Systematic Reviews/Meta-analyses

The influence of comorbidities on the treatment outcome in symptomatic lumbar spinal stenosis: A systematic review and meta-analysis

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ABSTRACT

Background: Lumbar spinal stenosis (LSS) affects mainly elderly patients. To this day, it is unclear whether comorbidities influence treatment success. The aim of this systematic review and meta-analysis was to assess the impact of comorbidities on the treatment effectiveness in symptomatic LSS.

Methods: We conducted a systematic review and meta-analysis and reviewed prospective or retrospective studies from Medline, Embase, Cochrane Library and CINAHL from inception to May 2020, including adult patients with LSS undergoing surgical or conservative treatment. Main outcomes were satisfaction, functional and symptoms improvement, and adverse events (AE). Proportions of outcomes within two subgroups of a comorbidity were compared with risk ratio (RR) as summary measure. Availability of ≥3 studies for the same subgroup and outcome was required for meta-analysis.

Results: Of 72 publications, 51 studies, mostly assessing surgery, there was no evidence reported that patients with comorbidities were less satisfied compared to patients without comorbidities (RR 1.06, 95% confidence interval (CI) 0.77 to 1.45, I² 94%), but they had an increased risk for AE (RR 1.46, 95% CI 1.06 to 2.01, I² 72%). A limited number of studies found no influence of comorbidities on functional and symptoms improvement. Older age did not affect satisfaction, symptoms and functional improvement, and AE (age >80 years RR 1.22, 95% CI 0.98 to 1.52, I² 60%). Diabetes was associated with more AE (RR 1.72, 95% CI 1.19 to 2.47, I² 58%).

Conclusion: In patients with LSS and comorbidities (in particular diabetes), a higher risk for AE should be considered in the treatment decision. Older age alone was not associated with an increased risk for AE, less functional and symptoms improvement, and less treatment satisfaction.

Introduction

In lumbar spinal stenosis (LSS) degenerative processes lead to a narrowing of the lumbar spine resulting in a compression of neurovascular structures [1-3]. Typical symptoms include neurogenic claudication or radiculopathy [1-3]. In symptomatic patients, LSS results in disability, limited mobility [4], which affects the physical, psychological and social health [5-7]. Degenerative LSS is the most common reason for spinal surgery in the elderly population [1,2,7-9]. Treatment options include physical therapy, pain medications [1,2,10] and in selected cases epidural injections [1,2,11], and surgery to improve function and relief of pain [1,2,10,12,13].

In the ageing population multimorbidity, defined as the presence of two or more chronic diseases, is common [14] and may affect treatment outcome in patients with LSS. Multimorbidity was associated with less favorable functional outcome after surgery [15,16] and with an increased risk for perioperative complications and mortality [9,17,18]. However, results from various studies were conflicting. Whereas some studies showed an increased risk for complications in elderly patients after surgery [8,17-19], others found no influence of age on the risk

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for complications [20-26]. Cardiovascular disease was associated with worse post-surgical outcomes in one study [27], but not in another study [21]. Conflicting results were also found for diabetes [21,22], psychiatric [21,22,28], and musculoskeletal diseases [21,29].

To date, the evidence of the influence of comorbidities on the treatment outcome in patients with LSS undergoing surgical or non-surgical treatments has not been systematically reviewed. Therefore, the aim was to summarize the evidence of the influence of comorbidities on the treatment outcome of patients undergoing treatment for LSS.

Methods

Study design

Systematic review and meta-analysis. We followed the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (PRISMA) [30]. The study protocol has been described previously [7].

Literature search

We systematically searched on May 2, 2020: Medline (Ovid), Embase, the Cochrane Library, and CINAHL. All references from the inception of the database until the search date were considered. Search terms included MeSH terms (Medical Subject Headings) and keywords related to “lumbar spinal stenosis” and “comorbidities” (Appendix 1). We also searched bibliographies of studies, guidelines, and review articles and contacted authors of studies with insufficient details.

Eligibility criteria

Eligible were prospective or retrospective studies with adult patients with degenerative LSS undergoing surgical or conservative treatment. As subgroup analyses require a sufficient sample size to be robust, we included studies with at least 100 patients. All studies were considered in which we had sufficient language proficiency (i.e. English, French, German, Spanish, and Italian). Excluded were studies in patients aged <18 years or less than 100 patients, cross-sectional and case-control studies.

Study selection and data extraction

Two reviewers (AS, AB) independently screened all titles and abstracts, and reviewed all potentially relevant references in full text. Disagreement between the reviewers was discussed and resolved in consensus or by third party arbitration (MW). If there were several publications for the same study, we included publication(s) reporting findings relevant for the research question.

Data collection and data item

One reviewer (AS) extracted information, using a predefined and piloted extraction form. A second reviewer (AB) confirmed the accuracy of extracted data. All data included in the meta-analysis were confirmed by the third reviewer (MW). We extracted information on study characteristics, patients’ characteristics, comorbidities and comorbidity measures, treatments, and outcomes.

Outcomes of interest

The main outcomes of interest were treatment satisfaction, functional and symptoms improvement, and adverse events. Additional outcomes included mortality. All outcome variables were extracted as reported in the original studies and operationalized.

Comorbidities

We extracted information on comorbidity measures (Appendix 2) and comorbidities: disease specific (previous spine surgery, symptom duration), cardiovascular risk factors (age, obesity, smoking), chronic diseases (e.g. cardiovascular, lung, neurologic, or rheumatologic), and psychologic disease. Subgroup definitions were standardized into the most often reported categories: e.g. diabetes/no diabetes, obesity (body mass index (BMI) ≥30kg/m² versus (vs.) <30kg/m²), high comorbidity burden (i.e. American Society of Anesthesiology score (ASA) >3 vs. ≤3, Charlson >1 vs. ≤1, comorbidity score >3 vs. ≤3, presence of diseases/comorbidities vs. no diseases/comorbidities).

Study quality

Two reviewers (AB, AS) independently assessed study quality using Scottish Intercollegiate Guidelines Networks (SIGN) checklists for randomized controlled trials (RCTs) and cohort studies [31]. For each study, internal validity was assessed (yes/no/can’t say/don’t apply) and a global quality assessment assigned according to pre-defined criteria into high, acceptable, or low (Appendix 3). Disagreements were discussed and resolved by consensus or third-party arbitration (MW).

Data synthesis and statistical analysis

We provided a descriptive synthesis of evidence by categorizing findings into strong, weak, or conflicting evidence for or against an influence of a comorbidity. We summarized continuous and categorical variables with number/percentage, mean/standard deviation or median/interquartile range. We reported regression factors with coefficients, 95% confidence intervals (CI) and p-values.

In the meta-analysis, associations of comorbidities with treatment outcomes were analyzed by restricting subsets with the same treatment outcome for surgical or non-surgical treatment. The proportions of the two subgroups were compared with risk ratio (RR) as summary measure. We explored potential publication bias by using funnel plots. Funnel plots were exploratory, as a study could have multiple study arms, thus the study dots in the funnel plot were not independent. We performed meta-analyses in subsets with the same treatment and with specific comorbidity subgroups only, if at least three studies were available. We used random-effects models for pooling RRs due to expected large heterogeneity.

Studies were weighted by the standard error of their estimates, i.e. by sample size. Heterogeneity measures I² and T² were quantified. Results in RRs were visualized in forest plots including the study-specific estimates and their 95% confidence intervals (CI). The statistical analysis was performed in the R programming language [32] using base and analysis-specific packages: Amelia, biostatUZH, dplyr, ggpubr, meta, metaviz, readxl, tableone, xtable.

Results

Study selection

We screened title and abstract of 3244 references and read 157 potentially relevant full texts (Figure 1). In total, 72 publications based on 51 studies (the Spine Patient Outcomes Research Trial (SPORT) study was counted as two studies with a randomized and an observational study arm) were included and analyzed. Main reasons for exclusion were insufficient sample size (n=47), other study population/research question (n=27), study protocol/conference proceedings (n=7), and no language proficiency (n=4, Chinese, Japanese, and Czech).

Baseline characteristics

Two studies were RCTs, 14 prospective observational, and 32 retrospective studies (Table 1). Three studies used mixed methods (retro-
### Table 1
Baseline characteristics.

| Author, year, study number | Design | Setting | Inclusion criteria | Exclusion criteria | Treatment | Follow-up, months | Number of patients(% female) | Age: mean, years (SD) |
|-----------------------------|--------|---------|--------------------|-------------------|-----------|-------------------|------------------------------|----------------------|
| Turner J et al, 2015, [51]  | Randomized controlled trial (RCT) | Lumbar Epidural Steroid Injections for Spinal Stenosis trial (LESS), multicenter study at 16 clinical sites, United States of America (USA). Follow-up data assessed by telephone interview, in-person interview or mailed questionnaires. | Age ≥50 years, confirmed lumbar spinal stenosis (LSS) on computer tomography (CT)/magnetic resonance imaging (MRI); undergoing conservative treatment; average low back/buttock/leg pain while standing/walking/spinal extension in the past week of number rating scale (NRS) ≥5 (0-10); buttock/leg pain worse than back pain; Roland Morris Disability Questionnaire (RMDQ) physical disability score ≥7. | Epidural steroid injection (ESI) ≤6 months, previous lumbar spine surgery; cognitive impairment; fibromyalgia; chronic widespread pain; lower extremity amputation; Parkinson’s disease; head injury; stroke, other neurologic conditions; severe vascular, pulmonary or coronary artery disease; spinal instability; osteoporosis, metastatic cancer, excessive alcohol consumption/drug use; pregnancy; pain with internal rotation of hip; active infection; allergy to local anesthetic, steroid or contrast. | Double blind epidural steroid + lidocaine injections | 1.5 | 400 (45) | Median 68 |
| Friedly J et al, 2014, [67]  | Subgroup analysis with central canal stenosis | | | | 1.5 | 386 (57) | 68.1 (10) |
| Friedly J et al, 2018, [68]  | Subgroup analysis: degree of cortisol suppression and risk factors | | | | 0.75 | 307 (n.r.) | N.r. |
| Lurie JD et al, 2015, [69]  | Secondary analysis of a RCT and cohort study | Spine Patient Outcomes Research Trial (SPORT): RCT and cohort study; patient enrollment in 13 centers across 11 US-States 2000-2004, USA. | Adults (age ≥18 years), LSS group: neurogenic claudication and/or radicular leg symptoms; LSS confirmed on imaging (≥1 level(s)); ongoing symptoms ≥12 weeks without sufficient improvement after non-surgical interventions. | Degenerative spondylolisthesis, cauda equina syndrome, progressive symptoms with urgent surgery, overall health that makes spine surgery too life threatening; dramatic improvement with non-surgical care; pregnancy; active malignancy; current fracture, infection, significant deformity of the spine; previous lumbar spine surgery; unable to complete questionnaires or follow-up. | RCT-group: surgery (posterior decompression laminectomy) or conservative treatment (physical therapy (PT), education, non-steroidal anti-inflammatory drugs (NSAID), ESI, spinal manipulation). Cohort study: surgery or conservative treatment | 96 | 306 (37) | 61.1 (10.4) |
| Gerling M et al, 2016, [70]  | Subgroup analysis: risk factors for reoperation in patients treated surgically for LSS | | | | Surgery (posterior decompression laminectomy) | | 96 | 417 (39) | 63.3 (11.35) |

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### Table 1 (continued)

| Author, year, study number | Design | Setting | Inclusion criteria | Exclusion criteria | Treatment | Follow-up, months | Number of patients(% female) | Age: mean, years (SD) |
|----------------------------|--------|---------|--------------------|-------------------|-----------|------------------|-----------------------------|-----------------------|
| Freedman M et al, 2011, [59] 2.3 | Multicenter cohort study | Maine Lumbar Spine Study, community-based practices in Maine, USA; recruitment 1990-1992, interviews (baseline), mailed questionnaires (follow-up) | Subgroup analysis: influence of diabetes on the outcome after treatment for LSS | Spondylolysis and isthmic spondylolisthesis | Surgical or conservative treatment | 48 | 627 (40) | 65.75 (10.65) |
| McGuire K et al, 2014, [41] 2.4 | Multicenter prospective observational study | Four referral centers, Brigham and Women’s Hospital, and Beth Israel Hospital in Boston, University of Vermont and University of Iowa Hospitals and Clinics, USA. Baseline/follow-up questionnaires by mail and medical records | Subgroup analysis: influence of extreme obesity (BMI ≥35 kg/m²) on outcomes of treatment for LSS | | Surgical or conservative treatment | 48 | 634 (39) | 63.47 (10.87) |
| Rihn J et al, 2015, [71] 2.5 | Single center observational study | Multicenter | Subgroup analysis in old age (<80 years compared to ≥80) | | Surgical or conservative treatment | 48 | 1235 (54) | 73.35 (6.4) |
| Rihn J et al, 2012, [72] 2.6 | Single center observational study | Multicenter | Subgroup analysis: obesity (body mass index (BMI) > 30 kg/m²) compared with non-obese (BMI ≤30) | | Surgical or conservative treatment | 48 | 634 (39) | 64.25 (11.35) |
| Radcliff K et al, 2005, [74] 3 | Multicenter cohort study | Multicenter | Subgroup analysis: symptom duration | | | | | |
| Atlas SJ et al, 2011, [73] 2.7 | Multicenter | Multicenter | | | | | | |
| Katz JN et al, 1995, [27] 4.1 | Multicenter | Multicenter | Subgroup analysis: symptom duration | | | | | |
| Katz JN et al, 1995, [38] 4.2 | Multicenter | Multicenter | | | | | | |
| Herron L et al, 1991, [75] 5 | Multicenter | Multicenter | | | | | | |

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Table 1 (continued)

| Author, year, study number | Design                  | Setting                                                                 | Inclusion criteria                                                                                                                                                                                                 | Exclusion criteria                                                                 | Treatment                                                                                       | Follow-up, months | Number of patients(% female) | Age: mean, years (SD) |
|---------------------------|-------------------------|-------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|-------------------|-----------------------------|------------------------|
| Ilyas H et al, 2019, [54]  | Single center retrospective chart review | Cleveland Clinic, Cleveland, USA, Baseline and follow-up data from medical records | All patients with diagnosis of LSS with claudication undergoing surgery between 01/2014 and 12/2015                                                                                                           | Age <18 years, spinal tumor or infection, anterior lumbar surgery, planned elective readmission or reoperation | Posterior lumbar decompression (with/without fusion)                                           | 3                 | 1592 (45.5)                 | 67.4 (10.1)             |
| Lubelski D et al, 2015, [52]  | Single center retrospective chart review | Cleveland Clinic Center for Spine Health, Cleveland, USA, Baseline chart review; outcome measures prospectively collected in a database | Age ≥18 years; diagnosis of LSS (gluteal and/or lower extremity pain and/or fatigue with/without back pain, symptoms aggravated by upright exercise or position-induced neurogenic claudication and relief with forward flexion, sitting or recumbency) undergoing conservative treatment | Previous spine surgery or treatment with a membrane stabilizing agent (MSA); spinal tumors or fracture; cauda equina syndrome; foot drop; epilepsy; renal failure; not participating in Quality of Life outcome data collection | Membrane stabilizing agents (MSA): gabapentin, pregabalin (treatment duration and drug dose not reported) | Mean 6 (range 2-12) | 1346 (49)                   | 66.3 (10.1)             |
| Javalkar V et al, 2010, [76]  | Single center retrospective chart review | Department of Neurosurgery, Louisiana State University Health Sciences Center, Shreveport, Louisiana, USA; analysis of reoperation after surgery | Patients aged ≥18 years with symptomatic, confirmed LSS (MRI/x-rays) undergoing treatment for LSS after insufficient improvement during conservative treatment (epidural/facet/foraminal injections, PT) | N.r.                                                                                                                                   | Surgery (decompression +/- fusion)                                                                 | Undefined         | 335 (50)                    | Mean patients with re-operation: 60.8 (range 33-83) |
| Movassaghi K et al, 2019, [77]  | Single center retrospective chart review | Department of Orthopedic surgery, Rush University Medical Center, Chicago, USA | Age <18 years, previous lumbar surgery, herniated disc, follow-up <3 months | Decompressive laminectomy                                                                                                                   | Mean 24.1 (range 3-78)                                                                 | 210 (24.3)        | 54.1 (16.3)                 |                        |
| Ragab A et al, 2003, [78]  | Single center retrospective chart review | Spine Institute, Orthopedic surgery Department, Case Western Reserve University, Cleveland, USA, Medical charts review, follow-up questionnaire by mail | Age ≥70 years, follow-up ≥2 years (out of 1152 patients who underwent lumbar spinal surgery, 118 patients met these criteria) | Surgery (decompression +/- fusion)                                                                                                           | Mean 84 (range 24-168)                                                                 | 118 (56)          | 74 (range 70-101)          |                        |

