Title page

Persistent use of prescription opioids before and after lumbar spine surgery: Observational study with prospectively collected data from two Norwegian nationwide registries

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Persistent use of prescription opioids before and after lumbar spine surgery: Observational study with prospectively collected data from two Norwegian nationwide registries

Abstract

Study design: Prospective pharmacoepidemiological study

Objective: To investigate the relationship between clinical and sociodemographic variables among patients with persistent opioid use one-year preceding lumbar spine surgery.

Summary of background data: Persistent opioid use among patients undergoing surgery for degenerative spine disease is a concern.

Methods: Data from the Norwegian Registry for Spine Surgery and the Norwegian Prescription Database were linked for patients operated for degenerative lumbar spine disorders between 2007 and 2017. The primary outcome measure was persistent opioid use the second year after surgery. Functional disability was measured with the Oswestry Disability Index (ODI).

Results: The prevalence of persistent opioid use was 8.7% the year preceding surgery. Approximately two-thirds of these also met the criteria for persistent opioid use the second year after surgery. 991 (3.3%) opioid-naïve patients developed persistent opioid use the second year after surgery. The strongest predictor of sustained use was high doses of benzodiazepines the year preceding surgery (OR 1.7, 95% CI 1.26 to 2.19, P<.001). Among opioid-naïve patients, the most important predictor of new-onset opioid use the second year after surgery was the use of high doses of benzodiazepines (OR 1.8, 95% CI 1.26 to 2.44, P<.001), high doses of z-hypnotics (OR 2.6, 95% CI 2.10 to 3.23, P<.001) and previous surgery in the same lumbar level (OR 1.37, 95% CI 1.11 to 1.68, P = .003). Patients with persistent opioid use the year preceding surgery were less likely to achieve a minimal clinically important change in ODI score than patients who did not meet the criteria for persistent opioid use (OR 0.5, 95% CI 0.48 to 0.57 P <.001).

Conclusion:

Patients with persistent opioid use before surgery should be supported to taper off opioid treatment. Special efforts appear to be required to taper off persistent opioid use in patients using high doses of benzodiazepines.

Level of evidence: 2

Introduction

Considering the opioid epidemic affecting many western countries, opioid use for chronic non-malignant pain is a significant public health concern.[1,2] Short term opioid treatment has only been recommended for selected and closely montitored patients with chronic non-malignant pain.[3,4] Long-term treatment use seems to increase the risk of addiction and overdose deaths, both in the genral population and among patients with back pain.[5] Still, the use opioids for degenerative lumbar spine disorders has increased[6,78-10] Furthermore, co-medication with other addictive drugs, such as benzodiazepines, is prevalent in patients with persistent opioid use.[11-13] This tendency is alarming because benzodiazepines increase the risk of fatal opioid overdoses.[10,14]

In most contries degenerative disorders of the spine are major causes of pain related disability, representing significant costs for patients, their families and society.[15] It is well documented that many of these patients can benefit from spine surgery.[16] For those using prescription opioids, an additional goal is to reduce or eliminate opioid use, but it is not well documented that surgical treatment is successful in terms of tapering off long lasting opioid use.[7,17-19]

The Norwegian prescription database (NorPD) and the nationwide Norwegian Registry for Spine Surgery (NORspine) are both population based registries. This allows for an unique opportunity to combine individual data from two national cohorts, providing detailed information on drug use and comprehensive surgical, sosciodemographic and clinical data, including patient-reported outcome measures (PROMs).

The present study aimed to study the relationship between preoperative persistent opioid use and opioid use the second year after spinal surgery.

Material and methods

Study population

Patients were eligible if they had degenerative lumbar spine disease and underwent either microdiscectomy, decompressive surgery, or fusion surgery between 2007 and 2017. The study population was stratified subjects stratified by those meeting the criteria for persistent opioid use during 365 days preceding surgery and those who did not.

Data collection by NORspine

NORspine is a comprehensive registry for quality control and research and includes all centers performing spinal surgery in Norway.[20,21] On admission for surgery (baseline), the patients completed a self-administered questionnaire, including PROMs and demographics. Surgeons recorded data on diagnosis, comorbidity, radiological findings, surgical procedure, and complications. NORspine distributed questionnaires to the patients by mail three and 12 months after surgery for follow-up reporting of PROMs.

