Impact of the number of previous lumbar operations on patient-reported outcomes after surgery for lumbar spinal stenosis or lumbar disc herniation

A POPULATION-BASED COHORT STUDY FROM THE NORWEGIAN REGISTRY FOR SPINE SURGERY

A. S. Riksaasen, S. Kaur, T. K. Solberg, I. Austevoll, J-I. Brox, F. C. Dolatowski, C. Hellum, F. Kolstad, G. Lonne, Ø. P. Nygaard, T. Ingebrigtsen

From The University Hospital of North Norway, Tromsø, Norway

Aims

Repeated lumbar spine surgery has been associated with inferior clinical outcomes. This study aimed to examine and quantify the impact of this association in a national clinical register cohort.

Methods

This is a population-based study from the Norwegian Registry for Spine surgery (NORspine). We included 26,723 consecutive cases operated for lumbar spinal stenosis or lumbar disc herniation from January 2007 to December 2018. The primary outcome was the Oswestry Disability Index (ODI), presented as the proportions reaching a patient-acceptable symptom state (PASS; defined as an ODI raw score ≤ 22) and ODI raw and change scores at 12-month follow-up. Secondary outcomes were the Global Perceived Effect scale, the numerical rating scale for pain, the EuroQoL five-dimensions health questionnaire, occurrence of perioperative complications and wound infections, and working capability. Binary logistic regression analysis was conducted to examine how the number of previous operations influenced the odds of not reaching a PASS.

Results

The proportion reaching a PASS decreased from 66.0% (95% confidence interval (CI) 65.4 to 66.7) in cases with no previous operation to 22.0% (95% CI 15.2 to 30.3) in cases with four or more previous operations ($p < 0.001$). The odds of not reaching a PASS were 2.1 (95% CI 1.9 to 2.2) in cases with one previous operation, 2.6 (95% CI 2.3 to 3.0) in cases with two, 4.4 (95% CI 3.4 to 5.5) in cases with three, and 6.9 (95% CI 4.5 to 10.5) in cases with four or more previous operations. The ODI raw and change scores and the secondary outcomes showed similar trends.

Conclusion

We found a dose-response relationship between increasing number of previous operations and inferior outcomes among patients operated for degenerative conditions in the lumbar spine. This information should be considered in the shared decision-making process prior to elective spine surgery.

Cite this article: ***Bone Joint J*** **2023;105-B(4):422–430.**

Correspondence should be sent to T. Ingebrigtsen; email: tor.ingebrigtsen@unn.no

doi:10.1302/0301-620X.105B4.BJJ-2022-0704.R1 $2.00

Bone Joint J 2023;105-B(4):422–430.

Introduction

The rate of lumbar spinal surgery in Norway increased from 78 per 100,000 per year in 1999 to 120 per 100,000 per year in 2018, and repeated operations accounted for 15%.[1,2] Repeated operations have been associated with inferior outcomes in single-centre studies.[3,4] Five registry studies found an association between previous operations and worse outcomes.[5-9] Zehnder et al[6] used data from the Spine Tango Registry and analyzed 4,940 patients operated for degenerative disorders, while Sigmundsson et al[9] used data from the

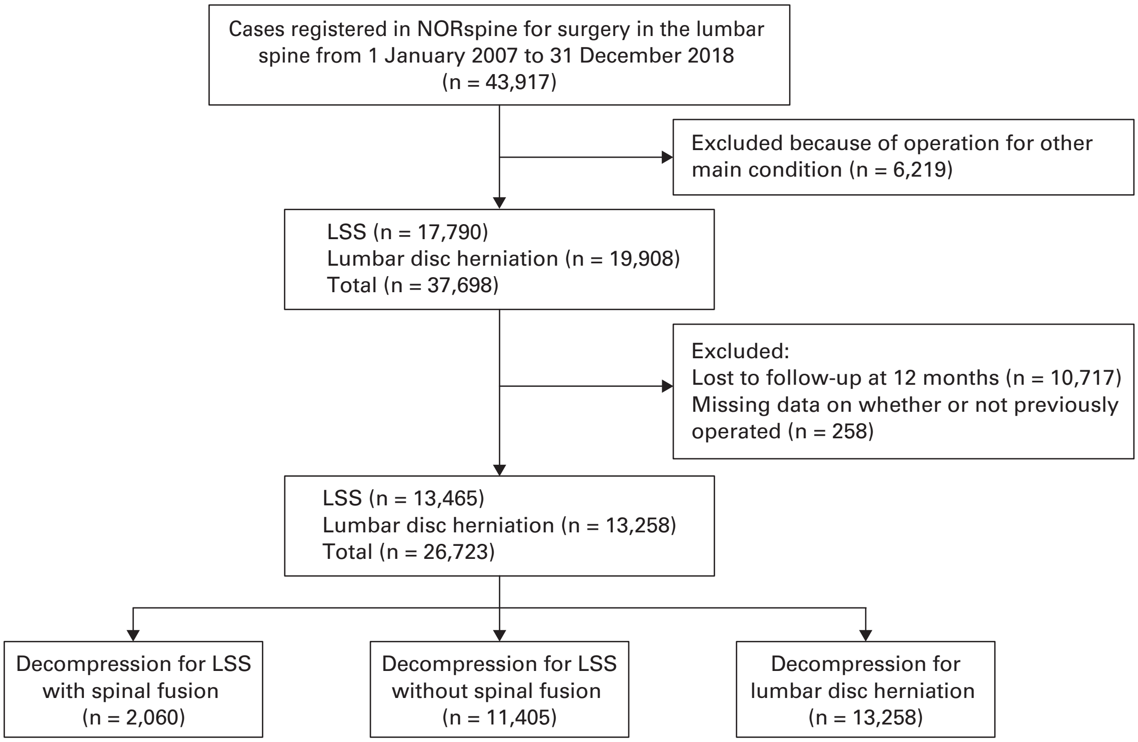

Fig. 1

Flowchart showing the recruitment process to the study. LSS, lumbar spinal stenosis; NORspine, Norwegian Registry for Spine Surgery.

Swedish spine registry (SweSpine) and analyzed 3,291 patients operated for lumbar disc herniation. Both found a dose-response effect of previous surgery: the risk of poor outcome after 12 months increased with the number of previous operations.[6,9] This study aimed to examine whether, and if so to what extent, the number of previous lumbar operations is associated with the outcomes after surgery for lumbar spinal stenosis or lumbar disc herniation.