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| Author, year, study number | Design | Setting | Inclusion criteria | Exclusion criteria | Treatment | Follow-up, months | Number of patients(% female) | Age: mean, years (SD) |
|----------------------------|--------|---------|-------------------|--------------------|-----------|------------------|-----------------------------|------------------------|
| Li G et al, 2008, [35] 11  | Database study | National Inpatient Sample (NIS) hospital discharge database (Agency for Healthcare Research and Quality), USA | All patients with primary diagnosis of LSS undergoing lumbar laminectomy without fusion from 1993 to 2002 | N.r. | Surgery (lumbar laminectomy) | Within the hospitalization time | 471215 (50) | 67 |
| Deyo R et al, 2010, [8] 12 | Insurance claims database analysis (Medicare) | Medicare claims data analysis (Medicare Provider Analysis and Review database (MedPAR)), 2002-2007, USA | Age ≥65 years; primary diagnosis of LSS or “spondylogenic compression of lumbar spinal cord”; all surgical procedure: patient identified by surgical procedure codes (international classification of disease 9th edition (ICD-9)) | Any diagnosis as cancer, vehicular accident, spinal infection, inflammatory spondyloarthropathy, vertebral fracture or dislocation or cervical or thoracic spine procedures | Surgery (decompression, simple fusion, complex fusion and any combination) | 1 | 32152 (54) | 75 |
| Drazin D et al, 2017, [55] 13 | Medicare claims data analysis, MedPAR data from 2005-2011 USA | Age ≥65 years; LSS diagnosis; patient identification by LSS diagnosis code (ICD-9) | Death during the index hospitalization; cancer <6 months prior to diagnosis; back surgery <1 year prior to the index hospitalization Cervical/thoracic spine diagnosis; cancer; spinal infection, inflammatory spondylitis; fracture; vehicular trauma; other surgical procedure; living outside the US; Medicare eligibility based on end-stage renal disease or disability; <12 months Medicare eligibility | Surgery (laminectomy or fusion) | Mean 40.4 (SD 23.5) | 12807 (58) | 75.4 (5.9) |
| Ciol M et al, 1996, [17] 14 | Medicare and National Hospital Discharge Survey (NDHS, for all acute-care non-federal hospitals in the USA) data | Age ≥65 years with primary diagnosis for spinal stenosis (ICD-9 for spinal stenosis or “spondylogenic compression of the lumbar spine”) undergoing surgery in 1985 or 1989 | | Surgery (decompression with or without fusion) | 36 (1989 cohort), 84 (1985 cohort) | 28915 (59) | 73.35 (5.35) |
| Lad S et al, 2013, [79] 15 | Insurance claims database analysis | Patient-level data from Medicaid and private insurance (Thomson Reuter’s MarketScan), USA | Primary diagnosis of LSS; laminectomy or fusion between 01-2000 and 12-2009; patient identification using procedure codes (current procedural terminology 4th edition (CTP-4) and international classification of disease 9th edition, clinical modification (ICD-9-CM)) | | Surgery (laminectomy or fusion) | 24 | 28462 (52) | 56 (8) |

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| Author, year, study number | Design | Setting | Inclusion criteria | Exclusion criteria | Treatment | Follow-up, months | Number of patients(% female) | Age: mean, years (SD) |
|---------------------------|--------|---------|-------------------|-------------------|-----------|-----------------|---------------------------|---------------------|
| Sharma M et al, 2019, [37] 16 | Insurance claims database analysis | MarketScan database from Truven Health Analytics - IBM Watson Health. Claims data from private, Medicaid, Medicare supplemental insurances | Age ≥80 years and older with primary diagnosis of LSS and decompression between 2000-2016 | Age <80 years, no insurance enrollment | Decompression +/- fusion (laminectomy, discectomy, laminec. ectomy, vertebrectomy, corpectomy, foreign body removal or repair of vertebral fracture) | 12 | 5387 (48.3) | 83.1 (2.9) |
| Basques B et al, 2014, [80] 17 | Database study | American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database; ≥370 hospitals, USA | Postoperative diagnosis of LSS (ICD-9) with the primary Current Procedural Terminology code for lumbar laminectomy | Other spinal procedures including lumbar fusion; urgent/emergent surgery; previous evidence of infection | Surgery (decompression) | 1 | 2358 (40) | 66.4 (11.7) |
| Merrill R et al, 2018, [50] 18 | Database study | Surgical database of procedures 2015-2016 performed by 4 surgeons in 1 academic center, USA. Questionnaires collected during clinical visits | Symptomatic LSS (claudication or radiculopathy), age ≥18 years; surgery with lumbar laminectomy without fusion | | Surgery (lumbar laminectomy) | 6 | 111 (51) | 60.0 (1.94) |
| Adogwa O et al, 2012, [81] 19 | Mixed methods (baseline chart review, prospective follow-up interview) | Clinic of Neurosurgery and Orthopedic Surgery and Rehabilitation, Vanderbilt University Medical Center, Nashville, USA | Revision lumbar decompression/instrumented fusion for symptomatic adjacent segment disease, pseudarthrosis, or same-level restenosis; age 18-70 years; no improvement after ≥6 months conservative therapy | Extra-spinal cause of back pain; an active worker's compensation lawsuit; having no wish to take part to follow-up; fractured rods and screws without evidence of nonunion | Revision surgery | 24 | 150 (63) | 57 (22) |
| Held U et al, 2019, [82] 20.1 | Multicenter cohort study | Lumbar stenosis outcome study (LSSOS), Rheumatology/Spine surgery units at 8 hospitals, Switzerland. Baseline/follow-up questionnaires/interview. | Follow-up results 1 year: age ≥50 years, symptomatic LSS (neurogenic claudication) and verified degenerative LSS (MRI/CT) | Cancer, infection, or significant deformity; previous lumbar spine surgery; clinically relevant peripheral artery disease | Treatment according to patient/physician preferences: surgery; non-surgical treatment (analgesics, physiotherapy, +/- lumbar ESI) | 12 | 222 (55) | 74.2 (8.1) |

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Table 1 (continued)

| Author, year, study number | Design | Setting | Inclusion criteria | Exclusion criteria | Treatment | Follow-up, months | Number of patients(% female) | Age: mean, years (SD) |
|----------------------------|--------|---------|-------------------|-------------------|-----------|------------------|-----------------------------|----------------------|
| Held U et al, 2018, [46]   | 20.2   |         | Subgroup analysis: | Exclusion from     | Surgery (open | 12               | 300 (51)                    | N.r.                 |
|                            |        |         | patients undergoing| analysis: patient did not undergo | posterior lumbar laminotomy +/-fusion) |                 |                             |                      |
|                            |        |         | surgical treatment; +/- previous spine surgery | surgery <6 months after enrollment; not completed follow-up at 12 months |                |                 |                             |                      |
| Fekete T et al, 2015, [83] | 20.3   |         | Subgroup analysis: | Surgery (first-time decompression without fusion) |                | 6                | 281 (52)                    | 75.0 (8.7)           |
|                            |        |         | ESI prior to surgical/non-surgical intervention | or conservative treatment (PT, oral analgesics) |                |                 |                             |                      |
| Burgstaller J et al, 2016, | 20.4   |         | Subgroup analysis in patients undergoing surgery: influence of obesity on postoperative outcome | Diagnosis of diabetes mellitus |                | 12               | 166 (48)                    | Median 74 (IQR 12)   |
| [64]                       |        |         |                  | Surgery (open posterior lumbar laminectomy or laminotomy (no instrumentation)) |                |                 |                             |                      |
| Burgstaller J et al, 2017,| 20.5   |         | Subgroup analysis in patients undergoing surgery: influence of pre- and postoperative fear avoidance beliefs on post-surgical pain and disability | Surgery (first-decompression only) |                | 12               | 234 (51)                    | Median 75.0 (IQR 68, 80) |
| [53]                       |        |         |                  |                  |                |                 |                             |                      |
| Ulrich NH et al, 2015, [20]| 20.6   |         | Subgroup analysis in patients aged >80 years undergoing surgery (compared to <80 years) |                  | Surgery (open posterior lumbar laminectomy or laminotomy (no instrumentation)) | 12               | 93 (39)                     | 78.0 (2.6)           |
| Aalto T et al, 2012, [40]  | 21.1   | Single center cohort study | Clinic of Orthopedics and Neurosurgery at Kuopio University Hospital, Kuopio, Finland. Baseline and follow-up questionnaires | Surgery for degenerative, symptomatic LSS; (back/buttock/lower extremity pain); radiographic evidence of cauda equina compression +/- exiting nerve roots; insufficient improvement after conservative treatment. Preoperative predictors for post-surgical outcome at 3 months [43] and 12 months [40] follow-up | Emergency spinal operation precluding recruitment and protocol investigations; failures in cooperation; MRI contraindications | 24               | 102 (58)                    | N.r.                 |
| Sinikallio S et al, 2007   | 21.2   |        |                  |                  | Surgery (open or microscopic decompression) |                |                             |                      |
| [43]                       |        |        |                  |                  |                |                 |                             |                      |
| Tuomainen I et al, 2018,  | 21.3   |        |                  |                  |                | 120              | 72 (60)                     | 68.5 (10.9)          |
| [46]                       |        |        |                  |                  |                |                 |                             |                      |
| Pakarinen M et al, 2014,   | 21.4   |        |                  |                  |                |                 |                             |                      |
| [85]                       |        |        |                  |                  |                |                 |                             |                      |
| Sinikallio S et al, 2011   | 21.5   |        |                  |                  |                |                 |                             |                      |
| [86]                       |        |        |                  |                  |                |                 |                             |                      |

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| Author, year, study number | Design | Setting | Inclusion criteria | Exclusion criteria | Treatment | Follow-up, months | Number of patients (gender) | Age: mean, years (SD) |
|---------------------------|--------|---------|--------------------|-------------------|-----------|-------------------|-----------------------------|----------------------|
| Airaksinen O et al, 1997, [22] 22 | Mixed methods (chart review baseline, follow-up interview) | Department of Surgery, Kuopio University Hospital, Kuopio, Finland | Surgery for LSS between 1974 and 1987 | Nr. | Surgery (decompression) | Mean 52 | 438 (42) | 53 (9.5) |
| Jakola A et al, 2010, [24] 23 | Single center cohort study | Department of Neurosurgery, St. Olavs Hospital, Trondheim, Norway | Age ≥70 years, isolated LSS undergoing conventional decompression laminectomy | Radiological signs of instability (spondylolisthesis) considered for fusion procedure | Surgery (decompression) | 12 | 101 (50) | 75.3 |
| Guigui P et al, 2002, [87] 24 | Single center prospective observational study | Orthopedic/Surgery Unit, Beaujon Hospital, Clichy, France | Patients undergoing surgery for LSS at hospital of Beaujon from 1998 to 2000 | Patients with a deviation of the spine (>20°) in the frontal or sagittal plane | Surgery (decompression, and/or fusion) | 12 | 306 (55) | 60 (range 22-90) |
| Ferrero E et al, 2018, [88] 25 | Single center prospective observational study | Department of orthopedic surgery, Hôpital européen Georges-Pompidou, Paris, France | LSS diagnosis based on clinical and imaging studies (CT/MRI; ≥1 level(s) narrowing of the central spinal canal [area <100mm2], a foraminal diameter or lateral recess diameter <3mm); neurogenic claudication and/or signs of chronic neurogenic compression | Previous spinal surgery; coronal Cobb angle ≥10°; other disease causing polyneuropathy; LSS secondary to tumor or infection; language limitations | Unspecified surgery | 12 | 250 (57) | 65.6 (12) |
| Papavero L et al, 2009, [89] 26 | Single center prospective observational study | Spine Surgery Center, Eilbek Medical Center, Hamburg, Germany | Baseline/outcome data assessed by independent observer | Mobile vertebral slip; previous surgery at one of the stenotic levels | Surgery (microsurgical bilateral decompression using unilateral laminotomy) | 12 | 165 (50) | 69.27 |
| Costa F et al, 2007, [90] 27 | Single center retrospective chart review | Department of Neurosurgery, Milan, Italy | Patients with confirmed single/multilevel LSS (CT/MRI) undergoing surgery; neurogenic claudication or radiculopathy; failure of conservative treatment with NSAID, corticosteroids, and physiotherapy for ≥3 months | Segmental instability | Surgery (unilateral laminotomy for bilateral microdecompression) | 30.3 (range 16-53) | 374 (51) | 64.7 (9) |

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| Author, year, study number | Design | Setting | Inclusion criteria | Exclusion criteria | Treatment | Follow-up, months | Number of patients(% female) | Age: mean, years (SD) |
|---------------------------|--------|---------|-------------------|-------------------|-----------|------------------|-----------------------------|---------------------|
| Rillardon L et al, 2003, [91] 28.1 | Single center retrospective chart review | Orthopedic Surgery Clinic, Hospital Beaujon, Clichy, France. Chart review. Additional in-person/phone questionnaire for follow-up | Surgery for symptomatic and confirmed LSS 1990-1992; symptoms: neurogenic claudication/compression of peripheral nerves; analysis of long-term outcome after surgery | Previous spine surgery: scoliosis of ≥20° | Surgery (decompression +/- fusion) | Mean 120 | 105 (66) | 58 (11.3) |
| Lenoir T et al, 2008, [36] 28.2 | | | Analysis on the long-term risk of reoperation after initial surgery between 1989 and 1992 | | | 180 | 262 (56) | 61 (10.8) |
| Aghayev E et al, 2019, [54] 29 | Spine Tango registry (Eurospine) | 38 centers, 10 countries. Pre- and postoperative questionnaires | Age 18-100 years; decompression surgery for LSS 2004-2017, known American Society of Anesthesiologists (ASA) classification, no other spinal pathology | Anterior dynamic stabilization, any previous spine surgery, no pre- or ≥1 postoperative Core Outcome Measure Index (COMI) between 3-30 months available | Surgery (decompression with at least laminotomy, hemi-/laminectomy, partial facet joint resection or interspinous spacer) | Mean 15.6 (10.8-24) | 4504 (46.6) | 67.1 (12) |
| Sobottke R et al, 2017, [23] 30 | | | Age ≥20 years; surgery for LSS 2004-2015; no other spinal pathology; no anterior surgical procedure | No ASA classification available, no pre- or ≥1 postoperative COMI between 3-30 months available | Surgery (open decompression +/- rigid or dynamic stabilization +/-fusion) | Mean 15.8 (8.5) | 4768 (47) | 67.4 (11.9) |
| Kleinstück F et al, 2009, [53] 31 | Spine Center, Schulthess Klinik, Zürich, Switzerland | | Degenerative LSS diagnosed by surgeons (clinical and radiological findings), decompression only (02-2004 to 03-2007); fluent in German/English; ≤3 segments affected | <1-year follow-up; disc herniation; previous surgery at the same level; fusion/stabilization | Surgery (decompression) without fusion | Mean 10.7 (50.4) | 221 (49) | 72.4 (9.4) |
| Iderberg H et al, 2018, [47] 32 | Swespine registry | National spine surgery registry (covers ≥80% of surgical procedures for degenerative lumbar spine disorders), Sweden. Mailed follow-up questionnaires | Patients who underwent surgery for LSS on 1 or 2 adjacent levels during 2008-2012 Analysis of predictors of surgical outcome | No information on case mix variables or without 1-year follow-up data | Surgery (decompression, mostly without fusion) | Mean 12 | 7643 (47) | 66.2 |
| Knutsson B et al, 2013, [92] 33 | | | Age ≥50 years; surgery for LSS 01-2006 to 06-2008. Analysis on influence of obesity (BMI groups: <25, 25-30, >30kg/m²) | No 2-year follow-up; invalid weight/height measures; invalid personal identification number; <50 years | Surgery | 24 | 2633 (43) | 68.67 (8.3) |

