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Current knowledge on spinal meningiomas: a systematic review protocol

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38 Abstract

39 Introduction

40 Meningiomas are primary CNS tumors that arise from both cranial and spinal meninges.
41 Spinal meningiomas occur less frequently than their cranial counterparts and are
42 consequently given less attention in the literature. Therefore, systematic studies are needed to
43 summarize the current knowledge on spinal meningiomas, providing a solid evidence base
44 for treatment strategies. This systematic review of the literature will therefore assess studies
45 describing spinal meningiomas, their epidemiology, diagnostics, treatment, and outcomes.
46

47 Methods and Analysis

48 Electronic databases including PubMed, Web of Science and Embase, will be searched using
49 the keywords "spinal" and "meningioma". The search will be set to provide only the studies
50 published after 2000 to avoid any conflicts regarding terminology and classification, as well
51 as to reflect the current status. Case reports, editorials, letters, and reviews will also be
52 excluded. Reference lists of relevant records will also be searched. Identified studies will be
53 screened for inclusion, by one reviewer in a first step and then three in the next step to
54 decrease the risk of bias. The results will be categorized to allow for a structured summary of
55 the outcomes and their evidence grade conforming to the GRADE approach. Categories may
56 include: epidemiology, histopathology, radiological diagnostics, surgery, complications, non-
57 surgical or adjuvant treatments, disease outcomes and predictors, and lastly recurrence.
58

59 Ethics and dissemination

60 This review will summarize the current knowledge on spinal meningiomas to allow for a
61 better understanding of the disease and contribute to improve its management. For clinicians,
62 the systematic collection and grading of available evidence may aid in decision-making and
63 for those seeking to further the scientific field, this review may help to identify areas where
64 knowledge is currently lacking.
65

66 **Strengths and limitations**

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

79 Introduction

80 Meningiomas originate from the arachnoid cap cells in the leptomeninges surrounding the
81 brain and spinal cord. Hence, they occur most frequently in an intradural extramedullary
82 location. Meningiomas of the spinal cord are less common, making up only about 2-12% of
83 all meningiomas¹⁻³. In fact, much of what we know today is derived from studies on
84 intracranial meningiomas. Spinal meningiomas are the most common primary spinal tumor in
85 adults, representing 25-45% of all tumors and occur with an age-adjusted incidence of 0.33
86 per 100, 000 population¹. Most spinal meningiomas (90%) are benign, WHO I tumors⁴⁻⁶,
87 mainly seen in the elderly with a peak incidence between the seventh and ninth decades of
88 life^{2,4}. Regardless of their location, meningiomas are more commonly found in females. For
89 spinal meningiomas the female to male ratio is around 4:1^{2,4,7,8}. Most meningiomas occur
90 sporadically but a known genetic association to neurofibromatosis type 2 (NF2) is
91 established, and it is estimated that up to 20% of patients with NF2 will develop spinal
92 meningiomas, which might even appear earlier on in life^{9,10}. Mutations of the NF2 tumor
93 suppressor gene or loss of chromosome 22 harboring this gene was found to be more frequent
94 among spinal meningiomas of WHO grades II and III^{11,12}. Exposure to high-dose ionizing
95 radiation is also associated with earlier onset of spinal meningioma^{1,13}. Meningiomas often
96 carry estrogen or progesterone receptors¹⁴, suggesting pregnancy as a potential risk factor for
97 tumor growth^{15,16}. This association was however refuted by a large population-based cohort
98 study¹⁷. Spinal meningiomas may produce neurologic deficits and pain related to local
99 compression of the spinal cord, nerves and adjacent structures^{4,18}. The diagnosis is best made
100 using MRI where meningiomas show homogenous enhancement on gadolinium enhanced T1
101 sequences. Meningiomas also typically display dural tails, enhancement and thickening of the
102 dura extending from the tumor¹⁹. The treatment of choice is surgery, where tumor removal
103 typically alleviates symptoms with little risk of complications or recurrence^{4,7}. In surgery of
104 meningiomas, Simpson grading is used to describe the radicality of tumor removal and to
105 predict the risk for tumor recurrence. Whether Simpson grade I, which includes complete
106 removal of dural attachments, should be the goal of spinal meningioma surgery, remains a
107 topic of debate^{4,20-23}. The Simpson scale also addresses the removal or coagulation of the
108 affected dura. Aggressive removal of the dura may reduce the risk of recurrence but increases
109 the risk of spinal cord injury and postoperative leakage of cerebrospinal fluid. The most
110 commonly reported postoperative complications are wound infections, cerebrospinal fluid
111 leaks, kyphosis, venous thromboembolisms, and transient or permanent neurologic
112 deficits^{4,7,24-26}. However, these complications are rare and improvement of neurological
113 function after tumor removal is expected in the majority of patients^{4,27}. For patients having
114 undergone Simpson Grade 2 resection of a spinal meningioma, Heon Kim et al have
115 estimated a mean clinical recurrence-free survival period of 17 years²¹. Poor outcomes on the
116 other hand, are reportedly associated with factors like: WHO tumor grade > 1, high Ki-67
117 index, long time to diagnosis, large tumor size and the degree of spinal cord compression^{4,6,28}
118 while mortality mainly reflects high age or co-morbidities^{4,7}. Very little data on health-related
119 quality of life after spinal meningioma surgery is available. Two studies with mixed groups
120 of intradural extramedullary tumors found that the vast majority of patients who underwent
121 surgery saw a significant improvement of activity, mood, walking ability, quality of relations,
122 sleep, and a decrease in pain^{29,30}. These findings are consistent with the results of a quality-
123 of-life questionnaire our group conducted on 84 spinal meningioma patients at an average of
124 8.7 years after surgery³¹. The need for alternative or adjuvant therapies is emphasized in the
125 literature, especially for recurring and higher-grade tumors (WHO II-III) or for patients who
126 are poor surgical candidates^{26,32}. In these cases, other treatment modalities may have to be

