BMJ Open

Current knowledge on spinal meningiomas: a systematic review protocol

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2022-061614
Article Type:	Protocol
Date Submitted by the Author:	31-Jan-2022
Complete List of Authors:	El-Hajj, Victor Gabriel; Karolinska University Hospital, Department of Neurosurgery; Karolinska Institute, Department of Clinical Neuroscience Pettersson Segerlind, Jenny; Karolinska University Hospital, Department of Neurosurgery; Karolinska Institute, Department of Clinical Neuroscience Burström, Gustav ; Karolinska University Hospital, Department of Neurosurgery; Karolinska Institute, Department of Clinical Neuroscience Edström, Erik; Karolinska University Hospital, Department of Neurosurgery; Karolinska Institute, Department of Clinical Neuroscience Elmi-Terander, Adrian; Karolinska University Hospital, Department of Neurosurgery; Karolinska Institute, Department of Clinical Neuroscience
Keywords:	NEUROSURGERY, Neurological oncology < NEUROLOGY, Neurosurgery < SURGERY, Spine < ORTHOPAEDIC & TRAUMA SURGERY, ONCOLOGY

Title: Current knowledge on spinal meningiomas: a systematic review protocol

Author information

Author notes

[1,2]Victor Gabriel El-Hajj (victor.gababriel.elhajj@stud.ki.se)
[1,2]Jenny Pettersson-Segerlind, MD (jenny.pettersson.segerlind@ki.se)
[1,2]Gustav Burström, MD, PhD (gustav.burstrom@ki.se)
[1,2]Erik Edström, MD, PhD (erik.edstrom.1@ki.se)
[1,2]Adrian Elmi-Terander, Md, PhD (adrian.elmi.terander@ki.se)

Affiliations

[1]Department of Neurosurgery, Karolinska University Hospital, Stockholm, Sweden
[2]Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden

Corresponding and author

Victor Gabriel El-Hajj
Adress: Karolinska University Hospital, Department of Neurosurgery, Eugeniavägen 6, 4th floor, Solna, Stockholm 17164.
ORCID: https://orcid.org/0000-0001-9479-761X
Email: victor.gabriel.elhajj@stud.ki.se
Number: +467659889449

Keywords: systematic review, spinal meningioma, current knowledge, treatment, outcomes.

Word count: 2700 (excluding title page, abstract, statements & references).

Abstract

Introduction

Meningiomas are primary CNS tumors that arise from both cranial and spinal meninges. Spinal meningiomas occur less frequently than their cranial counterparts and are consequently given less attention in the literature. Therefore, systematic studies are needed to summarize the current knowledge on spinal meningiomas, providing a solid evidence base for treatment strategies. This systematic review of the literature will therefore assess studies describing spinal meningiomas, their epidemiology, diagnostics, treatment, and outcomes.

Methods and Analysis

Electronic databases including PubMed, Web of Science and Embase, will be searched using the keywords ”spinal” and “meningioma”. The search will be set to provide only the studies published after 2000 to avoid any conflicts regarding terminology and classification, as well as to reflect the current status. Case reports, editorials, letters, and reviews will also be excluded. Reference lists of relevant records will also be searched. Identified studies will be screened for inclusion, by one reviewer in a first step and then three in the next step to decrease the risk of bias. The results will be categorized to allow for a structured summary of the outcomes and their evidence grade conforming to the GRADE approach. Categories may include: epidemiology, histopathology, radiological diagnostics, surgery, complications, non-surgical or adjuvant treatments, disease outcomes and predictors, and lastly recurrence.

Ethics and dissemination

This review will summarize the current knowledge on spinal meningiomas to allow for a better understanding of the disease and contribute to improve its management. For clinicians, the systematic collection and grading of available evidence may aid in decision-making and for those seeking to further the scientific field, this review may help to identify areas where knowledge is currently lacking.

Strengths and limitations

- We developed a thorough strategy to assess both risk of bias in individual studies as well as the collective quality of evidence with respect to the GRADE guidelines.
- To our knowledge there are no other studies systematically reviewing the current knowledge on spinal meningiomas.
- The predicted high heterogeneity among studies prevents the conduction of a meta-analysis, which constitutes the main limitation to this review.

Introduction

Meningiomas originate from the arachnoid cap cells in the leptomeninges surrounding the brain and spinal cord. Hence, they occur most frequently in an intradural extramedullary location. Meningiomas of the spinal cord are less common, making up only about 2-12% of all meningiomas[1–3]. In fact, much of what we know today is derived from studies on intracranial meningiomas. Spinal meningiomas are the most common primary spinal tumor in adults, representing 25-45% of all tumors and occur with an age-adjusted incidence of 0.33 per 100, 000 population[1]. Most spinal meningiomas (90%) are benign, WHO I tumors[4–6], mainly seen in the elderly with a peak incidence between the seventh and ninth decades of life[2,4]. Regardless of their location, meningiomas are more commonly found in females. For spinal meningiomas the female to male ratio is around 4:1[2,4,7,8]. Most meningiomas occur sporadically but a known genetic association to neurofibromatosis type 2 (NF2) is established, and it is estimated that up to 20% of patients with NF2 will develop spinal meningiomas, which might even appear earlier on in life[9,10]. Mutations of the NF2 tumor suppressor gene or loss of chromosome 22 harboring this gene was found to be more frequent among spinal meningiomas of WHO grades II and III[11,12]. Exposure to high-dose ionizing radiation is also associated with earlier onset of spinal meningioma[1,13]. Meningiomas often carry estrogen or progesterone receptors[14], suggesting pregnancy as a potential risk factor for tumor growth[15,16]. This association was however refuted by a large population-based cohort study[17]. Spinal meningiomas may produce neurologic deficits and pain related to local compression of the spinal cord, nerves and adjacent structures[4,18]. The diagnosis is best made using MRI where meningiomas show homogenous enhancement on gadolinium enhanced T1 sequences. Meningiomas also typically display dural tails, enhancement and thickening of the dura extending from the tumor[19]. The treatment of choice is surgery, where tumor removal typically alleviates symptoms with little risk of complications or recurrence[4,7]. In surgery of meningiomas, Simpson grading is used to describe the radicality of tumor removal and to predict the risk for tumor recurrence. Whether Simpson grade I, which includes complete removal of dural attachments, should be the goal of spinal meningioma surgery, remains a topic of debate[4,20–23]. The Simpson scale also addresses the removal or coagulation of the affected dura. Aggressive removal of the dura may reduce the risk of recurrence but increases the risk of spinal cord injury and postoperative leakage of cerebrospinal fluid. The most commonly reported postoperative complications are wound infections, cerebrospinal fluid leaks, kyphosis, venous thromboembolisms, and transient or permanent neurologic deficits.[4,7,24–26]. However, these complications are rare and improvement of neurological function after tumor removal is expected in the majority of patients.[4,27]. For patients having undergone Simpson Grade 2 resection of a spinal meningioma, Heon Kim et al have estimated a mean clinical recurrence-free survival period of 17 years[21]. Poor outcomes on the other hand, are reportedly associated with factors like: WHO tumor grade > 1, high Ki-67 index, long time to diagnosis, large tumor size and the degree of spinal cord compression.[4,6,28] while mortality mainly reflects high age or co-morbidities[4,7]. Very little data on health-related quality of life after spinal meningioma surgery is available. Two studies with mixed groups of intradural extramedullary tumors found that the vast majority of patients who underwent surgery saw a significant improvement of activity, mood, walking ability, quality of relations, sleep, and a decrease in pain[29,30]. These findings are consistent with the results of a quality-of-life questionnaire our group conducted on 84 spinal meningioma patients at an average of 8.7 years after surgery[31]. The need for alternative or adjuvant therapies is emphasized in the literature, especially for recurring and higher-grade tumors (WHO II-III) or for patients who are poor surgical candidates[26,32]. In these cases, other treatment modalities may have to be

explored. However, the role of nonsurgical treatment options in the management of spinal meningiomas remains poorly defined.
The systematic review proposed with this protocol aims to create a comprehensive overview of the current understanding of spinal meningiomas, as well as to clarify the evidence base for the treatment strategies employed today. Topics which will be reviewed include epidemiology, tumor characteristics, diagnostics, treatment options with their potential risks and benefits, as well as outcomes including quality of life, mortality, and recurrence. The created overview will serve as a foundation for treatment choices and possibly to identify areas of insufficient knowledge, warranting renewed scientific effort.
Instead of the more classic PICO criteria (Population, Intervention, Comparison, Outcome), we decide to use the SPIDER criteria[33] (Sample, Phenomenon of Interest, Design, Evaluation, Research type) which we believe are more suited to the purpose of this review (Table 1).

Table 1: SPIDER criteria[33].

Sample	Any patient
Phenomenon of Interest	Spinal meningiomas
Design	Studies presenting original numeric data on the different topics of interest
Evaluation	Epidemiology, tumor characteristics, diagnostics, treatment, patient outcome, and recurrence
Research Type	Experimental and observational studies

Methods/Design

Patient and public involvement:

Patients were not involved in the design or conception of the study.

Study registration

This protocol for an intended systematic review is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocol (PRISMA-P) statement of 2015[34]. The PRISMA-P checklist is provided as supplementary material (see *supplementary file 1*). The systematic review protocol will also be registered on PROSPERO, before submission of the final manuscript to a peer reviewed journal.

Eligibility criteria

Inclusion criteria

Type of studies

All peer reviewed and original studies, written in English and available in the PubMed, Embase, or Web of Science databases, will be eligible for inclusion. Only studies published after 2000 will be included to limit our review to the more current publications within the field.

Type of participant

All patients will be included, regardless of age, ethnicity, and sex. Similarly, all spinal meningiomas irrespective of size, tumor grading or anatomical locations along the spine will be included. However, an adequate diagnosis of the tumor must be available and based on histological examination or MRI investigations.

Type of interventions

All modes of diagnosis and treatment of spinal meningiomas will be included.

Type of outcome measurements

Epidemiological data such as age, sex and socioeconomic factors, possible predictors of poor preoperative or postoperative decline such as comorbidity and spinal cord compression will also be addressed. Furthermore, outcome parameters including pain, neurological function, quality of life, tumor recurrence and mortality, tumor characteristics including expression of specific receptors, markers of proliferative activity, and WHO grade will also be included. Additional outcomes used in the selected studies may be considered. In those cases, the possibility of reporting biases will be recognized.

Exclusion criteria

Non-original publications such as reviews, editorials, and letters to the editor will be disregarded together with case reports and conference abstracts. Studies found in languages other than English will be excluded for practical reasons. Publications prior to the year of 2000 will also be excluded to reduce the number of included studies and give priority to more current publications.

Databases and search strategy

An electronic database search will be performed on PubMed, Embase, and Web of Science. The search will be broad, excluding case reports by adding a filter to the search. Appropriate filters will also be used to exclude non-English studies and those published prior to the year 2000. To illustrate the process, the preliminary search strategy specific to the Web of Science database is provided (see *supplementary file 2*). A reference list search of the included studies will be performed, to screen for any eligible article that was missed.

