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Impairment correlates in lumbar spinal stenosis: perceived health status and depression. A protocol of a systematic review and meta-analysis

Running head: depression and health status in lumbar spinal stenosis

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Abstract

Background. Lumbar spinal stenosis (LSS) is a common degenerative spine disease associated with the natural process of aging leading to narrowing of the lumbar spinal canal and foramen. Health-related quality of life is the perceived health status on the ability to lead a fulfilling daily life. LSS is associated with a strong impairment in various areas, particularly the ability to perform work-related activity. Depression is a condition frequently associated with this pathology. There is no systematic review on health-related quality of life in LSS and knowledge is scarce about potential moderators of impaired quality of life. This paper presents the protocol of the first systematic review and meta-analysis summarising evidence about health-related quality of life in patients with LSS compared with healthy controls. Comorbidity of depressive disorders will be investigated as a moderator of health-related quality of life impairment.

Methods. The protocol of the systematic review and meta-analysis is reported according to PRISMA-P guidelines. Studies will be included if they were conducted on patients aged 18 years old or older with primary LSS and if they reported data on the differences in the levels of health-related quality of life between patients with LSS and healthy controls. Independent reviewers will search published/unpublished studies through electronic databases and additional sources, will extract the data and assess the methodological quality. Random-effect meta-analysis will be carried out by calculating effect sizes as Cohen's *d* indices. Heterogeneity will be investigated by calculating the I^2 index and the *Q* statistic. Comorbidity of depressive disorders will be explored as a moderator of the effect sizes through meta-regression.

Conclusions. A summary of the evidence on depression and quality of life in LSS may suggest clinical and occupation health medicine strategies aimed at timely detect and prevent these outcomes to attenuate illness deterioration and increase patients' wellbeing.

Ethics and dissemination. The current review does not require ethics approval. The results will be disseminated through publications in peer-reviewed journals.

Review registration: PROSPERO on CRD42019132209.

Strengths and limitations of the study

- The first review and meta-analysis on perceived health status in patients with lumbar spinal stenosis.
- Study selection and data extraction will be performed by independent reviewers.
- Methodological quality of each study will be assessed through a specific tool.
- Another strength will be the analysis of depression as a moderator.
- Potential limitations concern a small number of studies and heterogeneity of instruments assessing quality of life.

Introduction

Health-related quality of life: a relevant outcome in lumbar spine stenosis

Health-related quality of life can be defined as the perceived health status on the ability to lead a fulfilling daily life [1-10]. Lumbar spinal stenosis (LSS) is a common phenomenon associated with the natural process of aging leading to narrowing of the lumbar spinal canal and foramen, as a consequence of degenerative disease. When stenosis is clinically relevant, it results in a syndrome known as neurogenic claudication. Patients typically describe activity-related low-back and leg pain that worsens with prolonged standing or ambulation, limiting their walking distance and compromising their quality of life. LSS is relatively common among the elderly, affecting more than 200,000 adults in the United States, and it is the most common reason for spinal surgery in patients over 65 years [11-12]. As a degenerative spine disease, its prevalence is expected to increase with the continued aging of the population [13]. Symptoms are often chronic, frequently missed, and frequently misdiagnosed, leading to severe disability or reduction in patients' quality of life [13-14]. One of the most affected areas in the patient's life is the ability to perform work-related activity [14].

LSS is a condition in which there is diminished space available for the neural and vascular elements in the lumbar spine secondary to degenerative changes in the spinal canal. When symptomatic, this causes a variable clinical syndrome of gluteal and/or lower extremity pain and/or fatigue that may occur with or without back pain. Symptomatic LSS has certain characteristic provocative and palliative features. Provocative features include upright exercise such as walking or positionally induced neurogenic claudication. Palliative features commonly include symptomatic relief with forward flexion, sitting, and/or recumbency [15].

The presence of a narrowed spinal canal on radiographic imaging does not define LSS, and a correlation between narrowing of the spinal canal and clinical symptoms of spinal stenosis is not established yet [11, 13]. Therefore, LLS is mainly a clinical diagnosis supported by consistent radiological findings.

The diagnosis of LSS may be considered in older patients presenting with neurogenic claudication and imaging studies demonstrating narrowing of the spinal canal. Neurogenic claudication is the core symptom of LSS, defined as intermittent pain radiating to the buttocks, thighs and/or lower legs that is induced with standing, walking and/or lumbar extension, and relieved with sitting, lying down or lumbar flexion. When of severe intensity, neurogenic claudication causes considerable limitations for walking. Patients whose pain is not made worse with walking have a low likelihood of stenosis [16-18].

In patients with history and physical examination evidence consistent with LSS, magnetic resonance imaging is suggested as the most appropriate non-invasive test to confirm the presence of anatomic

narrowing of the spinal canal or the presence of nerve root impingement. It can also help in the differential diagnosis with peripheral neuropathy, lumbar spondylosis, and peripheral artery disease, whose symptoms may resemble LSS [15, 17, 19].

A number of studies demonstrated that health-related quality of life is poorer in patients with LSS compared with healthy individuals without this condition and even compared with patients diagnosed with chronic back pain [20-21]. There is a number of reasons why assessing health-related quality of life in LSS is an important strategy for the management of this condition. Patients with poorer quality of life may be expected to have worse self-management skills of symptoms, to engage less in activities to maintain function, to collaborate with healthcare providers and navigate effectively the healthcare system [22]. Patients with worse quality of life may believe to a less extent that an active role is important in the management of this condition, have lower optimism and hope, lower self-efficacy and locus of control on health behaviour [23].

Patients with LSS experience significantly lower job satisfaction than individuals without this condition [24]. In addition, about 20-40% of the patients with LSS present clinically significant depressive symptoms [25-26].

Rationale and objectives of the present protocol

Health-related quality of life is an important outcome in the assessment and management of LSS. The assessment of this aspect during clinical practice may suggest the introduction of psychological interventions directed at promoting psychological resources to improve long-term outcome. Indeed, patient education has been proven effective for the improvement of both clinical outcomes and quality of life in these patients [27-28].

In the scientific literature, there is no systematic review summarising the evidence of health-related quality of life in LSS. The current paper presents the protocol of the first systematic review and meta-analysis aimed at providing a quantitative summary of the levels of health-related quality of life in patients with LSS compared with healthy control groups. Comorbidity of depressive disorders will be investigated as a moderator if significant heterogeneity in the effect sizes is found. The rationale for investigating this moderator relies on the research data suggesting that (a) comorbid depression levels are frequent in LSS and higher in patients with LSS than in controls, (b) they are associated with worse wellbeing, (c) they predict more severe long-term disability, particularly a combination of symptoms of pain, numbness, weakness, and balance issues, (d) they are associated with more dysfunctional coping such as lower sense of coherence, lower engagement in physical exercise, more severe pain sensitivity, more catastrophic beliefs about pain [29-32].

Methods

The review protocol is presented according to the guidelines of the PRISMA-Protocol (PRISMA-P) [33] and was registered in PROSPERO on CRD42019132209.

Eligibility criteria

In accordance with the PRISMA-P guidelines, the criteria considered for inclusion of studies will be related to (a) participants, (b) outcomes, (c) comparators, and (d) design. Studies will be included if (a) they are conducted on adult clinical groups aged 18 years old or older with a primary diagnosis of LSS; (b) they reported quantitative data on differences in the levels of health-related quality of life between a group of patients with LSS and a healthy control group or the authors are willing to provide the necessary data when contacted if such data are missing in the study paper; (c) they used the criteria of neurogenic claudication and/or radicular leg symptoms and confirmatory imaging showing lumbar spinal stenosis at one or more levels to establish the diagnosis of LSS [34]; (d) they measured health-related quality of life through a validated standardized interview or a validated self-report questionnaire (i.e., the psychometric properties such as reliability values are reported in the literature) (an overview of the eligible measures of health-related quality of life is presented in Table 1); (e) they used a case-control research design (the study may use any other design if it reports the necessary data to compute effect sizes according to inclusion criterion "*b*"). Controls include healthy individuals recruited from the general population/community without LSS; the absence of LSS should be ascertained by a physician through history and physical examination or imaging ruling out lumbar spinal stenosis. Trials on the effects of a treatment will be excluded unless they reported (or the authors are available to provide them on request) data regarding the requested outcomes at baseline (i.e. before trial entry). No language restriction will be applied. Studies will be included whether they used inpatients or outpatients. No restriction on publication dates will be used. Studies where patients had any comorbid psychiatric disorders according to any version of the Diagnostic and Statistical Manual of Mental Disorders (e.g., DSM-IV-TR) [35-36] will not be excluded because psychiatric comorbidity can be observed in one in three patients [37].

Table 1. Eligible measures of health-related quality of life.