Methods

Study design. This cohort study is a population-based retrospective analysis of prospectively collected data from the Norwegian registry for spine surgery (NORspine). Patients were categorized based on the number of previous lumbar spinal operations, enabling comparison of baseline scores and outcomes after first-time operations, and one or more previous operations. We report the results according to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.[10]

Setting. NORspine is a national clinical quality registry collecting data from public and private hospitals.[11] The operations are performed by orthopaedic surgeons or neurosurgeons. In 2017, the national coverage was 100% at the institutional level and 70.2% at the individual level for lumbar spine surgery. The response rate at 12-month follow-up is 70%. Data completeness is high (96.6% for the primary outcome measure, Oswestry Disability Index[12] (ODI)).[11]

Patients completed questionnaires on patient-reported outcome measures (PROMs), demographic data, and lifestyle preoperatively (baseline), and after three and 12 months. Patients also reported wound infections after three months. The surgeon recorded previous spine operations, diagnosis, comorbidity, treatment details, and perioperative complications after the operation.[11] At follow-up, the questionnaires were distributed by and returned to NORspine without involvement of the surgeons or other hospital staff.

Participants. All patients being operated for degenerative disorders in the lumbar spine are eligible for registration in NORspine. Exceptions are those precluded from consenting because of cognitive failure, severe psychiatric disorders, language barriers, or age < 16 years. Patients operated for fractures, primary infections, or tumours are not eligible.[11]

We included all cases registered with operations for lumbar spinal stenosis or lumbar disc herniation between 1 January 2007 and 31 December 2018. The operations were decompression with or without discectomy for disc herniation and decompression with or without fusion for spinal stenosis. NORspine defines reoperation within three months as a postoperative complication to the index operation, and not as a new case. Operations conducted three months or more apart are registered as separate cases, irrespective of the previously operated spinal level. We excluded cases with missing outcome data after 12 months and cases with missing data on whether they were previously operated.

Figure 1 defines the study population. A total of 37,698 cases operated for spinal stenosis or disc herniation were registered in NORspine during the study period. At 12 months, 10,717 (28.4%) were lost to follow-up. Another 258 (0.6%) were not

Table I. Distribution of the operations for all included cases, stratified by the number of previous operations.

Operation	All included cases	Previous operations				
		None	One	Two	Three	Four or more
Lumbar disc herniation, n (%)						
Microdiscectomy	12,199 (92.0)	9,632 (92.1)	1,751 (92.1)	424 (93.6)	104 (89.7)	24 (85.7)
Open decompression	1,059 (8.0)	822 (7.9)	150 (7.9)	29 (6.4)	12 (10.3)	4 (14.3)
Total	13,258 (100)	10,454 (100)	1,901 (100)	453 (100)	116 (100)	28 (100)
Lumbar spinal stenosis, n (%)						
Midline preserving decompression	9,559 (71.0)	7,450 (74.8)	1,365 (61.9)	382 (55.8)	113 (51.4)	46 (46.0)
Laminectomy	1,846 (13.7)	1,296 (13.0)	361 (16.4)	100 (14.6)	30 (13.6)	12 (12.0)
Fusion, n (%)	2,060 (15.3)	1,212 (12.2)	480 (21.8)	202 (29.5)	77 (35.0)	42 (42.0)
Posterior lumbar fusion	1,206 (58.5)	737 (60.8)	264 (55.0)	102 (50.4)	39 (50.6)	30 (71.4)
Posterior lumbar interbody fusion	79 (3.8)	51 (4.2)	16 (3.3)	6 (3.0)	3 (3.9)	1 (2.4)
Transforaminal lumbar interbody fusion	760 (36.9)	418 (34.5)	196 (40.8)	93 (46.0)	33 (42.9)	9 (21.4)
Anterior lumbar interbody fusion	7 (0.3)	4 (0.3)	1 (0.2)	0 (0.0)	1 (1.3)	1 (2.4)
Extreme lateral interbody fusion	3 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.3)	1 (2.4)
Undefined fusion	5 (0.2)	2 (0.2)	2 (0.4)	1 (0.5)	0 (0.0)	0 (0.0)
Total	13,465 (100)	9,958 (100)	2,206 (100)	684 (100)	220 (100)	100 (100)

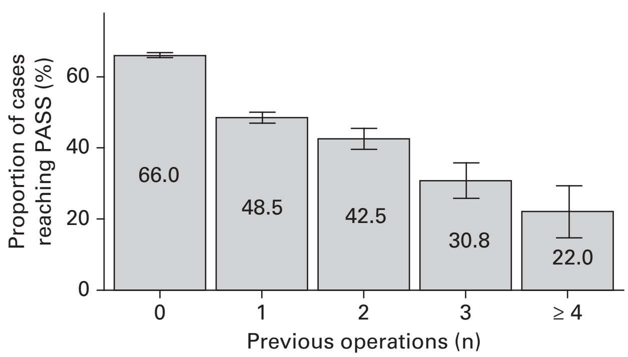

Fig. 2

Proportion of cases reaching a patient-acceptable symptom state (PASS; Oswestry Disability Index raw score ≤ 22) at 12-month follow-up, stratified by the number of previous operations. Error bars represent 95% confidence intervals.

analyzed for reasons specified in Figure 1. We included 26,723 cases (70.9%). Supplementary Table i shows that 20,412 (76.4%) had no previous lumbar operation for degenerative disorders, 4,107 (15.4%) had one, 1,137 (4.3%) had two, 336 (1.3%) had three, and 128 (0.4%) had four or more previous operations. The sensitivity analysis, in which we analyzed available three-month outcome data for cases with missing data at 12-month follow-up, included 30,075 cases (80.8%).