Study selection

The records retrieved from the different databases will be exported into Zotero[35], to eliminate duplicates. The records will then be screened based on title and abstract by one reviewer, to eliminate records that are plainly irrelevant. This is necessary as an unmanageable number of records is foreseen due to the broad search strategy that will be used. In the next step, three independent and blinded reviewers will be assigned the task of examining the remaining records applying the eligibility criteria based on full-text reading. This will be performed using Rayyan Software[36]. Potential disagreements after pooling of the results will be resolved by discussion with a fourth reviewer. Finally, reference lists of the selected articles will be reviewed for any potentially eligible studies that were previously missed. The process will be illustrated in a PRISMA flowchart which will be provided.

Data extraction

Data from selected records will be extracted using a predefined extraction template, preliminarily including (1) general information—title, first author, journal, publication year, etc.; (2) patient characteristics and epidemiology—age, sex, tumor location, and grade, etc.; (3) intervention characteristics—imaging, Simpson grade, adjuvant therapy, etc.; (4) study characteristics—study type, sample size, follow-up time, etc.; and (5) outcomes—neurological outcomes, quality of life, recurrence rate, mortality rate, follow-up time, adverse events and their management, main conclusions, etc. The collaboration of multiple reviewers will be sought to achieve thorough extraction of the data. The final work will even be assessed and cross-checked to prevent any error.

Assessment of risk of bias

The Oxford Center for Evidence-Based Medicine system[37], modified by Wright et al, will be used to assess evidence levels[38,39] (table 2). The selected articles will first be allocated to one of only four levels based on methodological quality, since the fifth level (V) is solely associated to expert opinions which are systematically excluded from our study. Then, an individual score (IS) will be proposed, as we account for the risk of bias accordingly: studies with lower risk of bias will be upgraded while those with higher risk of bias will get downgraded. Risk of bias will be assessed using the appropriate tools specific to the type of study, as defined by Ma et al[40]. The final IS will also range from I to IV.

Table 2 Level of evidence based on primary research question, by Wright et al[38].

	Therapeutic Studies—Investigating the results of treatment	Prognostic Studies—Investigating the outcome of disease	Diagnostic Studies—Investigating a diagnostic test
Level I	1. Good-quality randomized controlled trial, 2. Systematic review of Level-I studies	1. Prospective study, 2. Systematic review of Level-I studies	1. Testing of previously developed diagnostic criteria in series of consecutive patients (with universally applied reference "gold" standard), 2. Systematic review of Level-I studies
Level II	1. Prospective cohort study, 2. Poor-quality randomized controlled trial, 3. Systematic review, a. Level-II studies, b. Nonhomogeneous Level-I studies	1. Retrospective study, 2. Study of untreated controls from a previous randomized controlled trial, 3. Systematic review of Level-II studies	1. Development of diagnostic criteria on basis of consecutive patients (with universally applied reference "gold" standard), 2. Systematic review of Level-II studies
Level III	1. Case-control study, 2. Retrospective cohort study, 3. Systematic review of Level-III studies		1. Study of nonconsecutive patients (no consistently applied reference "gold" standard), 2. Systematic review of Level-III studies
Level IV	Case series (with no, or historical, control group)	Case series	1. Case-control study, 2. Poor reference standard
Level V	Expert opinion	Expert opinion	Expert opinion

Quality of evidence across studies.

The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE)[41] approach will be used to rate the body of evidence behind key study outcomes assessing their strength or certainty level. First, a baseline level will be set for each study outcome based on the IS of the majority of studies contributing to that specific outcome, such as: if the majority of studies have an individual score of I or II the baseline grade of evidence supporting the study outcome will be classified as ”high”, and if the majority have individual scores of either III or IV, the baseline grade of evidence will be classified as ”low”. After that, we will properly adjust the baseline score after different factors like, large effect magnitude, dose-response gradient, inconsistency, indirectness, imprecision, etc.[41] to obtain a final quality of evidence grade of “high”, “moderate”, “low” or “very low”[39] (Table 3).

Table 3: Quality of Evidence Grades, from the GRADE Handbook (Chapter 5)[41].

Quality	Definition
High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there it may be substantially different.
Low	Our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.
Very low	We have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

We will refer to the GRADE handbook[41] for further assistance on this approach.
A summary of findings table will be generated using the Guideline development tool (GRADEpro GDT)[42]. The table will convey the key study outcomes with their corresponding level of certainty (grade of evidence), in a structured and transparent manner.

Data synthesis:

After extraction, the data obtained from eligible studies will be systematically presented.
Topics of interest to this review are chosen as follows:

1. Patient characteristics: epidemiology,
2. Tumor characteristics: histopathology, WHO grading,
3. Radiological diagnostics,
4. Surgical treatment: technique, Simpson grading, intraoperative monitoring,
5. Complications and their management,
6. Non-surgical or adjuvant treatment including radiotherapy,
7. Patient outcomes: neurological outcomes, quality of life, mortality,
8. Recurrence.

Relevant data will be compiled under corresponding headings. Areas with lack of data will still be mentioned. After going through the GRADE approach, all study outcomes will be condensed in a summary of findings table, each contrasted to their respective grade of evidence. Meta-analysis will not be performed due to the anticipated high heterogeneity across the selected studies, with regards to participant and tumor characteristics as well as outcomes. In these settings, a quantitative study would therefore likely be less valuable. If an adequate number of studies is identified, subgroup analyses regarding interethnic variations and socioeconomic factors may be performed. Moreover, other subgroups reported in the eligible studies will be considered, as long as an adequate number of studies exists to support the analysis. When dealing with any such subgroups the possibility of selective reporting bias will be closely monitored[43].

Ethics and dissemination

The intended systematic review outlined in this protocol aims to summarize the current scientific literature on spinal meningiomas to provide guidance to clinicians and identify areas in need of further study. The available literature covers many aspects of spinal meningiomas, such as incidence[2,8,44], age[2,4], and gender distribution[2,4,7,8], treatments and their outcomes[4,45,46], but many studies are limited by small sample[3,46–54] sizes and short follow-up times[3,48,50,55]. Regarding the effect of preoperative neurological impairment, tumor grade and size on postoperative outcomes[3,28,48,50–57] and adjuvant therapies[26,32] the available data is conflicting. These issues will be addressed by the systematic review's design, as integrating data from diverse origins will allow for a more representative synthesis that reflects the population of patients with spinal meningiomas more accurately[58]. The absence of both randomized trials and high-quality evidence within the literature as well as the dominance of observational and cohort studies is already apparent, making up the largest limitation to our review. Other limitations eventually encountered during the writing of the manuscript will be discussed in the corresponding part of the review.

This study ought to be regarded as a reliable source for clinicians to access current evidence compiled in a systematic way and hence better understand the tumor, its epidemiology, management, and prognosis. Greater knowledge of the subject will eventually contribute to improving the diagnosis and care delivery of affected patients. Moreover, the planned systematic review could also help disclose knowledge gaps in the field, identifying and highlighting future research priorities[59]. To the best of our knowledge, no systematic review outlining the current understanding of spinal meningiomas has been attempted to this date, making our study the first of its kind. The protocol hereby presented is in accordance with the PRISMA-P guidelines, (see *supplementary file 1*). For further transparency, this protocol will also be registered on PROSPERO in due time. The record on PROSPERO will be updated should significant changes to the procedure take place. The final manuscript is intended for submission to peer-reviewing.

Abbreviations

IS = individual score
GRADE = Grading of Recommendations, Assessment, Development and Evaluation
MRI = Magnetic Resonance Imaging
NF2 = Neurofibromatosis type 2
PICO = Population, Intervention, Comparison, Outcome
PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses
SPIDER = Sample, Phenomenon of Interest, Design, Evaluation, Research type
WHO = World health Organization

Availability of data and materials

Not applicable.

Competing interests

No competing interests are reported by any of the authors.

Contributions

- Victor Gabriel El-Hajj: conception & design of the work, drafting of the article, critical revision, and final approval of the version to be published.
- Jenny Pettersson-Segerlind: conception & design of the work, drafting of the article, and final approval of the version to be published.
- Gustav Liu Burström: conception & design of the work, drafting of the article, and final approval of the version to be published.
- Erik Edström: conception & design of the work, drafting of the article, critical revision, and final approval of the version to be published.
- Adrian Elmi-Terander: guarantor of the review, conception & design of the work, drafting of the article, critical revision, and final approval of the version to be published.

Funding

Not applicable.

Ethics declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Acknowledgements

Not applicable.

References

1. Ogasawara, C., Philbrick, B. D., & Adamson, D. C. (2021). Meningioma: A Review of Epidemiology, Pathology, Diagnosis, Treatment, and Future Directions. *Biomedicines*, *9*(3), 319. https://doi.org/10.3390/biomedicines9030319
2. Kshettry, V. R., Hsieh, J. K., Ostrom, Q. T., Kruchko, C., Benzel, E. C., & Barnholtz-Sloan, J. S. (2015). Descriptive Epidemiology of Spinal Meningiomas in the United States. *Spine*, *40*(15), E886-9. https://doi.org/10.1097/BRS.0000000000000974
3. Maiti, T. K., Bir, S. C., Patra, D. P., Kalakoti, P., Guthikonda, B., & Nanda, A. (2016). Spinal meningiomas: clinicoradiological factors predicting recurrence and functional outcome. *Neurosurgical Focus*, *41*(2), E6. https://doi.org/10.3171/2016.5.FOCUS16163
4. Pettersson-Segerlind, J., Fletcher-Sandersjöö, A., Tatter, C., Burström, G., Persson, O., Förander, P., Mathiesen, T., Bartek, J., Edström, E., & Elmi-Terander, A. (2021). Long-

Term Follow-Up and Predictors of Functional Outcome after Surgery for Spinal Meningiomas: A Population-Based Cohort Study. *Cancers 2021, Vol. 13, Page 3244*, *13*(13), 3244. https://doi.org/10.3390/CANCERS13133244