Eligible measures to assess dimensions of quality of life
Medical Outcome Survey Short Form-36 [SF-36; 38]
Psychological General Well-being Index [PGWBI; 39]
Quality of Life Inventory [QLI; 40]
WHOQOL.BREF [41]
WHOQOL-100 [42]

Information sources and search procedure

The search procedure will be conducted on 3 July 2019 for one week overall (end of search: 10 July 2019). Studies will be identified by conducting a systematic search of electronic databases using Medical Subject Headings (MeSH terms) and keywords related to "Health-Related Quality of Life" which will be combined through the Boolean operator "AND" with MeSH terms and keywords related to "Lumbar Spinal Stenosis". MeSH terms were created by using the PubMed MeSH on Demand Tool which allowed us to identify relevant MeSH terms. The search procedure will be conducted using the databases Scopus, PubMed, EMBASE and the Cochrane Library. An overview of the electronic search strategy is provided in Table 2.

In addition, to identify any further published or unpublished studies, all the authors of the studies included will be contacted. Reference sections of included studies will be checked. Conference proceedings will be hand-searched from inception for abstracts, papers, or posters presented at the following international scientific societies relevant to research on LSS: American Association of Neurological Surgeons, World Federation of Neurosurgical Societies, North American Spine Society, British Association of Spine Surgeons, Spine Society of Europe (Eurospine), AO Spine, American Psychological Association, European Association of Neurosurgical Societies, Society for Health Psychology, European Health Psychology Society. This search will be carried out independently by the two reviewers (AP, VFM) by accessing the websites of these scientific societies. Eligible theses and doctoral dissertations will be searched and identified by the two independent reviewers who will run the same queries using the same keywords on the Open Access Theses and Dissertations website. All the searches will be re-run just before the final analyses.

Table 2. Electronic search procedure.

Electronic databases	Search terms (MeSH and keywords)
Scopus PubMed EMBASE Cochrane Library	MeSH: "Quality of Life", "Health-Related Quality of Life" Keywords: HRQOL Health-Related Quality Of Life Life Quality AND MeSH: "Spinal Stenosis" Keywords: Constriction, Pathologic Lumbar Vertebrae Spinal Canal Spinal Diseases

Note. MeSH = Medical Subject Heading.

Selection of studies

Studies will be assessed and screened by two independent reviewers (AP, VFM) in three stages using inclusion/exclusion criteria. During the first stage, studies will be assessed independently by the reviewers with regards to inclusion criteria after reading the title. Then, the reviewers will meet to compare their selections. During the abstract selection stage, the two reviewers will independently assess each of the retained studies by reading the abstract and again they will meet to compare their selections. During both these stages (exclusion by title and by abstract), only studies on which both reviewers are in complete agreement on exclusion will be excluded. On the contrary, studies will be retained if there is disagreement between the reviewers on inclusion or exclusion. Studies for which there is complete agreement between the reviewers on inclusion will be included. During the final stage, studies will be assessed independently by the two reviewers by assessing the full text of the paper. Potential discrepancies on inclusion or exclusion at this stage and their reasons will be discussed and resolved in a meeting with two other independent reviewers (FF, AC) to obtain an agreed-upon number of included studies. Between-reviewer agreement on inclusion will be calculated by the Kappa index [43].

Data extraction

All information will be extracted from each of the included studies by two independent reviewers (AP, VFM) and inserted into an Excel worksheet after an initial pilot using 3 included studies. Table 3 provides information on what will be extracted and coded from the primary studies. A third independent reviewer (FF) not involved in the extraction process will check the correctness of the data inserted in the worksheet. After data insertion is completed, potential discrepancies in the data extracted by the two reviewers will be discussed at a meeting between the reviewers who conducted the data extraction and the third independent reviewer.

Table 3. Information extracted from the primary studies and coding procedure

Information extracted	Coding
Title of the paper	Full title of the paper
First author name	First author's last name
Publication date	Publication date of the paper
Language of the paper	Language in which the paper is written
Publication on a peer-review journal	"Yes", "No"
Publication type	"Published on a journal", "Conference paper", "Thesis/doctoral dissertation"
Country where the study was conducted	Name of the country
Participants' inclusion criteria	Quote the inclusion criteria reported in the study paper
Participants' exclusion criteria	Quote the exclusion criteria reported in the study paper
Total sample size in the study	
Participants with Lumbar Spinal Stenosis	Number of clinical participants with Lumbar Spinal Stenosis
Control participants	Number of control participants
Matched controls	"Yes", "No". If Yes, specify if match was made on age or gender or both
Age	Total study mean age and standard deviation
Females	Total percentage of females in the study
Married/cohabitant patients	Total percentage of married/cohabitant patients
Employed patients	Percentage of employed patients
Research design	"Cross-sectional case-control", "Longitudinal"
Lumbar Spinal Stenosis diagnosis	Diagnostic criteria used to establish diagnosis
Instrument(s) used to establish Lumbar Spinal Stenosis diagnosis	Acronym of the instrument(s)
Instrument(s) used to assess health-related quality of life	Acronym of the instrument(s)
Type of instrument(s) used to assess health-related quality of life	"Clinician-administered interview", "Self-report questionnaire"
Duration of Lumbar Spinal Stenosis	Study mean duration of Lumbar Spinal Stenosis in months
Clinical population	"Outpatient", "Inpatient"
Strategies used to recruit clinical participants	Quote the strategies reported in the study paper
Strategies used to recruit controls	Quote the strategies reported in the study paper
Setting where clinical participants were recruited	Quote the setting where patients were recruited
Comorbidity of depressive disorders	Percentage of patients with comorbid depressive disorders in the study according to any version of the DSM

Evaluation of study quality

The quality of each study will be independently evaluated using the Newcastle-Ottawa Quality Assessment Scale [44]. This tool assigns a maximum score of nine: four points regarding inclusion criteria for cases and controls (definition of cases, selection of cases, definition of controls, selection of controls), two points regarding the comparability criteria of cases and controls according to study design and statistical analysis (comparability in terms of age and in terms of gender) and three points for exposure verification criteria of cases and controls (exposure verification, same method of verification, no response point). Studies scoring nine are classified as high quality, those scoring seven or eight as medium quality, and those scoring less than seven as low quality. Disagreement in score attribution between the two authors will be settled by discussion.

Meta-analytic procedure

Summary measures

A random-effect meta-analysis will be conducted using the software *Comprehensive Meta-Analysis, CMA version 2.00* [45]. For all the analyses, the *p*-value will be set at 0.05. Random-effect models assume that included studies are drawn from populations of studies that systematically differ from each other [40]. According to these models, effect sizes extracted from included studies differ not only because of random error within studies (as in fixed-effect models), but also because of true variation in effect sizes from one study to another. Summary measures will consist of effect-size indexes related to the levels of health-related quality of life in clinical groups as compared to control groups. Effect-size indexes will be calculated using the following formula proposed by Cohen [46]: $d = (M_{CASE} - M_{CONTROL})/SD_{COMBINED}$, where M_{CASE} and $M_{CONTROL}$ represent the means of the clinical group and control groups, respectively, and $SD_{COMBINED}$ is the combined standard deviation. If a study used a measure of health-related quality of life that contains subscales (e.g. the SF-36), a global effect-size index will be computed by pooling all the effect-size indexes obtained from the comparison between the clinical group and the controls on each subscale.

The score of each index will be weighted using the following correction formula: $W_{zr} = 1/SE^2$, where SE^2_{zr} is the standard error of the effect-size index calculated for each study. Using Cohen's model, effect-size indexes greater than or equal to 0.80 are considered high, indexes in the range of 0.80–0.50 moderate and indexes less than or equal to 0.20 low. Hedges' correction for small sample bias will be applied [47].

Publication bias

To assess the likelihood that effect sizes have been subject to publication bias, two procedures will be used: Duval and Tweedie's trim and fill procedure and a visual inspection of the funnel plot [48]. A funnel plot is a scatter plot in which the effect sizes computed from the included studies are plotted on the horizontal axis against an indicator of study precision, the Standardized Error, on the vertical axis [49]. In the absence of bias, the graph resembles a symmetrical inverted funnel because the effect sizes derived from smaller studies scatter more widely at the bottom of the graph, with the spread narrowing as precision increases among larger studies. If there is publication bias because smaller studies reporting no significant effect sizes remain unpublished, then the funnel plot appears asymmetrical [49].

Inconsistency analysis

To verify heterogeneity in effect sizes, the I^2 statistic [49] and the Q index [47] will be calculated. The I^2 index is the percentage of variation across studies that is attributable to heterogeneity rather than chance [49]. A value approximating zero suggests homogeneity, whereas values of 25%–50%, 50%–75%, and 75%–100% represent low, moderate, and high heterogeneity, respectively. The Q index is calculated by summing the squared deviation of each study's effect estimate from the overall effect estimate, while weighting the contribution of each study by its inverse variance [47]. In the hypothesis of homogeneity among effect sizes, the Q statistic follows a chi-square distribution with $k - 1$ degrees of freedom, k being the number of studies.

Moderator coding and analysis

If inconsistency between effect sizes is found, comorbidity of depressive disorders will be investigated as a moderator of the effect sizes through a meta-regression. Comorbidity of depressive disorders will be coded as the percentage of patients with comorbid depressive disorders in the study according to any version of the DSM.

