according to self/ clinician |
| | | Overall improvement |
| | | Patient satisfaction |
| | | Patient-centered outcomes |
| | | Tolerability |
| | | Patient satisfaction at 1 year |
| | | Successful outcome proportion |
| | | Proportion of individuals with good outcome from surgery according to prognostic factors |
| | | Global assessment of efficacy |
| | | Dichotomized success |
| | Mental health | Mood |
| | | Emotional state |
| | Function | Glasgow Outcome Score |
| | | GOS at 30 days/end of trial follow-up |
| | | Neurological outcome at 6 or 12 months |
| | | Ambulation |
| | | Oswestry Disability Index |
| | | Disability and functional status |

Continues

**Supplementary Table 2.** Continued

| Core area | Outcome domain | |
|---|---|---|
| | | Walking capacity |
| | | Functional disability |
| | | Final postsurgical neurological status |
| | | Return to work |
| | | Improvement in neurological status |
| | | Back-specific functional status |
| | | Functional performance |
| | | Measures of objective physical impairment |
| | | Function |
| | | Functional impairment |
| | | Fatigue |
| | | Clinical status |
| | | Functional capacity |
| | | Walking distance |
| | | Employment |
| | | Disability |
| | | Motor function/sensory function |
| | | Daily tasks |
| | | Functionally independent survival |
| | | Survival with severe disability |
| | | mrs=5 at 6 to 12 months |
| | | Poor functional outcome |
| | | Work status |
| | | Progression-free survival |
| | | Time to deterioration |
| | | Functionally independent survival |
| | | Recovery—Japanese Orthopaedic Association score |
| | Death or severe disability | Death or mrs>4 at 6 to 12 months |
| | | Death or dependence |

ICP, intracranial pressure; LOS, length of stay; ICH, intracranial haemorrhage; GOS, Glasgow Outcome Score; SCS, spinal cord stimulation; HRQoL, health-related quality of life.

Continues

**Supplementary Table 2.** Continued

| Core area | Outcome domain | |
|---|---|---|
| | | Death or dependence at 12 months |
| | | Death or dependence at the end of follow-up |
| | | Death or mrs>3 at 6 to 12 months |
| **Core area** | **Outcome domain** | |
| Resource use | Economic | Cost data |
| | | Economic data |
| | | Economic evaluation |
| | Hospital | Healthcare use |
| | | LOS |
| | Operative | Length of procedure |
| **Core area** | **Outcome domain** | |
| Adverse events | Adverse events/effects | Treatment failure 2–6 years |
| | | Morbidity $\leq$ 30 days + > 30 days |
| | | Postop complications |
| | | Morbidity rates |
| | | Adverse events |
| | | Rate of complications |
| | | Deterioration in neurological status |
| | | Surgical morbidity |
| | | Adverse complications: early and late |
| | | Long-term complications |
| | | Stroke |
| | | Blood loss |
| | | Symptomatic ICH |
| | | Symptomatic radiation necrosis |
| | | Delayed cerebral ischemia |
| | | Rebleeding postprocedure(1 and 10 years) |
| | | Symptomatic rebleed |
| | | Voice alteration or hoarseness |
| | | Cough |
| | | Dyspnea |
| | | Severe adverse events |
| | | Neurological adverse events |

Continues

**Supplementary Table 2.** Continued

| Core area | Outcome domain | |
|---|---|---|
| | | Postop complications |
| | | Surgical morbidity after 1 year |
| | | Side effects |
| | | Failure rates |
| | | Treatment-specific complications |
| | | General perioperative complications |
| | | Return to theater |
| | | Repeat surgery |
| | | SCS complications |
| | | Dural tear |
| | | Surgical reintervention |
| | | Rehospitalization |
| | | Lead failure/displacement |
| | | Myocardial infarction |
| | | Pulmonary embolism |
| | | Serious vascular event |
| | | Major extracranial hemorrhage |
| | | Transient ischemic attack |
| | | Local hemorrhage requiring surgery |

ICP, intracranial pressure; LOS, length of stay; ICH, intracranial haemorrhage; GOS, Glasgow Outcome Score; SCS, spinal cord stimulation; HRQoL, health-related quality of life.