127 explored. However, the role of nonsurgical treatment options in the management of spinal
 128 meningiomas remains poorly defined.
 129 The systematic review proposed with this protocol aims to create a comprehensive overview
 130 of the current understanding of spinal meningiomas, as well as to clarify the evidence base
 131 for the treatment strategies employed today. Topics which will be reviewed include
 132 epidemiology, tumor characteristics, diagnostics, treatment options with their potential risks
 133 and benefits, as well as outcomes including quality of life, mortality, and recurrence. The
 134 created overview will serve as a foundation for treatment choices and possibly to identify
 135 areas of insufficient knowledge, warranting renewed scientific effort.
 136 Instead of the more classic PICO criteria (Population, Intervention, Comparison, Outcome),
 137 we decide to use the SPIDER criteria³³ (Sample, Phenomenon of Interest, Design, Evaluation,
 138 Research type) which we believe are more suited to the purpose of this review (Table 1).

139
 140 *Table 1: SPIDER criteria³³.*

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

141 142 143 **Methods/Design**

144 Patient and public involvement:

145 Patients were not involved in the design or conception of the study.
 146

147 Study registration

148 This protocol for an intended systematic review is reported according to the Preferred
 149 Reporting Items for Systematic Reviews and Meta-Analyses Protocol (PRISMA-P) statement
 150 of 2015³⁴. The PRISMA-P checklist is provided as supplementary material (see
 151 *supplementary file 1*). The systematic review protocol will also be registered on PROSPERO,
 152 before submission of the final manuscript to a peer reviewed journal.
 153

154 Eligibility criteria

155 **Inclusion criteria**

156 Type of studies

157 All peer reviewed and original studies, written in English and available in the PubMed,
 158 Embase, or Web of Science databases, will be eligible for inclusion. Only studies published
 159 after 2000 will be included to limit our review to the more current publications within the
 160 field.
 161

162 Type of participant

1
2
3 163 All patients will be included, regardless of age, ethnicity, and sex. Similarly, all spinal
4 164 meningiomas irrespective of size, tumor grading or anatomical locations along the spine will
5 165 be included. However, an adequate diagnosis of the tumor must be available and based on
6 166 histological examination or MRI investigations.

8
9 167

10 168 Type of interventions

12 169 All modes of diagnosis and treatment of spinal meningiomas will be included.

13 170

15 171 Type of outcome measurements

16 172 Epidemiological data such as age, sex and socioeconomic factors, possible predictors of poor
17 173 preoperative or postoperative decline such as comorbidity and spinal cord compression will
18 174 also be addressed. Furthermore, outcome parameters including pain, neurological function,
19 175 quality of life, tumor recurrence and mortality, tumor characteristics including expression of
20 176 specific receptors, markers of proliferative activity, and WHO grade will also be included.

22 177 Additional outcomes used in the selected studies may be considered. In those cases, the
23 178 possibility of reporting biases will be recognized.

25 179

27 180 **Exclusion criteria**

28 181 Non-original publications such as reviews, editorials, and letters to the editor will be
29 182 disregarded together with case reports and conference abstracts. Studies found in languages
30 183 other than English will be excluded for practical reasons. Publications prior to the year of
31 184 2000 will also be excluded to reduce the number of included studies and give priority to more
32 185 current publications.