Patient and public involvement

Patients and the public were not involved in the development phase of the research question, of the outcome measures, and of the systematic review and meta-analysis protocol. The study does not involve patient recruitment, and patients were not involved in the conduction of the study. The findings will be disseminated through a publication in a peer-reviewed journal.

Ethics and dissemination

The current review does not require ethics approval. The results will be disseminated through publication in peer-reviewed journals.

Discussion and conclusions

Health-related quality of life is an impaired psychological outcome among patients with LSS [20]. Several psychological processes may explain why patients with LSS have poorer quality of life than controls such as worse self-management skills of symptoms, lower engagement in daily activities and physical exercise, lower tendency to collaborate with healthcare providers and navigate effectively the healthcare system, more catastrophic beliefs about pain [22]. Health-related quality of life is a key outcome in the management of LSS and its assessment during clinical practice may suggest the introduction of psychological interventions directed at promoting psychological resources in the patient with the aim to improve long-term outcome or even enhance recovery. Indeed, cognitive behavioural patient education has been proven effective for the improvement of both clinical and quality of life outcomes in these patients [27-28].

In the scientific literature, there is no systematic review summarising the evidence of health-related quality of life in LSS. The current paper presents a study protocol of the first systematic review and meta-analysis aimed at summarising health-related quality of life impairment in patients with LSS compared with healthy control groups. Comorbidity of depressive disorders will be investigated as a moderator if significant heterogeneity in the effect sizes is found.

Some methodological strengths of the review may be highlighted. First, the review is based on a study selection and a data extraction performed by two independent reviewers; in addition, inter-rater agreement will be evaluated and meeting with other reviewers will be carried out. Comorbid psychiatric disorders will not be excluded as they are quite frequent among patients with LSS; in addition, this allows the review to have sufficient external validity. Any research design will be considered as eligible and this may allow additional eligible data to be located and included even if the focus of the paper is not the comparison of health-related quality of life between patients and controls. Moreover, the search strategy is based on the identification of published and unpublished studies. Lastly, another strength is the evaluation of the study's methodological quality through a specific tool.

The review may have important clinical implications: for example, it can highlight the importance of focusing the assessment also on quality of life in patients with LSS to improve prognosis and treatment response, because some psychological interventions have been proven effective for this condition [27].

Since one of the most strongly affected areas of daily life in LSS is the ability to perform work-related activity, a summary of the evidence about depression and impaired quality of life in this condition can suggest that occupational health professionals should assess these outcomes during occupational medicine practice with the aim to improve work-related health and functioning. For example, well informed physician-patient communication in consultations on back pain may prevent deterioration of the LSS and improve patients' perceived health status [50]. Our paper may suggest that occupational medicine practice may be improved by the use of instruments aimed at a timely detection of depression and perceived health status impairment.

Finally, potential limitations of the review regard a small number of studies in the literature and the heterogeneity of the studies in terms of the instruments used to assess health-related quality of life and the difference in the definitions used to conceptualize this construct.

In conclusion, this is a protocol of the first systematic review of health-related quality of life in patients with LSS. A summary of the evidence on this topic may support clinical practice highlighting the importance of the assessment of quality of life and suggesting the use of psychological interventions dedicated to this outcome with the aim of improving patients' quality of life.

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Contributors

FF conceived and designed the study, wrote the first draft of the paper.

AC conceived and designed the study, critically reviewed the first draft of the paper.

VFM conceived and designed the study, critically reviewed the first draft of the paper.

AP conceived and designed the study, wrote the first draft of the paper.

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References

[1] DuBois CM, Beach SR, Kashdan TB, Nyer MB, Park ER, Celano CM et al. Positive psychological attributes and cardiac outcomes: associations, mechanisms, and interventions. *Psychosomatics* 2012;53:303-318.

[2] Sheldon KM, King L. Why positive psychology is necessary. *American Psychologist* 2001;56:216.

[3] Bullinger M, Anderson R, Cella D, Aaronson N. Developing and evaluating cross-cultural instruments from minimum requirements to optimal models. *Quality of Life Research* 1993;2:451-459.

[4] Castro EM, Van Regenmortel T, Vanhaecht K, Sermeus W, Van Hecke A. Patient empowerment, patient participation and patient-centeredness in hospital care: a concept analysis based on a literature review. *Patient Education and Counseling* 2016;99:1923-1939.

[5] Coluccia A, Fagiolini A, Ferretti F, Pozza A, Costoloni G, Bolognesi S, et al. Adult obsessive–compulsive disorder and quality of life outcomes: a systematic review and meta-analysis. *Asian Journal of Psychiatry* 2016;22:41-52.

[6] Coluccia A, Fagiolini A, Ferretti F, Pozza A, Goracci A. Obsessive-Compulsive Disorder and quality of life outcomes: protocol for a systematic review and meta-analysis of cross-sectional case-control studies. *Epidemiology, Biostatistics and Public Health* 2015;12:e11037.

[7] Coluccia A, Ferretti F, Fagiolini A, Pozza A. Quality of life in children and adolescents with obsessive–compulsive disorder: a systematic review and meta-analysis. *Neuropsychiatric Disease and Treatment* 2017;13:597-608.

[8] Johansson P, Dahlström U, Broström A. Factors and interventions influencing health-related quality of life in patients with heart failure: a review of the literature. *European Journal of Cardiovascular Nursing* 2006;5:5-15.

[9] Leadley RM, Armstrong N, Lee YC, Allen A, Kleijnen J. Chronic diseases in the European Union: the prevalence and health cost implications of chronic pain. *Journal of Pain and Palliative Care Pharmacotherapy* 2012;26:310-325.

[10] World Health Organization. Preamble to the Constitution of the World Health Organization. In Official records of the World Health Organization, No. 2 (p. 100). Geneva: Author. Retrieved from http://whqlibdoc.who.int/hist/official_records/2e.pdf, 1948.

[11] Resnick DK, Watters WC, Sharan A, Mummaneni PV, Dailey AT, Wang JC et al. Guideline update for the performance of fusion procedures for degenerative disease of the lumbar spine. Part 9: lumbar fusion for stenosis with spondylolisthesis. *Journal of Neurosurgery Spine* 2014;21:54-61.

[12] Lurie J, Tomkins-Lane C. Management of lumbar spinal stenosis. *BMJ* 2016 4;352:6234.

[13] Konno S, Hayashino Y, Fukuhara S, Kikuchi S, Kaneda K, Seichi A et al. Development of a clinical diagnosis support tool to identify patients with lumbar spinal stenosis. *European Spine Journal* 2007;16:1951-7.

[14] Spengler DM. Degenerative stenosis of the lumbar spine. *J Bone and Joint Surgery American Volume* 1987;69:305-308.

[15] Kreiner DS, Shaffer WO, Baisden JL, Gilbert TJ, Summers JT, Toton JF et al. An evidence-based clinical guideline for the diagnosis and treatment of degenerative lumbar spinal stenosis (update). *Spine Journal* 2013;13:734-43.

[16] Katz JN, Dalgas M, Stucki G, Katz NP, Bayley J, Fossel AH et al. Degenerative lumbar spinal stenosis. Diagnostic value of the history and physical examination. *Arthritis Rheumatology* 1995;38:1236–41.

[17] Katz JN, Harris MB. Clinical practice. Lumbar spinal stenosis. *New England Journal of Medicine* 2008;358:818-25.

[18] Rainville J, Childs LA, Peña EB, Suri P, Limke JC, Jouve C et al. Quantification of Walking Ability in Subjects with Neurogenic Claudication from Lumbar Spinal Stenosis – A Comparative Study. *Spine Journal* 2012;12:101-9.

[19] Kent DL, Haynor DR, Larson EB, Deyo RA. Diagnosis of lumbar spinal stenosis in adults: a meta-analysis of the accuracy of CT, MR, and myelography. *American Journal of Roentgenology* 1992;158:1135-44.

[20] Otani K, Kikuchi S, Yabuki S, Igarashi T, Nikaido T, Watanabe K et al. Lumbar spinal stenosis has a negative impact on quality of life compared with other comorbidities: an epidemiological cross-sectional study of 1862 community-dwelling individuals. *The Scientific World Journal* 2013:590652.

[21] Saban KL, Penckofer SM, Androwich I, Bryant FB. Health-related quality of life of patients following selected types of lumbar spinal surgery: A pilot study. *Health Quality of Life Outcomes* 2007;5:71.

[22] Skolasky RL, Mackenzie EJ, Riley LH, Wegener ST. Psychometric properties of the Patient Activation Measure among individuals presenting for elective lumbar spine surgery. *Quality of Life Research* 2009;18:1357-1366.

[23] Von Korff M, Gruman J, Schaefer J, Curry SJ, Wagner EH. Collaborative management of chronic illness. *Annals of Internal Medicine* 1997;127:1097–1102.

[24] Sekiguchi M, Yonemoto K, Kakuma T, Nikaido T, Watanabe K, Kato K et al. Relationship between lumbar spinal stenosis and psychosocial factors: a multicenter cross-sectional study (DISTO project). *European Spine Journal* 2015;24:2288-2294.