5. Westwick, H. J., & Shamji, M. F. (2015). Effects of sex on the incidence and prognosis of spinal meningiomas: a Surveillance, Epidemiology, and End Results study. *Journal of Neurosurgery: Spine*, *23*(3), 368–373. https://doi.org/10.3171/2014.12.SPINE14974
6. Hua, L., Zhu, H., Deng, J., Tian, M., Jiang, X., Tang, H., Luan, S., Wakimoto, H., Xie, Q., & Gong, Y. (2018). Clinical and prognostic features of spinal meningioma: a thorough analysis from a single neurosurgical center. *Journal of Neuro-Oncology*, *140*(3), 639–647. https://doi.org/10.1007/S11060-018-2993-3/TABLES/4
7. Kwee, L. E., Harhangi, B. S., Ponne, G. A., Kros, J. M., Dirven, C. M. F., & Dammers, R. (2020). Spinal meningiomas: Treatment outcome and long-term follow-up. *Clinical Neurology and Neurosurgery*, *198*, 106238. https://doi.org/10.1016/J.CLINEURO.2020.106238
8. Duong, L. M., McCarthy, B. J., McLendon, R. E., Dolecek, T. A., Kruchko, C., Douglas, L. L., & Ajani, U. A. (2012). Descriptive epidemiology of malignant and nonmalignant primary spinal cord, spinal meninges, and cauda equina tumors, United States, 2004-2007. *Cancer*, *118*(17), 4220–4227. https://doi.org/10.1002/CNCR.27390
9. Evans, D. G. R., Sainio, M., & Baser, M. E. (2000). Neurofibromatosis type 2. *Journal of Medical Genetics*, *37*(12), 897. https://doi.org/10.1136/JMG.37.12.897
10. Karsy, M., Guan, J., Sivakumar, W., Neil, J. A., Schmidt, M. H., & Mahan, M. A. (2015). The genetic basis of intradural spinal tumors and its impact on clinical treatment. *Neurosurgical Focus*, *39*(2), E3. https://doi.org/10.3171/2015.5.FOCUS15143
11. Arslantas, A., Artan, S., Öner, Ü., Durmaz, R., Müslümanoğlu, H., Atasoy, M. A., Başaran, N., & Tel, E. (2003). Detection of Chromosomal Imbalances in Spinal Meningiomas by Comparative Genomic Hybridization. *Neurologia Medico-Chirurgica*, *43*(1), 12–19. https://doi.org/10.2176/NMC.43.12
12. Pawloski, J. A., Fadel, H. A., Huang, Y.-W., Lee, I. Y., Pawloski, C. :, Fadel, J. A. ;, Huang, H. A. ;, Lee, Y.-W. ;, Genomic, I. Y., & Baldi, A. (2021). Genomic Biomarkers of Meningioma: A Focused Review. *International Journal of Molecular Sciences 2021, Vol. 22, Page 10222*, *22*(19), 10222. https://doi.org/10.3390/IJMS221910222
13. Cohen-Gadol, A. A., Zikel, O. M., Koch, C. A., Scheithauer, B. W., & Krauss, W. E. (2003). Spinal meningiomas in patients younger than 50 years of age: a 21-year experience. *Journal of Neurosurgery: Spine*, *98*(3), 258–263. https://doi.org/10.3171/SPI.2003.98.3.0258
14. Maiuri, F., Mariniello, G., de Divitiis, O., Esposito, F., Guadagno, E., Teodonno, G., Barbato, M., & del Basso De Caro, M. (2021). Progesterone Receptor Expression in Meningiomas: Pathological and Prognostic Implications. *Frontiers in Oncology*, *11*, 2585. https://doi.org/10.3389/FONC.2021.611218/BIBTEX
15. Antolínez Ayala, V. E., García Arias, M. D., Bautista Vargas, S. E., Báez Cárdenas, L. M., & Castellanos Peñaranda, C. (2021). Paraplegia due to spinal meningioma during the third trimester of pregnancy: case report and literature review. *Spinal Cord Series and Cases 2021 7:1*, *7*(1), 1–5. https://doi.org/10.1038/s41394-020-00368-0
16. Hortobágyi, T., Bencze, J., Murnyák, B., Kouhsari, M. C., Bognár, L., & Marko-Varga, G. (2017). Pathophysiology of meningioma growth in pregnancy. *Open Medicine (Poland)*, *12*(1), 195–200. https://doi.org/10.1515/MED-2017-0029/MACHINEREADABLECITATION/RIS
17. Pettersson-Segerlind, J., Mathiesen, T., Elmi-Terander, A., Edström, E., Talbäck, M., Feychting, M., & Tettamanti, G. (2021). The risk of developing a meningioma during

and after pregnancy. *Scientific Reports 2021 11:1*, *11*(1), 1–8. https://doi.org/10.1038/s41598-021-88742-2

18. Abul-Kasim, K., Thurnher, M. M., McKeever, P., & Sundgren, P. C. (2008). Intradural spinal tumors: current classification and MRI features. *Neuroradiology*, *50*(4), 301–314. https://doi.org/10.1007/S00234-007-0345-7
19. Watts, J., Box, G., Galvin, A., Brotchie, P., Trost, N., & Sutherland, T. (2014). Magnetic resonance imaging of meningiomas: A pictorial review. *Insights into Imaging*, *5*(1), 113–122. https://doi.org/10.1007/S13244-013-0302-4/FIGURES/21
20. Tsuda, K., Akutsu, H., Yamamoto, T., Nakai, K., Ishikawa, E., & Matsumura, A. (2014). Is Simpson Grade I Removal Necessary in All Cases of Spinal Meningioma? Assessment of Postoperative Recurrence during Long-Term Follow-up. *Neurologia Medico-Chirurgica*, *54*(11), 907–913. https://doi.org/10.2176/NMC.OA.2013-0311
21. Kim, C. H., Chung, C. K., Lee, S. H., Jahng, T. A., Hyun, S. J., Kim, K. J., Yoon, S. H., Kim, E. S., Eoh, W., Kim, H. J., Kim, K. T., Sung, J. K., & Choi, Y. (2016). Long-term recurrence rates after the removal of spinal meningiomas in relation to Simpson grades. *European Spine Journal*, *25*(12), 4025–4032. https://doi.org/10.1007/S00586-015-4306-2/FIGURES/2
22. Voldřich, R., Netuka, D., & Beneš, V. (2020). Spinal meningiomas: is Simpson grade II resection radical enough? *Acta Neurochirurgica*, *162*(6), 1401–1408. https://doi.org/10.1007/S00701-020-04280-2/FIGURES/2
23. Nakamura, M., Tsuji, O., Fujiyoshi, K., Hosogane, N., Watanabe, K., Tsuji, T., Ishii, K., Toyama, Y., Chiba, K., & Matsumoto, M. (2012). Long-term surgical outcomes of spinal meningiomas. *Spine*, *37*(10). https://doi.org/10.1097/BRS.0B013E31824167F1
24. Tatter, C., Fletcher-Sandersjöö, A., Persson, O., Burström, G., Grane, P., Edström, E., & Elmi-Terander, A. (2020). Incidence and predictors of kyphotic deformity following resection of cervical intradural tumors in adults: a population-based cohort study. *Acta Neurochirurgica*, *162*(11), 2905–2913. https://doi.org/10.1007/S00701-020-04416-4/FIGURES/5
25. Yoon, S. H., Chung, C. K., & Jahng, T. A. (2007). Surgical Outcome of Spinal Canal Meningiomas. *Journal of Korean Neurosurgical Society*, *42*(4), 300–304. https://doi.org/10.3340/JKNS.2007.42.4.300
26. Westwick, H. J., Yuh, S. J., & Shamji, M. F. (2015). Complication Avoidance in the Resection of Spinal Meningiomas. *World Neurosurgery*, *83*(4), 627–634. https://doi.org/10.1016/J.WNEU.2014.12.015
27. Bydon, M., & Gokaslan, Z. L. (2015). Spinal Meningioma Resection. *World Neurosurgery*, *83*(6), 1032–1033. https://doi.org/10.1016/J.WNEU.2015.01.049
28. Frati, A., Pesce, A., Toccaceli, G., Fraschetti, F., Caruso, R., & Raco, A. (2019). Spinal Meningiomas Prognostic Evaluation Score (SPES): predicting the neurological outcomes in spinal meningioma surgery. *Neurosurgical Review*, *42*(1), 115–125. https://doi.org/10.1007/S10143-018-0961-1/FIGURES/4
29. Newman, W. C., Berry-Candelario, J., Villavieja, J., Reiner, A. S., Bilsky, M. H., Laufer, I., & Barzilai, O. (2021). Improvement in Quality of Life Following Surgical Resection of Benign Intradural Extramedullary Tumors: A Prospective Evaluation of Patient-Reported Outcomes. *Neurosurgery*, *88*(5), 989–995. https://doi.org/10.1093/NEUROS/NYAA561
30. Viereck, M. J., Ghobrial, G. M., Beygi, S., & Harrop, J. S. (2016). Improved patient quality of life following intradural extramedullary spinal tumor resection. *Journal of Neurosurgery: Spine*, *25*(5), 640–645. https://doi.org/10.3171/2016.4.SPINE151149
31. Pettersson-Segerlind, J., Vogelsang, A.-C. von, Fletcher-Sandersjöö, A., Tatter, C., Mathiesen, T., Edström, E., & Elmi-Terander, A. (2021). Health-Related Quality of Life

and Return to Work after Surgery for Spinal Meningioma: A Population-Based Cohort Study. *Cancers 2021, Vol. 13, Page 6371*, *13*(24), 6371. https://doi.org/10.3390/CANCERS13246371

32. Yolcu, Y. U., Goyal, A., Alvi, M. A., Moinuddin, F. M., & Bydon, M. (2019). Trends in the utilization of radiotherapy for spinal meningiomas: insights from the 2004–2015 National Cancer Database. *Neurosurgical Focus*, *46*(6), E6. https://doi.org/10.3171/2019.3.FOCUS1969
33. Cooke, A., Smith, D., & Booth, A. (2012). Beyond PICO: The SPIDER tool for qualitative evidence synthesis. *Qualitative Health Research*, *22*(10), 1435–1443. https://doi.org/10.1177/1049732312452938
34. Moher, D., Shamseer, L., Clarke, M., Ghersi, D., Liberati, A., Petticrew, M., Shekelle, P., Stewart, L. A., Estarli, M., Barrera, E. S. A., Martínez-Rodríguez, R., Baladia, E., Agüero, S. D., Camacho, S., Buhring, K., Herrero-López, A., Gil-González, D. M., Altman, D. G., Booth, A., … Whitlock, E. (2016). Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Revista Espanola de Nutricion Humana y Dietetica*, *20*(2), 148–160. https://doi.org/10.1186/2046-4053-4-1/TABLES/4
35. *Roy Rosenzweig Center for History and New Media. (2016) Zotero [Computer software]. Retrieved from www.zotero.org/download*. (n.d.).
36. Ouzzani, M., Hammady, H., Fedorowicz, Z., & Elmagarmid, A. (2016). Rayyan—a web and mobile app for systematic reviews. *Systematic Reviews*, *5*(1), 210. https://doi.org/10.1186/s13643-016-0384-4
37. *OCEBM Levels of Evidence Working Group*. "The Oxford 2011 Levels of Evidence". Oxford Centre for Evidence-Based Medicine. http://www.cebm.net/index.aspx?o=5653 * OCEBM Table of Evidence Working Group = Jeremy Howick, Iain Chalmers (James Lind Library), Paul Glasziou, Trish Greenhalgh, Carl Heneghan, Alessandro Liberati, Ivan Moschetti, Bob Phillips, Hazel Thornton, Olive Goddard and Mary Hodgkinson*. (n.d.).
38. Wright, J. G., Swiontkowski, M. F., & Heckman, J. D. (2003). Introducing levels of evidence to the journal. *The Journal of Bone and Joint Surgery. American Volume*, *85*(1), 1–3.
39. Anderson, K. K., Tetreault, L., Shamji, M. F., Singh, A., Vukas, R. R., Harrop, J. S., Fehlings, M. G., Vaccaro, A. R., Hilibrand, A. S., & Arnold, P. M. (2015). Optimal Timing of Surgical Decompression for Acute Traumatic Central Cord Syndrome. *Neurosurgery*, *77*, S15–S32. https://doi.org/10.1227/NEU.0000000000000946
40. Ma, L. L., Wang, Y. Y., Yang, Z. H., Huang, D., Weng, H., & Zeng, X. T. (2020). Methodological quality (risk of bias) assessment tools for primary and secondary medical studies: What are they and which is better? *Military Medical Research*, *7*(1), 1–11. https://doi.org/10.1186/S40779-020-00238-8/TABLES/1
41. *Schünemann H, Brożek J, Guyatt G, Oxman A, editors. GRADE handbook for grading quality of evidence and strength of recommendations. Updated October 2013. The GRADE Working Group, 2013. Available from guidelinedevelopment.org/handbook*. (n.d.).
42. *GRADEpro GDT: GRADEpro Guideline Development Tool [Software]. McMaster University, 2020 (developed by Evidence Prime, Inc.). Available from gradepro.org*. (n.d.).
43. Reid, E. K., Tejani, A. M., Huan, L. N., Egan, G., O'Sullivan, C., Mayhew, A. D., & Kabir, M. (2015). Managing the incidence of selective reporting bias: A survey of Cochrane review groups. *Systematic Reviews*, *4*(1), 1–8. https://doi.org/10.1186/S13643-015-0070-Y/FIGURES/3