(continued on next page)
### Table 1 (continued)

| Author, year, study number | Design | Setting | Inclusion criteria | Exclusion criteria | Treatment | Follow-up, months | Number of patients(%) female | Age: mean, years (SD) |
|----------------------------|--------|---------|--------------------|--------------------|-----------|-------------------|--------------------------|----------------------|
| Sanden B et al, 2011, [44] 34 | DaneSpine registry | DaneSpine database, 3 regional centers in Denmark: Middelfart, Køge, Silkeborg Hospitals, Denmark. Mailed follow-up questionnaires | Age ≥50 years; diagnosis of central LSS; undergoing surgery before 10-2006. Analysis smoking/no smoking | Invalid personal identification number; age <50 years; <2-year follow-up | Surgery | 24 | 4555 (56) | 67.3 (8.55) |
| Strömqvist F et al, 2011, [93] 35 | Mixed methods (baseline chart review, prospective follow-up interview) | Clinic of Neurosurgery at Evangelismos Hospital (4 surgeons), Athens, Greece | Patients aged ≥65 years undergoing laminectomy without fusion for LSS within 1999-2004 | Predominant back pain as preoperative symptom and/or imaging findings implying probable spinal instability or discopathy | Surgery (decompression) | Mean 61 | 125 (55) | 71.3 |
| Keorochana G et al, 2011, [94] 38 | Single center prospective observational study | Department of Orthopedics, Ramathibodi Hospital, Bangkok, Thailand. Database for baseline data, mailed follow-up questionnaires | Patients with symptomatic and confirmed LSS (CT, CT-mycelangiography, or MRI) undergoing surgery; limitation of the functional activities; back, buttock and/or leg pain | Previous surgery for spinal stenosis; not able to complete questionnaires | Surgery (decompression and instrumented fusion) | Mean 2.6 | 158 (82) | 60.3 (range 34-87) |
| Kim HJ et al, 2015, [49] 39 | Single center prospective observational study | Spine Center, Seoul National University College of Medicine and Seoul National University Bundang Hospital, Republic of Korea. Baseline chart review, follow-up structured questionnaires | Age 40-80 years, symptomatic and confirmed (MRI) LSS; undergoing spine surgery between 06-2012 and 04-2013; ≥1 symptom(s): walking intolerance due to neurogenic claudication, pain/numbness/tingling sensation in the buttocks and lower extremities, motor weakness, bladder/bowel dysfunction | History of major psychiatric disorders or peripheral vascular disease; concurrent serious medical condition such as sepsis or cancer | Surgery (decompression with/without fusion) all performed by 1 surgeon | 12 | 157 (66) | 65.7 (9.6) |
| Miyamoto H et al, 2008, [95] 40 | Single center prospective observational study | Department of Orthopedic Surgery, National Hospital Kobe Medical Center, Japan. Baseline clinical assessment, follow-up questionnaires | Patients with LSS who underwent extended in-hospital conservative treatment between 1982 and 1998 after non-surgical outpatient treatments failed | Lumbar disc herniation; osteoarthritis of the knee/hip; spondylolysis; traumatic spinal deformity; cerebrovascular diseases; dementia; previous surgery | Non-surgical treatment (in-bed pelvic traction, body cast in lumbar spine, epidural block, selective nerve root block) | Minimum 60, mean 95 (range 60-216) | 120 (42) | 63.6 (8.2) |

(continued on next page)
### Table 1 (continued)

| Author, year, study number | Design | Setting | Inclusion criteria | Exclusion criteria | Treatment | Follow-up, months | Number of patients(% female) | Age: mean, years (SD) |
|----------------------------|--------|---------|--------------------|-------------------|-----------|-------------------|-----------------------------|----------------------|
| Hara N et al, 2010, [96] 41 | Single center prospective observational study | Department of Orthopedic Surgery, University hospital of Tokyo, Japan. Clinical baseline and follow-up assessment and questionnaires | Surgery for symptomatic and confirmed LSS (plain radiographs, MRI/myelography followed by contrast-enhanced CT scan); leg pain/numbness and/or gait disturbance with no response to conservative therapy ≥3 months | Severe spinal deformity; spondylolysis; post-traumatic stenosis or re-stenosis after prior decompression surgery | Surgery (decompression) | 24 | 89 (37) | 66.3 (11.2) |
| Kim HJ et al, 2008, [97] 42 | Single center retrospective chart review | Orthopedic Surgery Unit (2 surgeons), Yonsei University, Seoul, Korea. Hospital records and national health insurance data Neurosurgery units of 2 university hospitals, Turkey. Chart review and clinical follow-up visit | Surgery for degenerative LSS between 01-2013 and 01-2014; ≥2 levels of laminectomy and facetectomy | N.r. | Surgery (decompression with/without fusion) | Min 12 | 1015 (63) | 60 (n.r.) |
| Yaldiz C et al, 2015, [98] 43 | Single center retrospective chart review | Neurosurgery units of 2 university hospitals, Turkey. Chart review and clinical follow-up visit | Surgery for degenerative LSS between 01-2013 and 01-2014; ≥2 levels of laminectomy and facetectomy | N.r. | Surgery (posterior stabilization) | 1 | 540 (28) | 56.45 (9.81) |
| Gepstein R et al, 2006, [99] 44.1 | Single center retrospective chart review and follow-up interview | Spinal Care Unit, Sapir Medical Center, Kfar-Saba, Israel. Database including baseline in-person interview (structured questionnaire) and follow-up telephone interview | Age ≥65 years; surgery for degenerative LSS between 1990 and 2000 | Patients in whom fusion procedures were performed; spondylolisthesis | Surgery (decompression and/or discectomy) | Mean 41.6 | 298 (51) | 71.4 (5.4) |
| Gepstein R et al, 2004, [100] 44.2 | Subgroup analysis: influence of obesity | Mean 44.8 | 298 (51) | 71.4 (5.4) |
| Shabat S et al, 2011, [101] 44.3 | Subgroup analysis: revision surgery | Mean 64 | 357 (n.r.) | 72 |
| Shabat S et al, 2005, [102] 44.4 | Subgroup analysis: gender | Mean 66 (range 12-125) | 367 (48) | 71.42 (5.4) |
| Arinzon Z et al, 2004, [103] 44.5 | Subgroup analysis: comparison of diabetic/non-diabetic patients | Mean 41 | 124 (48) | 71 (4.8) |
| Arinzon Z et al, 2003, [104] 44.6 | Subgroup analysis: influence of age on surgical outcome | Mean 42.2 | 283 (40) | 73.6 (3.1) |
| Nanjo Y et al, 2013, [105] 45 | Six orthopedic surgery units, Japan | Age ≥40 years; confirmed LSS (physical and radiographic examination); undergoing decompression surgery between 2006-2010 | Age ≤40 years; previous surgery for LSS or locomotor disease ≤1 year; hemodialysis; lumbar disc herniation; spondylolisthesis | Surgery (decompression without fusion) | Mean 14, range 6-60 | 241 (40) | 72.2 (range 45-93) |

(continued on next page)
| Author, year, study number | Design | Setting | Inclusion criteria | Exclusion criteria | Treatment | Follow-up, months | Number of patients(% female) | Age: mean, years (SD) |
|---------------------------|--------|---------|-------------------|-------------------|-----------|------------------|----------------------------|---------------------|
| Kong C et al, 2019, [56] 46 | Single center retrospective chart review | Department of Orthopedics, Beijing Xuanwu Hospital, Capital Medical University, Beijing, China | Department of Orthopedic Surgery, Wakayama, Japan | Patients >70 years with main diagnosis lumbar stenosis with instability +/- spondylolisthesis or scoliosis. | Surgery for symptomatic (neurogenic claudication and/or radicular leg pain with associated neurologic signs) and confirmed (MRI) LSS after failed conservative treatment for ≥3 months | No. | 215 (63.7) | 75.7 (4.6) |
| Minamide A et al, 2017, [104] 47 | Single center retrospective chart review | Department of Orthopedic Surgery, Wajokai, Japan | Patients >70 years with main diagnosis lumbar stenosis with instability +/- spondylolisthesis or scoliosis. | Previous lumbar surgery, malignancy, infection, or trauma | Surgery | No. | 122 (53) | 70.4 (8.0) |
| Choi J et al, 2017, [105] 48 | Single center retrospective chart review | Department of Neurosurgery, Kyung Hee University Hospital, Seoul, Korea | Korean National Health Insurance System (KNHIS) on all national in-/outpatient data, South Korea | Patients >70 years with main diagnosis lumbar stenosis with instability +/- spondylolisthesis or scoliosis. | Surgery for symptomatic (neurogenic claudication and/or radicular leg pain with associated neurologic signs) and confirmed (MRI) LSS after failed conservative treatment for ≥3 months | No. | 116 (57) | 74.3 |
| Lee CK et al, 2018, [61] 49 | Insurance claims database analysis | | Cases with LSS diagnosis codes in KNHIS database, 2005 - 2007 | Cobb angle <10°; missing data (socio-demographic, clinical, or imaging studies); prior spine surgery or trauma; intraoperative complication; incomplete follow-up data | Surgery for symptomatic (neurogenic claudication and/or radicular leg pain with associated neurologic signs) and confirmed (MRI) LSS after failed conservative treatment for ≥3 months | No. | 96 | 64 (8.5) |
| Kim C et al, 2011, [60] 50 | Single center retrospective chart review | | | Lumbar surgery in the preceding 5 years; age ≤20 years; concomitant disease (fracture, neoplasm, infection), spondylolisthesis | Surgery (decompression or fusion) | No. | 11027 (56) | 57.3 (11.8) |
| Yamada K et al, 2018, [106] 51 | Mixed methods (chart review preoperative data, cross-sectional survey) | Department of Orthopedic Surgery, Wajokai Eniwa Hospital, Osaka, Japan (4 spine surgeons) | | Prior spinal surgery, vertebral fracture, spinal malignant neoplasm, spinal infection; age ≤50 years; lack of radiographs | Surgery (decompression alone or with fusion) | No. | 1063 (47) | 66.6 (7.7) |

Abbreviations: SD, standard deviation; N.r., not reported; IQR, interquartile range.
Identification

Records identified through database searching
n = 3175

Records after removal of duplicates
- Medline (n = 1211)
- Embase (n = 379)
- Cochrane Library (n = 49)
- CINAHL (n = 148)
- Total n = 1787

Eligibility

Full-text articles assessed for eligibility
n = 157

Inclusion

Full-text articles included in the qualitative synthesis
n = 72

Studies included in the systematic review
n = 72 publications based on 51 studies

Full-text articles excluded n = 85:
- small sample size <100 patients (n = 47)
- other study population/research question (n = 27)
- other article type (abstract, protocol, n = 7)
- no language proficiency (n = 4)

Records excluded n = 1674

Additional records identified through other sources
n = 44

Follow-up duration ranged from hospital discharge [35] to 180 months [36], sample sizes ranged from 101 [24] to 471215 [35] subjects, and mean age from 53 [22] to 83 [37] years. The treatment type was surgical in 43 studies (84.3%), conservative in three (5.9%), both conservative and surgical in five studies (9.8%). Due to heterogeneous reporting of outcomes and comorbidities, only 37 of 72 publications had in total 170 arms suitable for subgroup analyses.

The quality was high in two RCTs (100%) and acceptable in the other studies (Appendix 3). No study was excluded due to a high risk of bias. Visual inspection of the funnel plot (Appendix 4) was symmetrical.

Studies reported different sets of comorbidities and the prevalence of comorbidities varied widely (Appendix 5, 6): diabetes (7.8% to 37.1%), cardiovascular disease (43.1% to 59.9%), lung disease (1.7% to 26.1%), nonspecific musculoskeletal disorders (1.8% to 55.9%), osteoporosis (6.2% to 35.6%). Neurological diseases (excluded in 16 studies (31.4%)) had a low prevalence (2.1% to 8.0%).

Fig. 1. Study flow.
Table 2
Association of comorbidities with function, symptoms and satisfaction.

| Comorbidity                                      | Function score | Evidence strength for/against association | Symptoms score | Evidence strength for/against association | Satisfaction score | Evidence strength for/against association |
|--------------------------------------------------|----------------|------------------------------------------|----------------|------------------------------------------|--------------------|------------------------------------------|
| Comorbidities, comorbidity measures (CM)         | 3              | weak against                             | 4              | weak for                                 | 1                  | weak against                             |
| Previous spine surgery                           | 3              | conflicting                              | 1              | weak against                             | 1                  | weak for                                 |
| Symptom duration                                 | 3              | weak against                             | 4              | strong against                          | 1                  | weak against                             |
| Body weight                                      | 1              | strong against                          | 0              | weak against                            | 2                  | weak against                             |
| Hypertension                                     | 0              | no evidence                             | 0              | no evidence                             | 0                  | no evidence                              |
| Diabetes                                         | 1              | weak against                             | 2              | weak against                            | 2                  | conflicting                              |
| Cardiovascular disease                           | 1              | conflicting                              | 2              | weak for                                | 1                  | conflicting                              |
| Lung disease                                     | 0              | weak against                             | 0              | weak against                            | 0                  | no evidence                              |
| Depression                                       | 0              | no evidence                             | 0              | no evidence                             | 0                  | no evidence                              |
| Age                                               | 0              | no evidence                             | 0              | no evidence                             | 0                  | no evidence                              |
| Continuous pain                                  | 1              | strong against                          | 0              | strong against                         | 1                  | strong against                           |
| Categorical pain                                 | 1              | strong against                          | 0              | strong against                         | 1                  | conflicting                              |

| Abbreviations: n, number of studies; sign., significant; n.s., not significant. |
| Evidence strength defined as follows: strong: 3 or more studies difference (no effect vs. significant effect), weak: difference of 1-2 studies, conflicting: equal number of studies with or without an effect. |

Predictors for satisfaction

Table 2 provides an overview of studies reporting results for satisfaction, and symptoms and functional improvement. Although one study reported higher satisfaction in patients with comorbidities compared to patients without comorbidities [38], there was no evidence for an association (RR 1.06, 95% CI 0.77 to 1.45; Figure 2).

Older age (>80 years and >75 years) did not influence satisfaction in five studies, whereas one study showed an association of younger age with more satisfaction. Diabetes was associated with lower satisfaction in one study [39], but not in another study [40].

There was a (not significant) trend in obese patients towards less satisfaction after surgery (RR 0.90, 95% CI 0.74 to 1.11), which was comparable for non-surgical treatments in one study [41]. Smoking was associated with less satisfaction in all three studies with an overall RR of 0.86 (95% CI 0.81 to 0.90). Whereas heterogeneity was very high in studies using comorbidity measures (I² > 93.7%) and BMI (I² > 82.4%), heterogeneity was 0% for smoking.

One study assessed the influence of previous lumbar surgery and found a higher satisfaction in patients without previous lumbar operation (odds ratio (OR) 3.65, 95% CI 1.13 to 11.79) [40]. In a registry study, patients with neurologic disease and cancer were less satisfied with surgery [42]. Depression was associated with lower satisfaction rate in one study [43] but not in another study [38]. Findings from individual studies are summarized in Appendix 7.