34 186

36 187 Databases and search strategy

38 188 An electronic database search will be performed on PubMed, Embase, and Web of Science.
39 189 The search will be broad, excluding case reports by adding a filter to the search. Appropriate
40 190 filters will also be used to exclude non-English studies and those published prior to the year
41 191 2000. To illustrate the process, the preliminary search strategy specific to the Web of Science
42 192 database is provided (see *supplementary file 2*). A reference list search of the included studies
43 193 will be performed, to screen for any eligible article that was missed.

45 194

47 195 Study selection

49 196 The records retrieved from the different databases will be exported into Zotero³⁵, to eliminate
50 197 duplicates. The records will then be screened based on title and abstract by one reviewer, to
51 198 eliminate records that are plainly irrelevant. This is necessary as an unmanageable number of
52 199 records is foreseen due to the broad search strategy that will be used. In the next step, three
53 200 independent and blinded reviewers will be assigned the task of examining the remaining
54 201 records applying the eligibility criteria based on full-text reading. This will be performed
55 202 using Rayyan Software³⁶. Potential disagreements after pooling of the results will be resolved
56 203 by discussion with a fourth reviewer. Finally, reference lists of the selected articles will be
57 204 reviewed for any potentially eligible studies that were previously missed. The process will be
58 205 illustrated in a PRISMA flowchart which will be provided.

206

207 Data extraction

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

218 Assessment of risk of bias

219 The Oxford Center for Evidence-Based Medicine system³⁷, modified by Wright et al, will be
 220 used to assess evidence levels^{38,39} (table 2). The selected articles will first be allocated to one
 221 of only four levels based on methodological quality, since the fifth level (V) is solely
 222 associated to expert opinions which are systematically excluded from our study. Then, an
 223 individual score (IS) will be proposed, as we account for the risk of bias accordingly: studies
 224 with lower risk of bias will be upgraded while those with higher risk of bias will get
 225 downgraded. Risk of bias will be assessed using the appropriate tools specific to the type of
 226 study, as defined by Ma et al⁴⁰. The final IS will also range from I to IV.

227
 228 *Table 2 Level of evidence based on primary research question, by Wright et al³⁸.*

	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

229

230 Quality of evidence across studies.

231 The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE)⁴¹
 232 approach will be used to rate the body of evidence behind key study outcomes assessing their
 233 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 handbook⁴¹ 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 monitored⁴³.

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272
273

Ethics and dissemination

274 The intended systematic review outlined in this protocol aims to summarize the current
275 scientific literature on spinal meningiomas to provide guidance to clinicians and identify
276 areas in need of further study. The available literature covers many aspects of spinal
277 meningiomas, such as incidence^{2,8,44}, age^{2,4}, and gender distribution^{2,4,7,8}, treatments and their
278 outcomes^{4,45,46}, but many studies are limited by small sample^{3,46–54} sizes and short follow-up
279 times^{3,48,50,55}. Regarding the effect of preoperative neurological impairment, tumor grade and
280 size on postoperative outcomes^{3,28,48,50–57} and adjuvant therapies^{26,32} the available data is
281 conflicting. These issues will be addressed by the systematic review's design, as integrating
282 data from diverse origins will allow for a more representative synthesis that reflects the
283 population of patients with spinal meningiomas more accurately⁵⁸. The absence of both
284 randomized trials and high-quality evidence within the literature as well as the dominance of
285 observational and cohort studies is already apparent, making up the largest limitation to our
286 review. Other limitations eventually encountered during the writing of the manuscript will be
287 discussed in the corresponding part of the review.

288 This study ought to be regarded as a reliable source for clinicians to access current evidence
289 compiled in a systematic way and hence better understand the tumor, its epidemiology,
290 management, and prognosis. Greater knowledge of the subject will eventually contribute to
291 improving the diagnosis and care delivery of affected patients. Moreover, the planned
292 systematic review could also help disclose knowledge gaps in the field, identifying and
293 highlighting future research priorities⁵⁹. To the best of our knowledge, no systematic review
294 outlining the current understanding of spinal meningiomas has been attempted to this date,
295 making our study the first of its kind. The protocol hereby presented is in accordance with the
296 PRISMA-P guidelines, (see *supplementary file 1*). For further transparency, this protocol will
297 also be registered on PROSPERO in due time. The record on PROSPERO will be updated
298 should significant changes to the procedure take place. The final manuscript is intended for
299 submission to peer-reviewing.