[25] Levy HI, Hanscom B, Boden SD. Three-question depression screener used for lumbar disc herniations and spinal stenosis. *Spine* 2002;27:1232-1236.

[26] Sinikallio S, Aalto T, Airaksinen O, Herno A, Kröger H, Savolainen S et al. Depression and associated factors in patients with lumbar spinal stenosis. *Disability Rehabilitation* 2006;28:415-422.

[27] Archer KR, Devin CJ, Vanston SW, Koyama T, Phillips SE, George et al. Cognitive-behavioral–based physical therapy for patients with chronic pain undergoing lumbar spine surgery: a randomized controlled trial. *Journal of Pain* 17;76-89.

[28] Rolving N, Sogaard R, Nielsen CV, Christensen FB, Bünger C, Oestergaard LG. Preoperative cognitive-behavioral patient education versus standard care for lumbar spinal fusion patients: economic evaluation alongside a randomized controlled trial. *Spine* 2016;41:18-25.

[29] Coronado RA, George SZ, Devin CJ, Wegener ST, Archer KR. Pain sensitivity and pain catastrophizing are associated with persistent pain and disability after lumbar spine surgery. *Archives of Physical Medicine and Rehabilitation* 2015;96:1763-1770.

[30] McKillop AB, Carroll LJ, Battié MC. Depression as a prognostic factor of lumbar spinal stenosis: a systematic review. *Spine* 2014;14:837-846.

[31] Sinikallio S, Aalto T, Airaksinen O, Lehto SM, Kröger H, Viinamäki H. Depression is associated with a poorer outcome of lumbar spinal stenosis surgery: a two-year prospective follow-up study. *Spine* 2011;36:677-682.

[32] Sinikallio S, Aalto T, Koivumaa-Honkanen, H, Airaksinen O, Herno A, Kröger H et al. Life dissatisfaction is associated with a poorer surgery outcome and depression among lumbar spinal stenosis patients: a 2-year prospective study. *European Spine Journal* 2009;18:1187-1193.

[33] Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ* 2015;349:g7647.

[34] Birkmeyer NJ, Weinstein JN, Tosteson AN, et al. Design of the Spine Patient outcomes Research Trial (SPORT). *Spine* 2002;27:1361-1372.

[35] American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed. Washington, DC: American Psychiatric Association, 2000.

[36] American Psychiatric Association. Diagnostic and statistical manual of mental disorders (5th ed.). Washington, DC: American Psychiatric Association, 2013.

[37] Diebo BG, Lavian JD, Murray DP, Liu S, Shah NV, Beyer GA et al. The impact of comorbid mental health disorders on complications following adult spinal deformity surgery with minimum 2-year surveillance. *Spine* 2018;43:1176-1183.

[38] Ware JE, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). *Medical Care* 1992;30:473–483.

[39] Dupuy HJ. The psychological general well-being (PGWB) index. In: Wenger NK, Mattson ME, Fuberg CL, eds. Assessment of quality of life in clinical trials of cardiovascular therapies. New York: Le Jacq, 1984.

[40] Frisch MB, Cornell J, Villanueva M, Retzlaff PJ. Clinical validation of the Quality of Life Inventory. A measure of life satisfaction for use in treatment planning and outcome assessment. *Psychological Assessment* 1992;4:92-101.

[41] WHOQOL Group. Development of the World Health Organization WHOQOL-BREF Quality of Life Assessment. *Psychological Medicine* 1998;28:551-558.

[42] Skevington SM, Carse MS, Williams ACDC. Validation of the WHOQOL-100: pain management improves quality of life for chronic pain patients. *The Clinical Journal of Pain* 2001;17:264-275.

[43] Cohen J. A coefficient of agreement for nominal scales. *Educational and Psychological Measurement* 1960;20:37-46

[44] Wells GA, Shea B, O'Connell D et al. The Newcastle–Ottawa Scale (NOS) for assessing the quality of non-randomised studies in meta-analyses. http://www. ohri.ca/programs/clinical_epidemiology/oxford.asp, 2000.

[45] Borenstein M, Hedges LV, Higgins JPT, Rothstein HR. Introduction to meta-analysis. Chichester: John Wiley & Sons, 2009.

[46] Cohen J. Statistical power analysis for the behavioural sciences. 2nd ed. Hillsdale, NK: Erlbaum Ed; 1988.

[47] Hedges LV. Estimation of effect size from a series of independent experiments. *Psychological Bulletin* 1982:92:490-499.

[48] Duval S, Tweedie R. Trim and fill: a simple funnel-plot–based method of testing and adjusting for publication bias in meta-analysis. *Biometrics* 2000;56:455-463.

[49] Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003;327:557-60.

[50] Voigt-Radloff S, Schöpf AC, Boeker M, Frank L, Farin E, Kaier K, et al. Well informed physician-patient communication in consultations on back pain–study protocol of the cluster randomized GAP trial. *BMC Family Practice* 2019;20:33.

PRISMA-P checklist indicating page numbers where the information can be found.

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Quality of life and objective functional impairment in lumbar spinal stenosis: A protocol for a systematic review and meta-analysis of moderators

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Quality of life and objective functional impairment in lumbar spinal stenosis: A protocol for a systematic review and meta-analysis of moderators

Running head: subjective and objective impairment in lumbar spinal stenosis

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Abstract

Background. Lumbar spinal stenosis (LSS) is a common degenerative spine disease associated with a strong impairment in various quality of life areas, particularly the ability to perform work-related activity. Depression is a condition frequently associated. There is no comprehensive review on quality of life and objective functional impairment in LSS. This paper presents the protocol of the first systematic review and meta-analysis summarising evidence about quality of life and functional impairment in patients with LSS compared with healthy controls. Comorbid depressive disorders, age, gender, LSS duration, disability, pain severity and study methodological quality will be investigated as moderators.

Methods. The protocol is reported according to PRISMA-P guidelines. Studies will be included if they were conducted on patients aged 18 years old or older with primary LSS and if they reported data on differences in the levels of quality of life or objective functional impairment between patients with LSS and healthy controls. Independent reviewers will search published/unpublished studies through electronic databases and additional sources, will extract the data and assess the methodological quality. Random effects meta-analysis will be carried out by calculating effect sizes as Cohen's *d* indices. Heterogeneity will be examined by the I^2 and the Q statistics. Moderators will be investigated through meta-regression.

Conclusions. A summary of the evidence on quality of life and functional impairment in LSS may suggest clinical and occupational health medicine strategies aimed to timely detect and prevent these outcomes. Higher percentages of LSS patients with depression may be expected to be related to poorer quality of life. Depressive comorbidity might impact negatively on quality of life because it is associated with dysfunctional coping, disability and psychophysiological symptoms.

Ethics and dissemination. The current review does not require ethics approval. The results will be disseminated through publications in peer-reviewed journals.

Review registration: PROSPERO on CRD42019132209.

Strengths and limitations of the study

- Study selection and data extraction will be performed by independent reviewers.
- If heterogeneity is found, subgroup analyses will be conducted for studies using only clinician-administered interviews or self-report questionnaires.
- Another strength will be the moderator analysis of comorbid depressive disorders based on international standardized classification systems.
- Potential limitations concern a small number of studies and heterogeneity of instruments assessing quality of life.
- Another limitation might be that some studies do report data for moderator coding or the authors do not provide them upon request.

Introduction

Health-related quality of life: a relevant outcome in lumbar spinal stenosis

Health-related quality of life can be defined as the perceived health status on the ability to lead a fulfilling daily life [1-11]. Lumbar spinal stenosis (LSS) is a condition associated with the natural process of aging leading to narrowing of the lumbar spinal canal and foramen, resulting from a degenerative process. When stenosis is clinically relevant, it results in a syndrome known as neurogenic claudication. Patients generally experience and report activity-related low-back and leg pain that worsens with prolonged standing or ambulation, limiting their walking distance and impacting their capacity to live a fulfilling life. LSS is relatively common among the elderly, affecting more than 200,000 adults in the United States, and it is the most frequent reason for spinal surgery in patients over 65 years [12-13]. As a degenerative spine disease, its prevalence is expected to increase with the continued aging of the population [14]. Symptoms are often chronic, frequently missed or misdiagnosed, leading to strong impairment or reduction in quality of life [14-15]. One of the most impaired domains in the patient's life is the ability to perform work-related activity [15].

The clinical picture of LSS is characterized by a diminished space available for the neural and vascular elements in the lumbar spine secondary to degenerative changes in the spinal canal [16-17]. When symptomatic, this causes a variable clinical syndrome of gluteal and/or lower extremity pain and/or fatigue that may occur with or without back pain [17]. Symptomatology of LSS consists of specific provocative and palliative features. Provocative features include upright exercise such as walking or positionally induced neurogenic claudication. Palliative features typically involve symptomatic relief with forward flexion, sitting, and/or recumbency [16-17].