Predictors for functional and symptoms improvement

Only a limited number of studies assessed clinically relevant functional improvement and provided sufficient information to perform subgroup analyses (Figure 3). Patients with comorbidities seemed to have comparable functional improvement (Figure 3, Table 2) compared to patients without comorbidities. Findings for symptoms improvement showed a weak association of comorbidities with less improvement (Table 2). Most studies were performed using data from the Eurospine registry [25,33,34]. Higher ASA scores were associated with lower improvement rates (Core Outcome Measures Index (COMI) sum-score) [23,33] and global outcome [34].

Older age and obesity were in most studies not associated with worse symptoms and functional improvement. Based on one study [39], diabetes was associated with less clinical meaningful improvement in symptoms (RR 0.76, 95% CI 0.61 to 0.96). Smoking was not associated with functional improvement (RR 0.84, 95% CI 0.62 to 1.13, I² 0%). One study reported that patients who smoked less needed more additional pain medication [44].

Findings for previous spine surgery were conflicting. Whereas three studies found no influence on the Oswestry Disability Index (ODI) [24,40,45], three other studies found less functional improvement [22,46,47]. Previous lumbar surgery was associated with less functional improvement at one year (Spinal Stenosis Measure (SSM) function) [46], more disability (ODI) [47], and good functional outcome (ODI at 4.3 years) [22].

Less cardiovascular comorbidity was only associated with less symptoms at two years [27]. Other factors with conflicting findings on functional improvement based on a few studies were symptom duration, obesity, and rheumatologic disease (see Table 2).

Whereas patients with depression had less functional improvement in four studies of moderate quality and small sample size [27,48-50], this contrasted with three other studies without evidence for depression to influence function [45,46,51]. Particularly the high quality Lumbar Epidural Steroid Injections for Spinal Stenosis trial (LESS) including 400 patients found no evidence that baseline depression scores would influence improvement in the Roland Morris Questionnaire (RMQ) at six weeks [51]. Baseline depression scores seemed to be associated with less symptoms improvement in most studies [46,48,50,52]. Although baseline fear avoidance beliefs (FAB) were not associated with functional improvement [51,53], persisting FAB was associated with less symptoms improvement [53].

Predictors for adverse events (AE)

Overall, 13 studies reported AE (Figure 4). Comorbidities were associated with an increased risk for postoperative complications (RR 1.46, 95% CI 1.06 to 2.01, I² 72%). Patients with comorbidities showed higher rates of overall complications, wound complications, and hospital readmissions.

There was a non-significant trend that older age was associated with an increased risk for complications (age >80 years: RR 1.22, 95% CI 0.98 to 1.52). Diabetes was associated with an increased risk for AE (RR 1.72, 95% CI 1.19 to 2.47) mainly due to increased postoperative and in-hospital complication rates, but not with postoperative wound infections (Appendix 7).
Obesity was associated with an increased risk for surgical site infections [54], and in-hospital complications in one study [41] but not in two other studies [55,56]. Smoking did not influence the risk for AE. Congestive heart failure was associated with increased in-hospital complications [57], and 90-day readmission rate [54]. Ischemic heart disease was associated with an increased risk for in-hospital perioperative complications [57] and surgical site infection [54]. Evidence for the influence of previous spine surgery was conflicting.

**Discussion**

This synthesis of 51 studies revealed an increased risk for adverse events (AE) in patients with comorbidities or higher comorbidity burden compared to patients without comorbidities. Comorbidities did not influence satisfaction, and improvement in function and pain after surgery. Older age alone did not affect satisfaction, symptoms and functional improvement, or the risk of AE. Diabetes was associated with a higher risk for AE and less symptoms improvement with conflicting influence on satisfaction. Other factors that may be associated with less satisfaction were smoking, previous spine surgery, neurological disease, and active cancer disease. There is some indication that patients with depressive symptoms may experience less symptoms improvement.

**Discussion in context of the literature**

Current disease specific treatment guidelines such as the North American Spine Society (NASS) guideline [58] offer only limited guidance on how comorbidities should be considered in the treatment decision. In addition to one study [39] included in the NASS guideline [58] four additional studies identified in this review confirmed an increased risk for AE in patients with diabetes compared to non-diabetic patients [57,59-61].

In the SPORT trial patients with diabetes had an increased rate of postoperative complications [59]. In patients undergoing surgery, dia-
betes did not influence functional and symptoms improvement, and satisfaction [59]. In the current systematic review we observed less symptoms improvement in diabetic patients. One reason for this finding may be that lower extremity symptoms due to LSS may sometimes be difficult to distinguish from diabetic peripheral neuropathy. However, the overall prevalence of diabetes in the studies was low and ranged from 4 to 37% and two studies excluded diabetic patients. Therefore, the full extent of long-term diabetes and diabetic peripheral neuropathy on symptoms improvement may be underestimated.

Further, symptoms due to undiagnosed peripheral arterial disease in patients with diabetes may also reduce the efficacy of surgery for LSS. The prevalence of diagnosed peripheral arterial disease in the studies included in the systematic review was very low (2-11%) and three studies excluded patients with the diagnosis.

We observed conflicting findings for previous spine surgery. Whereas in three studies previous spine surgery did not influence the improvement of function [24,40,45], three other studies observed less functional improvement [22,46,47]. One explanation may be that the proportion of postoperative perineural fibrosis and/or arachnoiditis varies among different study populations [62].

Other spine surgeries (e.g. disc herniation [63]) guidelines discuss an increased risk of preoperative depression, older age, and longer symptom duration with poorer outcomes.

| Author, Year | Endpoint | Treatment | Events (CM) | Events (No CM) |
|--------------|----------|-----------|-------------|---------------|
| Koerlich, 2011 | FI ODI S | 33/54 | 68/104 |
| Aghayev, 2020 | S | 840/999 | 3016/3505 |
| Narjo, 2013 | SI IODA score S | 28/46 | 130/195 |
| Rihn, 2015 | SI S | 32/58 | 498/742 |
| Rihn, 2015 | Non-S S | 15/47 | 95/381 |
| Ahko, 2012 | FI ODI S | 13/20 | 45/92 |
| Koerlich, 2011 | FI ODI S | 24/48 | 77/112 |
| Annin, 2004 | SI MCID VAS S | 38/62 | 51/82 |
| Knutsen, 2013 | FI Walking abil S | 291/806 | 1050/2027 |
| McGuire, 2014 | SI S | 117/183 | 35/295 |
| McGuire, 2014 | Non-S S | 10/98 | 35/123 |
| Ilburgmaker, 2018 | SI BMI F. and S | 2144/46 | 68/122 |
| Koerlich, 2011 | FI ODI S | 7/11 | 46/147 |
| Ahko, 2012 | S | 9/20 | 55/82 |
| Kim, 2015 | FI ODI S | 6/15 | 58/124 |
| RE Model (Q = 1.27, df = 2, p = 0.33; I² = 0%) | |
| Sanden, 2011 | SI Pain medication S | 450/738 | 2605/3797 |
| Arakishin, 1997 | FI ODI S | 46/99 | 227/339 |
| Ahko, 2012 | S | 7/17 | 56/85 |

Fig. 3. Risk Ratio for Functional Improvement and Symptoms Improvement. Risk ratios for outcomes functional improvement (FI) and symptoms improvement (SI) comparing different subgroups in surgical and non-surgical treatment (S and Non-S). Meta-analyses were performed only if at least three studies with the same outcome and treatment were available. Subgroup abbreviations: comorbidity (CM), diabetes mellitus (DM), smoking (SM), previous surgery (PS).
Fig. 4. Risk Ratio for Adverse Events in Different Subgroups.
Risk ratios for outcome adverse events (AE) and different subgroup comparisons in surgical treatment (S). Asterisks in the author column indicates that this study had a different age split. Li and Sharma were split at age 85 and 90, respectively. Meta-analyses were performed only if at least three studies with the same outcome and treatment were available. Subgroup abbreviations: binary comorbidity measure (CM), diabetes mellitus (DM), smoking (SM).

A systematic review published in 2006 [28] assessed preoperative predictors and found cardiovascular disease, depression and higher comorbidity burden to be negative predictors for treatment outcomes after LSS surgery [28]. The conclusion was mainly based on one study [27], which was also included in our review. Despite the frequency of the disease, we identified only one additional study that found in patients with coronary artery disease or heart failure a decreased symptoms improvement [46]. Further, three studies reported an increased rate of AE in patients with cardiovascular disease [54,57,61]. Therefore, cardiovascular disease may be an important factor to consider in the treatment decision.

A systematic review assessed the influence of preoperative depression on treatment outcome in LSS and found a negative influence [64]. For the current review, ten additional studies with a sample size of more than 100 patients were available. Although there was some indication that depression may have a negative impact on symptoms improvement [46,48,50,52], it remains a matter of debate whether preoperative depression is causal or a result of the functional limitation. Two studies observed that depressive symptoms improve with global improvement after spine surgery [65,66], which may indicate that preoperative assessment of depression alone may not be sufficient to fully assess the influence of depression on treatment outcome.
Strengths and limitations

Although we used rigorous and standardized methods to identify all relevant studies, there are several limitations that need to be discussed. Despite a considerable number of studies available for the analysis, only data from 37 studies could be used for the meta-analysis. The findings of the meta-analysis are therefore of exploratory nature and additional studies should provide high-quality evidence to support or refute the findings.

Further, reporting of comorbidities and outcomes was very heterogeneous and not comparable between the studies. Although we aimed to analyze the influence of comorbidities on non-surgical and surgical treatments, only limited number of studies for non-surgical treatments were available. Therefore, the influence of comorbidities on non-surgical treatments remains unclear.

Finally, comorbidities may influence treatment outcome depending on the surgical technique used. Due to the limited number of studies assessed comorbidities and the limited information on the surgical techniques (e.g. open surgery vs. minimal-invasive surgery) that were used, we were unable to address this aspect.

Implications for research

Future studies should report comorbidities of patients in a standardized fashion. In addition, the influence of diabetic peripheral neuropathy and peripheral arterial disease on the treatment outcome in patients undergoing surgery for symptomatic LSS should be assessed. Further, the influence of comorbidities should be assessed for different surgical techniques (e.g. obesity may influence open surgery but not minimally invasive approaches). To assess the impact of comorbidities on treatment outcome, studies need to have sufficient power to assess the treatment effect in subgroups. Further, study outcome assessments should be standardized and comparable. Future studies should assess whether systematic management or improvement of comorbidities preoperatively may influence potential negative factors.

Implications for clinical practice

There was no evidence that age alone influences surgical outcomes for symptomatic LSS. In clinical practice, modifiable prognostic factors that may result in worse treatment outcomes when untreated should be identified and considered. Relevant and potentially modifiable factors identified in this systematic review include diabetes, cardiovascular disease, and smoking. Further, depression and psychological factors may, if they persist, negatively influence treatment outcome [53].

Conclusion

In patients with LSS and comorbidities (particularly diabetes), a higher risk for AE should be considered in the treatment decision. Older age alone does not expose to an increased risk for AE. Elderly patients undergoing surgery for LSS were equally likely to experience functional and symptoms improvement, and to be satisfied.

FDA device/drug status

Not applicable.

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Author’s disclosures

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Affirmation of authorship

All authors had access to the data and a role in writing this manuscript. MW, AB, AS designed the study. AS and AB performed the independent literature screening, data extraction and quality assessment. MW, AB, AS, LH, UH analyzed the data. The first draft of the article was written by MW, AB, AS and revised by ERB, FB, JS, LH, and UH. All authors approved the final version of the article.

Declarations of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.xnsj.2021.100072.
Appendix 1. Search strategy

Tables A1 and A2.

Table A1
Medline – with Epub Ahead of Print, In-process, Other Non-Indexed Citations.

| Step | Search strategy | References |
|------|-----------------|------------|
| 1    | exp Spinal Stenosis/ or ((spinal OR spine or lumbar or root or foraminal) adj3 stenosis),ti,ab. | 8966 |
| 2    | exp Diabetes Mellitus/ or exp Hypertension/ or exp Heart Disease/ or exp Cardiomyopathies/ or exp Cerebrovascular Disorders/ or exp Asthma/ or exp Pulmonary Disease, Chronic Obstructive/ or exp Hyperlipidemias/ or exp Hypercholesterolemia/ or exp Thyroid Diseases/ or exp Arthritis, Rheumatoid/ or exp Mental Disorders/ or exp Neoplasms/ or exp Kidney Diseases/ or exp Liver Diseases/ or exp Osteoporosis/ or (diabetes OR hypertension) OR (high blood pressure) OR arthritia).ti,lab or (((heart or cardiac or cardiovascular or coronary) adj3 (disease OR disorder) OR failure)).ti,lab or (((cerebrovascular or vascular or carotid OR arter) adj3 (disorder OR disease)).ti,lab OR (((mental OR anxiety OR mood or psychological OR sleep) adj3 (disease OR disorder))).ti,lab OR (((kidney OR renal) adj3 (disease OR disorder OR failure))).ti,lab OR (((liver adj3 (disease OR disorder))).ti,lab OR (((asthma OR hyperlipidemia OR hypercholesterolemia OR hypertriglyceridemia OR rheumatoid arthritis OR neoplasm OR cancer OR osteoporosis))).ti,lab. | 8368814 |
| 3    | ((co-occur or co-ocur or coexist or co-occurring) adj3 (disease OR ill OR care OR condition OR disorder OR health OR medication OR symptom OR syndrome)).ti,lab or (((heart or cardiac or cardiovascular or coronary) adj3 (disease OR disorder) OR failure))).ti,lab OR (((cerebrovascular or vascular or carotid OR arter) adj3 (disease OR disorder))).ti,lab OR (((mental OR anxiety OR mood OR psychological OR sleep) adj3 (disease OR disorder))).ti,lab OR (((kidney OR renal) adj3 (disease OR disorder))).ti,lab or (((liver adj3 (disease OR disorder))).ti,lab OR (((asthma OR hyperlipidemia OR hypercholesterolemia OR hypertriglyceridemia OR rheumatoid arthritis OR neoplasm OR cancer OR osteoporosis))).ti,lab | 1142402 |
| 4    | 2 and 3 | 622591 |
| 5    | exp Comorbidity/ or exp Chronic Disease/ or exp "Severity of Illness Index" OR exp risk factors/ or (comorbid OR co-morbid OR multimorbid OR multi-morbid OR multidisease OR multi-disease).ti,lab OR (multiple adj3 (ill OR disease OR condition OR syndrome OR disorder)).ti,lab OR (chronic adj3 (disease OR ill OR care OR condition OR disorder OR health OR medication OR syndrome OR symptom)).ti,lab, or "severity of illness index",ti,ab, or "risk factor",ti,ab | 1868150 |
| 6    | 4 or 5 | 2160985 |
| 7    | 1 and 6 | 1217 |
| 8    | 7 not (animals not humans).sh. | 1195 |
| 9    | 8 not ((exp child OR exp infant OR exp adolescent/) not exp adult/) | 1182 |

Table A2
Embase.