300

Abbreviations

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

310

Availability of data and materials

312 Not applicable.

313

314 Competing interests

315 No competing interests are reported by any of the authors.

316

317 Contributions

- 318 • Victor Gabriel El-Hajj: conception & design of the work, drafting of the article, critical
319 revision, and final approval of the version to be published.
- 320 • Jenny Pettersson-Segerlind: conception & design of the work, drafting of the article,
321 and final approval of the version to be published.
- 322 • Gustav Liu Burström: conception & design of the work, drafting of the article, and
323 final approval of the version to be published.
- 324 • Erik Edström: conception & design of the work, drafting of the article, critical
325 revision, and final approval of the version to be published.
- 326 • Adrian Elmi-Terander: guarantor of the review, conception & design of the work,
327 drafting of the article, critical revision, and final approval of the version to be
328 published.
- 329

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336 Consent for publication

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338

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341

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559 **Supplementary information**

- 14 560 Supplementary file 1: PRISMA-P 2015 Checklist.
15 561 Supplementary file 2: Search strategy for Web of Science.
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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

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3	Support		
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5	Sources	#5a	Indicate sources of financial or other support for the review
6			n/a
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9	Sponsor	#5b	Provide name for the review funder and / or sponsor
10			n/a
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12			
13	Role of sponsor or funder	#5c	Describe roles of funder(s), sponsor(s), and / or institution(s), if any, in developing the protocol
14			n/a
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Introduction

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17	Introduction		
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19	Rationale	#6	Describe the rationale for the review in the context of what is already known
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23	Objectives	#7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)
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Methods

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31	Methods		
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33	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
34			4, 5
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41	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
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48	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
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54	Study records - data management	#11a	Describe the mechanism(s) that will be used to manage records and data throughout the review
55			5, 6
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1	Study records -	#11b	State the process that will be used for selecting	5
2	selection process		studies (such as two independent reviewers)	
3			through each phase of the review (that is,	
4			screening, eligibility and inclusion in meta-	
5			analysis)	
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10	Study records -	#11c	Describe planned method of extracting data	6
11	data collection		from reports (such as piloting forms, done	
12	process		independently, in duplicate), any processes for	
13			obtaining and confirming data from investigators	
14				
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17	Data items	#12	List and define all variables for which data will	6
18			be sought (such as PICO items, funding	
19			sources), any pre-planned data assumptions	
20			and simplifications	
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24	Outcomes and	#13	List and define all outcomes for which data will	7
25	prioritization		be sought, including prioritization of main and	
26			additional outcomes, with rationale	
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29	Risk of bias in	#14	Describe anticipated methods for assessing risk	6
30	individual studies		of bias of individual studies, including whether	
31			this will be done at the outcome or study level,	
32			or both; state how this information will be used	
33			in data synthesis	
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38	Data synthesis	#15a	Describe criteria under which study data will be	n/a (only qualitative
39			quantitatively synthesised	synthesis will be sought
40				due to expected
41				heterogeneity)
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45	Data synthesis	#15b	If data are appropriate for quantitative synthesis,	n/a (qualitative only)
46			describe planned summary measures, methods	
47			of handling data and methods of combining data	
48			from studies, including any planned exploration	
49			of consistency (such as I ² , Kendall's τ)	
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54	Data synthesis	#15c	Describe any proposed additional analyses	n/a
55			(such as sensitivity or subgroup analyses, meta-	
56			regression)	
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1	Data synthesis	#15d	If quantitative synthesis is not appropriate, describe the type of summary planned	7
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5	Meta-bias(es)	#16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	6
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10	Confidence in	#17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	6, 7
11	cumulative			
12	evidence			
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18 The PRISMA-P elaboration and explanation paper is distributed under the terms of the Creative
19 Commons Attribution License CC-BY. This checklist was completed on 29. January 2022 using
20 <https://www.goodreports.org/>, a tool made by the [EQUATOR Network](#) in collaboration with
21 [Penelope.ai](#)
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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

BMJ Open

Current knowledge on spinal meningiomas: a systematic review protocol

Journal:	<i>BMJ Open</i>
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

SCHOLARONE™
Manuscripts

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

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

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38 Abstract

39 Introduction

40 Meningiomas are primary CNS tumors that arise from both cranial and spinal meninges.
41 Spinal meningiomas occur less frequently than their cranial counterparts and are
42 consequently given less attention in the literature. Therefore, systematic studies are needed to
43 summarize the current knowledge on spinal meningiomas, providing a solid evidence base
44 for treatment strategies. This systematic review of the literature will therefore assess studies
45 describing spinal meningiomas, their epidemiology, diagnostics, treatment, and outcomes.
46