44. Weber, C., Gulati, S., Jakola, A. S., Habiba, S., Nygaard, Ø. P., Johannesen, T. B., & Solheim, O. (2014). Incidence rates and surgery of primary intraspinal tumors in the era of modern neuroimaging: a national population-based study. *Spine*, *39*(16). https://doi.org/10.1097/BRS.0000000000000412
45. Sandalcioglu, I. E., Hunold, A., Müller, O., Bassiouni, H., Stolke, D., & Asgari, S. (2008). Spinal meningiomas: Critical review of 131 surgically treated patients. *European Spine Journal*, *17*(8), 1035–1041. https://doi.org/10.1007/S00586-008-0685-Y/TABLES/4
46. Hohenberger, C., Gugg, C., Schmidt, N. O., Zeman, F., & Schebesch, K. M. (2020). Functional outcome after surgical treatment of spinal meningioma. *Journal of Clinical Neuroscience*, *77*, 62–66. https://doi.org/10.1016/J.JOCN.2020.05.042
47. Morandi, X., Haegelen, C., Riffaud, L., Amlashi, S., Adn, M., & Brassier, G. (2004). Results in the operative treatment of elderly patients with spinal meningiomas. *Spine*, *29*(19), 2191–2194. https://doi.org/10.1097/01.BRS.0000141173.79572.40
48. Arima, H., Takami, T., Yamagata, T., Naito, K., Abe, J., Shimokawa, N., & Ohata, K. (2014). Surgical management of spinal meningiomas: A retrospective case analysis based on preoperative surgical grade. *Surgical Neurology International*, *5*(Suppl 7), S333. https://doi.org/10.4103/2152-7806.139642
49. Sacko, O., Haegelen, C., Mendes, V., Brenner, A., Sesay, M., Brauge, D., Lagarrigue, J., Loiseau, H., & Roux, F. E. (2009). SPINAL MENINGIOMA SURGERY IN ELDERLY PATIENTS WITH PARAPLEGIA OR SEVERE PARAPARESISA MULTICENTER STUDY. *Neurosurgery*, *64*(3), 503–510. https://doi.org/10.1227/01.NEU.0000338427.44471.1D
50. Haegelen, C., Morandi, X., Riffaud, L., Amlashi, S. F. A., Leray, E., & Brassier, G. (2005). Results of spinal meningioma surgery in patients with severe preoperative neurological deficits. *European Spine Journal*, *14*(5), 440–444. https://doi.org/10.1007/S00586-004-0809-Y/TABLES/3
51. Schaller, B. (2005). Spinal Meningioma: Relationship Between Histological Subtypes and Surgical Outcome? *Journal of Neuro-Oncology 2005 75:2*, *75*(2), 157–161. https://doi.org/10.1007/S11060-005-1469-4
52. Setzer, M., Vatter, H., Marquardt, G., Seifert, V., & Vrionis, F. D. (2007). Management of spinal meningiomas: surgical results and a review of the literature. *Neurosurgical Focus*, *23*(4), E14. https://doi.org/10.3171/FOC-07/10/E14
53. Gilard, V., Goia, A., Ferracci, F. X., Marguet, F., Magne, N., Langlois, O., Perez, A., & Derrey, S. (2018). Spinal meningioma and factors predictive of post-operative deterioration. *Journal of Neuro-Oncology*, *140*(1), 49–54. https://doi.org/10.1007/S11060-018-2929-Y/TABLES/4
54. Gezen, F., Kahraman, S., Çanakci, Z., & Bedük, A. (2000). Review of 36 Cases of Spinal Cord Meningioma. *Spine*, *25*(6), 727–731. https://doi.org/10.1097/00007632-200003150-00013
55. Bayoumi, A. B., Laviv, Y., Karaali, C. N., Ertilav, K., Kepoglu, U., Toktas, Z. O., Konya, D., & Kasper, E. M. (2020). Spinal meningiomas: 61 cases with predictors of early postoperative surgical outcomes. *Journal of Neurosurgical Sciences*, *64*(5), 446–451. https://doi.org/10.23736/S0390-5616.17.04102-9
56. Raco, A., Pesce, A., Toccaceli, G., Domenicucci, M., Miscusi, M., & Delfini, R. (2017). Factors leading to a poor functional outcome in spinal meningioma surgery: Remarks on 173 cases. *Neurosurgery*, *80*(4), 602–609. https://doi.org/10.1093/NEUROS/NYW092
57. Klekamp, J., & Samii, M. (1999). Surgical results for spinal meningiomas. *Surgical Neurology*, *52*(6), 552–562. https://doi.org/10.1016/S0090-3019(99)00153-6

58. Edwards, T. B. (2014). What is the value of a systematic review? *Journal of Shoulder and Elbow Surgery*, *23*(1), 1–2. https://doi.org/10.1016/J.JSE.2013.09.001
59. *Lasserson TJ, Thomas J, Higgins JPT. Chapter 1: Starting a review. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.2 (updated February 2021). Cochrane, 2021. Available from www.training.cochrane.org/handbook*. (n.d.).

Supplementary information

Supplementary file 1: PRISMA-P 2015 Checklist.
Supplementary file 2: Search strategy for Web of Science.

Reporting checklist for protocol of a systematic review and meta analysis.

Based on the PRISMA-P guidelines.

Reference: Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA. Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 statement. Syst Rev. 2015;4(1):1.

		Reporting Item	Page Number
Title			
Identification	#1a	Identify the report as a protocol of a systematic review	1
Update	#1b	If the protocol is for an update of a previous systematic review, identify as such	n/a
Registration			
	#2	If registered, provide the name of the registry (such as PROSPERO) and registration number	n/a (this protocol is planned for registration on PROSPERO)
Authors			
Contact	#3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contribution	#3b	Describe contributions of protocol authors and identify the guarantor of the review	9
Amendments			
	#4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol	n/a

		amendments	
Support			
Sources	#5a	Indicate sources of financial or other support for the review	n/a
Sponsor	#5b	Provide name for the review funder and / or sponsor	n/a
Role of sponsor or funder	#5c	Describe roles of funder(s), sponsor(s), and / or institution(s), if any, in developing the protocol	n/a
Introduction			
Rationale	#6	Describe the rationale for the review in the context of what is already known	2, 4
Objectives	#7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	4
Methods			
Eligibility criteria	#8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	4, 5
Information sources	#9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	5
Search strategy	#10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	5
Study records - data management	#11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	5, 6

Study records - selection process	#11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	5
Study records - data collection process	#11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	6
Data items	#12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	6
Outcomes and prioritization	#13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	7
Risk of bias in individual studies	#14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	6
Data synthesis	#15a	Describe criteria under which study data will be quantitatively synthesised	n/a (only qualitative synthesis will be sought due to expected heterogeneity)
Data synthesis	#15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I2, Kendall's τ)	n/a (qualitative only)
Data synthesis	#15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	n/a

Data synthesis	#15d	If quantitative synthesis is not appropriate, describe the type of summary planned	7
Meta-bias(es)	#16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	6
Confidence in cumulative evidence	#17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	6, 7

 This checklist was completed on 29. January 2022 using https://www.goodreports.org/, a tool made by the EQUATOR Network in collaboration with Penelope.ai

Supplementary file 2: Draft search strategy inclusive to the Web of Science database

#1	Spinal AND meningioma* (title)
#2	Case report (title)
#3	#1 NOT #2
#4	“spinal meningioma” (All fields)
#5	”case report” (Topic)
#6	#4 NOT #5
#7	Search #3 OR #6
#8	2000-2500 (Year Published)
#9	English (Language)
#10	Veterinary sciences (Exclude – Web of Science Categories)
#11	Editorial Materials or Letters or Meeting Abstracts (Exclude – Document Types)
#12	Search #7 AND #8 AND #9 NOT #10 NOT #11

Current knowledge on spinal meningiomas: a systematic review protocol

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2022-061614.R1
Article Type:	Protocol
Date Submitted by the Author:	15-May-2022
Complete List of Authors:	El-Hajj, Victor Gabriel; Karolinska University Hospital, Department of Neurosurgery; Karolinska Institute, Department of Clinical Neuroscience Pettersson Segerlind, Jenny; Karolinska University Hospital, Department of Neurosurgery; Karolinska Institute, Department of Clinical Neuroscience Burström, Gustav ; Karolinska University Hospital, Department of Neurosurgery; Karolinska Institute, Department of Clinical Neuroscience Edström, Erik; Karolinska University Hospital, Department of Neurosurgery; Karolinska Institute, Department of Clinical Neuroscience Elmi-Terander, Adrian; Karolinska University Hospital, Department of Neurosurgery; Karolinska Institute, Department of Clinical Neuroscience
Primary Subject Heading:	Surgery
Secondary Subject Heading:	Surgery, Neurology, Epidemiology, Oncology
Keywords:	NEUROSURGERY, Neurological oncology < NEUROLOGY, Neurosurgery < SURGERY, Spine < ORTHOPAEDIC & TRAUMA SURGERY, ONCOLOGY

Title: Current knowledge on spinal meningiomas: a systematic review protocol

Author information

Author notes

[1,2]Victor Gabriel El-Hajj (victor.gababriel.elhajj@stud.ki.se)
[1,2]Jenny Pettersson-Segerlind, MD (jenny.pettersson.segerlind@ki.se)
[1,2]Gustav Burström, MD, PhD (gustav.burstrom@ki.se)
[1,2]Erik Edström, MD, PhD (erik.edstrom.1@ki.se)
[1,2]Adrian Elmi-Terander, Md, PhD (adrian.elmi.terander@ki.se)

Affiliations

[1]Department of Neurosurgery, Karolinska University Hospital, Stockholm, Sweden
[2]Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden

Corresponding and author

Victor Gabriel El-Hajj
Adress: Karolinska University Hospital, Department of Neurosurgery, Eugeniavägen 6, 4th floor, Solna, Stockholm 17164.
ORCID: https://orcid.org/0000-0001-9479-761X
Email: victor.gabriel.elhajj@stud.ki.se
Number: +467659889449

Keywords: systematic review, spinal meningioma, current knowledge, treatment, outcomes.