Variables and outcomes. The primary outcome was ODI, evaluating back-related disability in activities of daily living. Scores range from 0 (no disability) to 100 (maximum disability).[12] We present the proportion of patients who reached a patient-acceptable symptom state (PASS; defined as an ODI raw score ≤ 22), and their raw and change scores at 12 months postoperatively. [13]

Secondary outcomes were the Global Perceived Effect scale (GPE),[14] numerical rating scale (NRS) for back and leg pain,[15] EuroQoL five-dimension three-level health questionnaire (EQ-5D-3L),[16] perioperative complications, wound infections, and working capability. The GPE is a balanced Likert scale assessing patient-rated benefit of the operation, with response alternatives ranging from 1 (completely recovered) to 7 (worse than ever). The NRS measures back and leg pain intensity on a unidimensional scale ranging from 0 (no pain) to 10 (worst conceivable pain). EQ-5D-3L is a generic measure of health-related quality of life, comprising five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Index scores range from -0.594 to 1, where 1 corresponds to perfect health and 0 to death.

We calculated the proportion of cases who received sickness or disability benefits preoperatively and the proportion continuing to do so after 12 months.

Statistical analysis. Descriptive data are presented as means and 95% confidence intervals (CIs) for continuous variables and counts and percentages for proportions. Differences between samples were examined by one-way analysis of variance (ANOVA) for continuous and the chi-squared test for categorical variables. The level of significance was a p-value < 0.05. Comparative analysis of baseline characteristics of respondents and those lost to follow-up after 12 months was done to assess selection bias.

We used bivariate analyses to examine associations between possible confounders and the exposure variable.[17–22] Continuous variables were: BMI and baseline PROM scores; i.e. ODI, EQ-5D-3L, and NRS. Some categorical variables were dichotomized to improve the data-to-model fit and facilitate interpretation of the analyses. The following categorical variables were included: age (five-year categories: 15 to 19, 20 to 24, etc.); female sex (yes or no); smoking (yes or no); level of education: completed college or university education (yes or no); marital status: living alone (yes or no); native language: Norwegian (yes or no); working status: sickness or disability benefit recipient (full or partial sick leave, or work assessment allowance or disability pension) (yes or no); have applied or plan to apply for disability pension (yes or no); duration of back pain: longer than 12 months (yes or no); duration of radiating pain: longer than 12 months (yes or no); use of any painkillers

Table II. The Global Perceived Effect scale at 12 months' follow-up, stratified by the number of previous operations.

To what degree did you benefit from the operation?	Previous operations, n (%)				
	None	One	Two	Three	Four or more
Completely recovered	4,898 (24.1)	591 (14.5)	125 (11.0)	23 (7.0)	4 (3.1)
Much improved	9,078 (44.7)	1,569 (38.5)	416 (36.7)	111 (33.6)	41 (32.3)
Slightly improved	3,669 (18.1)	954 (23.4)	300 (26.5)	86 (26.1)	40 (31.5)
Unchanged	1,199 (5.9)	404 (9.9)	121 (10.7)	45 (13.6)	21 (16.5)
Slightly worsened	742 (3.7)	263 (6.5)	91 (8.0)	22 (6.7)	11 (8.7)
Much worsened	493 (2.4)	202 (5.0)	64 (5.7)	30 (9.1)	7 (5.5)
Worse than ever	220 (1.1)	90 (2.2)	15 (1.3)	13 (3.9)	3 (2.4)

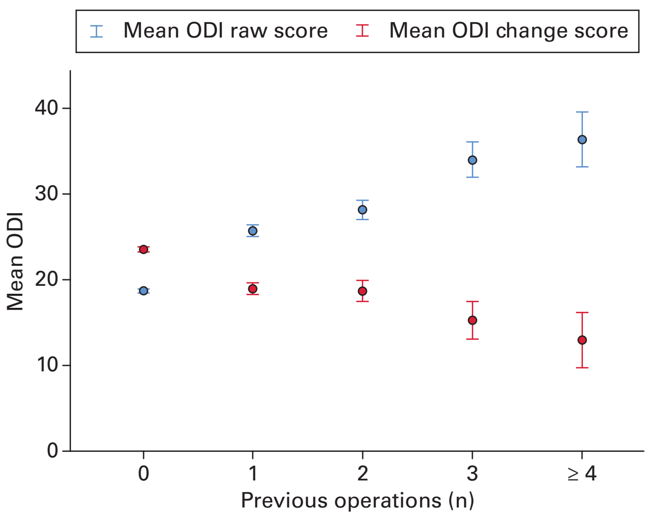

Fig. 3

Mean Oswestry Disability Index (ODI) raw score and mean ODI change score at 12-month follow-up, stratified by the number of previous operations. Error bars represent 95% confidence intervals.

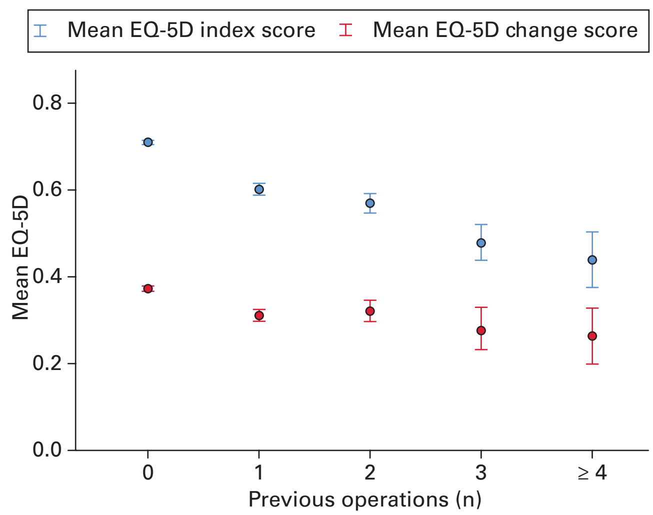

Fig. 4

Mean EuroQol five-dimension (EQ-5D) index score and mean EQ-5D change score at 12-month follow-up, stratified by the number of previous operations. Error bars represent 95% confidence intervals.

(yes or no); any comorbidity (yes or no); American Society of Anesthesiologists grade (ASA):[23] > II (yes or no); anxiety and/or depression: moderate to severe problems (yes or no); and fusion surgery (yes or no). Confounding was defined as present if a covariate altered the β of the association between the exposure variable and the outcome by more than 10%. The exposure variable was categorized as no (reference), one, two, three, and four or more previous operations.

A binary logistic regression analysis was conducted to examine how the exposure variable (number of previous operations) influenced the primary outcome (dependent variable: reaching PASS (no or yes)). We also conducted subgroup analyses with the exposure variable dichotomized to patients previously operated at the same spinal level or at different levels only.