47 Methods and Analysis

48 Electronic databases including PubMed, Web of Science and Embase, will be searched using
49 the keywords "spinal" and "meningioma". The search will be set to provide only English
50 studies published after 2000 to avoid any conflicts regarding terminology and classification,
51 as well as to reflect the current status. Case reports, editorials, letters, and reviews will also be
52 excluded. Reference lists of relevant records will also be searched. Identified studies will be
53 screened for inclusion, by one reviewer in a first step and then three in the next step to
54 decrease the risk of bias. The results will be categorized to allow for a structured summary of
55 the outcomes and their evidence grade conforming to the GRADE approach. Categories may
56 include: epidemiology, histopathology, radiological diagnostics, surgery, complications, non-
57 surgical or adjuvant treatments, disease outcomes and predictors, and lastly recurrence. This
58 review will summarize the current knowledge on spinal meningiomas to allow for a better
59 understanding of the disease and contribute to improve its management. For clinicians, the
60 systematic collection and grading of available evidence may aid in decision-making and for
61 those seeking to further the scientific field, this review may help to identify areas where
62 knowledge is currently lacking.
63

64 Ethics and dissemination

65 Ethics approval was not required for our systematic review as it is based on existing
66 publications. The results will be disseminated via submission for publication in a peer-
67 reviewed journal.
68

69 Strengths and limitations

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

79

80

81 Introduction

82 Meningiomas originate from the arachnoid cap cells in the leptomeninges surrounding the
83 brain and spinal cord. Hence, they occur most frequently in an intradural extramedullary
84 location. Meningiomas of the spinal cord are less common, making up only about 2-12% of
85 all meningiomas¹⁻³. In fact, much of what we know today is derived from studies on
86 intracranial meningiomas. Spinal meningiomas are the most common primary spinal tumor in
87 adults, representing 25-45% of all tumors and occur with an age-adjusted incidence of 0.33
88 per 100, 000 population¹. Most spinal meningiomas (90%) are benign, WHO I tumors⁴⁻⁶,
89 mainly seen in the elderly with a peak incidence between the seventh and ninth decades of
90 life^{2,4}. Regardless of their location, meningiomas are more commonly found in females. For
91 spinal meningiomas the female to male ratio is around 4:1^{2,4,7,8}. Most meningiomas occur
92 sporadically but a known genetic association to neurofibromatosis type 2 (NF2) is
93 established, and it is estimated that up to 20% of patients with NF2 will develop spinal
94 meningiomas, which might even appear earlier on in life^{9,10}. Mutations of the NF2 tumor
95 suppressor gene or loss of chromosome 22 harboring this gene was found to be more frequent
96 among spinal meningiomas of WHO grades II and III^{11,12}. Exposure to high-dose ionizing
97 radiation is also associated with earlier onset of spinal meningioma^{1,13}. Meningiomas often
98 carry estrogen or progesterone receptors¹⁴, suggesting pregnancy as a potential risk factor for
99 tumor growth^{15,16}. This association was however refuted by a large population-based cohort
100 study¹⁷. Spinal meningiomas may produce neurologic deficits and pain related to local
101 compression of the spinal cord, nerves and adjacent structures^{4,18}. The diagnosis is best made
102 using MRI where meningiomas show homogenous enhancement on gadolinium enhanced T1
103 sequences. Meningiomas also typically display dural tails, enhancement and thickening of the
104 dura extending from the tumor¹⁹. The treatment of choice is surgery, where tumor removal
105 typically alleviates symptoms with little risk of complications or recurrence^{4,7}. In surgery of
106 meningiomas, Simpson grading is used to describe the radicality of tumor removal and to
107 predict the risk for tumor recurrence. Whether Simpson grade I, which includes complete
108 removal of dural attachments, should be the goal of spinal meningioma surgery, remains a
109 topic of debate^{4,20-23}. The Simpson scale also addresses the removal or coagulation of the
110 affected dura. Aggressive removal of the dura may reduce the risk of recurrence but increases
111 the risk of spinal cord injury and postoperative leakage of cerebrospinal fluid. Surgical
112 techniques with removal of the inner dural layer, may constitute an intermediate solution^{24,25}.
113 The most commonly reported postoperative complications are wound infections,
114 cerebrospinal fluid leaks, kyphosis, venous thromboembolisms, and transient or permanent
115 neurologic deficits^{4,7,26-28}. However, these complications are rare and improvement of
116 neurological function after tumor removal is expected in the majority of patients^{4,29}. For
117 patients having undergone Simpson Grade 2 resection of a spinal meningioma, Heon Kim et
118 al have estimated a mean clinical recurrence-free survival period of 17 years²¹. Poor
119 outcomes on the other hand, are reportedly associated with factors like: WHO tumor grade >
120 1, high Ki-67 index, long time to diagnosis, large tumor size and the degree of spinal cord
121 compression^{4,6,30} while mortality mainly reflects high age or co-morbidities^{4,7}. Very little data
122 on health-related quality of life after spinal meningioma surgery is available. Two studies
123 with mixed groups of intradural extramedullary tumors found that the vast majority of
124 patients who underwent surgery saw a significant improvement of activity, mood, walking
125 ability, quality of relations, sleep, and a decrease in pain^{31,32}. These findings are consistent
126 with the results of a quality-of-life questionnaire our group conducted on 84 spinal
127 meningioma patients at an average of 8.7 years after surgery³³. The need for alternative or
128 adjuvant therapies is emphasized in the literature, especially for recurring tumors refractory
129 to conventional therapies and higher-grade tumors (WHO II-III) or for patients who are poor