Word count: 2700 (excluding title page, abstract, statements & references).

Abstract

Introduction

Meningiomas are primary CNS tumors that arise from both cranial and spinal meninges. Spinal meningiomas occur less frequently than their cranial counterparts and are consequently given less attention in the literature. Therefore, systematic studies are needed to summarize the current knowledge on spinal meningiomas, providing a solid evidence base for treatment strategies. This systematic review of the literature will therefore assess studies describing spinal meningiomas, their epidemiology, diagnostics, treatment, and outcomes.

Methods and Analysis

Electronic databases including PubMed, Web of Science and Embase, will be searched using the keywords ”spinal” and “meningioma”. The search will be set to provide only English studies published after 2000 to avoid any conflicts regarding terminology and classification, as well as to reflect the current status. Case reports, editorials, letters, and reviews will also be excluded. Reference lists of relevant records will also be searched. Identified studies will be screened for inclusion, by one reviewer in a first step and then three in the next step to decrease the risk of bias. The results will be categorized to allow for a structured summary of the outcomes and their evidence grade conforming to the GRADE approach. Categories may include: epidemiology, histopathology, radiological diagnostics, surgery, complications, non-surgical or adjuvant treatments, disease outcomes and predictors, and lastly recurrence. This review will summarize the current knowledge on spinal meningiomas to allow for a better understanding of the disease and contribute to improve its management. For clinicians, the systematic collection and grading of available evidence may aid in decision-making and for those seeking to further the scientific field, this review may help to identify areas where knowledge is currently lacking.

Ethics and dissemination

Ethics approval was not required for our systematic review as it is based on existing publications. The results will be disseminated via submission for publication in a peer-reviewed journal.

Strengths and limitations

- We developed a thorough strategy to assess both risk of bias in individual studies as well as the collective quality of evidence with respect to the GRADE guidelines.
- Our broad search strategy and limited set of exclusion criteria allows for more studies to be included, ensuring adequate coverage of the topic and identification of knowledge gaps.
- By providing a comprehensive synthesis of the body of evidence, the possibility to focus future research efforts will be improved.
- We suspect that the quality of data does not suffice to perform a meta-analysis, consequently limiting the level of evidence that can be achieved.

Introduction

Meningiomas originate from the arachnoid cap cells in the leptomeninges surrounding the brain and spinal cord. Hence, they occur most frequently in an intradural extramedullary location. Meningiomas of the spinal cord are less common, making up only about 2-12% of all meningiomas[1–3]. In fact, much of what we know today is derived from studies on intracranial meningiomas. Spinal meningiomas are the most common primary spinal tumor in adults, representing 25-45% of all tumors and occur with an age-adjusted incidence of 0.33 per 100, 000 population[1]. Most spinal meningiomas (90%) are benign, WHO I tumors[4–6], mainly seen in the elderly with a peak incidence between the seventh and ninth decades of life[2,4]. Regardless of their location, meningiomas are more commonly found in females. For spinal meningiomas the female to male ratio is around 4:1[2,4,7,8]. Most meningiomas occur sporadically but a known genetic association to neurofibromatosis type 2 (NF2) is established, and it is estimated that up to 20% of patients with NF2 will develop spinal meningiomas, which might even appear earlier on in life[9,10]. Mutations of the NF2 tumor suppressor gene or loss of chromosome 22 harboring this gene was found to be more frequent among spinal meningiomas of WHO grades II and III[11,12]. Exposure to high-dose ionizing radiation is also associated with earlier onset of spinal meningioma[1,13]. Meningiomas often carry estrogen or progesterone receptors[14], suggesting pregnancy as a potential risk factor for tumor growth[15,16]. This association was however refuted by a large population-based cohort study[17]. Spinal meningiomas may produce neurologic deficits and pain related to local compression of the spinal cord, nerves and adjacent structures[4,18]. The diagnosis is best made using MRI where meningiomas show homogenous enhancement on gadolinium enhanced T1 sequences. Meningiomas also typically display dural tails, enhancement and thickening of the dura extending from the tumor[19]. The treatment of choice is surgery, where tumor removal typically alleviates symptoms with little risk of complications or recurrence[4,7]. In surgery of meningiomas, Simpson grading is used to describe the radicality of tumor removal and to predict the risk for tumor recurrence. Whether Simpson grade I, which includes complete removal of dural attachments, should be the goal of spinal meningioma surgery, remains a topic of debate[4,20–23]. The Simpson scale also addresses the removal or coagulation of the affected dura. Aggressive removal of the dura may reduce the risk of recurrence but increases the risk of spinal cord injury and postoperative leakage of cerebrospinal fluid. Surgical techniques with removal of the inner dural layer, may constitute an intermediate solution[24,25]. The most commonly reported postoperative complications are wound infections, cerebrospinal fluid leaks, kyphosis, venous thromboembolisms, and transient or permanent neurologic deficits[4,7,26–28]. However, these complications are rare and improvement of neurological function after tumor removal is expected in the majority of patients[4,29]. For patients having undergone Simpson Grade 2 resection of a spinal meningioma, Heon Kim et al have estimated a mean clinical recurrence-free survival period of 17 years[21]. Poor outcomes on the other hand, are reportedly associated with factors like: WHO tumor grade > 1, high Ki-67 index, long time to diagnosis, large tumor size and the degree of spinal cord compression[4,6,30] while mortality mainly reflects high age or co-morbidities[4,7]. Very little data on health-related quality of life after spinal meningioma surgery is available. Two studies with mixed groups of intradural extramedullary tumors found that the vast majority of patients who underwent surgery saw a significant improvement of activity, mood, walking ability, quality of relations, sleep, and a decrease in pain[31,32]. These findings are consistent with the results of a quality-of-life questionnaire our group conducted on 84 spinal meningioma patients at an average of 8.7 years after surgery[33]. The need for alternative or adjuvant therapies is emphasized in the literature, especially for recurring tumors refractory to conventional therapies and higher-grade tumors (WHO II-III) or for patients who are poor surgical candidates[28,34]. In these cases, other treatment modalities, including targeted, hormonal, micro-RNA, or different forms of radiation therapy, may have to be explored. However, the role of nonsurgical treatment options in the management of spinal meningiomas remains poorly defined.

The systematic review proposed with this protocol aims to create a comprehensive overview of the current understanding of spinal meningiomas, as well as to clarify the evidence base for the treatment strategies employed today. Topics which will be reviewed include epidemiology, tumor characteristics, diagnostics, treatment options with their potential risks and benefits, as well as outcomes including quality of life, mortality, and recurrence. The created overview will serve as a foundation for treatment choices and possibly to identify areas of insufficient knowledge, warranting renewed scientific effort.

Instead of the more classic PICO criteria (Population, Intervention, Comparison, Outcome), we decide to use the SPIDER criteria[35] (Sample, Phenomenon of Interest, Design, Evaluation, Research type) which we believe are more suited to the purpose of this review (Table 1).

Table 1: SPIDER criteria[35].

Sample	Any patient
Phenomenon of Interest	Spinal meningiomas
Design	Studies presenting original numeric data on the different topics of interest
Evaluation	Epidemiology, tumor characteristics, diagnostics, treatment, patient outcome, and recurrence
Research Type	Experimental and observational studies

Methods and analysis

Study registration

This protocol for an intended systematic review is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocol (PRISMA-P) statement of 2015[36]. The PRISMA-P checklist is provided as supplementary material (see *supplementary file 1*). The systematic review protocol will also be registered on PROSPERO, before submission of the final manuscript to a peer reviewed journal.

Eligibility criteria

Inclusion criteria

Type of studies

All peer reviewed and original studies, written in English and available in the PubMed, Embase, or Web of Science databases, will be eligible for inclusion. Only studies published after 2000 will be included to limit our review to the more current publications within the field.

Type of participant

All patients will be included, regardless of age, ethnicity, and sex. Similarly, all spinal meningiomas irrespective of size, tumor grading or anatomical locations along the spine will be included. However, an adequate diagnosis of the tumor must be available and based on histological examination or MRI investigations.

Type of interventions

All modes of diagnosis and treatment of spinal meningiomas will be included.

Type of outcome measurements

Epidemiological data such as age, sex and socioeconomic factors, possible predictors of poor preoperative or postoperative decline such as comorbidity and spinal cord compression will also be addressed. Furthermore, outcome parameters including pain, neurological function, quality of life, tumor recurrence and mortality, tumor characteristics including expression of specific receptors, markers of proliferative activity, and WHO grade will also be included. Additional outcomes used in the selected studies may be considered. In those cases, the possibility of reporting biases will be recognized.

Exclusion criteria

Non-original publications such as reviews, editorials, and letters to the editor will be disregarded together with case reports and conference abstracts. Studies found in languages other than English will be excluded for practical reasons. Publications prior to the year of 2000 will also be excluded to reduce the number of included studies and give priority to more current publications.

Databases and search strategy

An electronic database search will be performed on PubMed, Embase, and Web of Science. The search will be broad, excluding case reports by adding a filter to the search. Appropriate filters will also be used to exclude non-English studies and those published prior to the year 2000. To illustrate the process, the preliminary search strategy for each of the databases is provided (see *supplementary file 2*). A reference list search of the included studies will be performed, to screen for any eligible article that was missed.

Study selection

The records retrieved from the different databases will be exported into Zotero[37], to eliminate duplicates. The records will then be screened based on title and abstract by one reviewer, to eliminate records that are plainly irrelevant. This is necessary as an unmanageable number of records is foreseen due to the broad search strategy that will be used. In the next step, three independent and blinded reviewers will be assigned the task of examining the remaining records applying the eligibility criteria based on full-text reading. This will be performed using Rayyan Software[38]. Potential disagreements after pooling of the results will be resolved by discussion with a fourth reviewer. Finally, reference lists of the selected articles will be reviewed for any potentially eligible studies that were previously missed. The process will be illustrated in a PRISMA flowchart which will be provided.