| Step | Search strategy | References |
|------|-----------------|------------|
| 1    | 'lumbar spinal stenosis'/exp OR (((spinal OR spine OR lumbar OR root OR foraminal) NEAR/3 stenosis),ti,ab) | 9969 |
| 2    | 'diabetes mellitus'/exp OR 'hypertension'/exp OR 'heart disease'/exp OR 'myocardial disease'/exp OR 'cerebrovascular disease'/de OR 'asthma'/exp OR 'chronic obstructive lung disease'/exp OR 'hyperlipidemia'/exp OR 'hypercholesterolemia'/exp OR 'thyroid disease'/exp OR 'rheumatoid arthritis'/exp OR 'mental disease'/exp OR 'neoplasm'/exp OR 'kidney disease'/exp OR 'liver disease'/exp OR 'osteoporosis'/exp OR 'diabetes'.ti,lab OR 'hypertens'.ti,lab OR 'high blood pressure'.ti,lab OR 'arthritis'.ti,lab OR (((heart OR cardiac OR cardiovascular OR coronary) NEAR/3 (disease OR disorder) OR failure)).ti,lab OR (((cerebrovascular OR vascular OR carotid OR arter) NEAR/3 (disease OR disorder))).ti,lab OR (((mental OR anxiety OR mood OR psychological OR sleep) NEAR/3 (disease OR disorder))).ti,lab OR DEPRESSION.ti,lab OR SCHIZOPHRENIA.ti,lab OR PSYCHOSIS.ti,lab OR ADDICTION.ti,lab OR (((kidney OR renal) NEAR/3 (disease OR disorder))).ti,lab OR (((liver NEAR/3 (disease OR disorder))).ti,lab) OR (((asthma OR hyperlipidemia OR hypercholesterolemia OR hypertriglyceridemia OR rheumatoid arthritis OR neoplasm OR cancer OR osteoporosis))).ti,lab | 11835749 |
| 3    | (((co-occur or co-occur or coexist or co-exist or multiplicity) adj3 (disease OR ill OR care OR condition OR disorder OR health OR medication OR symptom OR syndrome))).ti,lab OR (((heart or cardiac or cardiovascular or coronary) NEAR/3 (disease OR disorder) OR failure))).ti,lab OR (((cerebrovascular or vascular or carotid OR arter) NEAR/3 (disease OR disorder))).ti,lab OR (((mental OR anxiety OR mood OR psychological OR sleep) NEAR/3 (disease OR disorder))).ti,lab OR DEPRESSION.ti,lab OR SCHIZOPHRENIA.ti,lab OR PSYCHOSIS.ti,lab OR ADDICTION.ti,lab OR (((kidney OR renal) NEAR/3 (disease OR disorder))).ti,lab OR (((liver NEAR/3 (disease OR disorder))).ti,lab) OR (((asthma OR hyperlipidemia OR hypercholesterolemia OR hypertriglyceridemia OR rheumatoid arthritis OR neoplasm OR cancer) OR osteoporosis)).ti,lab | 1612598 |
| 4    | #2 AND #3 | 998846 |
| 5    | 'comorbidity'/exp OR 'chronic disease'/exp OR 'severity of illness index'/exp OR 'risk factor'/exp OR 'comorbid'.ti,lab OR 'co morbid'.ti,lab OR 'multimorbid'.ti,lab OR 'multi-morbid'.ti,lab OR 'multidisease'.ti,lab OR 'multi-disease'.ti,lab OR (((multiple NEAR/3 (ill OR disease OR condition OR syndrome OR disorder))).ti,lab) OR (((chronic NEAR/3 (disease OR ill OR care OR condition OR disorder OR health OR medication OR syndrome OR symptom))).ti,lab) OR (((severity of illness index)).ti,lab OR 'risk factor'.ti,lab | 2093321 |
| 6    | #4 OR #5 | 2621159 |
| 7    | #1 AND #6 | 1278 |
| 8    | #7 NOT ([animals]lim NOT [humans]lim) | 1263 |
| 9    | #8 NOT ([infant]lim OR [child]lim OR [adolescent]lim) NOT ([adult]lim OR [aged]lim) | 1255 |
| 10   | #9 NOT [conference abstract]lim | 863 |

Appendix 2. Description of Comorbidity Measures (CM)

The extracted comorbidity measures were: American Society of Anesthesiologists score (ASA, range 0-5), Cumulative Illness Rating Scale (CIRS, range 0-52 or 0-56), Charlson Comorbidity Index (CCI, range 0-31), Functional Comorbidity Index (FCI, range 0-18), Gagne score (range -2.26), and the Elixhauser index (0-12).
Appendix 3. Quality Assessed with the Scottish Intercollegiate Guidelines Network (SIGN) Methodology Checklist

Assessment criteria: **High quality** (++): yes in ≥50% items and <1 item as “no”, **Acceptable quality** (+): yes in <50% items and ≤50% items “no”. Retrospective and single cohort studies were assigned to the acceptable (+) quality due to their weaker study design. **Low quality** (-): no in >50% items or concerns by reviewers about a high risk of bias (Tables A3 and A4).

| Table A3 Quality of RCTs |
|--------------------------|
| **ID** | **Author** | **Year** | **1.1** | **1.2** | **1.3** | **1.4** | **1.5** | **1.6** | **1.7** | **1.8** | **1.9** | **1.10** | **2.1** | **2.2** | **2.3** |
| 1.1-1.3 | LESS Trial (Lumbar Epidural injections for Spinal Stenosis trial) | 2014-2018 | Y | Y | Y | Y | Y | Y | 3.5% | Y | CS | ++ | Y | Y |
| 2.1-2.5 | SPORT (Spine Patient Outcomes Research Trial) randomized arm | 2011-2016 | Y | Y | CS | DA | Y | Y | DA | Y | CS | ++ | Y | Y |

**Abbreviations:** ID, identification number; Y, yes; N, no; CS, can’t say; DA, does not apply; ++, high quality; +, acceptable; 0, low quality.

1.1 The study addresses an appropriate and clearly focused question.
1.2 The assignment of subjects to treatment groups is randomized.
1.3 An adequate concealment method is used.
1.4 The design keeps subjects and investigators "blind" about treatment allocation.
1.5 The treatment and control groups are similar at the start of the trial.
1.6 The only difference between groups is the treatment under investigation.
1.7 All relevant outcomes are measured in a standard, valid and reliable way.
1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?.
1.9 All the subjects are analyzed in the groups to which they were randomly allocated (often referred to as intention to treat analysis).
1.10 Where the study is carried out at more than one site, results are comparable for all sites.
2.1 How well was the study done to minimize bias?.
2.2 Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention?.
2.3 Are the results of this study directly applicable to the patient group targeted in this guideline?
**Table A4**

Quality of cohort studies.

| ID | Author | Year | 1.1 | 1.2 | 1.3 | 1.4 | 1.5 | 1.6 | 1.7 | 1.8 | 1.9 | 1.10 | 1.11 | 1.12 | 1.13 | 1.14 | 2.1 | 2.2 | 2.3 |
|----|--------|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-------|-------|-------|-------|-----|-----|-----|
| 1  | Aalto S et al. | 2016 | Y   | N   | N   | N   | N   | N   | N   | N   | N   | Y     | Y     | Y     | Y     | Y   | Y   | Y   |
| 2  | North Airaksinen O et al. | 1997 | Y   | Y   | N   | Y   | Y   | Y   | N   | Y   | N   | +     | +     | Y     | Y     | Y   | Y   | Y   |
| 3  | Katz J et al. | 1999 | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y   | N     | N     | Y     | Y     | Y   | Y   | Y   |
| 4  | Herron L et al. | 2001 | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y     | Y     | Y     | Y     | Y   | Y   | Y   |
| 5  | Ilyas G et al. | 2005 | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y     | Y     | Y     | Y     | Y   | Y   | Y   |
| 6  | Liang G et al. | 2008 | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y     | Y     | Y     | Y     | Y   | Y   | Y   |
| 7  | Papavero L et al. | 2009 | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y     | Y     | Y     | Y     | Y   | Y   | Y   |
| 8  | Costa F et al. | 2010 | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y     | Y     | Y     | Y     | Y   | Y   | Y   |
| 9  | Araki Y et al. | 2011 | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y     | Y     | Y     | Y     | Y   | Y   | Y   |
| 10 | Merrill J et al. | 2012 | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y     | Y     | Y     | Y     | Y   | Y   | Y   |
| 11 | Rosenfield N et al. | 2013 | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y     | Y     | Y     | Y     | Y   | Y   | Y   |
| 12 | Costa F et al. | 2014 | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y     | Y     | Y     | Y     | Y   | Y   | Y   |
| 13 | Aalto S et al. | 2015 | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y     | Y     | Y     | Y     | Y   | Y   | Y   |
| 14 | Aalto S et al. | 2016 | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y     | Y     | Y     | Y     | Y   | Y   | Y   |
| 15 | Aalto S et al. | 2017 | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y     | Y     | Y     | Y     | Y   | Y   | Y   |
| 16 | Aalto S et al. | 2018 | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y   | Y     | Y     | Y     | Y     | Y   | Y   | Y   |

**Notes:**

- The table continues on the next page.

-NASSJ: North American Spine Society Journal

-NCS: Not considered significant

-DA: Discrepant analysis

-CS: Considered significant

-+Y: Yes

-N: No
### Table A4 (continued)

| Study | Year | Focused question | Selection of subjects | Assessment | Confounding | Statistical analysis | Overall assessment | Clinical judgment | Applicability |
|-------|------|------------------|-----------------------|------------|-------------|----------------------|------------------|------------------|---------------|
| Iderberg H et al. | 2018 | Y | DA | DA | DA | 40% | DA | Y | DA | CS | Y | Y | CS | Y | Y | + | Y | Y |
| Knutsson B et al. | 2013 | Y | Y | N | DA | 43% | Y | Y | N | Y | Y | CS | N | Y | Y | + | Y | Y |
| Sanden B et al. | 2011 | Y | Y | N | DA | 29% | Y | Y | N | Y | Y | CS | N | Y | Y | + | Y | Y |
| Strömqvist F et al. | 2011 | Y | DA | DA | DA | 22% | DA | CS | DA | N | Y | DA | N | Y | Y | + | Y | Y |
| Paulsen B et al. | 2018 | Y | DA | DA | DA | 22% | Y | Y | DA | N | Y | N | Y | Y | Y | + | Y | Y |
| Boursa T et al. | 2010 | Y | DA | DA | DA | 31% | DA | Y | DA | Y | Y | Y | N | Y | N | + | Y | Y |
| Keorochana G et al. | 2011 | Y | DA | DA | DA | 34% | DA | Y | Y | Y | Y | Y | Y | Y | Y | + | Y | Y |
| Kim HJ et al. | 2015 | Y | DA | DA | DA | 11% | DA | Y | DA | Y | Y | Y | N | Y | Y | + | Y | Y |
| Miyamoto H et al. | 2008 | Y | DA | DA | DA | 30% | DA | Y | DA | CS | Y | Y | N | Y | Y | + | Y | Y |
| Hara N et al. | 2010 | Y | DA | DA | DA | 18% | DA | Y | DA | CS | Y | Y | N | N | Y | + | Y | Y |
| Kim HJ et al. | 2008 | Y | DA | DA | DA | DA | Y | DA | Y | Y | DA | DA | Y | Y | Y | + | Y | Y |
| Yaldiz C et al. | 2015 | Y | DA | DA | DA | DA | Y | DA | N | Y | DA | DA | CS | Y | Y | + | Y | Y |
| Gepstein R et al., Shabat S et al., Arinzon Z et al. | 2011 | Y | DA | DA | DA | DA | Y | DA | N | DA | DA | Y | N | Y | N | + | Y | Y |
| Nanjo Y et al. | 2013 | Y | Y | DA | DA | DA | DA | Y | DA | Y | DA | N | CS | Y | DA | Y | N | + | Y | Y |
| Kong C et al. | 2019 | Y | DA | DA | DA | DA | Y | DA | CS | Y | DA | Y | Y | DA | Y | Y | + | Y | Y |
| Minamide A et al. | 2017 | Y | DA | DA | DA | DA | Y | DA | Y | CS | Y | DA | CS | N | + | Y | Y |
| Choi J et al. | 2017 | Y | Y | DA | DA | DA | DA | Y | N | CS | Y | DA | N | N | N | + | CS | Y |
| Lee CK et al. | 2018 | Y | DA | DA | DA | DA | Y | N | CS | Y | DA | DA | Y | Y | Y | + | Y | Y |
| Kim C et al. | 2013 | Y | DA | DA | DA | DA | Y | DA | N | DA | DA | CS | Y | DA | Y | Y | + | Y | Y |
| Yamada K et al. | 2018 | Y | DA | DA | DA | 48% | DA | Y | DA | Y | DA | Y | Y | Y | Y | + | Y | Y |

Abbreviations: ID, identification number; Y, yes; N, no; CS, can’t say; DA, does not apply; ++, high quality; +, acceptable; 0, low quality.

1.1 The study addresses an appropriate and clearly focused question.
1.2 The two groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation.
1.3 The study indicates how many of the people asked to take part did so, in each of the groups being studied.
1.4 The likelihood that some eligible subjects might have the outcome at the time of enrolment is assessed and taken into account in the analysis.
1.5 What percentage of individuals or clusters recruited into each arm of the study dropped out before the study was completed? Only in prospective studies.
1.6 Comparison is made between full participants and those lost to follow-up, by exposure status.
1.7 The outcomes are clearly defined.
1.8 The assessment of outcome is made blind to exposure status.
1.9 Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome.
1.10 The method of assessment of exposure is reliable.
1.11 Evidence from other sources is used to demonstrate that the method of outcome assessment is valid and reliable.
1.12 Exposure level or prognostic factor is assessed more than once.
1.13 The main potential confounders are identified and taken into account in the design and analysis.
1.14 Confidence intervals are provided.
2.1 How well was the study done to minimize the risk of bias or confounding?.
2.2 Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, do you think there is clear evidence of an association between exposure and outcome?.
2.3 Are the results of this study directly applicable to the patient group targeted in this guideline?.
Appendix 4. Funnel Plot for Functional Improvement

Fig. A1.