We did a sensitivity analysis to assess whether missing data influenced the main results, i.e. the odds for not reaching a PASS (dependent variable). Follow-up data after three months were included in a generalized estimating equation with a logit link function. We used a combination of time (three and 12 months) and the number of previous operations (exposure) as fixed effects. An exchangeable covariance matrix was included to adjust for dependence between the repeated ODI measures.

Results

Study population. Comprehensive details of the baseline characteristics of the included cases are provided in Supplementary Table i. In brief, the mean age was 56.5 years (95% CI 56.3 to 56.7) for all included cases and 56.0 years (95% CI 55.7 to 56.2) for those who had no previous surgery. Overall, 14,047 cases (52.6%) were male. The ODI mean score increased from 42.1 (95% CI 41.8 to 42.4) in cases with no previous operations to 48.6 (95% CI 46.5 to 50.7) in cases with three previous operations. The proportion who were working decreased from 19.1% among cases with no previous operations to 8.9% among those with three previous operations, and the proportion receiving disability pension increased. Additionally, the proportion with comorbidity increased with the number of previous operations. Supplementary Table i also shows the distribution of previously operated spinal levels. The proportion with previous operations both at the same and different spinal levels increased from 2.9% among cases with one to 24.2% among those with four or more previous operations.

A comparison of baseline characteristics of the included cases with those lost to follow-up after 12 months found those lost to follow-up were younger, healthier, and more likely to

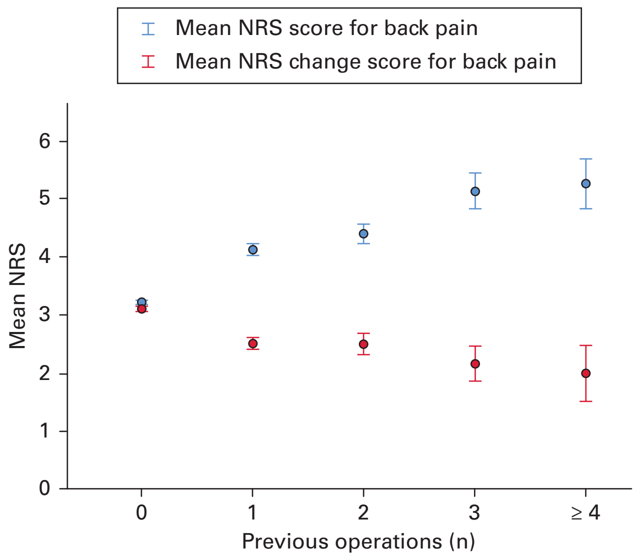

Fig. 5

Mean numerical rating scale (NRS) score for back pain and mean NRS change score at 12-month follow-up, stratified by the number of previous operations. Error bars represent 95% confidence intervals.

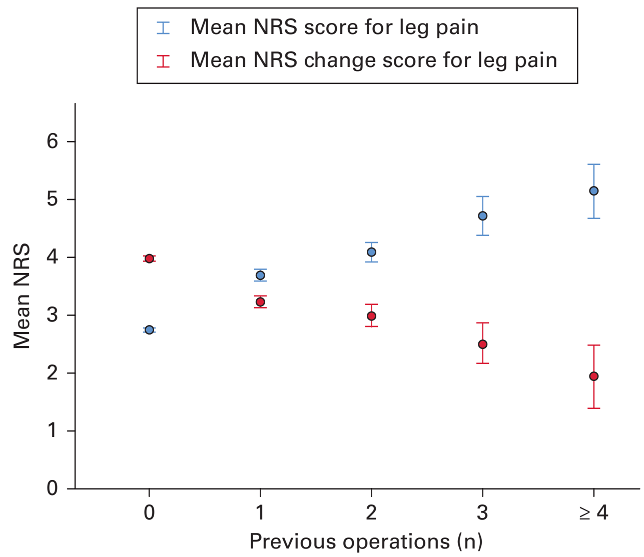

Fig. 6

Mean numerical rating scale (NRS) score for leg pain and mean NRS change score at 12-month follow-up, stratified by the number of previous operations. Error bars represent 95% confidence intervals.

be male, smoke, and live alone. The differences in the proportion previously operated and the distribution of the number of previous operations were small. The full analysis is presented in Supplementary Table ii.

Table I shows the distribution of operations. Among cases operated for spinal stenosis, the proportion operated with fusion increased from 12.2% in cases with no previous operations to 42.0% in cases with four or more previous operations.

Main results. Figure 2 shows the proportion who reached a PASS after 12 months, stratified by the number of previous operations. The proportion decreased stepwise and significantly from 66.0% (95% CI 65.4 to 66.7) in the group with no previous operations to 22.0% (95% CI 15.2 to 30.3) in the group with four or more previous operations ($p < 0.001$, chi-squared test). The differences were statistically significant at each step from no previous operations to three previous operations ($p < 0.001$, chi-squared test), but not from three to four or more previous operations ($p = 0.062$, chi-squared test).

Figure 3 shows mean ODI raw and change scores after 12 months, stratified by the number of previous operations. The mean raw score increased successively and significantly with the number of operations, from 18.6 (95% CI 18.4 to 18.8) for cases with no previous operations to 36.4 (95% CI 33.2 to 39.5) for cases with four or more previous operations ($p < 0.001$, ANOVA). The differences were statistically significant at each step from no previous operations to three previous operations ($p < 0.001$, ANOVA), but not from three to four or more previous operations ($p = 0.234$, ANOVA). The mean ODI raw score increased by a mean of 4.5 points (2.4 to 7.1) for each additional previous operation.

We found less improvement in ODI from baseline to 12 months with increasing number of previous operations. The mean change score decreased significantly from 23.5 (95 CI 23.3 to 23.8) for cases with no previous operations to 13.1 (95% CI 9.8 to 16.2) for cases with four or more previous operations ($p < 0.001$, ANOVA). There were statistically significant differences between cases with no and one previous operations, and between those with two and three previous operations. Between cases with one and two previous operations, and between those with three and four previous operations, there were no statistically significant differences.

Results for the secondary outcomes are presented in Table II and Figures 4 to 6. They showed the same trends as for the primary outcomes ($p < 0.001$, chi-squared test and ANOVA). The incidence of wound infection, requirement for disability benefits, and surgical complications all increased in parallel with the increasing number of operations received (Supplementary Figures a to c). The proportion reporting complete recovery or much improvement on the GPE scale decreased stepwise from 68.8% in the group with no previous operations to 35.4% in the group with four or more previous operations (Table II).