The presence of a narrowed spinal canal on radiographic imaging is not a sufficient criterion to diagnose LSS, and a correlation between narrowing of the spinal canal and clinical symptoms of spinal stenosis has not been demonstrated yet [12, 14, 17]. Therefore, LLS is mainly a clinical diagnosis supported by consistent radiological findings [17].

The diagnosis of LSS may be considered in older patients presenting with neurogenic claudication and imaging studies demonstrating narrowing of the spinal canal. Neurogenic claudication represents the key symptomatic aspect of LSS, defined as intermittent pain radiating to the buttocks, thighs and/or lower legs that is typically provoked by standing, walking and/or lumbar extension, and relieved with sitting, lying down or lumbar flexion. If the level of intensity is severe, neurogenic claudication determines considerable difficulties in walking [18-20].

In patients with history and physical examination evidence consistent with LSS, magnetic resonance imaging is generally considered as the most reliable non-invasive tool aimed to support the presence of anatomic narrowing of the spinal canal or the presence of nerve root impingement [17]. It can also enhance the differential diagnosis with peripheral neuropathy, lumbar spondylosis, and peripheral artery disease, whose symptoms may resemble LSS [16, 18, 21].

A number of studies demonstrated that health-related quality of life is poorer in patients with LSS compared with healthy individuals without this condition and even compared with patients diagnosed with chronic back pain [22-23]. There is a number of reasons why assessing health-related quality of life in LSS is an important strategy for the management of this condition. Patients with poorer quality of life may be expected to have worse self-management skills of symptoms, to engage less in activities to maintain function, to collaborate with healthcare providers and navigate effectively the healthcare system [24]. Patients with worse quality of life may believe to a less extent that an active role is important in the management of this condition, have lower optimism and hope, lower self-efficacy and locus of control on health behaviour [25].

Patients with LSS experience significantly lower job satisfaction than individuals without this condition [26]. In addition, about 20-40% of the patients with LSS present clinically significant depressive symptoms [27-28].

In patients with LSS, comorbid depressive disorders are frequent and higher than in controls; this type of comorbidity is often associated with worse wellbeing, more severe long-term disability (a combination of symptoms of pain, numbness, weakness, and balance issues), and more dysfunctional coping such as lower sense of coherence, lower engagement in physical exercise, more severe pain sensitivity, more catastrophic beliefs about pain [29-32].

Based on these points, some researchers pointed out the need for integrating the assessment of patient-reported quality of life with measures of objective functional impairment since functional status of the patient is less prone to a bias due to psychological health [33] Objective functional measures such as "Time Up and Go" test are based on a task to be performed by the patient, which is evaluated using an objective assessment of the patient's performance on that task through a standardized testing protocol (i.e., time taken, repetitions) and is rated by an observer and/or machine instead of the patient him/herself [34].

Rationale and objectives of the present protocol

Health-related quality of life and objective functional impairment are important outcomes in the assessment and management of LSS. The assessment of both these aspects during clinical practice may

suggest a comprehensive evaluation aimed to improve long-term outcome. For example, patient education and psychological interventions aimed to promote patient's resources have been proven effective for the improvement of both clinical outcomes and quality of life in these patients [35-36].

In the scientific literature, there is no systematic review providing a comprehensive summary of the evidence of health-related quality of life and functional impairment in LSS. The current paper presents the protocol of the first systematic review and meta-analysis aimed at providing a quantitative summary of the levels of health-related quality of life and objective functional impairment in patients with LSS compared with healthy control groups. Comorbidity of depressive disorders will be investigated as a moderator if significant heterogeneity in the effect sizes is found. Comorbidity of depressive disorders might impact negatively on quality of life because depression is associated with worse general wellbeing, dysfunctional coping strategies, long-term disability and psychophysiological symptoms. On one hand, higher percentages of LSS patients with comorbid depressive disorders may be expected to be related to poorer levels of quality of life; on the other hand, depressive comorbidity may impact less on objective functional impairment which is less influenced by psychological status [33-34]. Other moderators will be examined as potentially impacting negatively on quality of life and functional impairment including age, gender, LSS duration, LSS severity (self-reported disability and pain severity related to LSS), study methodological quality.

Methods

The planned start and end dates for the study are 1st November and 31st December 2019, respectively. The review protocol is presented according to the guidelines of the PRISMA-Protocol (PRISMA-P) [37] and was registered in PROSPERO on CRD42019132209.

Eligibility criteria

In accordance with the PRISMA-P guidelines, the criteria considered for inclusion of studies will be related to (a) participants, (b) outcomes, (c) comparators, and (d) design. Studies will be included if (a) they are conducted on adult clinical groups aged 18 years old or older with a primary diagnosis of LSS; (b) they reported quantitative data on differences in the levels of health-related quality of life between a group of patients with LSS and a healthy control group or the authors are willing to provide the necessary data when contacted if such data are missing in the study paper; (c) they used the criteria of neurogenic claudication and/or radicular leg symptoms and confirmatory imaging showing LSS at one or more levels to establish the diagnosis of LSS [38]; (d) they measured health-related quality of life through any validated standardized interview or a validated self-report questionnaire such as the Medical Outcome

Survey Short Form-36 (SF-36) [39] (i.e., the psychometric properties such as reliability values are reported in the literature) and/or they assessed objective functional impairment based on a task to be performed by the patient, evaluated using an objective assessment of the patient's performance on that task (i.e., time taken, repetitions), rated by an observer and/or machine instead of the patient him/herself through a standardized testing protocol; (e) they used a case-control research design (the study may use any other design if it reports the necessary data to compute effect sizes according to inclusion criterion "*b*"). Controls include healthy individuals recruited from the general population/community without LSS; the absence of LSS should be ascertained by a physician through history and physical examination or imaging ruling out lumbar spinal stenosis. Case series will be excluded. Trials on the effects of a treatment will be excluded unless they reported (or the authors are available to provide them on request) data regarding the requested outcomes at baseline (i.e. before trial entry). No language restriction will be applied. Studies will be included whether they used inpatients or outpatients. No restriction on publication dates will be used. Studies where patients had any comorbid psychiatric disorders according to any version of the Diagnostic and Statistical Manual of Mental Disorders (e.g., DSM-IV-TR) [40-41] will not be excluded because psychiatric comorbidity can be observed in one in three patients [42]. If the study assessed the number of patients with comorbid depressive disorders, this comorbidity had to be evaluated by the criteria for a major depressive disorder according to an international standardized diagnostic system such as the Diagnostic and Statistical Manual of Mental Disorders (DSM) or the International Classification of Diseases (ICD).

Information sources and search procedure

The search procedure will be conducted on 4th November 2019. Studies will be identified by conducting a systematic search of electronic databases using Medical Subject Headings (MeSH terms) and keywords related to "Health-Related Quality of Life" which will be combined through the Boolean operator "AND" with MeSH terms and keywords related to "Lumbar Spinal Stenosis". MeSH terms were created by using the PubMed MeSH on Demand Tool which allowed us to identify relevant MeSH terms. The search procedure will be conducted using the databases Scopus, PubMed, EMBASE and the Cochrane Library. An overview of the electronic search strategy is provided in Table 1. An example of the search strategy is provided in the Supplementary file. In order to define and validate the search string in the different electronic databases, an experienced librarian will be involved during this phase of the search.

In addition, to identify any further published or unpublished studies, all the authors of the studies included will be contacted. Reference sections of included studies will be checked. Conference proceedings will be hand-searched from inception for abstracts, papers, or posters presented at the following international

scientific societies relevant to research on LSS: American Association of Neurological Surgeons, World Federation of Neurosurgical Societies, North American Spine Society, British Association of Spine Surgeons, Spine Society of Europe (Eurospine), AO Spine, American Psychological Association, European Association of Neurosurgical Societies, Society for Health Psychology, European Health Psychology Society. This search will be carried out independently by the two reviewers (AP, VFM) by accessing the websites of these scientific societies. Eligible theses and doctoral dissertations will be searched and identified by the two independent reviewers who will run the same queries using the same keywords on the Open Access Theses and Dissertations website. All the searches will be re-run just before the final analyses.

Table 1. Electronic search procedure.

Electronic databases	Search terms (MeSH and keywords)
Scopus PubMed EMBASE Cochrane Library	MeSH: "Quality of Life", OR "Health-Related Quality of Life" Boolean operator and keywords: OR HRQOL OR Health-Related Quality of Life OR Life Quality AND MeSH: "Spinal Stenosis" Boolean operator and keywords: OR Constriction, Pathologic OR Lumbar Vertebrae OR Spinal Canal OR Spinal Diseases

Note. MeSH = Medical Subject Heading.

Selection of studies

Studies will be assessed and screened by two independent reviewers (AP, VFM) in two stages using inclusion/exclusion criteria. During the first stage, studies will be assessed independently by the reviewers with regards to inclusion criteria after reading the title and the abstract. Then, the reviewers

will meet to compare their selections. During this stage, only studies on which both reviewers are in complete agreement on exclusion will be excluded. On the contrary, studies will be retained if there is disagreement between the reviewers on inclusion or exclusion. Studies for which there is complete agreement between the reviewers on inclusion will be included. During the final stage, studies will be assessed independently by the two reviewers by assessing the full text of the paper. Potential discrepancies on inclusion or exclusion at this stage and their reasons will be discussed and resolved in a meeting with two other independent reviewers (FF, AC) to obtain an agreed-upon number of included studies. Between-reviewer agreement on inclusion will be calculated by the Kappa index [43]. During the whole selection process, potential duplicates will be handled and excluded by following the systematic detection heuristic proposed by Wood [44].