Norwegian Prescription Database

Since January 1st, 2004, all pharmacies in Norway have been obliged to submit monthly data to the NorPD on all dispensed prescriptions.[22] NorPD contains information on all prescription drugs, reimbursed or not, administered at pharmacies to individual patients outside institutions.

Study drugs

All drugs dispensed are classified according to the Anatomical Therapeutic Chemical (ATC) classification system. Drug quantities were measured as Defined Daily Doses (DDDs) and oral morphine equivalents (OMEQs).[23] OMEQs describe an equianalgesic dose of an opioid compared to oral morphine. The value can be computed from DDD quantities included in the NorPD data with equianalgesic conversion factors.[23] All prescription opioids (ATC: N02A) were included except those used primarily in opioid maintenance therapy (ATC: N07BC, methadone, buprenorphine 8 mg, buprenorphine/naloxone combination) and opioids only used by anesthesiologists in hospitals (alfentanil, remifentanil, and sufentanil). Information about drug use by individuals in hospitals and nursing homes, or drugs sold as supplies to physician offices, were not included. Data on dispensed prescriptions of benzodiazepines (ATC: N03AE01, N05BA, N05CD), z-hypnotics (ATC: N05CF), and gabapentinoids (ATC: N03AX16, N03AX12) were also included. Prescriptions of NSAIDs (ATC: M01A) and acetaminophen/paracetamol (ATC: N02B E01) were also included, but small quantities of these drugs are available without prescription and not captured by NorPD.

Definitions of drug consumption

Persistent opioid use was defined as using>180 DDD or >4500 OMEQ for 365 days and dispensing prescriptions in 3/4 quarters of the year.[24] This is an established “wide” definition used in several previous studies and clinically corresponds to using opioids most days of the week.[11,23] A limit of >100DDDs per year was chosen to define high doses of benzodiazepines and Z-hypnotics. This equals an average use of more than two times each week.[22]
The same definition of persistent opioid use was used to stratify the study population at baseline and as the primary outcome measure in the second year after surgery.

Patient-reported outcome measures

Functional outcome one year following surgery was measured with the Oswestry disability index (ODI) version 2.0. The ODI is scored 0-100, with increasing scores reflecting more disability.[25,26] We used 10 points as the minimal clinically important change (MCIC).[26]

Quality of life was measured with EQ-5D (EuroQol Research Foundation). Pain intensity in the lower back and the legs was measured with 0-10 numeric rating scales (NRS).

Statistical analysis

The statistical significance level was defined as $P \leq 0.05$. The analysis of drug consumption was based on the number of prescriptions and the amount of DDD and OMEQ. Multivariable logistic regression analyses were performed to identify predictors associated with persistent opioid use the year before surgery, and the chi-squared test was used to compare patients with persistent opioid use the year preceding surgery to patients without opioid use. Changes in ODI, EQ-5D, and NRS from baseline to one year were examined with paired sample T-test and mixed linear models. The fixed effect was time for the mixed linear models, and the random effect was the patient identification number. Mixed linear model analyses were used for handling missing data of PROMs.[27] In the mixed model, patients were not excluded from the analysis if a variable was missing at some, but not all, time points after baseline. The year before surgery is defined as the 365 days immediately preceding surgery, whereas the second year after surgery is defined as days 366 to 730 after the surgery date.
Statistical analyses were performed with SPSS version 28.01.0.

User involvement

The Norwegian Back Pain Association reviewed the study protocol and provided feedback concerning the study design.

Research ethics

The study was approved by the Regional Committee for Medical Research Ethics in Central Norway (2016/840), and all participants provided written informed consent.

Results

Figure 1 illustrates the inclusion criteria for the study population. Table one shows characteristics of patients with persistent opioid use the year preceding surgery (N=2864) and those without (N=30022), a statistically significant difference was observed in all group variables (table 1). Among the persistent users, we observed higher mean age (57.6 yrs. (±14.0) vs. 54.4 yrs. (±15.9), P <.001), more women (57.2% vs. 46.0%, P <.001) and more comorbidity (60.2% vs. 40.1%, P <.001), longer lasting back pain (71.2% vs. 51.8%, P <.001) and a higher proportion of persistent users had been operated previously at the same spinal level (28.6% vs. 13.0%, P <.001).