130 surgical candidates^{28,34}. In these cases, other treatment modalities, including targeted,
 131 hormonal, micro-RNA, or different forms of radiation therapy, may have to be explored.
 132 However, the role of nonsurgical treatment options in the management of spinal
 133 meningiomas remains poorly defined.
 134 The systematic review proposed with this protocol aims to create a comprehensive overview
 135 of the current understanding of spinal meningiomas, as well as to clarify the evidence base
 136 for the treatment strategies employed today. Topics which will be reviewed include
 137 epidemiology, tumor characteristics, diagnostics, treatment options with their potential risks
 138 and benefits, as well as outcomes including quality of life, mortality, and recurrence. The
 139 created overview will serve as a foundation for treatment choices and possibly to identify
 140 areas of insufficient knowledge, warranting renewed scientific effort.
 141 Instead of the more classic PICO criteria (Population, Intervention, Comparison, Outcome),
 142 we decide to use the SPIDER criteria³⁵ (Sample, Phenomenon of Interest, Design, Evaluation,
 143 Research type) which we believe are more suited to the purpose of this review (Table 1).
 144
 145

Table 1: SPIDER criteria³⁵.

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

146 147 148 **Methods and analysis**

149 Study registration

150 This protocol for an intended systematic review is reported according to the Preferred
 151 Reporting Items for Systematic Reviews and Meta-Analyses Protocol (PRISMA-P) statement
 152 of 2015³⁶. The PRISMA-P checklist is provided as supplementary material (see
 153 *supplementary file 1*). The systematic review protocol will also be registered on PROSPERO,
 154 before submission of the final manuscript to a peer reviewed journal.
 155

156 Eligibility criteria

157 **Inclusion criteria**

158 Type of studies

159 All peer reviewed and original studies, written in English and available in the PubMed,
 160 Embase, or Web of Science databases, will be eligible for inclusion. Only studies published
 161 after 2000 will be included to limit our review to the more current publications within the
 162 field.
 163

164 Type of participant

1
2
3 165 All patients will be included, regardless of age, ethnicity, and sex. Similarly, all spinal
4 166 meningiomas irrespective of size, tumor grading or anatomical locations along the spine will
5 167 be included. However, an adequate diagnosis of the tumor must be available and based on
6 168 histological examination or MRI investigations.

8
9 169

10 170 Type of interventions

12 171 All modes of diagnosis and treatment of spinal meningiomas will be included.

13 172

15 173 Type of outcome measurements

16 174 Epidemiological data such as age, sex and socioeconomic factors, possible predictors of poor
17 175 preoperative or postoperative decline such as comorbidity and spinal cord compression will
18 176 also be addressed. Furthermore, outcome parameters including pain, neurological function,
19 177 quality of life, tumor recurrence and mortality, tumor characteristics including expression of
20 178 specific receptors, markers of proliferative activity, and WHO grade will also be included.

22 179 Additional outcomes used in the selected studies may be considered. In those cases, the
23 180 possibility of reporting biases will be recognized.

25 181

27 182 **Exclusion criteria**

28 183 Non-original publications such as reviews, editorials, and letters to the editor will be
29 184 disregarded together with case reports and conference abstracts. Studies found in languages
30 185 other than English will be excluded for practical reasons. Publications prior to the year of
31 186 2000 will also be excluded to reduce the number of included studies and give priority to more
32 187 current publications.

34 188

36 189 Databases and search strategy

37 190 An electronic database search will be performed on PubMed, Embase, and Web of Science.
38 191 The search will be broad, excluding case reports by adding a filter to the search. Appropriate
39 192 filters will also be used to exclude non-English studies and those published prior to the year
40 193 2000. To illustrate the process, the preliminary search strategy for each of the databases is
41 194 provided (see *supplementary file 2*). A reference list search of the included studies will be
42 195 performed, to screen for any eligible article that was missed.