Data extraction

All information will be extracted from each of the included studies by two independent reviewers (AP, VFM) and inserted into an Excel worksheet after an initial pilot using 3 included studies. Table 2 provides information on what will be extracted and coded from the primary studies. A third independent reviewer (FF) not involved in the extraction process will check the correctness of the data inserted in the worksheet. After data insertion is completed, potential discrepancies in the data extracted by the two reviewers will be discussed at a meeting between the reviewers who conducted the data extraction and the third independent reviewer.

Table 2. Information extracted from the primary studies and coding procedure.

Information extracted	Coding
Title of the paper	Full title of the paper
First author name	First author's last name
Publication date	Publication date of the paper
Language of the paper	Language in which the paper is written
Publication on a peer-review journal	"Yes", "No"
Publication type	"Published on a journal", "Conference paper", "Thesis/doctoral dissertation"
Country where the study was conducted	Name of the country
Participants' inclusion criteria	Quote the inclusion criteria reported in the study paper
Participants' exclusion criteria	Quote the exclusion criteria reported in the study paper
Total sample size in the study	Total sample size in the study
Participants with Lumbar Spinal Stenosis	Number of clinical participants with Lumbar Spinal Stenosis
Control participants	Number of control participants
Matched controls	"Yes", "No". If Yes, specify if match was made on age or gender or both
Age	Total study mean age and standard deviation. If the study does not report these data, they will be requested from the

	corresponding author. If this is not the case, mean and standard deviation will be estimated from median and interquartile ranges through the formula proposed by Wan and colleagues [45]. Otherwise, the study will be excluded from the analyses involving data on age.
Females	Total percentage of females in the study
Married/cohabitant patients	Total percentage of married/cohabitant patients
Employed patients	Percentage of employed patients
Research design	"Cross-sectional case-control", "Longitudinal"
Lumbar Spinal Stenosis diagnosis	Diagnostic criteria used to establish diagnosis
Instrument(s) used to establish Lumbar Spinal Stenosis diagnosis	Acronym of the instrument(s)
Instrument(s) used to assess health-related quality of life	Acronym of the instrument(s)
Type of instrument(s) used to assess health-related quality of life	"Clinician-administered interview", "Self-report questionnaire"
Instrument(s) used to evaluate objective functional impairment	Acronym of the instrument(s)
Duration of Lumbar Spinal Stenosis	Study mean duration of Lumbar Spinal Stenosis in months
Clinical population	"Outpatient", "Inpatient"
Strategies used to recruit clinical participants	Quote the strategies reported in the study paper
Strategies used to recruit controls	Quote the strategies reported in the study paper
Setting where clinical participants were recruited	Quote the setting where patients were recruited
Comorbidity of depressive disorders	Percentage of patients with comorbid depressive disorders in the study according to any version of any international standardized classification systems
Instrument(s) used to assess disability related to Lumbar Spinal Stenosis	Acronym of the instrument(s)
Disability related to Lumbar Spinal Stenosis	Study mean scores on the Swiss Spinal Stenosis Questionnaire and Oxford Spinal Stenosis Score [46]
Instrument(s) used to assess self-reported pain severity	Acronym of the instrument(s)
Self-reported pain severity	Study mean scores on the Visual Analog Scale for pain, Numeric Rating Scale for pain, McGill Pain Questionnaire [47]

Measurement of methodological quality of studies

As in our previous meta-analytical works [11, 48], the Newcastle-Ottawa Quality Assessment Scale will be adopted by two independent meta-analysts to examine the methodological quality of each study [49]. This checklist is based on a maximum score of nine: four points are assigned to inclusion criteria of cases and controls (definition of cases, selection of cases, definition of control subjects, selection of control subjects), two points are assigned to the comparability criteria of cases and control subjects according to study design and statistical analysis (comparability in terms of age and gender) and three points to exposure verification criteria of cases and control subjects (exposure verification, same method of verification, no response point). Studies which obtain a nine score are considered as high quality, those receiving seven or eight as medium quality, and those scoring less than seven as poor quality. A

discussion meeting will be planned to resolve eventual disagreement in score attribution between the two meta-analysts.

Meta-analytic procedure

Summary measures

A random effects meta-analysis will be conducted using the software *Comprehensive Meta-Analysis, CMA version 2.00* [50]. For all the analyses, significance will be analysed by quantifying the evidence on a continuous scale. Random effects models assume that included studies are drawn from populations of studies that systematically differ from each other [50]. According to these models, effect sizes extracted from included studies differ not only because of random error within studies (as in fixed-effect models), but also because of true variation in effect sizes from one study to another. Summary measures will consist of effect-size indexes related to the levels of health-related quality of life in clinical groups as compared to control groups. In addition, effect-size indexes will be calculated for any measures of objective functional impairment (as defined in the "Eligibility criteria" paragraph).

Effect-size indexes will be calculated using the following formula proposed by Cohen [51]: $d = (M_{CASE}–M_{CONTROL})/SD_{COMBINED}$, where M_{CASE} and $M_{CONTROL}$ represent the means of the clinical group and control groups, respectively, and $SD_{COMBINED}$ is the combined standard deviation. If a study used a measure of health-related quality of life/objective functional impairment that contains subscales (e.g. the SF-36), a global effect-size of quality of life and/or functional impairment index will be computed by pooling all the effect-size indexes obtained from the comparison between the clinical group and the controls on each subscale.

The score of each index will be weighted using the following correction formula: $W_{zr} = 1/SE^2$, where SE^2_{zr} is the standard error of the effect-size index calculated for each study. Using Cohen's model, effect-size indexes greater than or equal to 0.80 are considered high, indexes in the range of 0.80–0.50 moderate and indexes in the range of 0.50-0.20 low. Hedges' correction for small sample bias will be applied [52].

Bias of publication

In order to investigate whether the effect sizes are subject to a bias of publication, two methods will be adopted: Duval and Tweedie's trim and fill technique and a visual examination of the funnel plot [53]. A funnel plot is a scatter plot in which the effect sizes derived from the included papers are plotted on the horizontal axis against an indicator of study precision, the Standardized Error, on the vertical axis [54]. In the absence of bias, the graph resembles a symmetrical inverted funnel because the effect sizes

calculated from smaller studies scatter more widely at the bottom of the graph, with the spread narrowing as precision increases among larger studies. If there is publication bias because smaller studies showing no significant effect sizes remain unpublished, then the funnel plot results asymmetrical [54]. The aim of the trim-and-fill method is to evaluate the effect of adjustment for bias related to small studies. It removes studies until symmetry in the funnel plot is achieved, recalculating the centre of the funnel before the removed studies are replaced together with their "missing" mirror-image counterparts [53]. This procedure will result in a revised summary estimate calculated using all of the original studies, together with the hypothetical "filled" studies. The new summary estimate (after trim-and-fill) will be reported together with the original estimate in every meta-analysis.

Inconsistency analysis

To verify heterogeneity in effect sizes, the I^2 statistic [54] and the Q index [52] will be calculated. The I^2 index is the percentage of variation across studies that is attributable to heterogeneity rather than chance [54]. A value approximating zero suggests homogeneity, whereas values of 25%–50%, 50%–75%, and 75%–100% represent low, moderate, and high heterogeneity, respectively. The Q index is calculated by summing the squared deviation of each study's effect estimate from the overall effect estimate, while weighting the contribution of each study by its inverse variance [52]. In the hypothesis of homogeneity among effect sizes, the Q statistic follows a chi-square distribution with $k - 1$ degrees of freedom, k being the number of studies.

Subgroup and moderator analyses

If significant inconsistency is found, subgroup analyses will be conducted for studies using (a) only clinician-administered interviews to measure health-related quality of life, (b) self-report questionnaires of health-related quality of life.

Comorbidity of depressive disorders will be investigated as a moderator of the effect sizes through a meta-regression. Comorbidity of depressive disorders will be coded as the percentage of patients with comorbid depressive disorders in the study according to the criteria for a major depressive disorder of any standardized international classification systems such as DSM or ICD. If such data is not given in the study paper (i.e., the paper does not report on depression, or does not explicitly state the percentage of patients with comorbid depressive disorders), the corresponding author will be contacted to request this information. In this case, the study will be included in the analysis only if the corresponding author is available to provide the necessary data.