Prediction analysis. Results from the bivariate logistic regression analysis are presented in Table III. None of the variables changed the β with 10% or more. Thus, we did not identify confounders significantly affecting the impact of the number of previous operations. Fusion surgery (cases operated for spinal stenosis) changed the β of the exposure variable most, reducing the odds ratio (OR) for an unfavourable outcome from 1.74 (95% CI 1.74 to 1.81) to 1.66 (95% CI 1.57 to 1.75). Table IV shows that there was a dose-response relationship between the number of previous operations and the odds of not reaching a PASS, increasing from 2.1 (95% CI 1.9 to 2.2) in cases with one previous operation, 2.6 (95% CI 2.3 to 3.0) in cases with two, 4.4 (95% CI 3.4 to 5.5) in cases with three, and 6.9 (95% CI 4.5 to 10.5) in cases with four or more previous operations. The increments were statistically significant ($p < 0.001$, binary

Table III. Bivariate analysis of associations between the exposure variable and possible confounders. The dependent variable was reaching a patient-acceptable symptom state at 12-month follow-up.

Variable	β	OR (95% CI)	Confounder	p-value
Exposure variable				
Number of previous operations	0.55	1.74 (1.67 to 1.81)		< 0.001
Possible confounders				
Age (5-year categories)	0.54	1.71 (1.64 to 1.78)	No	< 0.001
Female sex (Y/N)	0.57	1.77 (1.70 to 1.84)	No	< 0.001
Smoking (Y/N)	0.55	1.74 (1.67 to 1.81)	No	< 0.001
College or university education (Y/N)	0.56	1.74 (1.67 to 1.81)	No	< 0.001
Living alone (Y/N)	0.56	1.74 (1.68 to 1.82)	No	< 0.001
Native Norwegian language (Y/N)	0.56	1.75 (1.68 to 1.82)	No	< 0.001
BMI	0.55	1.73 (1.66 to 1.81)	No	< 0.001
Sickness or disability benefit recipient (Y/N)	0.56	1.74 (1.67 to 1.82)	No	< 0.001
Have applied or planning to apply for disability pension (yes/no)	0.55	1.74 (1.67 to 1.82)	No	< 0.001
NRS back pain (0 to 10)	0.52	1.68 (1.61 to 1.75)	No	< 0.001
NRS leg pain (0 to 10)	0.54	1.72 (1.65 to 1.79)	No	< 0.001
ODI (0 to 100)	0.52	1.68 (1.61 to 1.75)	No	< 0.001
EQ-5D (-0.594 to 1)	0.53	1.70 (1.63 to 1.77)	No	< 0.001
Longer than 12 months duration of back pain (Y/N)	0.56	1.76 (1.68 to 1.83)	No	< 0.001
Longer than 12 months duration of radiating pain (Y/N)	0.55	1.74 (1.67 to 1.81)	No	< 0.001
Use of painkillers (Y/N)	0.54	1.71 (1.64 to 1.78)	No	< 0.001
Any comorbidity (Y/N)	0.52	1.68 (1.61 to 1.75)	No	< 0.001
ASA grade > II (Y/N)	0.54	1.72 (1.65 to 1.79)	No	< 0.001
Moderate to severe anxiety and/or depression (Y/N)	0.56	1.75 (1.68 to 1.83)	No	< 0.001
Partial paralysis (Y/N)	0.56	1.75 (1.68 to 1.82)	No	< 0.001
Fusion surgery (lumbar spinal stenosis) (Y/N)	0.51	1.66 (1.57 to 1.75)	No	< 0.001

ASA, American Society of Anesthesiologists; CI, confidence interval; EQ-5D, EuroQol five-dimension health questionnaire; NRS, numerical rating scale; ODI, Oswestry Disability Index; OR, odds ratio; PASS, patient-acceptable symptom state.

logistic regression) from the reference (no previous operation) for all categories. The 95% CIs did not overlap between the steps except from three to four or more previous operations. Subgroup analysis of cases previously operated at different spinal levels showed the same result (Table IV).

The sensitivity analysis showed that missing data at 12-month follow-up did not influence the odds for not reaching a PASS (Table IV).

Discussion

In this large national register study of 26,723 cases operated for spinal stenosis or disc herniation, 5,708 (21%) had undergone one or more previous operations. We found that the likelihood of reaching a PASS decreased with each previous operation. There was a dose-response relationship between the number of previous operations and the proportion of cases reaching a PASS 12 months postoperatively, decreasing from 66% in cases with no previous operations to 22% in cases with four or more previous operations. The OR for not reaching a PASS was doubled in cases with one previous operation, nearly tripled in cases with two, four in cases with three, and nearly seven in cases with four or more previous operations. The ODI raw and change scores, and the secondary outcomes, showed similar trends.

This association between previous operations and inferior outcomes confirm the findings in previous but smaller studies, including one previous data analysis from NORspine.[3-9] Only the register-based studies by Zehnder et al[6] and Sigmundsson et al[9] categorized participants based on the number of previous operations.

Zehnder et al[6] analyzed 1,519 (31%) previously operated patients among 4,940 included patients, and reported 0.4 points less improvement of the Core Outcome Measurement Index (COMI) for each additional operation. This finding was statistically significant, but below the minimal clinically important change (MCIC) of two to three COMI points.[24] In the present study, we observed a mean stepwise increase in the ODI raw score at 12 months by 4.5 points for each additional operation. This change is larger than the effect size found by Zehnder et al,[6] since the MCIC cut-off for ODI is considered to be approximately ten points.[25] Importantly, the MCIC is not recommended for comparisons of mean outcomes between groups, since these thresholds are developed to determine a clinically relevant change at the individual level. Therefore, we compared the proportion of cases reaching a validated threshold for a PASS in each subgroup. This strategy allows for comparison of effect sizes across groups and has been recommended by several authors.[26–29] In addition, the Spine Tango comprises patients operated in different countries, and reporting is voluntary, implying that completeness and follow-up may be compromised.