Data extraction

Data from selected records will be extracted using a predefined extraction template, preliminarily including (1) general information—title, first author, journal, publication year, etc.; (2) patient characteristics and epidemiology—age, sex, tumor location, and grade, etc.; (3) intervention characteristics—imaging, Simpson grade, adjuvant therapy, etc.; (4) study characteristics—study type, sample size, follow-up time, etc.; and (5) outcomes—neurological outcomes, quality of life, recurrence rate, mortality rate, follow-up time, adverse events and their management, main conclusions, etc. The collaboration of multiple reviewers will be sought to achieve thorough extraction of the data. The final work will even be assessed and cross-checked to prevent any error.

Assessment of risk of bias

The Oxford Center for Evidence-Based Medicine system[39], modified by Wright et al, will be used to assess evidence levels[40,41] (table 2). The selected articles will first be allocated to one of only four levels based on methodological quality, since the fifth level (V) is solely associated to expert opinions which are systematically excluded from our study. Then, an individual score (IS) will be proposed, as we account for the risk of bias accordingly: studies with lower risk of bias will be upgraded while those with higher risk of bias will get downgraded. Risk of bias will be assessed using the appropriate tools specific to the type of study, as defined by Ma et al[42]. The final IS will also range from I to IV.

Table 2 Level of evidence based on primary research question, by Wright et al[40].

	Therapeutic Studies—Investigating the results of treatment	Prognostic Studies—Investigating the outcome of disease	Diagnostic Studies—Investigating a diagnostic test
Level I	1. Good-quality randomized controlled trial, 2. Systematic review of Level-I studies	1. Prospective study, 2. Systematic review of Level-I studies	1. Testing of previously developed diagnostic criteria in series of consecutive patients (with universally applied reference "gold" standard), 2. Systematic review of Level-I studies
Level II	1. Prospective cohort study, 2. Poor-quality randomized controlled trial, 3. Systematic review, a. Level-II studies, b. Nonhomogeneous Level-I studies	1. Retrospective study, 2. Study of untreated controls from a previous randomized controlled trial, 3. Systematic review of Level-II studies	1. Development of diagnostic criteria on basis of consecutive patients (with universally applied reference "gold" standard), 2. Systematic review of Level-II studies
Level III	1. Case-control study, 2. Retrospective cohort study, 3. Systematic review of Level-III studies		1. Study of nonconsecutive patients (no consistently applied reference "gold" standard), 2. Systematic review of Level-III studies
Level IV	Case series (with no, or historical, control group)	Case series	1. Case-control study, 2. Poor reference standard
Level V	Expert opinion	Expert opinion	Expert opinion

Quality of evidence across studies.

The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE)[43] approach will be used to rate the body of evidence behind key study outcomes assessing their strength or certainty level. First, a baseline level will be set for each study outcome based on the IS of the majority of studies contributing to that specific outcome, such as: if the majority of studies have an individual score of I or II the baseline grade of evidence supporting the study outcome will be classified as ”high”, and if the majority have individual scores of either III or IV, the baseline grade of evidence will be classified as ”low”. After that, we will properly adjust the baseline score after different factors like, large effect magnitude, dose-response gradient, inconsistency, indirectness, imprecision, etc.[43] to obtain a final quality of evidence grade of “high”, “moderate”, “low” or “very low”[41] (Table 3).

Table 3: Quality of Evidence Grades, from the GRADE Handbook (Chapter 5)[43].

Quality	Definition
High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there it may be substantially different.
Low	Our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.
Very low	We have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

We will refer to the GRADE handbook[43] for further assistance on this approach.
A summary of findings table will be generated using the Guideline development tool (GRADEpro GDT)[44]. The table will convey the key study outcomes with their corresponding level of certainty (grade of evidence), in a structured and transparent manner.

Data synthesis:

After extraction, the data obtained from eligible studies will be systematically presented. Topics of interest to this review are chosen as follows:

1. Patient characteristics: epidemiology,
2. Tumor characteristics: histopathology, WHO grading,
3. Radiological diagnostics,
4. Surgical treatment: technique, Simpson grading, intraoperative monitoring,
5. Complications and their management,
6. Non-surgical or adjuvant treatment including radiotherapy,
7. Patient outcomes: neurological outcomes, quality of life, mortality,
8. Recurrence.

Relevant data will be compiled under corresponding headings. Areas with lack of data will still be mentioned. After going through the GRADE approach, all study outcomes will be condensed in a summary of findings table, each contrasted to their respective grade of evidence. Meta-analysis will not be performed due to the anticipated high heterogeneity across the selected studies, with regards to participant and tumor characteristics as well as outcomes. In these settings, a quantitative study would therefore likely be less valuable. If an adequate number of studies is identified, subgroup analyses regarding interethnic variations and socioeconomic factors may be performed. Moreover, other subgroups reported in the eligible studies will be considered, as long as an adequate number of studies exists to support the analysis. When dealing with any such subgroups the possibility of selective reporting bias will be closely monitored[45].

Patient and public involvement:

Patients were not involved in the design or conception of the study.

Ethics and dissemination

Ethics approval is not required for this systematic review as it is based on existing publications. We also plan to submit our work to a peer-reviewed journal where the results will be openly available.

Discussion

The intended systematic review outlined in this protocol aims to summarize the current scientific literature on spinal meningiomas to provide guidance to clinicians and identify areas in need of further study. The available literature covers many aspects of spinal meningiomas, such as incidence[2,8,46], age[2,4], and gender distribution[2,4,7,8], treatments and their outcomes[4,47,48], but many studies are limited by small sample[3,48–56] sizes and short follow-up times[3,50,52,57]. Regarding the effect of preoperative neurological impairment, tumor grade and size on postoperative outcomes[3,30,50,52–59] and adjuvant therapies[28,34] the available data is conflicting. These issues will be addressed by the systematic review's design, as integrating data from diverse origins will allow for a more representative synthesis that reflects the population of patients with spinal meningiomas more accurately[60]. The absence of both randomized trials and high-quality evidence within the literature as well as the dominance of observational and cohort studies is already apparent, making up the largest limitation to our review. The high heterogeneity expected among studies, with regards to populations and outcome metrics, prevents the performance of a proper meta-analysis. This constitutes the main methodological limitation to this review. Other limitations eventually encountered during the writing of the manuscript will be discussed in the corresponding part of the review. This study ought to be regarded as a reliable source for clinicians to access current evidence compiled in a systematic way and hence better understand the tumor, its epidemiology, management, and prognosis. Greater knowledge of the subject will eventually contribute to improving the diagnosis and care delivery of affected patients. Moreover, the planned systematic review could also help disclose knowledge gaps in the field, identifying and highlighting future research priorities[61]. To the best of our knowledge, no systematic review outlining the current understanding of spinal meningiomas has been attempted to this date, making our study the first of its kind. The protocol hereby presented is in accordance with the PRISMA-P guidelines, (see *supplementary file 1*). For further transparency, this protocol will also be registered on PROSPERO in due time. The record on PROSPERO will be updated should significant changes to the procedure take place. The final manuscript is intended for submission to peer-reviewing.

Abbreviations

IS = individual score

GRADE = Grading of Recommendations, Assessment, Development and Evaluation
MRI = Magnetic Resonance Imaging
NF2 = Neurofibromatosis type 2
PICO = Population, Intervention, Comparison, Outcome
PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses
SPIDER = Sample, Phenomenon of Interest, Design, Evaluation, Research type
WHO = World health Organization

Competing interests

No competing interests are reported by any of the authors.

Contributions

- Victor Gabriel El-Hajj: conception & design of the work, drafting of the article, critical revision, and final approval of the version to be published.
- Jenny Pettersson-Segerlind: conception & design of the work, drafting of the article, and final approval of the version to be published.
- Gustav Liu Burström: conception & design of the work, drafting of the article, and final approval of the version to be published.
- Erik Edström: conception & design of the work, drafting of the article, critical revision, and final approval of the version to be published.
- Adrian Elmi-Terander: guarantor of the review, conception & design of the work, drafting of the article, critical revision, and final approval of the version to be published.

Funding

Not applicable.

Ethics declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Acknowledgements

Not applicable.

References

1. Ogasawara, C., Philbrick, B. D., & Adamson, D. C. (2021). Meningioma: A Review of Epidemiology, Pathology, Diagnosis, Treatment, and Future Directions. *Biomedicines*, *9*(3), 319. https://doi.org/10.3390/biomedicines9030319

2. Kshettry, V. R., Hsieh, J. K., Ostrom, Q. T., Kruchko, C., Benzel, E. C., & Barnholtz-Sloan, J. S. (2015). Descriptive Epidemiology of Spinal Meningiomas in the United States. *Spine*, *40*(15), E886-9. https://doi.org/10.1097/BRS.0000000000000974
3. Maiti, T. K., Bir, S. C., Patra, D. P., Kalakoti, P., Guthikonda, B., & Nanda, A. (2016). Spinal meningiomas: clinicoradiological factors predicting recurrence and functional outcome. *Neurosurgical Focus*, *41*(2), E6. https://doi.org/10.3171/2016.5.FOCUS16163
4. Pettersson-Segerlind, J., Fletcher-Sandersjöö, A., Tatter, C., Burström, G., Persson, O., Förander, P., Mathiesen, T., Bartek, J., Edström, E., & Elmi-Terander, A. (2021). Long-Term Follow-Up and Predictors of Functional Outcome after Surgery for Spinal Meningiomas: A Population-Based Cohort Study. *Cancers 2021, Vol. 13, Page 3244*, *13*(13), 3244. https://doi.org/10.3390/CANCERS13133244
5. Westwick, H. J., & Shamji, M. F. (2015). Effects of sex on the incidence and prognosis of spinal meningiomas: a Surveillance, Epidemiology, and End Results study. *Journal of Neurosurgery: Spine*, *23*(3), 368–373. https://doi.org/10.3171/2014.12.SPINE14974
6. Hua, L., Zhu, H., Deng, J., Tian, M., Jiang, X., Tang, H., Luan, S., Wakimoto, H., Xie, Q., & Gong, Y. (2018). Clinical and prognostic features of spinal meningioma: a thorough analysis from a single neurosurgical center. *Journal of Neuro-Oncology*, *140*(3), 639–647. https://doi.org/10.1007/S11060-018-2993-3/TABLES/4
7. Kwee, L. E., Harhangi, B. S., Ponne, G. A., Kros, J. M., Dirven, C. M. F., & Dammers, R. (2020). Spinal meningiomas: Treatment outcome and long-term follow-up. *Clinical Neurology and Neurosurgery*, *198*, 106238. https://doi.org/10.1016/J.CLINEURO.2020.106238
8. Duong, L. M., McCarthy, B. J., McLendon, R. E., Dolecek, T. A., Kruchko, C., Douglas, L. L., & Ajani, U. A. (2012). Descriptive epidemiology of malignant and nonmalignant primary spinal cord, spinal meninges, and cauda equina tumors, United States, 2004-2007. *Cancer*, *118*(17), 4220–4227. https://doi.org/10.1002/CNCR.27390
9. Evans, D. G. R., Sainio, M., & Baser, M. E. (2000). Neurofibromatosis type 2. *Journal of Medical Genetics*, *37*(12), 897. https://doi.org/10.1136/JMG.37.12.897
10. Karsy, M., Guan, J., Sivakumar, W., Neil, J. A., Schmidt, M. H., & Mahan, M. A. (2015). The genetic basis of intradural spinal tumors and its impact on clinical treatment. *Neurosurgical Focus*, *39*(2), E3. https://doi.org/10.3171/2015.5.FOCUS15143
11. Arslantas, A., Artan, S., Öner, Ü., Durmaz, R., Müslümanoğlu, H., Atasoy, M. A., Başaran, N., & Tel, E. (2003). Detection of Chromosomal Imbalances in Spinal Meningiomas by Comparative Genomic Hybridization. *Neurologia Medico-Chirurgica*, *43*(1), 12–19. https://doi.org/10.2176/NMC.43.12
12. Pawloski, J. A., Fadel, H. A., Huang, Y.-W., Lee, I. Y., Pawloski, C. :, Fadel, J. A. ;, Huang, H. A. ;, Lee, Y.-W. ;, Genomic, I. Y., & Baldi, A. (2021). Genomic Biomarkers of Meningioma: A Focused Review. *International Journal of Molecular Sciences 2021, Vol. 22, Page 10222*, *22*(19), 10222. https://doi.org/10.3390/IJMS221910222
13. Cohen-Gadol, A. A., Zikel, O. M., Koch, C. A., Scheithauer, B. W., & Krauss, W. E. (2003). Spinal meningiomas in patients younger than 50 years of age: a 21-year experience. *Journal of Neurosurgery: Spine*, *98*(3), 258–263. https://doi.org/10.3171/SPI.2003.98.3.0258
14. Maiuri, F., Mariniello, G., de Divitiis, O., Esposito, F., Guadagno, E., Teodonno, G., Barbato, M., & del Basso De Caro, M. (2021). Progesterone Receptor Expression in Meningiomas: Pathological and Prognostic Implications. *Frontiers in Oncology*, *11*, 2585. https://doi.org/10.3389/FONC.2021.611218/BIBTEX
15. Antolínez Ayala, V. E., García Arias, M. D., Bautista Vargas, S. E., Báez Cárdenas, L. M., & Castellanos Peñaranda, C. (2021). Paraplegia due to spinal meningioma during