Additional moderators will be examined including (a) age coded by the total mean age in the study, (b) female gender coded by the total percentage of females in the study, (c) duration of LSS coded by the mean number of months since the diagnosis in the study, (d) self-reported disability related to LSS coded by the mean scores on the Swiss Spinal Stenosis Questionnaire and Oxford Spinal Stenosis Score [46] (the moderating effects will be computed separately for each of these two scales if available), (e) pain severity coded by the mean scores on the Visual Analog Scale for pain, Numeric Rating Scale for pain, McGill Pain Questionnaire [47] (as for disability scores, the moderating effects will be computed separately for each of these scales), (f) study methodological quality (coded by the scores on the NOS). As for data related to depressive disorders, studies will be included if the paper provides the necessary information or the corresponding author is available to provide it when asked. The relationship between the effect sizes and all these moderators will be investigated by conducting weighted least squares meta-regression analyses.

If studies with controls without depressive disorders are retrieved, in order to disentangle depression and LSS effects in such studies, the percentage of controls with depressive disorders will be included as moderator in the analysis. This strategy will aim to examine whether the percentage of controls with depression moderates the effect sizes. It can be expected that in studies where the percentage of controls with comorbid depressive disorders is higher, the difference in the quality of life/functional impairment levels between patients and control is lower.

According to Valentine et al.'s recommendations [55], the minimum number of studies for pooling the data and performing effect size calculation will be 2. Following the guidelines for a continuous study level variable proposed by Fu et al. [56], at least 6 to 10 studies will be necessary to investigate the moderating effects through meta-regression.

Patient and public involvement

Patients and the public were not involved in the development phase of the research question, of the outcome measures, and of the systematic review and meta-analysis protocol. The study does not involve patient recruitment, and patients were not involved in the conduction of the study. The findings will be disseminated through a publication in a peer-reviewed journal.

Ethics and dissemination

The current review does not require ethics approval. The results will be disseminated through publication in peer-reviewed journals.

Discussion and conclusions

Health-related quality of life is an impaired psychological outcome among patients with LSS [22]. Several psychological processes may explain why patients with LSS have poorer quality of life than controls such as worse self-management skills of symptoms, lower engagement in daily activities and physical exercise, lower tendency to collaborate with healthcare providers and navigate effectively the healthcare system, more catastrophic beliefs about pain [24]. Health-related quality of life is a key outcome in the management of LSS and its assessment during clinical practice may suggest the introduction of psychological interventions directed at promoting psychological resources in the patient with the aim to improve long-term outcome or even enhance recovery. Indeed, cognitive behavioural patient education has been proven effective for the improvement of both clinical and quality of life outcomes in these patients [35-36].

In the scientific literature, there is no systematic review summarising the evidence of health-related quality of life in LSS. The current paper presents a study protocol of the first systematic review and meta-analysis aimed at summarising health-related quality of life impairment in patients with LSS compared with healthy control groups. Comorbidity of depressive disorders will be investigated as a moderator if significant heterogeneity in the effect sizes is found. Comorbid depressive disorders may be expected to impact on the levels of quality of life because this type of comorbidity is associated with more dysfunctional coping strategies, long-term disability and psychophysiological symptoms interfering with general functioning [31-32].

Some methodological strengths of the review may be highlighted. First, the review is based on a study selection and a data extraction performed by two independent reviewers; in addition, inter-rater agreement will be evaluated and meeting with other reviewers will be carried out. Comorbid psychiatric disorders will not be excluded as they are quite frequent among patients with LSS; in addition, this allows the review to have sufficient external validity. Any research design will be considered as eligible and this may allow additional eligible data to be located and included even if the focus of the paper is not the comparison of health-related quality of life between patients and controls. Moreover, the search strategy is based on the identification of published and unpublished studies. Lastly, another strength is the evaluation of the study's methodological quality through a specific tool.

The review may have important clinical implications: for example, it can highlight the importance of focusing the assessment also on quality of life in patients with LSS to improve prognosis and treatment response, because some psychological interventions have been proven effective for this condition [35].

Since one of the most strongly affected areas of daily life in LSS is the ability to perform work-related activity, a summary of the evidence about depression and impaired quality of life in this condition can suggest that occupational health professionals should assess these outcomes during occupational medicine practice with the aim to improve work-related health and functioning. For example, well informed physician-patient communication in consultations on back pain may prevent deterioration of the LSS and improve patients' perceived health status [57]. Our paper may suggest that occupational medicine practice may be improved by the use of instruments aimed at a timely detection of depression and perceived health status impairment.

Finally, potential limitations of the review regard a small number of studies in the literature and the heterogeneity of the studies in terms of the instruments used to assess health-related quality of life and the difference in the definitions used to conceptualize this construct. Another potential problem is that some studies will not report on the data necessary to code the moderators (e.g., they will not explicitly state the percentage of depressive disorders) or the authors are not available to provide them.

In conclusion, this is a protocol of the first systematic review of health-related quality of life in patients with LSS. A summary of the evidence on this topic may support clinical practice highlighting the importance of the assessment of quality of life and suggesting the use of psychological interventions dedicated to this outcome with the aim of improving patients' quality of life.

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Contributors

FF conceived and designed the study, wrote the first draft of the paper, reviewed the final draft.

AC conceived and designed the study, critically reviewed the first draft of the paper, reviewed the final draft.

RG critically reviewed the last draft of the paper.

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VFM conceived and designed the study, critically reviewed the first draft of the paper.

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References

[1] DuBois CM, Beach SR, Kashdan TB, Nyer MB, Park ER, Celano CM et al. Positive psychological attributes and cardiac outcomes: associations, mechanisms, and interventions. *Psychosomatics* 2012;53:303-318.

[2] Sheldon KM, King L. Why positive psychology is necessary. *American Psychologist* 2001;56:216.

[3] Bullinger M, Anderson R, Cella D, Aaronson N. Developing and evaluating cross-cultural instruments from minimum requirements to optimal models. *Quality of Life Research* 1993;2:451-459.

[4] Castro EM, Van Regenmortel T, Vanhaecht K, Sermeus W, Van Hecke A. Patient empowerment, patient participation and patient-centeredness in hospital care: a concept analysis based on a literature review. *Patient Education and Counseling* 2016;99:1923-1939.

[5] Coluccia A, Fagiolini A, Ferretti F, Pozza A, Goracci A. Obsessive-Compulsive Disorder and quality of life outcomes: protocol for a systematic review and meta-analysis of cross-sectional case-control studies. *Epidemiology, Biostatistics and Public Health* 2015;12:e11037.

[6] Coluccia A, Ferretti F, Fagiolini A, Pozza A. Quality of life in children and adolescents with obsessive–compulsive disorder: a systematic review and meta-analysis. *Neuropsychiatric Disease and Treatment* 2017;13:597-608.

[7] Pozza A, Lochner C, Ferretti F, Cuomo A, Coluccia A. Does higher severity really correlate with a worse quality of life in obsessive–compulsive disorder? A meta-regression. *Neuropsychiatric Disease and Treatment* 2018;14:1013.

[8] Johansson P, Dahlström U, Broström A. Factors and interventions influencing health-related quality of life in patients with heart failure: a review of the literature. *European Journal of Cardiovascular Nursing* 2006;5:5-15.

[9] Leadley RM, Armstrong N, Lee YC, Allen A, Kleijnen J. Chronic diseases in the European Union: the prevalence and health cost implications of chronic pain. *Journal of Pain and Palliative Care Pharmacotherapy* 2012;26:310-325.

[10] World Health Organization. Preamble to the Constitution of the World Health Organization. In Official records of the World Health Organization, No. 2 (p. 100). Geneva: Author. Retrieved from http://whqlibdoc.who.int/hist/official_records/2e.pdf, 1948.

[11] Porcelli B, Pozza A, Bizzaro N, Fagiolini A, Costantini MC, Terzuoli L, Ferretti F. Association between stressful life events and autoimmune diseases: A systematic review and meta-analysis of retrospective case-control studies. *Autoimmunity Reviews* 2015;15:325-334.

[12] Resnick DK, Watters WC, Sharan A, Mummaneni PV, Dailey AT, Wang JC et al. Guideline update for the performance of fusion procedures for degenerative disease of the lumbar spine. Part 9: lumbar fusion for stenosis with spondylolisthesis. *Journal of Neurosurgery Spine* 2014;21:54-61.

[13] Lurie J, Tomkins-Lane C. Management of lumbar spinal stenosis. *BMJ* 2016 4;352:6234.

[14] Konno S, Hayashino Y, Fukuhara S, Kikuchi S, Kaneda K, Seichi A et al. Development of a clinical diagnosis support tool to identify patients with lumbar spinal stenosis. *European Spine Journal* 2007;16:1951-7.

[15] Spengler DM. Degenerative stenosis of the lumbar spine. *J Bone and Joint Surgery American Volume* 1987;69:305-308.

[16] Kreiner DS, Shaffer WO, Baisden JL, Gilbert TJ, Summers JT, Toton JF et al. An evidence-based clinical guideline for the diagnosis and treatment of degenerative lumbar spinal stenosis (update). *Spine Journal* 2013;13:734-43.

[17] Cowley P. Neuroimaging of Spinal Canal Stenosis. *Magnetic Resonance Imaging Clinics of North America* 2016;24:523-539.