Sigmundsson et al[9] analyzed 681 (21%) additional operations after 3,291 primary operations, and reported a stepwise decrease in change scores for NRS leg pain from 5.5 among cases with no previous operations to 1.2 among cases with three previous operations.[9] The corresponding figures in the present

Table IV. Binary logistic regression analysis of the number of previous operations as a predictor of not reaching a patient-acceptable symptom state at 12-month follow-up, including subgroup (same or different spinal level) and sensitivity analysis (using both three- and 12-month follow-up data).

Previous operations	Primary analysis		Sensitivity analysis	
	OR (95% CI)	p-value	OR (95% CI)	p-value
None	Reference	< 0.001	Reference	< 0.001
One				
All	2.1 (1.9 to 2.2)	< 0.001	2.0 (1.9 to 2.1)	< 0.001
Different level	2.2 (2.0 to 2.4)	< 0.001		
Same level	2 (1.8 to 2.2)	< 0.001		
Two				
All	2.6 (2.3 to 3.0)	< 0.001	2.7 (2.4 to 3.0)	< 0.001
Different level	2.5 (2.0 to 3.1)	< 0.001		
Same level	2.7 (2.3 to 3.1)	< 0.001		
Three				< 0.001
All	4.4 (3.4 to 5.5)	< 0.001	4.3 (3.5 to 5.2)	< 0.001
Different level	3.7 (2.5 to 5.5)	< 0.001		
Same level	4.7 (3.5 to 6.3)	< 0.001		
Four or more				< 0.001
All	6.9 (4.5 to 10.5)	< 0.001	5.7 (4.1 to 7.8)	< 0.001
Different level	8.2 (4.0 to 17.0)	< 0.001		
Same level	6.2 (3.7 to 10.5)	< 0.001		

CI, confidence interval; OR, odds ratio.

study were 4.0 and 2.5. There were similar corresponding observations between the studies for NRS back pain and EQ-5D. SweSpine, the Swedish equivalent of NORspine, and NORspine are comparative national clinical quality registries with high coverage and data completeness.

In the analyses of the dose-response effects, we did not find statistically significant differences between groups with three and four or more previous operations. This is most likely due to lack of statistical power (type II error), since the number of cases with four or more previous operations was low (n = 128).

No covariate met the predefined criteria for confounding. Importantly, established risk factors for an unfavourable outcome, such as age, female sex, smoking status, duration of symptoms, ASA grade, having moderate to severe anxiety and/or depression, or being a sickness or disability benefit recipient, did not influence the impact of the number of previous operations on the outcome. This was also the case for the baseline ODI mean score, even though it increased with the number of previous operations. Additional fusion in cases operated for lumbar spinal stenosis did not reduce the negative impact of previous operations on the outcome considerably. In contrast, Osterman et al[30] reported that additional fusion surgery could reduce the risk of subsequent surgery after lumbar discectomy.

The present study aimed to quantify the impact of the number of previous operations on outcomes. However, due to the study design we cannot draw conclusions about causal inferences between increasing number of previous operations and unfavourable outcome. Possible explanations could be a weak indication already for the first operation, increasing pain sensitization and neuropathic radicular pain among cases undergoing repeated operations, or underlying genetic predisposition, e.g. for progressive degenerative spinal disorder.

Our findings were consistent and may be used in shared decision-making, particularly in cases where there is uncertainty regarding the indication for surgery.

The large study population allowed us to categorize participants into five groups based on the number of previous operations. NORspine is population-based with high individual-level coverage and data completeness. This yields low risk for selection bias at inclusion. The external validity is high since the data were retrieved from routine clinical practice.

Loss to follow-up introduces a risk of selection bias in the reporting of outcomes. The drop-out analysis revealed no notable difference in pre-scores for the primary and secondary outcomes, and the differences in the distribution of the number of previous operations were small. However, the cases lost to follow-up were younger, and the proportions of males, smokers, participants living alone, and participants with comorbidity were higher. This corresponds with findings in studies from the Scandinavian spine surgery registries.[31–33] Previous Scandinavian registry studies found no statistically significant differences in outcomes between respondents and non-respondents.[32–34] The robustness of our findings is supported by the sensitivity analysis, in which we used data from both three- and 12-month follow-up, showing only negligible deviations from the primary analyses. However, we cannot rule out that loss to follow-up may lead to overestimation of clinical outcomes.[31]

Some of the minor differences may have been statistically significant by incident (type I error), but our main findings were consistent across all the outcomes. The study may also be subject to unmeasured confounding. For instance, we did not have information about imaging-based grading of spinal stenosis, description of disc herniation morphology, or the laterality or complications of previous lumbar spine operations.

PROMs may have some shortcomings. The disease-specific ODI could fail to address issues important to patients, who also may weigh the importance of the items differently. However, we also used the generic and preference-weighted EQ-5D, which revealed similar trends as we found for the ODI. We used a GPE scale to assess patient-rated benefit of the operation. An answer can reflect both preferences and expectations, and may be strongly influenced by the current health status at 12-month follow-up.[14] The accuracy of reporting may also decrease as the time from intervention increases due to recall bias.[28] Some authors argue that the criteria for measurement of global effects should be defined more objectively. However, no such scale exists. Therefore, we consider the GPE most suitable for assessing a global perceived effect.

We found a dose-response relationship between increasing number of previous operations and inferior outcomes among cases operated for degenerative conditions in the lumbar spine. The odds for not reaching a PASS were doubled in patients with one previous operation, nearly tripled in patients with two, and four to nearly seven times increased in patients with three or more previous operations. This information should be taken into consideration in the shared decision-making process prior to surgery.

Take home message

- Repeated lumbar spine operations have been associated with inferior outcomes.
- We found a dose-response relationship between increasing number of previous operations and inferior outcomes among patients operated for degenerative conditions.
- This information should be considered in the shared decision making-process prior to elective spine surgery.

Supplementary material

Tables showing baseline characteristics for all included cases and those lost to follow-up, and figures showing outcomes stratified by the number of previous operations.