the third trimester of pregnancy: case report and literature review. *Spinal Cord Series and Cases 2021 7:1*, *7*(1), 1–5. https://doi.org/10.1038/s41394-020-00368-0

16. Hortobágyi, T., Bencze, J., Murnyák, B., Kouhsari, M. C., Bognár, L., & Marko-Varga, G. (2017). Pathophysiology of meningioma growth in pregnancy. *Open Medicine (Poland)*, *12*(1), 195–200. https://doi.org/10.1515/MED-2017-0029/MACHINEREADABLECITATION/RIS
17. Pettersson-Segerlind, J., Mathiesen, T., Elmi-Terander, A., Edström, E., Talbäck, M., Feychting, M., & Tettamanti, G. (2021). The risk of developing a meningioma during and after pregnancy. *Scientific Reports 2021 11:1*, *11*(1), 1–8. https://doi.org/10.1038/s41598-021-88742-2
18. Abul-Kasim, K., Thurnher, M. M., McKeever, P., & Sundgren, P. C. (2008). Intradural spinal tumors: current classification and MRI features. *Neuroradiology*, *50*(4), 301–314. https://doi.org/10.1007/S00234-007-0345-7
19. Watts, J., Box, G., Galvin, A., Brotchie, P., Trost, N., & Sutherland, T. (2014). Magnetic resonance imaging of meningiomas: A pictorial review. *Insights into Imaging*, *5*(1), 113–122. https://doi.org/10.1007/S13244-013-0302-4/FIGURES/21
20. Tsuda, K., Akutsu, H., Yamamoto, T., Nakai, K., Ishikawa, E., & Matsumura, A. (2014). Is Simpson Grade I Removal Necessary in All Cases of Spinal Meningioma? Assessment of Postoperative Recurrence during Long-Term Follow-up. *Neurologia Medico-Chirurgica*, *54*(11), 907–913. https://doi.org/10.2176/NMC.OA.2013-0311
21. Kim, C. H., Chung, C. K., Lee, S. H., Jahng, T. A., Hyun, S. J., Kim, K. J., Yoon, S. H., Kim, E. S., Eoh, W., Kim, H. J., Kim, K. T., Sung, J. K., & Choi, Y. (2016). Long-term recurrence rates after the removal of spinal meningiomas in relation to Simpson grades. *European Spine Journal*, *25*(12), 4025–4032. https://doi.org/10.1007/S00586-015-4306-2/FIGURES/2
22. Voldřich, R., Netuka, D., & Beneš, V. (2020). Spinal meningiomas: is Simpson grade II resection radical enough? *Acta Neurochirurgica*, *162*(6), 1401–1408. https://doi.org/10.1007/S00701-020-04280-2/FIGURES/2
23. Nakamura, M., Tsuji, O., Fujiyoshi, K., Hosogane, N., Watanabe, K., Tsuji, T., Ishii, K., Toyama, Y., Chiba, K., & Matsumoto, M. (2012). Long-term surgical outcomes of spinal meningiomas. *Spine*, *37*(10). https://doi.org/10.1097/BRS.0B013E31824167F1
24. Tominaga, H., Kawamura, I., Ijiri, K., Yone, K., & Taniguchi, N. (2021). Surgical results of the resection of spinal meningioma with the inner layer of dura more than 10 years after surgery. *Scientific Reports*, *11*(1). https://doi.org/10.1038/S41598-021-83712-0
25. Saito, T., Arizono, T., Maeda, T., Terada, K., & Iwamoto, Y. (2001). A novel technique for surgical resection of spinal meningioma. *Spine*, *26*(16), 1805–1808. https://doi.org/10.1097/00007632-200108150-00017
26. Tatter, C., Fletcher-Sandersjöö, A., Persson, O., Burström, G., Grane, P., Edström, E., & Elmi-Terander, A. (2020). Incidence and predictors of kyphotic deformity following resection of cervical intradural tumors in adults: a population-based cohort study. *Acta Neurochirurgica*, *162*(11), 2905–2913. https://doi.org/10.1007/S00701-020-04416-4/FIGURES/5
27. Yoon, S. H., Chung, C. K., & Jahng, T. A. (2007). Surgical Outcome of Spinal Canal Meningiomas. *Journal of Korean Neurosurgical Society*, *42*(4), 300–304. https://doi.org/10.3340/JKNS.2007.42.4.300
28. Westwick, H. J., Yuh, S. J., & Shamji, M. F. (2015). Complication Avoidance in the Resection of Spinal Meningiomas. *World Neurosurgery*, *83*(4), 627–634. https://doi.org/10.1016/J.WNEU.2014.12.015
29. Bydon, M., & Gokaslan, Z. L. (2015). Spinal Meningioma Resection. *World Neurosurgery*, *83*(6), 1032–1033. https://doi.org/10.1016/J.WNEU.2015.01.049

30. Frati, A., Pesce, A., Toccaceli, G., Fraschetti, F., Caruso, R., & Raco, A. (2019). Spinal Meningiomas Prognostic Evaluation Score (SPES): predicting the neurological outcomes in spinal meningioma surgery. *Neurosurgical Review*, *42*(1), 115–125. https://doi.org/10.1007/S10143-018-0961-1/FIGURES/4
31. Newman, W. C., Berry-Candelario, J., Villavieja, J., Reiner, A. S., Bilsky, M. H., Laufer, I., & Barzilai, O. (2021). Improvement in Quality of Life Following Surgical Resection of Benign Intradural Extramedullary Tumors: A Prospective Evaluation of Patient-Reported Outcomes. *Neurosurgery*, *88*(5), 989–995. https://doi.org/10.1093/NEUROS/NYAA561
32. Viereck, M. J., Ghobrial, G. M., Beygi, S., & Harrop, J. S. (2016). Improved patient quality of life following intradural extramedullary spinal tumor resection. *Journal of Neurosurgery: Spine*, *25*(5), 640–645. https://doi.org/10.3171/2016.4.SPINE151149
33. Pettersson-Segerlind, J., Vogelsang, A.-C. von, Fletcher-Sandersjöö, A., Tatter, C., Mathiesen, T., Edström, E., & Elmi-Terander, A. (2021). Health-Related Quality of Life and Return to Work after Surgery for Spinal Meningioma: A Population-Based Cohort Study. *Cancers 2021, Vol. 13, Page 6371*, *13*(24), 6371. https://doi.org/10.3390/CANCERS13246371
34. Yolcu, Y. U., Goyal, A., Alvi, M. A., Moinuddin, F. M., & Bydon, M. (2019). Trends in the utilization of radiotherapy for spinal meningiomas: insights from the 2004–2015 National Cancer Database. *Neurosurgical Focus*, *46*(6), E6. https://doi.org/10.3171/2019.3.FOCUS1969
35. Cooke, A., Smith, D., & Booth, A. (2012). Beyond PICO: The SPIDER tool for qualitative evidence synthesis. *Qualitative Health Research*, *22*(10), 1435–1443. https://doi.org/10.1177/1049732312452938
36. Moher, D., Shamseer, L., Clarke, M., Ghersi, D., Liberati, A., Petticrew, M., Shekelle, P., Stewart, L. A., Estarli, M., Barrera, E. S. A., Martínez-Rodríguez, R., Baladia, E., Agüero, S. D., Camacho, S., Buhring, K., Herrero-López, A., Gil-González, D. M., Altman, D. G., Booth, A., … Whitlock, E. (2016). Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Revista Espanola de Nutricion Humana y Dietetica*, *20*(2), 148–160. https://doi.org/10.1186/2046-4053-4-1/TABLES/4
37. *Roy Rosenzweig Center for History and New Media. (2016) Zotero [Computer software]. Retrieved from www.zotero.org/download*. (n.d.).
38. Ouzzani, M., Hammady, H., Fedorowicz, Z., & Elmagarmid, A. (2016). Rayyan—a web and mobile app for systematic reviews. *Systematic Reviews*, *5*(1), 210. https://doi.org/10.1186/s13643-016-0384-4
39. *OCEBM Levels of Evidence Working Group*. "The Oxford 2011 Levels of Evidence". Oxford Centre for Evidence-Based Medicine. http://www.cebm.net/index.aspx?o=5653 * OCEBM Table of Evidence Working Group = Jeremy Howick, Iain Chalmers (James Lind Library), Paul Glasziou, Trish Greenhalgh, Carl Heneghan, Alessandro Liberati, Ivan Moschetti, Bob Phillips, Hazel Thornton, Olive Goddard and Mary Hodgkinson*. (n.d.).
40. Wright, J. G., Swiontkowski, M. F., & Heckman, J. D. (2003). Introducing levels of evidence to the journal. *The Journal of Bone and Joint Surgery. American Volume*, *85*(1), 1–3.
41. Anderson, K. K., Tetreault, L., Shamji, M. F., Singh, A., Vukas, R. R., Harrop, J. S., Fehlings, M. G., Vaccaro, A. R., Hilibrand, A. S., & Arnold, P. M. (2015). Optimal Timing of Surgical Decompression for Acute Traumatic Central Cord Syndrome. *Neurosurgery*, *77*, S15–S32. https://doi.org/10.1227/NEU.0000000000000946