44 196

47 197 Study selection

48 198 The records retrieved from the different databases will be exported into Zotero³⁷, to eliminate
49 199 duplicates. The records will then be screened based on title and abstract by one reviewer, to
50 200 eliminate records that are plainly irrelevant. This is necessary as an unmanageable number of
51 201 records is foreseen due to the broad search strategy that will be used. In the next step, three
52 202 independent and blinded reviewers will be assigned the task of examining the remaining
53 203 records applying the eligibility criteria based on full-text reading. This will be performed
54 204 using Rayyan Software³⁸. Potential disagreements after pooling of the results will be resolved
55 205 by discussion with a fourth reviewer. Finally, reference lists of the selected articles will be
56 206 reviewed for any potentially eligible studies that were previously missed. The process will be
57 207 illustrated in a PRISMA flowchart which will be provided.

208

209 Data extraction

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

220 Assessment of risk of bias

221 The Oxford Center for Evidence-Based Medicine system³⁹, modified by Wright et al, will be
 222 used to assess evidence levels^{40,41} (table 2). The selected articles will first be allocated to one
 223 of only four levels based on methodological quality, since the fifth level (V) is solely
 224 associated to expert opinions which are systematically excluded from our study. Then, an
 225 individual score (IS) will be proposed, as we account for the risk of bias accordingly: studies
 226 with lower risk of bias will be upgraded while those with higher risk of bias will get
 227 downgraded. Risk of bias will be assessed using the appropriate tools specific to the type of
 228 study, as defined by Ma et al⁴². The final IS will also range from I to IV.

230 *Table 2 Level of evidence based on primary research question, by Wright et al⁴⁰.*

	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

231

232 Quality of evidence across studies.

233 The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE)⁴³
 234 approach will be used to rate the body of evidence behind key study outcomes assessing their
 235 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 handbook⁴³ 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 monitored⁴⁵.

273

274 Patient and public involvement:

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

276

277

278 **Ethics and dissemination**

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

282

283 **Discussion**

284 The intended systematic review outlined in this protocol aims to summarize the current
285 scientific literature on spinal meningiomas to provide guidance to clinicians and identify
286 areas in need of further study. The available literature covers many aspects of spinal
287 meningiomas, such as incidence^{2,8,46}, age^{2,4}, and gender distribution^{2,4,7,8}, treatments and their
288 outcomes^{4,47,48}, but many studies are limited by small sample^{3,48-56} sizes and short follow-up
289 times^{3,50,52,57}. Regarding the effect of preoperative neurological impairment, tumor grade and
290 size on postoperative outcomes^{3,30,50,52-59} and adjuvant therapies^{28,34} the available data is
291 conflicting. These issues will be addressed by the systematic review's design, as integrating
292 data from diverse origins will allow for a more representative synthesis that reflects the
293 population of patients with spinal meningiomas more accurately⁶⁰. The absence of both
294 randomized trials and high-quality evidence within the literature as well as the dominance of
295 observational and cohort studies is already apparent, making up the largest limitation to our
296 review. The high heterogeneity expected among studies, with regards to populations and
297 outcome metrics, prevents the performance of a proper meta-analysis. This constitutes the
298 main methodological limitation to this review. Other limitations eventually encountered
299 during the writing of the manuscript will be discussed in the corresponding part of the review.
300 This study ought to be regarded as a reliable source for clinicians to access current evidence
301 compiled in a systematic way and hence better understand the tumor, its epidemiology,
302 management, and prognosis. Greater knowledge of the subject will eventually contribute to
303 improving the diagnosis and care delivery of affected patients. Moreover, the planned
304 systematic review could also help disclose knowledge gaps in the field, identifying and
305 highlighting future research priorities⁶¹. To the best of our knowledge, no systematic review
306 outlining the current understanding of spinal meningiomas has been attempted to this date,
307 making our study the first of its kind. The protocol hereby presented is in accordance with the
308 PRISMA-P guidelines, (see *supplementary file 1*). For further transparency, this protocol will
309 also be registered on PROSPERO in due time. The record on PROSPERO will be updated
310 should significant changes to the procedure take place. The final manuscript is intended for
311 submission to peer-reviewing.