**Supplementary Table 3.** Table Demonstrating the Ability of Reviews to Deliver on Aims and Objectives

| Subspecialty | Author | Quality | Answer | Effect Size of Primary Outcomes |
|---|---|---|---|---|
| Hydrocephalus | Garegnani (2020) | Low | Similar outcomes but low quality evidence. | |
| Hydrocephalus | Tudor (2015) | Very low | Conclusions uncertain due to low or very low nature of the quality of the evidence. | |
| Neurovascular | Dower (2022) | High | Surgical decompression improves outcomes in a select group of patients. | Death at 6 to 12 months: OR 0.18 (0.12—0.27) Death or severe disability at 6 to 12 months: OR 0.22 (0.15—0.32) Death or moderate disability at 6 to 12 months: OR 0.34 (0.22—0.52) Severe disability at 6 to 12 months: OR 0.73 (0.36—1.44) |
| Neurovascular | Pontes (2021) | Very low | Conclusions uncertain due to low or very low nature of the quality of the evidence. | |
| Neurovascular | Zuurbier (2019) | Moderate | Moderate quality evidence that conservative management was superior to intervention with respect to functional outcome and symptomatic intracranial hemorrhage over one year post-randomization. | Death or dependence: RR 2.53 (1.28—4.98) Symptomatic ICH: RR 6.75 (2.07—21.96) Epileptic seizure: RR 1.14 (0.63—2.06) |
| Neurovascular | Lindgren (2018) | High | For people in good clinical condition with a ruptured aneurysm then coiling is associated with a better outcome than clipping. | Poor outcome (death or dependence 12 months): RR 0.77 (0.67—0.87) Poor outcome (death or dependence 10 years): RR 0.81 (0.70—0.92) Rebleeding postprocedure 1 year: RR 1.81 (1.04—3.23) |
| Epilepsy | Panebianco (2022) | Moderate | VNS for focal seizures appears to be effective and well tolerated. High frequency stimulation reduced seizures better than low. | 50% reduction in seizure frequency: RR 1.73 (1.13—2.64) Voice alteration or hoarseness: RR 2.17 (1.49—3.17) |
| Epilepsy | Sprengers (2017) | High | Compared to sham stimulation, 1—3 months of anterior thalamic DBS, responsive ictal onset zone stimulation and hippocampal DBS moderately reduce seizure frequency in refractory epilepsy. | Seizure frequency %: −17.4% lower (−31.2% - −1.0%) QOLIE-31: −0.30 lower (−3.50—2.90) |
| Neuro-oncology | McBain (2021) | High | For patients previously treated with surgery and chemotherapy, combination treatments have no survival benefit compared with LOM monotherapy in recurrence. | Overall survival + Progression free survival HR confidence intervals all cross 1 SAE in LOM versus. LOM + BEV: RR 2.51 (1.72—3.66) SAE in LOM versus. CED + LOM: RR 2.51 (1.29—4.90) |
| Neuro-oncology | Hanna (2020) | Moderate | For elderly people with GBM who are self-caring, CRT prolongs survival compared with RT and may prolong survivall compared with TMZ alone. | Progression-free survival (CRT vs. RT): HR 0.5 (0.41—0.61) CRT probably increases risk of hematological Aes |
| Neuro-oncology | Fuentes (2018) | Low | Conclusions uncertain due to low or very low nature of the quality of the evidence. | |
| Neuro-oncology | Jenkninson (2018) | Low | Conclusions uncertain due to low or very low nature of the quality of the evidence. | |
| Neuro-oncology | Barone (2014) | Low | Conclusions uncertain due to low or very low nature of the quality of the evidence. | |
| Neuro-oncology | Soon (2005) | Low | Conclusions uncertain due to low or very low nature of the quality of the evidence. | |
| Cranial trauma | Sahuquillo (2019) | Moderate | In adults with severe TBI and high ICP refractory to medical management, decompressive craniectomy reduces mortality at 6 months but may occur at the expense of more dependent survivors. | Mortality at 6 months: RR 0.66 (0.43–1.01) Mortality at 12 months: RR 0.59 (0.45–0.76) Unfavorable outcome as per Cochrane protocol: RR 0.95 (0.83–1.09) |