References

1. **Ingebrigtsen T**, **Balteskard L**, **Guldhaugen KA**, **et al**. Treatment rates for lumbar spine surgery in Norway and Northern Norway Regional Health Authority 2014-18. *Tidsskr Nor Laegeforen*. 2020;140(17).
2. **Grotle M**, **Småstuen MC**, **Fjeld O**, **et al**. Lumbar spine surgery across 15 years: trends, complications and reoperations in a longitudinal observational study from Norway. *BMJ Open*. 2019;9(8):e028743.
3. **Vik A**, **Zwart JA**, **Hulleberg G**, **Nygaard OP**. Eight year outcome after surgery for lumbar disc herniation: a comparison of reoperated and not reoperated patients. *Acta Neurochir (Wien*). 2001;143(6):607–610; .
4. **Waddell G**, **Kummel EG**, **Lotto WN**, **Graham JD**, **Hall H**, **McCulloch JA**. Failed lumbar disc surgery and repeat surgery following industrial injuries. *J Bone Joint Surg Am*. 1979;61-A(2):201–207.
5. **Sobottke R**, **Herren C**, **Siewe J**, **Mannion AF**, **Röder C**, **Aghayev E**. Predictors of improvement in quality of life and pain relief in lumbar spinal stenosis relative to patient age: a study based on the Spine Tango registry. *Eur Spine J*. 2017;26(2):462–472.
6. **Zehnder P**, **Aghayev E**, **Fekete TF**, **Haschtmann D**, **Pigott T**, **Mannion AF**. Influence of previous surgery on patient-rated outcome after surgery for degenerative disorders of the lumbar spine. *Eur Spine J*. 2016;25(8):2553–2562.
7. **Fritzell P**, **Knutsson B**, **Sanden B**, **Strömqvist B**, **Hägg O**. Recurrent versus primary lumbar disc herniation surgery: patient-reported outcomes in the Swedish Spine Register Swespine. *Clin Orthop Relat Res*. 2015;473(6):1978–1984.
8. **Nerland US**, **Jakola AS**, **Giannadakis C**, **et al**. The risk of getting worse: predictors of deterioration after decompressive surgery for lumbar spinal stenosis: a multicenter observational study. *World Neurosurg*. 2015;84(4):1095–1102.
9. **Sigmundsson FG**, **Joelson A**, **Strömqvist F**. Additional operations after surgery for lumbar disc prolapse : indications, type of surgery, and long-term follow-up of primary operations performed from 2007 to 2008. *Bone Joint J*. 2022;104-B(5):627–632.
10. **von Elm E**, **Altman DG**, **Egger M**, **et al**. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol*. 2008;61(4):344–349.
11. **Solberg T**, **Olsen L**, **Berglund M**. Annual report for NORspine 2018. Nasjonalt Kvalitetsregister for Ryggkirugi. 2019. https://unn.no/Documents/Kvalitetsregistre/Nasjonalt%20kvalitetsregister%20for%20ryggkirurgi/%C3%85rsrapporter/%C3%85rsrapport_NKR_2018%20.pdf (date last accessed 17 February 2023).
12. **Fairbank JC**, **Pynsent PB**. The Oswestry Disability Index. *Spine (Phila Pa 1976)*. 2000;25(22):2940–2952.
13. **van Hooff ML**, **Mannion AF**, **Staub LP**, **Ostelo RWJG**, **Fairbank JCT**. Determination of the Oswestry Disability Index score equivalent to a "satisfactory symptom state" in patients undergoing surgery for degenerative disorders of the lumbar spine-a Spine Tango registry-based study. *Spine J*. 2016;16(10):1221–1230.
14. **Kamper SJ**, **Ostelo R**, **Knol DL**, **Maher CG**, **de Vet HCW**, **Hancock MJ**. Global Perceived Effect scales provided reliable assessments of health transition in people with musculoskeletal disorders, but ratings are strongly influenced by current status. *J Clin Epidemiol*. 2010;63(7):760–766.
15. **Hawker GA**, **Mian S**, **Kendzerska T**, **French M**. Measures of adult pain: Visual Analog Scale for Pain (VAS Pain), Numeric Rating Scale for Pain (NRS Pain), McGill Pain Questionnaire (MPQ), Short-Form McGill Pain Questionnaire (SF-MPQ), Chronic Pain Grade Scale (CPGS), Short Form-36 Bodily Pain Scale (SF-36 BPS), and Measure of Intermittent and Constant Osteoarthritis Pain (ICOAP). *Arthritis Care Res*. 2011;63(S11):S240–S252.
16. **The EuroQol Group**. EuroQol-a new facility for the measurement of health-related quality of life. *Health Policy*. 1990;16(3):199–208.
17. **Fjeld O**, **Grotle M**, **Siewers V**, **Pedersen LM**, **Nilsen KB**, **Zwart J-A**. Prognostic factors for persistent leg-pain in patients hospitalized with acute sciatica. *Spine (Phila Pa 1976)*. 2017;42(5):E272–E279.
18. **Haugen AJ**, **Brox JI**, **Grøvle L**, **et al**. Prognostic factors for non-success in patients with sciatica and disc herniation. *BMC Musculoskelet Disord*. 2012;13(1):183.
19. **Järvimäki V**, **Kautiainen H**, **Haanpää M**, **et al**. Depressive symptoms are associated with poor outcome for lumbar spine surgery. *Scand J Pain*. 2016;12:13–17.
20. **Kleinstueck FS**, **Fekete T**, **Jeszenszky D**, **et al**. The outcome of decompression surgery for lumbar herniated disc is influenced by the level of concomitant preoperative low back pain. Eur Spine J. 2011;20(7):1166–1173.
21. **Koerner JD**, **Glaser J**, **Radcliff K**. Which variables are associated with patient-reported outcomes after discectomy? Review of SPORT disc herniation studies. *Clin Orthop Relat Res*. 2015;473(6):2000–2006.
22. **Pieber K**, **Salomon N**, **Inschlag S**, **Amtmann G**, **Resch K-L**, **Ebenbichler G**. Predictors of an unfavorable outcome 1.5 and 12 years after a first, uncomplicated lumbar disc surgery. *Eur Spine J*. 2016;25(11):3520–3527.
23. **Saklad M**. Grading of patients for surgical procedures. *Anesthesiol*. 1941;2(3):281–284.
24. **Mannion AF**, **Porchet F**, **Kleinstück FS**, **et al**. The quality of spine surgery from the patient's perspective: part 2. Minimal clinically important difference for improvement and deterioration as measured with the Core Outcome Measures Index. *Eur Spine J*. 2009;18 Suppl 3(Suppl 3):374–379.
25. **Ostelo RWJG**, **de Vet HCW**. Clinically important outcomes in low back pain. *Best Pract Res Clin Rheumatol*. 2005;19(4):593–607.
26. **Dworkin RH**, **Turk DC**, **Wyrwich KW**, **et al**. Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. *J Pain*. 2008;9(2):105–121.
27. **Austevoll IM**, **Gjestad R**, **Grotle M**, **et al**. Follow-up score, change score or percentage change score for determining clinical important outcome following surgery? An observational study from the Norwegian registry for Spine surgery evaluating patient reported outcome measures in lumbar spinal stenosis and lumbar degenerative spondylolisthesis. *BMC Musculoskelet Disord*. 2019;20(1):31.
28. **McLeod LD**, **Coon CD**, **Martin SA**, **Fehnel SE**, **Hays RD**. Interpreting patient-reported outcome results: US FDA guidance and emerging methods. *Expert Rev Pharmacoecon Outcomes Res*. 2011;11(2):163–169.
29. **Katz NP**, **Paillard FC**, **Ekman E**. Determining the clinical importance of treatment benefits for interventions for painful orthopedic conditions. *J Orthop Surg Res*. 2015;10:24.
30. **Osterman H**, **Sund R**, **Seitsalo S**, **Keskimäki I**. Risk of multiple reoperations after lumbar discectomy: a population-based study. *Spine (Phila Pa 1976*). 2003;28(6):621–627.
31. **Parai C**, **Hägg O**, **Willers C**, **Lind B**, **Brisby H**. Characteristics and predicted outcome of patients lost to follow-up after degenerative lumbar spine surgery. *Eur Spine J*. 2020;29(12):3063–3073.
32. **Højmark K**, **Støttrup C**, **Carreon L**, **Andersen MO**. Patient-reported outcome measures unbiased by loss of follow-up. Single-center study based on DaneSpine, the Danish spine surgery registry. *Eur Spine J*. 2016;25(1):282–286.