42. Ma, L. L., Wang, Y. Y., Yang, Z. H., Huang, D., Weng, H., & Zeng, X. T. (2020). Methodological quality (risk of bias) assessment tools for primary and secondary medical studies: What are they and which is better? *Military Medical Research*, *7*(1), 1–11. https://doi.org/10.1186/S40779-020-00238-8/TABLES/1
43. *Schünemann H, Brożek J, Guyatt G, Oxman A, editors. GRADE handbook for grading quality of evidence and strength of recommendations. Updated October 2013. The GRADE Working Group, 2013. Available from guidelinedevelopment.org/handbook*. (n.d.).
44. *GRADEpro GDT: GRADEpro Guideline Development Tool [Software]. McMaster University, 2020 (developed by Evidence Prime, Inc.). Available from gradepro.org*. (n.d.).
45. Reid, E. K., Tejani, A. M., Huan, L. N., Egan, G., O'Sullivan, C., Mayhew, A. D., & Kabir, M. (2015). Managing the incidence of selective reporting bias: A survey of Cochrane review groups. *Systematic Reviews*, *4*(1), 1–8. https://doi.org/10.1186/S13643-015-0070-Y/FIGURES/3
46. Weber, C., Gulati, S., Jakola, A. S., Habiba, S., Nygaard, Ø. P., Johannesen, T. B., & Solheim, O. (2014). Incidence rates and surgery of primary intraspinal tumors in the era of modern neuroimaging: a national population-based study. *Spine*, *39*(16). https://doi.org/10.1097/BRS.0000000000000412
47. Sandalcioglu, I. E., Hunold, A., Müller, O., Bassiouni, H., Stolke, D., & Asgari, S. (2008). Spinal meningiomas: Critical review of 131 surgically treated patients. *European Spine Journal*, *17*(8), 1035–1041. https://doi.org/10.1007/S00586-008-0685-Y/TABLES/4
48. Hohenberger, C., Gugg, C., Schmidt, N. O., Zeman, F., & Schebesch, K. M. (2020). Functional outcome after surgical treatment of spinal meningioma. *Journal of Clinical Neuroscience*, *77*, 62–66. https://doi.org/10.1016/J.JOCN.2020.05.042
49. Morandi, X., Haegelen, C., Riffaud, L., Amlashi, S., Adn, M., & Brassier, G. (2004). Results in the operative treatment of elderly patients with spinal meningiomas. *Spine*, *29*(19), 2191–2194. https://doi.org/10.1097/01.BRS.0000141173.79572.40
50. Arima, H., Takami, T., Yamagata, T., Naito, K., Abe, J., Shimokawa, N., & Ohata, K. (2014). Surgical management of spinal meningiomas: A retrospective case analysis based on preoperative surgical grade. *Surgical Neurology International*, *5*(Suppl 7), S333. https://doi.org/10.4103/2152-7806.139642
51. Sacko, O., Haegelen, C., Mendes, V., Brenner, A., Sesay, M., Brauge, D., Lagarrigue, J., Loiseau, H., & Roux, F. E. (2009). SPINAL MENINGIOMA SURGERY IN ELDERLY PATIENTS WITH PARAPLEGIA OR SEVERE PARAPARESISA MULTICENTER STUDY. *Neurosurgery*, *64*(3), 503–510. https://doi.org/10.1227/01.NEU.0000338427.44471.1D
52. Haegelen, C., Morandi, X., Riffaud, L., Amlashi, S. F. A., Leray, E., & Brassier, G. (2005). Results of spinal meningioma surgery in patients with severe preoperative neurological deficits. *European Spine Journal*, *14*(5), 440–444. https://doi.org/10.1007/S00586-004-0809-Y/TABLES/3
53. Schaller, B. (2005). Spinal Meningioma: Relationship Between Histological Subtypes and Surgical Outcome? *Journal of Neuro-Oncology 2005 75:2*, *75*(2), 157–161. https://doi.org/10.1007/S11060-005-1469-4
54. Setzer, M., Vatter, H., Marquardt, G., Seifert, V., & Vrionis, F. D. (2007). Management of spinal meningiomas: surgical results and a review of the literature. *Neurosurgical Focus*, *23*(4), E14. https://doi.org/10.3171/FOC-07/10/E14
55. Gilard, V., Goia, A., Ferracci, F. X., Marguet, F., Magne, N., Langlois, O., Perez, A., & Derrey, S. (2018). Spinal meningioma and factors predictive of post-operative

deterioration. *Journal of Neuro-Oncology*, *140*(1), 49–54. https://doi.org/10.1007/S11060-018-2929-Y/TABLES/4

56. Gezen, F., Kahraman, S., Çanakci, Z., & Bedük, A. (2000). Review of 36 Cases of Spinal Cord Meningioma. *Spine*, *25*(6), 727–731. https://doi.org/10.1097/00007632-200003150-00013
57. Bayoumi, A. B., Laviv, Y., Karaali, C. N., Ertilav, K., Kepoglu, U., Toktas, Z. O., Konya, D., & Kasper, E. M. (2020). Spinal meningiomas: 61 cases with predictors of early postoperative surgical outcomes. *Journal of Neurosurgical Sciences*, *64*(5), 446–451. https://doi.org/10.23736/S0390-5616.17.04102-9
58. Raco, A., Pesce, A., Toccaceli, G., Domenicucci, M., Miscusi, M., & Delfini, R. (2017). Factors leading to a poor functional outcome in spinal meningioma surgery: Remarks on 173 cases. *Neurosurgery*, *80*(4), 602–609. https://doi.org/10.1093/NEUROS/NYW092
59. Klekamp, J., & Samii, M. (1999). Surgical results for spinal meningiomas. *Surgical Neurology*, *52*(6), 552–562. https://doi.org/10.1016/S0090-3019(99)00153-6
60. Edwards, T. B. (2014). What is the value of a systematic review? *Journal of Shoulder and Elbow Surgery*, *23*(1), 1–2. https://doi.org/10.1016/J.JSE.2013.09.001
61. *Lasserson TJ, Thomas J, Higgins JPT. Chapter 1: Starting a review. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.2 (updated February 2021). Cochrane, 2021. Available from www.training.cochrane.org/handbook*. (n.d.).

Supplementary information

Supplementary file 1: PRISMA-P 2015 Checklist.

Supplementary file 2: Search strategy.

Reporting checklist for protocol of a systematic review and meta analysis.

Based on the PRISMA-P guidelines.

Reference: Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA. Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 statement. Syst Rev. 2015;4(1):1.

		Reporting Item	Section
Title			
Identification	#1a	Identify the report as a protocol of a systematic review	Title
Update	#1b	If the protocol is for an update of a previous systematic review, identify as such	n/a
Registration			
	#2	If registered, provide the name of the registry (such as PROSPERO) and registration number	n/a (this protocol is planned for registration on PROSPERO)
Authors			
Contact	#3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	Author information
Contribution	#3b	Describe contributions of protocol authors and identify the guarantor of the review	Contributions
Amendments			
	#4	If the protocol represents an amendment of a previously completed or published protocol,	n/a

		identify as such and list changes; otherwise, state plan for documenting important protocol amendments	
Support			
Sources	#5a	Indicate sources of financial or other support for the review	n/a
Sponsor	#5b	Provide name for the review funder and / or sponsor	n/a
Role of sponsor or funder	#5c	Describe roles of funder(s), sponsor(s), and / or institution(s), if any, in developing the protocol	n/a
Introduction			
Rationale	#6	Describe the rationale for the review in the context of what is already known	Abstract and last part of Introduction
Objectives	#7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	Last part of introduction
Methods			
Eligibility criteria	#8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	Methods and analysis: Eligibility criteria section
Information sources	#9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	Methods and analysis: Databases and search strategy section
Search strategy	#10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	Methods and analysis: Databases and search strategy section and

			supplementary file 2
Study records - data management	#11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	Methods and analysis: Study selection section
Study records - selection process	#11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	Methods and analysis: Study selection section
Study records - data collection process	#11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	Methods and analysis: Data extraction section
Data items	#12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	Methods and analysis: Data extraction section
Outcomes and prioritization	#13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	Methods and analysis: Data synthesis section
Risk of bias in individual studies	#14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	Methods and analysis: Risk of bias assessment and Quality of evidence sections
Data synthesis	#15a	Describe criteria under which study data will be quantitatively synthesised	n/a (only qualitative synthesis will be sought due to expected heterogeneity)
Data synthesis	#15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies,	n/a (qualitative synthesis only)

		including any planned exploration of consistency (such as I2, Kendall's τ)	
Data synthesis	#15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	n/a
Data synthesis	#15d	If quantitative synthesis is not appropriate, describe the type of summary planned	Methods and analysis: Data synthesis section
Meta-bias(es)	#16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	Methods and analysis: Risk of bias section
Confidence in cumulative evidence	#17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	Methods and analysis: Risk of bias and Quality of evidence sections

 This checklist was completed on 29. January 2022 using https://www.goodreports.org/, a tool made by the EQUATOR Network in collaboration with Penelope.ai

Database	Queries
PubMed	((("spinal meningioma*"[Title] NOT "case report"[All Fields]) AND 2000/01/01:3000/12/31[Date - Publication] AND "english"[Language] AND ("loattrfull text"[Filter] AND "humans"[MeSH Terms] AND "english"[Language])) OR ((("spin*"[All Fields] AND ("meningioma"[MeSH Terms] OR "meningioma"[All Fields] OR "meningiomas"[All Fields])) NOT ("case reports"[Publication Type] OR "case report"[All Fields])) AND 2000/01/01:3000/12/31[Date - Publication] AND ("loattrfull text"[Filter] AND "humans"[MeSH Terms] AND "english"[Language]))) AND ((fft[Filter]) AND (humans[Filter]) AND (english[Filter]))
Web of Science	((ALL=("spinal meningioma") AND PY=(2000-2500) AND LA=(English) NOT TS=("CASE REPORT")) NOT (TASCA==("VETERINARY SCIENCES") OR DT==("EDITORIAL MATERIAL" OR "LETTER" OR "MEETING ABSTRACT"))) OR ((TI=(spinal AND meningioma*) AND PY=(2000-2500) AND LA=(English) NOT TI=(case report)) NOT (TASCA==("VETERINARY SCIENCES") OR DT==("EDITORIAL MATERIAL" OR "LETTER" OR "MEETING ABSTRACT")))
Embase	spinal meningioma*':ab,ti NOT 'case report' AND [2000-2021]/py NOT ('spinal meningioma*':ab,ti NOT 'case report' AND [2000-2021]/py) AND ('animal experiment'/de OR 'animal model'/de OR 'animal tissue'/de OR 'nonhuman'/de)