Persistent opioid use before and after surgery

2864 (8.7%) patients were defined as persistent opioid users in the year preceding surgery. Among these, 1763 patients (61.6%) also met the criteria for persistent opioid use in the second year after surgery. The use of high doses of benzodiazepines was the strongest predictor for sustained persistent opioid use the second year after surgery (OR 1.66, 95% CI 1.26 to 2.19, P<.001) (table 2). Among patients with sustained opioid use two years after surgery, there was an increase in both DDD (454 DDD to 472,5 DDD, mean difference 18,5 DDD, 95% CI 1.99 to 34.7, P <.001), and OMEQ (15258,7 OMEQ to 20913,4 OMEQ, mean difference 5654,7 OMEQ, 95% CI 4209 to 7099, P<.001) compared to the year preceding surgery.

Persistent opioid use in the second year after surgery

A total of 2754/32886 (8.4%) patients were defined as persistent opioid users the second year after surgery. Among the patients who did not meet the criteria for persistent opioid use the year preceding surgery, 991 patients (3.3%) developed persistent opioid use the second year after surgery. In the multivariable analysis, increasing ODI score (OR 1.06, 95% CI 1.05 to 1.07, P <.001), previous surgery in the same level (OR 1.37, 95% CI 1.11 to 1.68, P = .003), use of both high doses of benzodiazepines (OR 1.76, 95% CI 1.26 to 2.44, P <.001) and high doses of z-hypnotics the year preceding surgery (OR 2.60, 95% CI 2.10 to 3.23, P <.001) were strong predictors of new-onset use of prescriptions opioids two years after surgery (table 3).

PROMs

PROMs for the stratified cohort is presented in table 4. Compared to patients without persistent opioid use patients, persistent users reported a higher mean ODI score (51.0 points vs. 41.9 points, P <. 001) prior to surgery. One year after the operation, pesistent users also reported less ODI score improvement (mean 7.05 points, 95% CI 6.0 to 8.0, P <.001), more back- and leg pain, and they were less likely to achieve the ODI MCIC score (OR 0.5, 95% CI 0.48 to 0.56, P <.001). The back-and leg pain scales and the EQ-5D showed similar trends.

Patients without persistent opioid use the year preceding surgery had a larger mean EQ5D score than patients with persistent opioid use preceding surgery (0.70 vs. 0.43, difference in mean change -0.95, 95% CI -0.11 to -0.07, P <.001). The mean change in EQ-5D among patients with persistent opioid use at one year represents a clinically important change with an effect size of 0.8 (Cohen’s d). For patients without persistent opioid use, there was an effect size of 1.13 (Cohen’s d).

Discussion

This nationwide pharmacoepidemiologic study shows that 8.7% of patients who underwent surgery for degenerative lumbar spine conditions were persistent opioid users the year preceding surgery. Approximately two-thirds of these also met the criteria for persistent opioid use the second year after surgery. In addition, 991 (3.3%) opioid-naïve patients developed persistent opioid use the second year after surgery. In line with prior studies, patients with persistent use the year preceding surgery were more likely to have more comorbidity, back and leg pain exceeding one year, and a history of previous lumbar spine surgery and were less likely to have higher education.[28-30]

The escalating use of therapeutic opioids over the past two decades has becoome a public concern.[31] Compared to the general Norwegian population, the prevalence of persistent opioid use is more than eightfold the year preceding spine surgery.[23] Although higher age in the study population compared to the general population is a confounding factor, the age difference only explains a small part of the eightfold difference. Among patients with sustained opioid use the second year after surgery, a 30% increase in OMEQ was observed. This finding is a major concern, but in line with previous studies, where patients with preoperative opioid use are at a higher risk of sustained use and dose escalation.[32] The strongest predictor for sustained opioid use was high doses of benzodiazepines the year preceding surgery. Similar results have been reported in previous studies with the growing use of opioids in combination with benzodiazepines for patients with back pain and chronic pain.[33,34] Such co-medication conflicts with existing guidelines for the treatment of chronic pain,[35] and the combination of these drugs is likely to increase the risk of developing problematic opioid use and risk of fatal opioid overdoses.[12,36]

An important finding in this study is the predictors of new-onset opioid use among opioid-naïve users. This study shows that 3.3% of opioid-naïve patients undergoing lumbar spine surgery become persistent opioid users two years after surgery. Patients with previous surgery at the same level had a 37% increased likelihood of new-onset opioid use after surgery. These findings concur with prior studies, reporting an increased risk of deterioration after multiple surgeries at the same level.[37] Further, the use of high doses of either benzodiazepines or z-hypnotics were strong predictors for new-onset opioid use. It is crucial to identify these high-risk patients when evaluating surgery, provide counseling regarding this risk and potentially arrange an alternative pain management plan for these patients postoperatively.