[18] Katz JN, Dalgas M, Stucki G, Katz NP, Bayley J, Fossel AH et al. Degenerative lumbar spinal stenosis. Diagnostic value of the history and physical examination. *Arthritis Rheumatology* 1995;38:1236–41.

[19] Katz JN, Harris MB. Clinical practice. Lumbar spinal stenosis. *New England Journal of Medicine* 2008;358:818-25.

[20] Rainville J, Childs LA, Peña EB, Suri P, Limke JC, Jouve C et al. Quantification of Walking Ability in Subjects with Neurogenic Claudication from Lumbar Spinal Stenosis – A Comparative Study. *Spine Journal* 2012;12:101-9.

[21] Kent DL, Haynor DR, Larson EB, Deyo RA. Diagnosis of lumbar spinal stenosis in adults: a meta-analysis of the accuracy of CT, MR, and myelography. *American Journal of Roentgenology* 1992;158:1135-44.

[22] Otani K, Kikuchi S, Yabuki S, Igarashi T, Nikaido T, Watanabe K et al. Lumbar spinal stenosis has a negative impact on quality of life compared with other comorbidities: an epidemiological cross-sectional study of 1862 community-dwelling individuals. *The Scientific World Journal* 2013:590652.

[23] Saban KL, Penckofer SM, Androwich I, Bryant FB. Health-related quality of life of patients following selected types of lumbar spinal surgery: A pilot study. *Health Quality of Life Outcomes* 2007;5:71.

[24] Skolasky RL, Mackenzie EJ, Riley LH, Wegener ST. Psychometric properties of the Patient Activation Measure among individuals presenting for elective lumbar spine surgery. *Quality of Life Research* 2009;18:1357-1366.

[25] Von Korff M, Gruman J, Schaefer J, Curry SJ, Wagner EH. Collaborative management of chronic illness. *Annals of Internal Medicine* 1997;127:1097–1102.

[26] Sekiguchi M, Yonemoto K, Kakuma T, Nikaido T, Watanabe K, Kato K et al. Relationship between lumbar spinal stenosis and psychosocial factors: a multicenter cross-sectional study (DISTO project). *European Spine Journal* 2015;24:2288-2294.

[27] Levy HI, Hanscom B, Boden SD. Three-question depression screener used for lumbar disc herniations and spinal stenosis. *Spine* 2002;27:1232-1236.

[28] Sinikallio S, Aalto T, Airaksinen O, Herno A, Kröger H, Savolainen S et al. Depression and associated factors in patients with lumbar spinal stenosis. *Disability Rehabilitation* 2006;28:415-422.

[29] Coronado RA, George SZ, Devin CJ, Wegener ST, Archer KR. Pain sensitivity and pain catastrophizing are associated with persistent pain and disability after lumbar spine surgery. Archives of Physical Medicine and Rehabilitation 2015;96:1763-1770.

[30] McKillop AB, Carroll LJ, Battié MC. Depression as a prognostic factor of lumbar spinal stenosis: a systematic review. Spine 2014;14:837-846.

[31] Sinikallio S, Aalto T, Airaksinen O, Lehto SM, Kröger H, Viinamäki H. Depression is associated with a poorer outcome of lumbar spinal stenosis surgery: a two-year prospective follow-up study. Spine 2011;36:677-682.

[32] Sinikallio S, Aalto T, Koivumaa-Honkanen, H, Airaksinen O, Herno A, Kröger H et al. Life dissatisfaction is associated with a poorer surgery outcome and depression among lumbar spinal stenosis patients: a 2-year prospective study. European Spine Journal 2009;18:1187-1193.

[33] Stienen MN, Smoll NR, Joswig H, Snagowski J, Corniola MV, Schaller K, et al. Influence of the mental health status on a new measure of objective functional impairment in lumbar degenerative disc disease. *The Spine Journal* 2017;17:807-813.

[34] Stienen N, Ho AL, Staartjes VE, Maldaner N, Veeravagu A, Desai A, et al. Objective measures of functional impairment for degenerative diseases of the lumbar spine: a systematic review of the literature. *The Spine Journal* 2019;19:1276-1293.

[35] Archer KR, Devin CJ, Vanston SW, Koyama T, Phillips SE, George et al. Cognitive-behavioral–based physical therapy for patients with chronic pain undergoing lumbar spine surgery: a randomized controlled trial. *Journal of Pain* 2016;17:76-89.

[36] Rolving N, Sogaard R, Nielsen CV, Christensen FB, Bünger C, Oestergaard LG. Preoperative cognitive-behavioral patient education versus standard care for lumbar spinal fusion patients: economic evaluation alongside a randomized controlled trial. *Spine* 2016;41:18-25.

[37] Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ* 2015;349:g7647.

[38] Birkmeyer NJ, Weinstein JN, Tosteson AN, et al. Design of the Spine Patient outcomes Research Trial (SPORT). *Spine* 2002;27:1361-1372.

[39] Ware JE, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). *Medical Care* 1992;30:473–483.

[40] American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed. Washington, DC: American Psychiatric Association, 2000.

[41] American Psychiatric Association. Diagnostic and statistical manual of mental disorders (5th ed.). Washington, DC: American Psychiatric Association, 2013.

[42] Diebo BG, Lavian JD, Murray DP, Liu S, Shah NV, Beyer GA et al. The impact of comorbid mental health disorders on complications following adult spinal deformity surgery with minimum 2-year surveillance. *Spine* 2018;43:1176-1183.

[43] Cohen J. A coefficient of agreement for nominal scales. *Educational and Psychological Measurement* 1960;20:37-46

[44] Wood, JA. Methodology for dealing with duplicate study effects in a meta-analysis. *Organizational Research Methods* 2008;11;79-95.

[45] Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. *BMC Medical Research Methodology* 2014;14:135.

[46] Pratt RK, Fairbank JC, Virr A. The reliability of the Shuttle Walking Test, the Swiss Spinal Stenosis Questionnaire, the Oxford Spinal Stenosis Score, and the Oswestry Disability Index in the assessment of patients with lumbar spinal stenosis. *The Spine Journal* 2002;27:84-91.

[47] Hawker GA, Mian S, Kendzerska T, French M. Measures of adult pain: Visual Analog Scale for pain (VAS pain), Numeric Rating Scale for pain (NRS pain), McGill Pain Questionnaire (MPQ), short-form, McGill Pain Questionnaire (SF-MPQ), Chronic Pain Grade Scale (CPGS), short form-36 Bodily Pain Scale (SF-36 bps), and measure of intermittent and constant osteoarthritis pain (ICOAP). *Arthritis Care & Research* 2011;63:S240-S252.

[48] Pozza A, Coluccia A, Kato T, Gaetani M, Ferretti F. The 'Hikikomori' syndrome: worldwide prevalence and co-occurring major psychiatric disorders: a systematic review and meta-analysis protocol. *BMJ Open* 2019;9:e025213.

[49] Wells GA, Shea B, O'Connell D et al. The Newcastle–Ottawa Scale (NOS) for assessing the quality of non-randomised studies in meta-analyses. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp, 2000.

[50] Borenstein M, Hedges LV, Higgins JPT, Rothstein HR. Introduction to meta-analysis. Chichester: John Wiley & Sons, 2009.

[51] Cohen J. Statistical power analysis for the behavioural sciences. 2nd ed. Hillsdale, NK: Erlbaum Ed; 1988.

[52] Hedges LV. Estimation of effect size from a series of independent experiments. *Psychological Bulletin* 1982:92:490-499.

[53] Duval S, Tweedie R. Trim and fill: a simple funnel-plot–based method of testing and adjusting for publication bias in meta-analysis. *Biometrics* 2000;56:455-463.

[54] Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003;327:557-60.

[55] Valentine JC, Pigott TD, Rothstein HR. How many studies do you need? A primer on statistical power for meta-analysis. *Journal of Educational and Behavioral Statistics* 2010;35:215-247.

[56] Fu R, Gartlehner G, Grant M, Shamliyan T, Sedrakya A, Wilt TJ, et al. Conducting quantitative synthesis when comparing medical interventions: AHRQ and the Effective Health Care Program. *Journal of Clinical Epidemiology* 2011;64:1187-1197.

[57] Voigt-Radloff S, Schöpf AC, Boeker M, Frank L, Farin E, Kaier K, et al. Well informed physician-patient communication in consultations on back pain–study protocol of the cluster randomized GAP trial. *BMC Family Practice* 2019;20:33.

Supplementary file.

Search strategy example in PubMed
"Quality of Life"[MeSH], OR "Health-Related Quality of Life"[MeSH] OR "HRQOL"[Title/Abstract] OR "Health-Related Quality Of Life"[Title/Abstract] OR "Life Quality"[Title/Abstract] AND "Spinal Stenosis"[MeSH] OR "Constriction, Pathologic"[Title/Abstract] OR "Lumbar Vertebrae"[Title/Abstract] OR "Spinal Canal"[Title/Abstract] OR "Spinal Diseases"[Title/Abstract]

PRISMA-P checklist indicating page numbers where the information can be found.

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