Appendix 5. Prevalence of Comorbidities

| Comorbidities                     | Randomized controlled trials | Observational studies | Retrospective, insurance database studies | Registries | Mixed methods |
|-----------------------------------|-----------------------------|----------------------|------------------------------------------|------------|---------------|
| **Prevalence (%)**                |                             |                      |                                          |            |               |
| Previous spine surgery            | 4.9 - 6.8 [8,36,102]        |                      | 17.0 - 19.4 [23,47,92,93]               |            |               |
| Symptom duration, years: mean     | 15.8 (13.9) [43]            |                      | 1.6 (1.7) [77]                          | -          |               |
| Obese (BMI > 30)                  | 1.0 (0.8) [49]              | 11.2 [55]            | -                                        | -          |               |
| Specified symptom duration, n (%) | 194 (87.4) [82]             | 3983 (51.2) [3009]   | -                                        | -          |               |
| Heart failure                     | 7.0 - 49.8 [54,55,57,80,101] |                      |                                          |            |               |
| Hypertension                      | 4.9 - 45.9 [41,59,69-71]    |                      | 7.8 - 71.6 [56,61,78,80,98,103,105]     |            |               |
| Diabetes                          | 4.2 - 37.1 [54-               |                      | 3.0 - 14.4 [22,45,106]                  |            |               |
| Smoking                           | 8.1 - 61.6 [54,77,80]        |                      | 11.7 - 24.3 [72,44,47,92,93]            |            |               |
| Cardiovascular disease            |                             |                      |                                          |            |               |
| All, not specified                | 59.9 [27]                   | 43.1 [61]            | -                                        | -          | 6.6 [22]      |
| Arhythmia                         | -                           | 3.3 - 4.2 [56,103]   | -                                        |            |               |
| Coronary artery disease (CAD)     | 7.1 - 23.6 [53,83]          |                      | 2.1 - 10.3 [54,60,103]                  | -          |               |
| Heart failure                     | 5.0 - 6.0 [53,83]           |                      | 1.3 - 11.3 [54,60,103]                  | -          |               |
| CAD/heart failure                 | 6.3 [46]                   |                      | -                                        | -          |               |
| CAD/heart disease                 | 17.8 [78]                  |                      | -                                        | -          |               |
| Heart disease                     | 4.8 [80]                    |                      | 4.4 [42]                                |            |               |
| Comorbidities | Randomized controlled trials | Observational studies | Retrospective, insurance database studies | Registries | Mixed methods |
|---------------|-----------------------------|-----------------------|------------------------------------------|------------|---------------|
| Previous myocardial infarction | - | - | 3.4 - 8.1 [60,78] | - | - |
| Aortic aneurysm | - | - | 1.2 [103] | - | - |
| Stroke/cardiovascular disease (CVD) | 2.1 [59] | - | 7.5 - 48.2 | - | - |
| Peripheral vascular disease (PVD) | 6.0 - 6.1 [41,59] | - | 5.9 - 11.3 | - | 2.1 [22] |
| Lung disease | 7.6 - 7.7 [41,59] | 5.6 - 15.7 [46,53,83] | 1.7 - 26.1 | - | 3.9 [22] |
| Neurologic disease | 2.1 [41,59] | - | - | 2.4 [42] | 8.0 [22] |
| Parkinson’s disease (PD)/peripheral neuropathy | - | 2.3 - 11.1 [46,53,83] | - | - | - |
| Dementia/hemi-/paraplegia | - | - | 2.9 [60] | - | - |
| PD/Alzheimer disease /hearing loss | - | - | 16.3 [54] | - | - |
| Rheumatologic disease | - | - | - | - | - |
| Musculoskeletal disorder, not specified | 51.0 - 55.9 [41,59,69,71] | 44.1 [27] | 13.3 [60] | - | 1.8 [22] |
| Osteoporosis | 6.2 - 10.4 [59,69,71] | - | 35.6 [60] | - | - |
| Osteoarthrits (OA) | - | - | 6.8 - 20.2 [39,78,101] | - | - |
| Knee OA | - | 4.9 - 15.8 [40,53,83] | - | - | 4.8 [22] |
| Hip OA | - | 2.0 - 13.7 [40,53,83] | - | - | 2.7 [22] |
| Hip/knee OA | - | 1.0 - 35.0 [40,46] | - | - | - |
| Rheumatoid arthritis | - | 2.0 [40] | 0.8 [78] | - | - |
| Pseudogout | - | - | 0.8 [78] | - | - |
| Diffuse idiopathic skeletal hyperostosis (DISH) | - | - | 0.8 [78] | - | - |
| Psychiatric disease | - | - | - | - | - |
| Depression | 11.0 - 53.4 [41,59,68,71] | 17.9 - 27.3 [46,53,82] | 5.7 - 7.3 [39,101] | - | 2.7 [45] |
| Anxiety | 4.8 - 38.1 [59,68] | 17.1-17.6 [53,82] | - | - | - |
| Drug addiction | 0.3 [59] | - | - | - | - |
| Cancer | 7.7 [59] | - | 4.6 - 9.3 [60,78,103,105] | - | 1.3 [42] |
| Kidney disease | 4.6 [41,59] | - | 0.8 - 9.4 [56,60,61,103,105] | - | - |
| Urologic disease | - | - | 2.5 - 17.7 [54,103] | - | - |
| Prostate hypertrophy | - | - | - | - | - |
| Gastrointestinal disease | - | - | - | - | - |
| Gastric disease | 20.6 - 22.2 [41,59,69,71] | - | 42.4 [60] | - | - |
| Intestinal disease | 10.4 - 13.7 [41,59,69,71] | - | 1.7 [78] | - | - |
| Liver disease | 1.6 [41,59] | - | 31.2 [60] | - | - |
| Endocrinologic disease | - | - | 0.8 [78] | - | - |
| Hypothyroidism | - | - | 0.1 [60] | - | - |
| Acquired immune deficiency syndrome (AIDS) | - | - | - | - | - |
| Ophthalmologic disease | - | - | 0.8 [78] | - | - |
| Glaucoma | - | - | - | - | 8.0 [22] |
| Other diseases | 29.7 - 78.5% [41,69,71] | - | - | - | - |

Abbreviations: SD, standard deviation; IQR, interquartile range; n, number of patients

a Value for back pain and leg pain respectively;
b symptom duration >5 years;
c symptom duration >6 months;
d symptom duration >3 months;
e duration of back pain >2 years;
f duration of leg pain >2 years;
g other diseases related to stroke, cancer, fibromyalgia, chronic fatigue syndrome, posttraumatic stress disorder, alcohol consumption, drug addiction, lung, liver, kidney, blood vessel, nervous system, migraine or anxiety;
h other diseases than hip or knee joint arthrosis, peripheral vascular disease, diabetes, cardiovascular, pulmonary, neurologic or rheumatic disease
## Appendix 6. Prevalence of Comorbidity Measures (CM)

| Comorbidity measures (CM) | Observational studies | Retrospective, insurance database studies | Registries | Mixed methods |
|---------------------------|------------------------|------------------------------------------|------------|---------------|
| Mean (SD) or prevalence n (%) | | | | |
| American Society of Anesthesiologists (ASA) 0-5 | 2.23 [89] | 2.27 (range 1-3.5) [105] | - | - |
| Cumulative Illness Rating Scale (CIRS, 0-52 or 0-56) | 9.3 (3.8), [82] | 4.8 (4.9), [91] | - | - |
| Charlson Comorbidity Index (CCI, 0-31)  | 1.2 (1.2) [88] | - | - | - |
| Functional Comorbidity Index (FCI, 0-18) | 3.2 (1.3) [88] | - | - | - |
| Gagne score (0-26) | - | 0.48 (1.41) [55] | - | - |
| Comorbidity scores/patient, median [range] | 2 (3) [88] | 2.85 (1.84), [57.99] | - | - |
| CIRS (0-56), median range | 8 [4.8] [84] | - | - | - |
| Comorbidity scores/patient, median [range] | 5.5 [0.7] [48] | - | - | - |
| Patients with ASA score ≥3 | 29 (28.7), [24] | 74 (62.7), [78] | 1135 (23.8), [23] | - |
| 25 (8) [67] | 1192 (50.6), [80] | 106 (48), [33] | 999 (22.2), [34] | - |
| 23 (18.5), [39] | 33 (11), [57.99,101] | 19 (6.7), [102] | 58 (27.6), [77] | - |
| 19 (6.7), [102] | 125 (58.1) [56] | 1756 (61.3), [17] | - | - |
| Patients with CCI or modified CCI (mCCI or mCCI-C) score 0-31 or 0-3+) score ≥3 | - | 2358 (73.3), [8] | 751 (13.94) [37] | - |
| Patients with CCI ≥2 | - | 1756 (61.3), [17] | 72 (39.6) [45] | - |
| Patients with Elixhauser index ≥3 | - | - | 2544 (33.3) [47] | - |
| Patients with any comorbid illnesses | 59 (60.8), [74] | 8338 (75.6) [60] | - | - |
| 54 (34.2) [94] | 49744 (10.6), [35] | - | - | - |
| Patients with ≥3 comorbidities | 74 (38.1) [38] | 138 (48.8), [102] | - | - |
| 78 (36.3) [56] | 8581 (2.25), [102] | - | - | - |
| Patients with ≥5 comorbidities | 55 (53.9) [40] | - | - | - |

**Abbreviations: SD, standard deviation; n (%), number of patients (%)**

## Appendix 7. Predictors of outcomes

**Tables A5–A8**

### Table A5

Predictors for satisfaction.

| Comorbidity | Significant predictors | Ref. | Not significant predictors | Ref. |
|-------------|------------------------|------|-----------------------------|------|
| **Comorbidities, Comorbidity measures (CM)** | Worse Cumulative Illness Rating Scale (CIRS, 0-56) associated with dissatisfaction (very/somewhat, 4-point scale) at 6 months: adjusted (adj) beta 0.08 (p=0.03) Less overall comorbidity associated with satisfaction at 2 years: univariate significant (sign.) Spearman correlation (r=0.23) | 4.2 [38] | Univariate, <5 comorbidities: no association with satisfaction (totally cured/condition has considerably improved, 7-point scale) at 2 years | 21.1 [40] |
| | Logistic regression (log.), higher American Society of Anesthesiologists (ASA, range 1-6) class and number of comorbidities: no association with less satisfaction (very/somewhat dissatisfied, 4-point scale) at a mean of 3.5 years | 44.1 [99] | | |
| | Univariate, comorbid illnesses not associated with satisfaction with current state (delighted/pleased/mostly satisfied, 7-point scale) at 10 years | 3 [74] | | |

(continued on next page)
| Comorbidity                  | Significant predictors                                                                 | Ref. | Not significant predictors                                                                 | Ref. |
|-----------------------------|----------------------------------------------------------------------------------------|------|-------------------------------------------------------------------------------------------|------|
| **Age**                     | <75 years associated with satisfaction (totally cured/condition has considerably improved, 7-point scale) at 2 years: adj. odds ratio (OR) 4.03 (95% confidence interval (CI) 1.35 to 12.02) Younger age associated with dissatisfaction (surgery total failure/condition slightly improved, 7-point scale) at 3 months: adj. OR 0.93 (95% CI 0.88 to 0.99) | 21.1 [40] | Univariate: no association with satisfaction with current state (delighted/pleased/mostly satisfied, 7-point scale) at 10 years | 3 [74] |
| **Previous spine surgery**  | No previous lumbar operation associated with satisfaction (totally cured/condition has considerably improved, 7-point scale) at 2 years: adj. OR 3.65 (95% CI 1.13 to 11.79) | 21.1 [40] | -                                                                                         | -    |
| **Symptom duration**        | Duration of leg pain >2 years associated with dissatisfaction (3-point scale) at 1 year, adj. OR 2.46 (95% CI 1.01 to 5.97) Multivariate, duration of back pain (<3 or 3-12 months or 1-2 or >2 years): no association with dissatisfaction (3-point scale) at 1 year | 36 [42] | Univariate, length of current episode >6 months: no association with satisfaction with current state (delighted/pleased/mostly satisfied, 7-point scale) at 10 years Bivariate, pain <1 year (reference) vs. >1 year: no association with satisfaction | 3 [74] |
| **Body weight**             | Compared to normal weight, obesity (body mass index (BMI) ≥30) associated with dissatisfaction (unsatisfied/uncertain with surgery, 3-point scale) at 2 years: adj. OR 1.73 (95% CI 1.36 to 2.19) | 33 [92] | Log. regression: no association with satisfaction (very/somewhat, 4-point scale) at a mean of 3.5 years | 44.1 [99] |
| **Diabetes**                | Significant difference in satisfaction (very/somewhat satisfied, 4-point scale) between patients with/without diabetes at a mean of 3.4 years: diabetes: 52%, no-diabetes: 78% (p=0.0067) | 44.5 [39] | Multivariate: no association with dissatisfaction (3-point scale) at 1 year Univariate, BMI <30: no association with satisfaction (totally cured/condition has considerably improved, 7-point scale) at 2 years BMI <24.9 vs. 25-29.9 vs. ≥30: obesity not associated with dissatisfaction (very/somewhat, 4-point scale) at a mean of 3.7 years BMI <30 vs. ≥30 to <35 vs. ≥35, surgical/non-surgical group: obesity not associated with dissatisfaction at 4 years | 21.1 [40] |
| **Smoking**                 | Smoking associated with dissatisfaction (3-point scale) at 1 year: adj. OR 1.61 (95% CI 1.19 to 2.17) Smoking associated with dissatisfaction at 2 years: adj. OR 1.79 (95% CI 1.51 to 2.12) | 36 [42] | Univariate, never smoking: no association with satisfaction (totally cured/condition has considerably improved, 7-point scale) at 2 years Multivariate, cigarette use (current or quit in <6 months): no association with satisfaction with current state (delighted/pleased/mostly satisfied, 7-point scale) at 10 years | 21.1 [40] |
| **Cardiovascular disease**  | Less cardiovascular comorbidity associated with satisfaction at 2 years: adj. beta 3.7 (p=0.0002) | 4.1 [27] | Multivariate, cardiac disease: no association with dissatisfaction (3-point scale) at 1 year | 36 [42] |
| **Neurologic disease**      | Neurological disease associated with dissatisfaction (3-point scale) at 1 year: adj. OR 2.05 (95% CI 1.00 to 4.20) | 36 [42] | -                                                                                         | -    |
| **Rheumatologic disease**   | -                                                                                         | -    | Univariate, no comorbidity affecting walking: no association with satisfaction (totally cured/condition has considerably improved, 7-point scale) at 2 years Univariate, less musculoskeletal comorbidity: no association with satisfaction at 2 years | 21.1 [40] |
| **Psychiatric disease**     | Depression associated with dissatisfaction (surgery total failure/condition slightly improved, 7-point scale) at 3 months: adj. OR 1.18 (95% CI 1.03 to 1.34) | 21.2 [43] | Multivariate, depression: no association with dissatisfaction (very/somewhat, 4-point scale) at 6 months Better mental health (3-item depression scale) associated univariate significant (Spearman correlation r=0.25), multivariate not significant with satisfaction at 2 years | 4.2 [38] |
| **Cancer**                  | Cancer disease associated with dissatisfaction (3-point scale) at 1 year: adj. OR 3.75 (95% CI 1.58 to 8.89) | 36 [42] | -                                                                                         | -    |
Table A6
Predicators for functional improvement.

| Comorbidities, Comorbidity measures (CM) | Significant predictors | Ref. | Not significant predictors | Ref. |
|-----------------------------------------|------------------------|------|-----------------------------|------|
| Higher comorbidity score (Elixhauser) associated with more disability (Oswevy disability index (ODI), range 0-100) at 1 year: adjusted (adj.) beta 2.04 (95% confidence interval [CI] 1.55 to 2.61) | 32 [47] | Logistic (log.) regression, no previously diagnosed comorbidity: no association with good outcome (ODI <40) at mean 4.3 years | 22 [22] |
| Less overall comorbidity associated with greater walking capacity at 2 years: univariate significant (sign.) Spearman correlation (r<0.33) with "able to walk 1 mile" | 4.1 [27] | Univariate: no association between <5 comorbidities and good improvement in disability (>30% ODI improvement) at 2 years | 21.1 [40] |
| Higher Cumulative Illness Rating Scale (CIRS, 0-52 or 0-56) associated with poor functional outcome (less Self-administered Beaujon Questionnaire score (SABQ, range 0-100)) at 1 year: adj. beta -0.94 (p=0.001) | 25 [88] | Univariate, associated diseases: no association with failed clinical improvement (ODI <15% improvement) at a mean of 2.64 years | 38 [94] |
| Older age associated with more disability (ODI) at 1 year: adj. beta 0.15 (95% CI 0.11 to 0.19) | 32 [47] | | |
| <65 years associated with failed improvement (ODI <15% improvement) at a mean of 2.64 years: adj. OR 2.16 (95% CI 1.02 to 4.57) | 38 [94] | | |
| Any previous lumbar surgery associated with less functional improvement at 1 year: regression analysis log OR -0.99 (95%CI -1.95 to -0.02), SSM function | 20.2 [46] | Log. regression, any previous back surgery: no association with less improvement in disability (ODI) at 1 year | 23 [24] |
| Any previous surgery associated with more disability (ODI) at 1 year: adj. beta 6.41 (95% CI 5.32 to 7.61) | 32 [47] | Univariate, any previous lumbar surgery: no association with less improvement in disability (ODI) at a mean of 5.1 years | 37 [45] |
| No previous surgery associated with good outcome (ODI <40) at mean 4.3 years: log. regression OR 2.4 (95% CI not reported) | 22 [22] | Multivariate, no previous lumbar operation: no association with good improvement in ODI (>30% improvement) at 2 years | 21.1 [40] |