Our study showed large and statistically important improvements in all PROMS for the two groups. Considerable disparities were observed in PROMs between patients who do not meet criteria for persistent use and persistent opioid users the year preceding surgery, with the latter reporting worse preoperative scores and less improvement. Surgeons are challenged to optimize postoperative pain management and limit opioid use after surgery. A recent study emphasizes the importance of prescription policy and patient instructions when prescribing opioids. Patient education has been recognized as essential in postoperative opioid reduction across surgical domains.[38] A prescription with instructions “as needed” might lead to incorrect self-administration of medications.[38] Caution should be exercised regardless of previous opioid exposure and education of patients regarding the proper way to manage their pain in the postoperative period.

Patients with persistent opioid use the year preceding surgery were less likely to achieve a MCIC one year after surgery than patients who did not meet the criteria for persistent use. One explanation for this might be that the MCIC value is a generic, predicted estimate based on a 30% difference in ODI score before and after surgery.[26] It may be appropriate to consider whether the MCIC value should be adjusted for patients experiencing a higher ODI score preoperative, as reported in our group of persistent opioid users, to achieve a correct MCIC measure.[26,39]

The proportion of patients with persistent opioid use is substantially lower than reported in US studies.[7,40,41] The explanation is probably multifaceted and may include a more restrictive prescription practice among Norwegian physicians and essential differences in patient selection, surgical strategies, the prevalence of substance abuse disorders, access to health care, and health care organization. Further, there are discrepancies in how persistent opioid use are being defined. Registry data can help monitor opioid use and the effects of interventions to reduce both persistent preoperative opioid use and postoperative use. Although awareness has increased in the medical community and general society in recent years, we are unaware of any strategies or policies in Norway during the study period to reduce opioid use following spine surgery. There has been substantial interest in developing and utilizing opioid-sparing protocols for postoperative pain management. A recent trial showed promising results among patients who underwent arthroscopic shoulder or knee surgery, where a postoperative opioid-sparing protocol significantly reduced postoperative opioid consumption among these patients.[38] Although these results were among another subpopulation of surgical patients, we strongly encourage clinical trials where patients with or at risk of opioid abuse are provided counseling. The widespread and increasing use of spinal cord stimulation for persistent pain following lumbar spine surgery does not appear to result in clinically meaningful cessation of opioids or improvement in pain or disability.[42-44]

Strengths and limitations

Strengths of our study include a large sample size, prospectively collected population based data, and an extended observation period. The heterogeneous study population recruited from everyday clinical practice ensures high external validity. A weakness of studies based on prescription databases is that it needs to be known whether the recipient uses drugs. Loss to follow-up regarding PROMs at one year represents a weakness. A previous study on a similar population from NORspine showed no differences in outcomes between responders and non-responders.[45]

Conclusion

A significant proportion of patients reported sustained opioid use after surgery. Patients with persistent opioid use before surgery should be supported to taper off opioid treatment. Special efforts appear to be required to taper off opioid use in patients using high doses of benzodiazepines.