ICP, intracranial pressure; CSDH, chronic subdural haematoma; ICH, intracranial haemorrhage; DBS, deep brain stimulation; VNS, vagal nerve stimulator; SAE, small area estimation; LOM, lomustine; CED, convection enhanced delivery; GBM, glioblastoma multiforme; TMZ, temozolamide; CRT, chemoradiotherapy; TBI, traumatic brain injury.

Continues

**Supplementary Table 3.** Continued

| Subspecialty | Author | Quality | Answer | Effect Size of Primary Outcomes |
|---|---|---|---|---|
| Cranial trauma | Peng (2016) | Moderate | Some evidence that postoperative drainage is effective in reducing symptomatic recurrence of CSDH. | Overall recurrence 3 weeks - 6 months: RR 0.45 (0.32—0.61) |
| Functional/Pain neurosurgery | Rodrigues (2019) | Low | Conclusions uncertain due to low or very low nature of the quality of the evidence. | |
| Functional/Pain neurosurgery | Traeger (2023) | Low | Conclusions uncertain due to low or very low nature of the quality of the evidence. | |
| Functional/Pain neurosurgery | O'Connell (2021) | Low | Conclusions uncertain due to low or very low nature of the quality of the evidence. | |
| Skull base | Caulley (2024) | Low | Conclusions uncertain due to low or very low nature of the quality of the evidence. | |
| Spinal surgery | George (2015) | Low | Conclusions uncertain due to low or very low nature of the quality of the evidence. | |
| Spinal surgery | Zaina (2016) | Low | Conclusions uncertain due to low or very low nature of the quality of the evidence. | |
| Spinal surgery | Overdevest (2015) | Low | Conclusions uncertain due to low or very low nature of the quality of the evidence. | |
| Spinal surgery | Del Curto (2014) | Very low | Conclusions uncertain due to low or very low nature of the quality of the evidence. | |
| Spinal surgery | Cheng (2013) | Low | Conclusions uncertain due to low or very low nature of the quality of the evidence. | |
| Spinal surgery | Jacobs (2012) | Moderate | The differences between lumbar disc replacement and conventional fusion for degenerative disc disease were not beyond generally accepted clinically important differences for pain relief, disability, QOL. | Patient satisfaction: OR 1.93 (1.36—2.76) Improvement in function (Oswestry score): 4.27 better (6.68—1.85) |
| Spinal surgery | Jacobs (2011) | Moderate | Low quality evidence that iliac crest autograft is best technique when working mechanism for pain relief and functional improvement is fusion of the motion segment. | Bone graft more effective than discectomy for fusion: RR 0.22 (0.17—0.48) No significant difference in complications: OR 1.56 (0.71—3.43) |
| Spinal surgery | Nikolaidis (2010) | Low | Conclusions uncertain due to low or very low nature of the quality of the evidence. | |
| Spinal surgery | Machado (2016) | High | Decompression + fusion and interspinous process spacers have not been shown to be superior to conventional decompression alone. | Reoperation (decompression vs. decompression + fusion): RR 1.25 (0.81—1.92) |
| Spinal surgery | Rasouli (2014) | Low | Conclusions uncertain due to low or very low nature of the quality of the evidence. | Reoperation (decompression vs. interspinous spacer): RR 0.25 (0.14—0.47) |

ICP, intracranial pressure; CSDH, chronic subdural haematoma; ICH, intracranial haemorrhage; DBS, deep brain stimulation; VNS, vagal nerve stimulator; SAE, small area estimation; LOM, lomustine; CED, convection enhanced delivery; GBM, glioblastoma multiforme; TMZ, temozolamide; CRT, chemoradiotherapy; TBI, traumatic brain injury.