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### Table A6 (continued)

| Comorbidity                  | Significant predictors                                                                 | Ref. | Not significant predictors                                                                 | Ref. |
|------------------------------|----------------------------------------------------------------------------------------|------|-------------------------------------------------------------------------------------------|------|
| Symptom duration             | Back pain for 1-2 years associated with more disability (ODI) at 1 year: adj. beta 3.50 (95% CI 1.56 to 5.27) | 32 [47] | Symptom duration ≥6 months: no association with less functional improvement at 1 year (SSM function) | 20.2 [46] |
|                             | Longer duration of leg pain associated with less improvement in disability (ODI) at 1 year: log regression beta 0.46 (p<0.001) | 23 [24] | Univariate, symptom duration: no association with unfavorable surgical outcome at 1 year (ODI >22) | 39 [49] |
|                             | Compared to buttock/leg/hip pain duration <3 months, longer duration associated with less improvement in disability (RMDQ) at 6 weeks: 3-12 months adj mean difference -0.7 (95% CI -2.3 to 1.0), 1-5 years adj mean difference 1.6 (95% CI -0.2 to 3.3), >5 years adj mean difference 0.6 (95% CI -1.2 to 2.3) (p<0.001) | 1.1 [51] | Multivariate, comparison pain <1 year (reference) vs. >1 year: no association with less functional improvement (ODI) at 2 years | 9 [77] |
|                             | Stieger, u., continued                                                                 |      | Multivariate, preoperative symptom duration: no association with bad functional score* at mean 10 years | 28.1 [91] |
|                             | BMI <30 vs. ≥30 to <35 vs. ≥35, non-surgical group: obesity associated with less improvement in disability (ODI) at 4 years: <30: mean -12.7 (standard deviation (SD) 1.7), ≥30 to <35: mean -2.3 (SD 2.6), ≥35: mean -6.4 (SD 3.4) (p<0.003) | 2.4 [41] | Multivariate, higher BMI: no association with poor functional outcome (less SABQ) at 1 year | 25 [88] |
|                             | Higher BMI associated with less functional improvement at 1 year: regression analysis log OR -0.96 (95% CI -1.63 to -0.28), SSM function. | 20.2 [46] | Multivariate: no association with an unfavorable surgical outcome (ODI >22) at 1 year | 39 [49] |
|                             | BMI <35 vs. ≥30 to <35 vs. ≥35, surgical group: obesity no association with less improvement in disability (ODI) at 4 years |      | No association with less improvement in disability (RMQ) at 6 weeks | 1.1 [51] |
|                             | BMI <25 vs. 25 to <30 and ≥30, obesity: no association with less functional improvement (SSM function) at 1 year | 20.4 [84] | Log. regression: no association with less improvement in disability (ODI) at 1 year | 23 [24] |
| Diabetes                     | Patients with diabetes: more disability compared to patients without diabetes in non-surgical group at 4 years: diabetes mean -2.6 (SD 3.5), no-diabetes mean -10.2 (SD 1.4) (p=0.044), Diabetes vs. no-diabetes, surgical group: diabetes no association with less improvement in disability (ODI) at 4 years | 2.3 [59] | No association between diabetes on insulin and less improvement in disability (RMQ) at 6 weeks | 1.1 [51] |
| Smoking                      | Non-smoking associated with good improvement in disability (ODI >30%) at 2 years: adj. OR 3.47 (95% CI 1.09 to 11.03) | 21.1 [40] | Univariate: no association between diabetes and improvement in disability (ODI) at a mean of 5.1 years | 37 [45] |
|                             | Smoking associated with more disability (ODI) at 1 year: adj. beta 4.72 (95% CI 3.73 to 5.61) | 32 [47] | Univariate: no association between diabetes and good improvement in disability (>30% ODI improvement) at 2 years | 21.1 [40] |
| Cardiovascular disease       | Less cardiovascular comorbidity associated with better walking capacity at 2 years: adj. beta 2.7 (p=0.008) with "able to walk 1 mile" | 4.1 [27] | Univariate, history of smoking: no association with failed improvement in disability (ODI improvement <15%) at mean 2.64 years | 38 [94] |
| Lung disease                 | -                                                                                       | -    | Univariate: no association with unfavorable surgical outcome (ODI >22) at 1 year | 39 [49] |
| Neurologic disease           | -                                                                                       | -    | Log. regression: no association with less improvement in disability (ODI) at 1 year | 23 [24] |
| Rheumatologic disease        | Cox-/gonarthrosis associated with less functional improvement at 1 year: regression analysis log OR -0.71 (95%CI -1.36 to -0.06), SSM function | 20.2 [46] | No association with less functional improvement (SSM function) at 6 weeks | 20.2 [46] |

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Table A6 (continued)

| Comorbidity | Significant predictors | Ref. | Not significant predictors | Ref. |
|-------------|------------------------|------|-----------------------------|------|
| Psychiatric disease | Higher depressive burden (higher Beck depression inventory [BDI], range 0-63) associated with more disability (ODI) at 10 years: adj. beta 0.25 (95%CI 0.18 to 0.33) | 21.3 [48] | Univariate, no comorbidity affecting walking: no association with good improvement in disability (>30% ODI improvement) at 2 years | 21.1 [40] |
| | Less depression associated with greater walking capacity at 2 years: univariate sign. Spearman correlation (r=0.19) with "able to walk 1 mile" | 4.1 [27] | Depression: no association with less functional improvement (SSM function) at 1 year | 20.2 [46] |
| | Higher depression scores associated with less functional improvement in Patient Reported Outcomes Measurement Information System (PROMIS) physical function: F (1, 109) = 6.11 (p=0.015) and higher depression scores associated with less functional improvement in disability (ODI): F (1, 58) = 28.59 (p=<0.0001) | 18 [50] | Log. regression, high Fear Avoidance Beliefs Questionnaire Physical activity (FABQ-P, range 0-24) baseline, high FABQ-P at 6 months and persistent high FABQ-P at baseline and at 6 months: no association with less clinical meaningful improvement at 1 year | 20.5 [53] |
| | Higher depression score (total Pain Sensitivity Questionnaire [PSQ, range 0-10]) associated with unfavorable outcome (ODI >22) at 1 year: adj. OR 1.29 (95% CI 1.03 to 1.62) | 39 [49] | | |

* Bad functional score, based on global/lumbar/radicular pain and signs of radicular ischemia (range 0-100, 0 = very bad function, 100 = very good function)

† Elixhauser comorbidity score (0-30), method for measuring patient comorbidity based on diagnosis codes in administrative data (includes mental disorders, drug and alcohol abuse, obesity, coagulopathy)

Table A7

Predictors for symptoms and global improvement.

| Comorbidity | Significant Predictors | Ref. | Not significant predictors | Ref. |
|-------------|------------------------|------|-----------------------------|------|
| Comorbidity measures (CM) | Less overall comorbidity associated with less symptom severity at 2 years: univariate significant (sign.) Spearman correlation (r=0.27) with "no severe pain" Compared to American Society of Anesthesiology (ASA, range 1-6) score 1, other ASA scores associated with lower Core Outcome Measure Index (COMI, range 8-40) sum-score improvement (in ≥1 domain) at mean 1.3 years: ASA 2: adjusted (adj.) odds ratio (OR) 0.86 (95% confidence interval [CI] 0.72 to 1.03); ASA ≥2: adj. OR 0.69 (95% CI 0.56 to 0.85) | 4.1 [27] | Univariate, Charlson Comorbidity Index (CCI, range 0-3+) >1: no association with less pain (Visual Analogue Scales [VAS]) improvement at a mean of 5.1 years | 37 [45] |
| | Higher ASA score (≥3 vs. 1) associated with negative global outcome in patients with predominant back pain at 1.3 year: OR 1.76 (1.15-2.70) Multivariate, higher ASA score (≥3 vs. 1): no association with negative global outcome in patients with predominant leg pain at 1.3 year Lower comorbidity (ASA score) associated with more improvement in COMI sum-score at 1 year: beta 0.619 (95% CI 0.06 to 1.18) Multivariate, lower comorbidity (ASA score): no association with good outcome (surgery helped a lot/hel ped, 5-point scale) at 1 year | 30 [23] | Logistic (log.) regression, higher ASA score (dichotomous ASA 1 and 2 versus [vs.] ASA 3 and 4): no association with less EuroQol 5 Dimensions Questionnaire (EQ-5D, 0-100); EuroQol Visual Analogue Scales (VAS, 0-100) at 1 year | 23 [24] |
| Age | <80 vs. ≥80 years, surgical group: older age associated with less improvement in Short Form 36 Questionnaire subscale bodily pain (SF-36 bodily pain, 0-100) sub-score at 4 years: <80: mean 28 (standard deviation [SD] 0.6), ≥80: 21.3 (2.2), p=0.004 <80 vs. ≥80 years, non-surgical group: older age not associated with less improvement in SF-36 bodily pain sub-score at 4 years | 2.5 [71] | Multivariate: no association with good outcome (surgery helped a lot/hel ped, 5-point scale) and COMI sum-score improvement at 1 year | 31 [33] |
Table A7 (continued)

| Comorbidity          | Significant Predictors                                                                 | Ref. | Not significant predictors                                                                 | Ref. |
|----------------------|----------------------------------------------------------------------------------------|------|-------------------------------------------------------------------------------------------|------|
| Previous spine surgery | After a mean of 1.3 years, ≥1 previous spine surgery compared to no previous surgery is associated with: - lower COMI sum-score ≥1 domain improvement: 1 previous surgery adj. OR 0.73 (95% CI 0.61 to 0.87), >1 previous surgery adj. OR 0.55 (95% CI 0.41-0.74) - less back pain improvement (GRS ≥2 points): 1 previous surgery adj. OR 0.75 (95% CI 0.62 to 0.90), >1 previous surgery adj. OR 0.72 (95% CI 0.53-0.98) - less leg pain improvement (GRS ≥2 points): 1 previous surgery adj. OR 0.72 (95% CI 0.60 to 0.86), >1 previous surgery adj. OR 0.58 (95% CI 0.43-0.78) | 30 [23] | No association between any lumbar surgery and less pain (VAS) improvement at a mean of 5.1 years | 37 [45] |
| Symptom duration     | -                                                                                       | -    | No association between any lumbar surgery and less pain (VAS) improvement at a mean of 5.1 years | 37 [45] |
| Body weight          | -                                                                                       | -    | No association between any lumbar surgery and less pain (VAS) improvement at a mean of 5.1 years | 37 [45] |
| Diabetes             | Diabetes vs. no-diabetes: diabetes associated with less decrease of ≥4 points of VAS: diabetes 63%, no-diabetes 83% χ²= 5.57, p=0.018 | 44.5 [30] | No association between obesity (body mass index (BMI) ≥30) and less symptom severity improvement (SSM symptoms) at 1 year | 20.2 [46] |
|                      | Univariate, diabetes: no association with less pain (VAS) improvement at a mean of 5.1 years | 37 [45] | No association between obesity (BMI ≥30)/overweight (BMI 25 to <30) compared to BMI <25 in symptom severity improvement (SSM symptoms) at 1 year | 20.4 [84] |
|                      | Diabetes vs. no-diabetes, surgical and non-surgical group: diabetes not associated with less improvement in SF-36 bodily pain sub-score at 4 years | 2.3 [59] | No association between obesity (BMI ≥30)/overweight (BMI 25 to <30) compared to BMI <25 in symptom severity improvement (SSM symptoms) at 1 year | 20.4 [84] |
|                      |                                                                                       |      | No association between obesity (BMI ≥30)/overweight (BMI 25 to <30) compared to BMI <25 in symptom severity improvement (SSM symptoms) at 1 year | 20.4 [84] |
|                      |                                                                                       |      | No association between obesity (BMI ≥30)/overweight (BMI 25 to <30) compared to BMI <25 in symptom severity improvement (SSM symptoms) at 1 year | 20.4 [84] |
|                      |                                                                                       |      | No association between obesity (BMI ≥30)/overweight (BMI 25 to <30) compared to BMI <25 in symptom severity improvement (SSM symptoms) at 1 year | 20.4 [84] |
|                      |                                                                                       |      | No association between obesity (BMI ≥30)/overweight (BMI 25 to <30) compared to BMI <25 in symptom severity improvement (SSM symptoms) at 1 year | 20.4 [84] |
|                      |                                                                                       |      | No association between obesity (BMI ≥30)/overweight (BMI 25 to <30) compared to BMI <25 in symptom severity improvement (SSM symptoms) at 1 year | 20.4 [84] |
|                      |                                                                                       |      | No association between obesity (BMI ≥30)/overweight (BMI 25 to <30) compared to BMI <25 in symptom severity improvement (SSM symptoms) at 1 year | 20.4 [84] |
|                      |                                                                                       |      | No association between obesity (BMI ≥30)/overweight (BMI 25 to <30) compared to BMI <25 in symptom severity improvement (SSM symptoms) at 1 year | 20.4 [84] |
|                      |                                                                                       |      | No association between obesity (BMI ≥30)/overweight (BMI 25 to <30) compared to BMI <25 in symptom severity improvement (SSM symptoms) at 1 year | 20.4 [84] |
|                      |                                                                                       |      | No association between obesity (BMI ≥30)/overweight (BMI 25 to <30) compared to BMI <25 in symptom severity improvement (SSM symptoms) at 1 year | 20.4 [84] |
|                      |                                                                                       |      | No association between obesity (BMI ≥30)/overweight (BMI 25 to <30) compared to BMI <25 in symptom severity improvement (SSM symptoms) at 1 year | 20.4 [84] |
|                      |                                                                                       |      | No association between obesity (BMI ≥30)/overweight (BMI 25 to <30) compared to BMI <25 in symptom severity improvement (SSM symptoms) at 1 year | 20.4 [84] |
|                      |                                                                                       |      | No association between obesity (BMI ≥30)/overweight (BMI 25 to <30) compared to BMI <25 in symptom severity improvement (SSM symptoms) at 1 year | 20.4 [84] |
|                      |                                                                                       |      | No association between obesity (BMI ≥30)/overweight (BMI 25 to <30) compared to BMI <25 in symptom severity improvement (SSM symptoms) at 1 year | 20.4 [84] |
| Comorbidity                  | Significant Predictors                                                                 | Ref.   | Not significant predictors                                                                 | Ref.   |
|-----------------------------|----------------------------------------------------------------------------------------|--------|-------------------------------------------------------------------------------------------|--------|
| Smoking                     | Smokers vs. non-smokers: smokers used more frequently analgesics at 2 years after surgery: OR 1.86 (95% CI 1.55 to 2.23) | 34 [44] | No association with less improvement in symptom severity (SSM symptoms) at 1 year          | 20.2 [46] |
| Cardiovascular disease      | Coronary heart disease or heart insufficiency associated with less symptom improvement at 1 year: regression analysis, log OR -1.21 (95% CI -2.35 to -0.09), SSM symptoms | 20.2 [46] | Log, regression: no association with less EQ-5D total score/EQ-VAS improvement at 1 year | 23 [24] |
|                             | Less cardiovascular comorbidity associated with less symptom severity (“no severe pain”) at 2 years: adj. beta 2.6 (p=0.01) with “able to walk 1 mile” | 4.1 [27] |                                                                                           |        |
| Lung disease                | -                                                                                      | -      | Asthma/Chronic Obstructive Pulmonary Disease (COPD): no association with less improvement in symptom severity (SSM symptoms) at 1 year | 20.2 [46] |
| Neurologic disease          | -                                                                                      | -      | Parkinson’s disease/peripheral neuropathy or hip-/knee arthritis: no association with less improvement in symptom severity (SSM symptoms) at 1 year | 20.2 [46] |
| Rheumatologic disease       | Greater depression score (per one-unit increase in Personal Health Questionnaire depression scale (PHQ-9, 0-24): -) associated with lower probability of any improvement in EQ-5D: adj. OR 0.95 (95% CI 0.90 to 0.998) and of MCID EQ-5D ≥0.1-point improvement: adj. OR 0.92 (95% CI 0.87 to 0.98) at mean 6 months | 7 [52]  | Univariate, less musculoskeletal comorbidity: no association with less symptom severity (“no severe pain”) at 2 years | 4.1 [27] |
| Psychiatric disease         | Higher depression scores associated with less depression improvement in Patient-Reported Outcomes Measurement Information System (PROMIS) depression: F (1, 109) = 148.3 (p<0.0001) and higher depression scores associated with less pain score improvement in PROMIS pain: F (1, 109) = 23.36 (p<0.0001) | 18 [50] | Multivariate, better mental health (3-item depression scale): no association with less symptom severity (“no severe pain”) at 2 years | 4.1 [27] |
|                             | Higher depression score (Hospital Anxiety and Depression Scale (HADS, range 0-21) ≥8 points) associated with less improvement in symptom severity at 1 year: log OR -1.09 (95% CI -1.87 to -0.31), SSM symptoms | 20.2 [46] |                                                                                           |        |
|                             | Higher Fear Avoidance Beliefs Questionnaire Physical activity (FABQ-P; 0-24) (at 6 months): less clinical meaningful improvement at 1 year: multiple log, regression, adj. OR 0.46 (95% CI 0.24-0.91) for SSM symptoms | 20.5 [53] |                                                                                           |        |
|                             | Persistent higher FABQ-P (at baseline and 6 months): less clinical meaningful improvement at 1 year: multiple log, regression, adj. OR 0.34 (95% CI 0.16-0.73) for SSM symptoms | 20.2 [46] |                                                                                           |        |
|                             | FABQ-P high (baseline) not associated with less clinical meaningful improvement (SSM symptoms) at 1 year | 20.5 [53] |                                                                                           |        |
|                             | Higher depressive burden (higher Beck depression inventory (BDI, range 0-63)) associated with higher pain scores (VAS (0-100)) at 10 years: mixed model, sign. beta 0.19 (95% CI 0.07 to 0.31) | 21.3 [48] |                                                                                           |        |
### Table A8
Predictors for adverse events (AE), mortality, and other outcomes.