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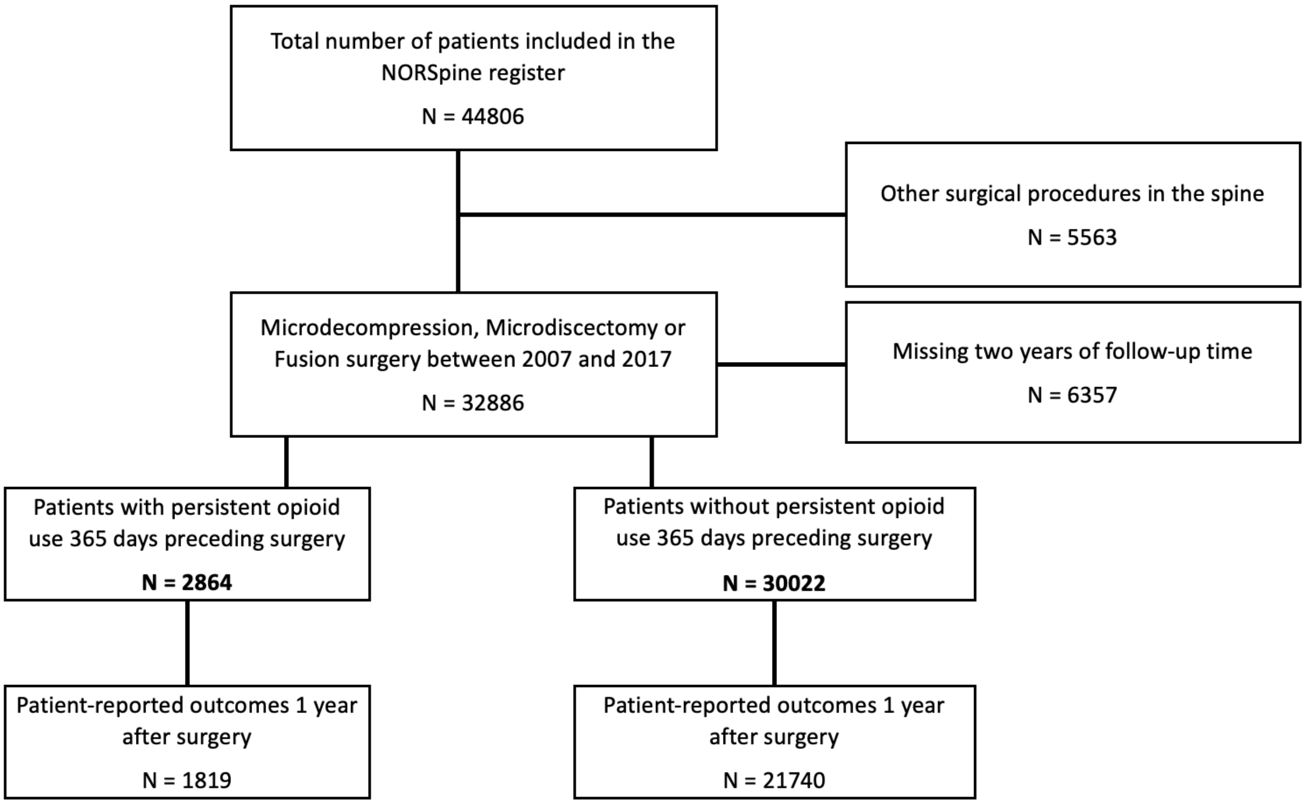

Figure 1. Flow sheet illustrating how the study population was defined based in NorSpine and NorPD

Table 1. Demographics and medical characteristics for the study population with persistent opioid use one year before surgery and patients without persistent opioid use.

Demographics (n= 32886)			
	Persistent opioid use the year preceding surgery (n= 2864)	**Not persistent opioid the year preceding surgery (n= 30022)**	**P-value**
Age, years, mean (SD)	57.6 (±14.0)	54.4 (±15.9)	<.001
Female, n (%)	1639 (57.2%)	13816 (46.0%)	<.001
Married or partner, n (%)	1964 (68.6%)	22356 (74.5)	<.001
Current tobacco smoker	1113 (38.9%)	7172 (23.9%)	<.001
Education >12 years	716 (25.0%)	10258 (34.2%)	<.001
Currently working	179 (6.3%)	5819 (19.4%)	<.001
Body Mass Index	27.5 (±5.0)	27.1 (±4.4)	
ASA Grade >2	638 (22.3%)	3216 (10.7%)	<.001
Comorbidity	1725 (60.2%)	12030 (40.1%)	<.001
ODI score preoperative	51.4 (±14.8)	42.2 (±17.4)	<.001
ODI score less than 22 points preoperative	43 (1.5%)	2878 (9.6%)	<.001
EQ5D score preoperative	0.15 (±0.3)	0.33 (±0.34)	<.001
Back pain >1 year	2038 (71.2%)	15551 (51.8%)	<.001
Radiculopathy >1 year	1972 (68.9%)	15025 (50.0%)	<.001
Previous spine surgery	1178 (41.1%)	5939 (19.8%)	<.001
Previous surgery in the same level	820 (28.6%)	3888 (13.0%)	<.001
Dispensed prescriptions of non-opioid analgesics three months preceding surgery			
NSAIDs	1165 (40.7%)	13270 (44.2%)	<.001
Gabapentinoids	660 (23.0%)	2448 (8.2%)	<.001
Paracetamol/Acetoaminophen	1217 (42.5%)	8872 (29.6%)	<.001
Dispensed prescriptions of gabapentin one-year preceding surgery			