33. **Solberg TK**, **Sørlie A**, **Sjaavik K**, **Nygaard ØP**, **Ingebrigtsen T**. Would loss to follow-up bias the outcome evaluation of patients operated for degenerative disorders of the lumbar spine? *Acta Orthop*. 2011;82(1):56–63.
34. **Endler P**, **Ekman P**, **Hellström F**, **Möller H**, **Gerdhem P**. Minor effect of loss to follow-up on outcome interpretation in the Swedish spine register. *Eur Spine J*. 2020;29(2):213–220.

Author information:
A. S. Riksaasen, MD, Resident Physician, Faculty of Health Sciences, Department of Clinical Medicine, University of Tromsø - the Arctic University of Norway, Tromsø, Norway.

S. Kaur, MD, Consultant Orthopaedic Surgeon, Martina Hansens Hospital, Sandvika, Norway.

T. K. Solberg, MD, PhD, Consultant Neurosurgeon, Professor, Faculty of Health Sciences, Department of Clinical Medicine, University of Tromsø - the Arctic University of Norway, Tromsø, Norway; Department of Neurosurgery and the Norwegian Registry for Spine Surgery, University Hospital of North Norway, Tromsø, Norway.

I. Austevoll, MD, PhD, Consultant Orthopaedic Surgeon, Orthopedic Department, Kysthospitalet in Hagevik, Haukeland University Hospital, Bergen, Norway.

J-I. Brox, MD, PhD, Professor, Consultant Physical Medicine, Rehabilitation Specialist, Department of Physical Medicine and Rehabilitation, Oslo University Hospital, Oslo, Norway.

F. C. Dolatowski, MD, PhD, Consultant Orthopaedic Surgeon
C. Hellum, MD, PhD, Consultant Orthopedic Surgeon
Division of Orthopedic Surgery, Oslo University Hospital, Oslo, Norway.

F. Kolstad, MD, PhD, Head of Department, Consultant Neurosurgeon, Department of Neurosurgery, Oslo University Hospital, Oslo, Norway.

G. Lonne, MD, PhD, Consultant Orthopaedic Surgeon, Department of Neuromedicine and Movement Science, Norwegian University of Science and Technology, Trondheim, Norway; Innlandet Hospital Trust, Brumunddal, Norway; Department of Neurosurgery, St. Olavs Hospital and the National Advisory Unit on Spinal Surgery, Trondheim, Norway.

Ø. P. Nygaard, MD, PhD, Consultant Neurosurgeon, Professor, Department of Neuromedicine and Movement Science, Norwegian University of Science and Technology, Trondheim, Norway; Department of Neurosurgery, St. Olavs Hospital and the National Advisory Unit on Spinal Surgery, Trondheim, Norway.

T. Ingebrigtsen, MD, PhD, Professor, Consultant Neurosurgeon, Faculty of Health Sciences, Department of Clinical Medicine, University of Tromsø - the Arctic University of Norway, Tromsø, Norway; Department of Neurosurgery and the Norwegian Registry for Spine Surgery, University Hospital of North Norway, Tromsø, Norway; Australian Institute of Health Innovation, Macquarie University, Sydney, Australia.

Author contributions:
A. S. Riksaasen: Methodology, Data curation, Formal analysis, Writing – original draft, Writing – review & editing.
S. Kaur: Writing – review & editing.
T. K. Solberg: Conceptualization, Methodology, Supervision, Data curation, Formal analysis, Writing – original draft, Writing – review & editing.
I. Austevoll: Writing – review & editing.
J-I. Brox: Writing – review & editing.
F. C. Dolatowski: Writing – review & editing.
C. Hellum: Writing – review & editing.
F. Kolstad: Writing – review & editing.
G. Lonne: Writing – review & editing.
Ø. P. Nygaard: Writing – review & editing.
T. Ingebrigtsen: Conceptualization, Methodology, Project administration, Supervision, Formal analysis, Writing – original draft, Writing – review & editing.

Funding statement:
The authors received no financial or material support for the research, authorship, and/or publication of this article.

Acknowledgements:
The authors thank Professor Tom Wilsgaard, UiT the Arctic University of Norway, for helpful advice and support with statistical analysis.

Ethical review statement:
All participants signed a written consent to collect, retain, and use their information for research and quality improvement purposes. The Data Protection Officer (DPO) approved the study (file number: 02388).

Open access funding:
The open access fee was funded by The University Hospital of North Norway.

This article was primary edited by G. Scott.