| Comorbidity                                | Significant predictors | Ref. | Not significant predictors | Ref. |
|--------------------------------------------|------------------------|------|----------------------------|------|
| **Comorbidities, Comorbidity measures (CM)** |                        |      |                            |      |
| Systemic disease (hypertension, diabetes or both) associated with higher postoperative wound infection rate: adjusted (adj.) odds ratio (OR) 3.99 (95% confidence interval (CI) 2.02 to 7.96) | 43 [98] | Compared to American Society of Anesthesiology (ASA, range 1-6) groups <3, ASA groups ≥3 not associated with more complications during hospitalization | 10 [78] |
| Compared to 0 comorbidity, 2-3 comorbidities associated with higher in-hospital complication rate: 2 comorbidities adj. OR 1.2 (95% CI 1.1 to 1.2), ≥3 comorbidities adj. OR 1.5 (95% CI 1.4 to 1.6) | 11 [35] | Multivariate, number of comorbidities: no association with reoperation rate 15 years after first surgery | 28.2 [36] |
| Multivariate, compared to 0 comorbidity, 1 comorbidity not associated with higher in-hospital complication rate | | | |
| Gagne comorbidity score: (1-year increment): association with more 30-days complications: adj. OR 1.25 (95% CI 1.02 to 1.29) | 13 [55] | | |
| Quan comorbidity score ≥1 (ref. Quan 0) associated with more cardiopulmonary/stroke complications or mortality <30 days: Quan 1 adj. OR 1.27 (95% CI 1.09 to 1.47); Quan 2 adj. OR 1.62 (95% CI 1.33 to 1.97); Quan 3 adj. OR 1.78 (95% CI 1.34 to 2.36); Quan 4 adj. OR 2.14 (95% CI 1.46 to 3.16); Quan 5 adj. OR 2.14 (95% CI 2.17 to 4.55) | 12 [8] | | |
| Comorbidity score ≥1 (ref. 0) associated with any complications <3 years after surgery: score 1: OR 1.31 (95% CI 1.06 to 1.61), 2: OR 1.48 (95% CI 1.13 to 1.94), 3: OR 1.63 (95% CI 1.22 to 2.19) | 14 [17] | | |
| ASA score 3 or 4 associated with increased length of stay: adj. beta 0.32 (95% CI 0.09 to 0.54), and with readmission <30 days after surgery: adj. beta 2.63 (95% CI 1.54 to 4.49) | 17 [80] | | |
| Compared to 0 comorbidity, adverse outcome (death) is associated with the presence of ≥2 comorbidities within hospitalization: 2 comorbidities adj. OR 2.3 (95% CI 1.5 to 3.6) and ≥3 comorbidities adj. OR 2.1 (95% CI 1.3 to 3.6) Multivariate, compared to 0 comorbidity, adverse outcome (death) not associated with the presence of 1 comorbidity within hospitalization | 11 [35] | | |
| Presence of comorbidities associated with overall reoperation rate up to 6 years: adj. hazard ratio (HR) 1.37 (95% CI 1.20 to 1.55), and with reoperation at specific time periods: early (<30 days): adj. HR 1.25 (95% CI 1.01 to 1.54), short-term (31-365 days): adj. HR 1.85 (95% CI 1.32 to 2.58), and midterm (1-6 years): adj. HR 1.30 (95% CI 1.09 to 1.55) | 50 [60] | | |
| **Age** | | | | |
| High age associated with higher occurrence of perioperative dural lesion: logistic (log.) regression significant (sign.) OR 1.03 (95% CI 1.01 to 1.04) | 35 [93] | 70-75 versus (vs.) >75 years: older age not associated with higher postoperative complication rate | 48 [105] |
| Age (1-year increment): associated with more 30-days complications: adj. OR 1.02 (95% CI 1.01 to 1.03) | 13 [55] | <80 vs. ≥80 years: older age not associated with more postoperative complications | 45 [103] |
| Compared to 18-44 years, ≥65 years associated with a higher in-hospital complication rate: 65-84 years adj. OR 1.8 (95% CI 1.5 to 2.1), >85 years adj. OR 2.3 (95% CI 1.9 to 2.7) Multivariate, compared to 18-44 years, 45-64 years not associated with higher in-hospital complication rate | 11 [35] | <80 vs. ≥80 years: older age not associated with more postoperative complications | 2.5 [71] |
| Compared to 66-70 years, 71-74, 75-79 and ≥80 years associated with more cardiopulmonary/stroke complications or mortality <30 days 71-74 years adj. OR 1.13 (95% CI 0.94 to 1.37), 75-79 years adj. OR 1.36 (95% CI 1.14 to 1.62), >80 years adj. OR 1.70 (95% CI 1.43 to 2.04) | 12 [8] | 80-89 vs. ≥90 years: older age not associated with more complications during hospitalization | 16 [37] |
| Compared to 65-69 years, 70-74 years not associated with any postoperative complications up to 3 years: 75-79 years OR 1.37 (95% CI 1.06 to 1.76), ≥80 years: OR 2.05 (95% CI 1.58 to 2.67) | 14 [17] | Multivariate, no association with time to reoperation until a mean of 8.6 years | 51 [106] |
| Compared to 65-69 years, age 70-74 years not associated with any postoperative complications up to 3 years 60-69 vs. 70-79 vs. ≥80 years: 60-69 and 70-79 years associated with increase of length of stay after surgery: 60-69 years beta 0.29 (95% CI 0.01 to 0.57), 70-79 beta 0.50 (95% CI 0.21 to 0.78) | 17 [80] | Multivariate, no association with reoperation rate up to 8 years | 2.2 [70] |
| Age ≥80 years associated with readmission <30 days after surgery: OR 2.09 (95% CI 1.05 to 4.14) | | Multivariate, no association with 90-day readmission | 6 [54] |
| Age 60-69 vs. 70-79 vs. ≥80 years: ≥80 years not associated with increase of length of stay after surgery (beta 0.92 (95% CI 0.55 to 1.29)) | 8 [76] | Multivariate, compared to ≥80 years, younger age not associated with reoperation rate (at undefined time) | |
| Age 60-69 and 70-79 years: no association with readmission <30 days (60-69 years OR 0.85 (95% CI 0.45 to 1.58), 70-79 years OR 0.79 (95% CI 0.42 to 1.49) | 16 [37] | 80-89 vs. >90 years: older age not associated with reoperations <12 months post-discharge | |
### Table A8 (continued)

| Comorbidity          | Significant predictors                                                                 | Ref.   | Not significant predictors | Ref.   |
|----------------------|----------------------------------------------------------------------------------------|--------|--------------------------|--------|
|                      | Age ≥70 years associated with reoperation rate at midterm (1-6 years): adj. HR 1.87 (95% CI 1.07 to 3.27) | 50 [60] |                          |        |
|                      | Multivariate, age >70 years: no association with overall (<6 years), early (<90 days) and short-term (90-365 days) reoperation rate |        |                          |        |
|                      | Higher age (per year) associated with shorter time until surgery since start of membrane stabilizing agent (MSA) treatment: adj. HR 1.02 (95% CI 1.00 to 1.04) | 7 [52] |                          |        |
|                      | Multivariate, higher age (per year) not associated with need for surgery <1 year since start of MSA treatment >85 years associated with adverse outcome (death) within hospitalization: adj. OR 8.7 (95% CI 2.0 to 38.5) | 11 [35] |                          |        |
|                      | Multivariate, compared to 18-44 years, 45-84 years not associated with adverse outcome (death) within hospitalization |        |                          |        |
|                      | Older age associated with higher 10-year survival rate: adj. HR 1.09 (95% CI 1.04 to 1.13) | 42 [97] |                          |        |
| Previous spine surgery | Any previous operation associated with occurrence of perioperative dural lesion: log. regression sign. OR 0.70 (95% CI 0.50 to 0.98) | 35 [93] |                          |        |
| Symptom duration | -                                                                                       |        |                          |        |
|                      | Morbid obesity associated with surgical site infection: log. regression OR 6.99 (95% CI 2.65-22.01), (p<0.001) | 6 [54] |                          |        |
|                      | Body mass index (BMI) <30 vs. 30 to <35 vs. ≥35: BMI 30 to <35 associated with no postoperative complication up to 8 weeks after surgery: BMI <30: 85% vs. 30 to <35: 95% vs. ≥35: 83% (p=0.02) | 2.4 [41] |                          |        |
|                      | BMI <30 vs. 30 to <35 vs. ≥35: obesity not associated with postoperative complications\(\) up to 8 weeks after surgery |        |                          |        |
|                      | Obesity (BMI ≥30) associated with increased length of stay after surgery: adj. beta 0.58 (95% CI 0.26 to 0.90), and with readmission <30 days after surgery: adj. beta 3.38 (95% CI 1.36 to 8.36) | 17 [80] |                          |        |
| Hypertension | -                                                                                       |        |                          |        |
|                      | Diabetes vs. no-diabetes: diabetes associated with more “other” complications (not specified) <8 weeks after surgery: diabetes 13%, no-diabetes 4% (p=0.021) | 2.3 [59] |                          |        |
|                      | Diabetes vs. no-diabetes: diabetes associated with no complication <8 weeks after surgery: diabetes 74%, no-diabetes 90% (p=0.002) |        |                          |        |
|                      | Diabetes vs. no-diabetes: diabetes not associated with postoperative wound infections/hematoma <8 weeks after surgery |        |                          |        |
|                      | Diabetes vs. no-diabetes: diabetes associated with more in-hospital perioperative complications\(\): diabetes 67%, no-diabetes 28% (p<0.0001) | 44.5 [39] |                          |        |
|                      | Diabetes mellitus associated with in-hospital perioperative complications\(\): log. regression sign. OR 1.85 (95% CI 1.03 ± 3.33) | 44.2 [57] |                          |        |
|                      | Diabetes associated with short-term reoperation rate (91-365 days): adj. HR 1.32 (95% CI 1.02 to 1.70), and with midterm reoperation rate (1-6 years): adj. HR 1.21 (95% CI 1.04 to 1.41) | 50 [60] |                          |        |

(continued on next page)
| Comorbidity          | Significant predictors                                                                 | Ref. | Not significant predictors                                                                 | Ref. |
|----------------------|----------------------------------------------------------------------------------------|------|-------------------------------------------------------------------------------------------|------|
| Diabetes             | Diabetes associated with mortality up to 8 years after surgery: adj. HR 1.12 (95% CI 1.0 to 1.25) | 49   |                                                                                           | [61] |
| Smoking              | Smoking associated with occurrence of perioperative dural lesion: logistic regression, sign. OR 0.70 (95% CI 0.49 to 0.999) | 35   | No association with increased length of stay after surgery (multivariate) and readmission <30 days (bivariate) | 17   |
| Cardiovascular       | Congestive heart failure associated with in-hospital perioperative complications: log. regression OR 2.96 (95% CI 1.55 ± 5.66) | 44.2 | Multivariate, no association with time to reoperation                                        | 51   |
| Lung                 | Ischemic heart disease associated with in-hospital perioperative complications: log. regression, sign. OR 2.02 (95% CI 1.22 ± 3.35) | 44.2 | Univariate, heart problem: no association with reoperation up to 8 years                     | 2.2  |
| Lung                 | Log. regression, peripheral vascular disease: no association with in-hospital perioperative complications| 44.2 |                                                                                           |      |
| Lung                 | History of coronary artery disease associated with surgical site infection: log. regression, sign. OR 2.26 (95% CI 1.31-3.84), p=0.003 | 6    | Anemia (hematocrit <36) associated with increased length of stay after surgery: adj. beta 0.65 (95% CI 0.28 to 1.02) | 17   |
| Cardiovascular       | Cardiovascular disease associated with mortality up to 8 years after surgery: adj. HR 1.64 (95% CI 1.48 to 1.82) | 49   | Bivariate, heart disease: no association with increased length of stay after surgery and readmission <30 days | 2.2  |
| Lung                 | History of congestive heart failure associated with 90-day readmission OR 3.03 (95% CI 1.69-5.28), p=0.001 | 6    | Bivariate, anemia (hematocrit <36): no association with readmission <30 days |      |
| Lung                 | Pulmonary disease associated with in-hospital perioperative complications: log. regression, sign. OR 2.63 (95% CI 1.42 ± 4.87) | 44.2 | Pulmonary disease: no association with increased length of stay (bivariate) after surgery and readmission <30 days after surgery (multivariate) | 17   |
| Neurologic disease   | Cerebrovascular disease associated with mortality up to 8 years after surgery: adj. HR 1.23 (95% CI 1.11 to 1.37) | 49   |                                                                                           |      |
| Rheumatologic disease| Osteoarthritis associated with reoperation rate after a mean of 5.3 years: linear regression sign. beta 0.14 (p<0.001) | 44.3 | Univariate, osteoporosis/joint problem: no association with reoperation up to 8 years          | 2.2  |
| Psychiatric disease  | -                                                                                       | -    |                                                                                           |      |
| Kidney disease       | Chronic kidney disease associated with mortality up to 8 years after surgery: adj. HR 2.83 (95% CI 2.51 to 3.19) | 49   |                                                                                           |      |

*Gagne score (-2–26);
*Charlson comorbidity score based on coexisting conditions (range 0–3+);
*Quan comorbidity score (adapted Charlson comorbidity score) based on comorbid conditions in any hospitalization during the previous year (range 0–3+);
*a urinary complications (retention, infection, incontinence), exacerbation of congestive heart failure/chronic obstructive pulmonary disease, atrial fibrillation, wound infection, delirium, unstable angina, depression, cerebrovascular accident, gastrointestinal bleeding, hypotension and in-hospital death; [57]
*b wound infections, wound hematoma and other complications;
*c renal, cardiac, neurological, pulmonary, deep vein thrombosis, pulmonary embolism, infection;
*d dural tears, confusion, pseudogout, ileus, hypotension, wound infection, urinary retention, dehiscence;
*e neurologic, pulmonary, thromboembolic, cardiac, urinary, renal, hemorrhage/hematoma complicating a procedure, fluid/electrolyte abnormalities;
*f cardiopulmonary, vascular, infectious;
*g infection, hematoma, pneumonia, urinary tract infection, delirium, cerebrovascular accident, acute renal failure, neutropenia;
*h cerebrospinal fluid leakage, delirium, epidural hematoma, infection, dysuria, insufficiency fracture, wound problem, ileus, acute cholecystitis, aortic aneurysm, deep venous thrombosis;
*i wound complications (infections, hematoma, dehiscence), nerve root injury or other complications;
*j cardiac, general neurologic, pulmonary, renal, deep vein thrombosis or pulmonary embolism, infection, wound infection.
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