Benzodiazepines in high doses one year before surgery	643 (22.5%)	751 (2.5%)	<.001
Z-hypnotics in high doses one year before surgery	898 (31.4%)	2677 (8.6%)	<.001

Abbreviations: ASA, American Society of Anesthesiologists; ODI, Oswestry Disability Index; EQ5D, EuroQol 5L – health related quality of life; NSAIDS, Non-Steroidal Anti-Inflammatory Drugs

Table 2. Predictors of sustained persistent opioid use the second year after surgery

Demographics	Univariable			Multivariable		
	OR	95% CI	P-Value	OR	95% CI	P-Value
Age	0.99	0.98 to 0.99	<.001	0.98	0.97 to 0.99	<.001
Female	1.10	0.95 to 1.28	.212			
Partner	1.00	0.99 to 1.00	.444			
Current tobacco smoker	1.00	1.00 to 1.00	.079			
Education >12 years	1.00	0.99 to 1.00	.596			
Body Mass Index	0.99	0.98 to 1.01	.666			
Working	1.00	1.00 to 1.00	.430			
ASA >2	1.00	1.00 to 1.00	.157			
Comorbidity	1.03	0.88 to 1.96	.745			
Preoperative mean ODI	1.01	1.00 to 1.01	.001	0.99	0.98 to 1.00	.064
Postoperative mean ODI	1.04	1.04 to 1.05	<.001	1.04	1.03 to 1.05	<.001
MCID ODI	0.50	0.43 to 0.58	<.001	0.86	0.63 to 1.18	.358
Preoperative back pain >1 year	1.00	1.00 to 1.00	.600			
Preoperative leg pain >1 year	1.00	1.00 to 1.00	.837			
Previous lumbar spine surgery	1.00	0.99 to 1.00	.552			
Previous surgery in the same level	1.30	1.10 to 1.55	.002	0.97	0.77 to 1.22	.812
Levels > 1	0.99	0.84 to 1.20	.985			
Microdiscectomy	0.87	0.74 to 1.03	.108			
Decompression only	1.08	0.93 to 1.26	.325			
Fusion	1.04	0.88 to 1.23	.657			

Complication within three months	1.00	1.00 to 1.00	.149			
Benzodiazepines in high doses one year before surgery	1.82	1.50 to 2.21	<.001	1.66	1.26 to 2.19	<.001
Z-hypnotics in high doses one year before surgery	1.31	1.11 to 1.55	.001	1.24	0.99 to 1.56	.062

Abbreviations: OR, Odds ratio; CI, Confidence Interval; ASA, American Society of Anesthesiologists; ODI, Oswestry Disability Index; EQ5D, EuroQoL 5L - health-related quality of life