312

313 **Abbreviations**

314 IS = individual score

1
2
3 315 GRADE = Grading of Recommendations, Assessment, Development and Evaluation
4 316 MRI = Magnetic Resonance Imaging
5 317 NF2 = Neurofibromatosis type 2
6 318 PICO = Population, Intervention, Comparison, Outcome
7 319 PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses
8 320 SPIDER = Sample, Phenomenon of Interest, Design, Evaluation, Research type
9 321 WHO = World health Organization
10 322

323 Competing interests

15 324 No competing interests are reported by any of the authors.
16 325

326 Contributions

- 21 327
- 22 328 • Victor Gabriel El-Hajj: conception & design of the work, drafting of the article, critical
23 329 revision, and final approval of the version to be published.
 - 24 329 • Jenny Pettersson-Segerlind: conception & design of the work, drafting of the article,
25 330 and final approval of the version to be published.
 - 26 331 • Gustav Liu Burström: conception & design of the work, drafting of the article, and
27 332 final approval of the version to be published.
 - 28 333 • Erik Edström: conception & design of the work, drafting of the article, critical
29 334 revision, and final approval of the version to be published.
 - 30 334 • Adrian Elmi-Terander: guarantor of the review, conception & design of the work,
31 335 drafting of the article, critical revision, and final approval of the version to be
32 336 published.
33 337
34 338

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342 Ethics declarations

43 343 Ethics approval and consent to participate

44 344 Not applicable.

45 345 Consent for publication

46 346 Not applicable.
47 347

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53 350

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Supplementary information

- 575 [Supplementary file 1: PRISMA-P 2015 Checklist.](#)
576 [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

1 identify as such and list changes; otherwise,
 2 state plan for documenting important protocol
 3 amendments
 4

5 Support

6 Sources [#5a](#) Indicate sources of financial or other support n/a
 7 for the review

8 Sponsor [#5b](#) Provide name for the review funder and / or n/a
 9 sponsor

10 Role of sponsor [#5c](#) Describe roles of funder(s), sponsor(s), and / n/a
 11 or funder or institution(s), if any, in developing the
 12 protocol

13 Introduction

14 Rationale [#6](#) Describe the rationale for the review in the Abstract and last part of
 15 context of what is already known Introduction

16 Objectives [#7](#) Provide an explicit statement of the question(s) Last part of introduction
 17 the review will address with reference to
 18 participants, interventions, comparators, and
 19 outcomes (PICO)

20 Methods

21 Eligibility criteria [#8](#) Specify the study characteristics (such as Methods and analysis:
 22 PICO, study design, setting, time frame) and Eligibility criteria section
 23 report characteristics (such as years
 24 considered, language, publication status) to be
 25 used as criteria for eligibility for the review

26 Information [#9](#) Describe all intended information sources Methods and analysis:
 27 sources (such as electronic databases, contact with Databases and search
 28 study authors, trial registers or other grey strategy section
 29 literature sources) with planned dates of
 30 coverage

31 Search strategy [#10](#) Present draft of search strategy to be used for Methods and analysis:
 32 at least one electronic database, including Databases and search
 33 planned limits, such that it could be repeated strategy section and

supplementary file 2

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3	Study records -	#11a	Describe the mechanism(s) that will be used to
4	data		manage records and data throughout the
5	management		review
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8	Study records -	#11b	State the process that will be used for
9	selection process		selecting studies (such as two independent
10			reviewers) through each phase of the review
11			(that is, screening, eligibility and inclusion in
12			meta-analysis)
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17	Study records -	#11c	Describe planned method of extracting data
18	data collection		from reports (such as piloting forms, done
19	process		independently, in duplicate), any processes for
20			obtaining and confirming data from
21			investigators
22			
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24			
25	Data items	#12	List and define all variables for which data will
26			be sought (such as PICO items, funding
27			sources), any pre-planned data assumptions
28			and simplifications
29			
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32	Outcomes and	#13	List and define all outcomes for which data will
33	prioritization		be sought, including prioritization of main and
34			additional outcomes, with rationale
35			
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37			
38	Risk of bias in	#14	Describe anticipated methods for assessing
39	individual studies		risk of bias of individual studies, including
40			whether this will be done at the outcome or
41			study level, or both; state how this information
42			will be used in data synthesis
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46	Data synthesis	#15a	Describe criteria under which study data will
47			be quantitatively synthesised
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53	Data synthesis	#15b	If data are appropriate for quantitative
54			synthesis, describe planned summary
55			measures, methods of handling data and
56			methods of combining data from studies,
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including any planned exploration of consistency (such as I², Kendall's τ)

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4	Data synthesis	#15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)
5			n/a
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10	Data synthesis	#15d	If quantitative synthesis is not appropriate, describe the type of summary planned
11			Methods and analysis: Data synthesis section
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14	Meta-bias(es)	#16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)
15			Methods and analysis: Risk of bias section
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19	Confidence in	#17	Describe how the strength of the body of
20	cumulative		evidence will be assessed (such as GRADE)
21	evidence		Methods and analysis: Risk of bias and Quality of evidence sections
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 28 Commons Attribution License CC-BY. This checklist was completed on 29. January 2022 using
 29 <https://www.goodreports.org/>, a tool made by the [EQUATOR Network](#) in collaboration with
 30 [Penelope.ai](#)
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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 ((ft[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)