Table 3. Predictors for new-onset persistent opioid use among naïve opioid users

Demographics (N= 991)	**Univariable**			**Multivariable**		
	OR	95% CI	P-Value	OR	95% CI	P-Value
Age	1.00	1.00 to 1.01	.002	0.98	0.97 to 0.99	<.001
Female	1.55	1.36 to 1.76	<.001	1.10	0.92 to 1.31	.298
Partner	1.00	0.99 to 1.00	.546			
Current tobacco smoker	1.00	0.99 to 1.00	.935			
Education >12 years	1.00	1.00 to 1.00	.676			
Body Mass Index	1.03	1.01 to 1.04	<.001	1.01	0.99 to 1.03	.182
Working	1.00	1.00 to 1.00	.354			
ASA >2	0.99	0.99 to 1.00	.115			
Comorbidity	1.70	1.50 to 1.93	<.001	1.90	0.98 to 1.44	.076
Preoperative mean ODI	1.02	1.02 to 1.03	<.001	1.00	0.98 to 1.01	.225
Postoperative mean ODI	1.06	1.06 to 1.07	<.001	1.06	1.05 to 1.07	<.001
MCIC ODI	0.30	0.26 to 0.35	<.001	0.91	0.70 to 1.20	.514
Preoperative back pain >1 year	1.00	1.00 to 1.00	.293			
Preoperative leg pain >1 year	1.00	1.00 to 1.00	.581			
Previous lumbar spine surgery	1.00	1.00 to 1.00	.709			
Previous surgery in the same level	2.00	1.74 to 2.33	<.001	1.37	1.11 to 1.68	.003
Levels > 1	1.49	1.28 to 1.73	<.001	1.08	0.87 to 1.32	.489
Microdiscectomy	0.55	0.48 to 0.63	<.001	1.48	0.33 to 6.10	.611
Decompression only	1.40	1.24 to 1.60	<.001	1.89	0.42 to 8.47	.404

Fusion	1.60	1.36 to 1.88	<.001	2.42	0.54 to 10.84	.249
Complication within three months	1.00	1.00 to 1.00	.001	1.00	1.00 to 1.00	.772
Benzodiazepines in high doses one year before surgery	4.83	3.87 to 6.03	<.001	1.76	1.26 to 2.44	<.001
Z-hypnotics in high doses one year before surgery	3.63	3.12 to 4.22	<.001	2.60	2.10 to 3.23	<.001

Abbreviations: OR, Odds ratio; CI, Confidence Interval; ASA, American Society of Anesthesiologists; ODI, Oswestry Disability Index; EQ5D, EuroQoL 5L - health-related quality of life; MCIC, Minimal Important Clinical Change.

Table 4. Outcome variables at baseline and one year after surgery

	Non-persistent opioid users prior (n= 21740)			Persistent users one year prior to surgery (n= 1819)				
Outcome variable (complete case analysis)	Baseline - mean (SD)	One year - mean (SD)	Mean difference (95% CI)	Baseline - mean (SD)	One year - mean (SD)	Mean difference (95% CI)	Difference in mean change (95% CI)	P-Value
ODI	41.9 (17.4)	19.3 (17.2)	22.6 (22.4 to 22.9)	51.0 (14.6)	35.4(19.3)	15.6 (14.7 to 16.5)	7.05 (6.0 to 8.0)	<.001
EQ-5D	0.34 (0.34)	0.70 (0.30)	-0.36 (-.036 to – 0.35)	0.16 (0.30)	0.43 (0.36)	-0.26 (-0.28 to -0.24)	-0.95 (-0.11 to -0.07)	<.001
VAS	47.3 (21.1)	71.4 (22.2)	- 24.1 (-24.5 to -23.6)	39.5 (20.8)	54.6 (23.5)	-15.1 (-16.5 to -13.7)	-8.9 (-10.4 to -7.5)	<.001
NRS Back pain	6.3 (2.3)	3.3 (2.7)	3.0 (2.9 to 3.0)	7.5 (1.9)	5.2 (2.7)	2.3 (2.1 to 2.4)	0.75 (0.60 to 0.90)	<.001
NRS Leg pain	6.6 (2.3)	2.8 (2.8)	3.8 (3.7 to 3.8)	7.1 (2.2)	4.5 (3.0)	2.6 (2.5 to 2.8)	1.14 (0.98 to 1.31)	<.001
Outcome variable (mixed linear model analysis)	Baseline - mean (SD)	One year - mean (SD)	Mean difference (95% CI)	Baseline - mean (SD)	One year - mean (SD)	Mean difference (95% CI)	Difference in mean change (95% CI)	P-Value
ODI	42.2 (17.9)	19.3 (21.0)	22.8 (22.6 to 23.1)	51.4 (17.2)	35.5 (17.3)	15.9 (15.0 to 16.8)	-12.7 (-13.3 to -12.1)	<.001
EQ-5D	0.33 (0.36)	0.70 (0.36)	- 0.36 (-0.37 to -0.36)	0.15 (0.33)	0.42 (0.28)	-0.28 (-0.30 to -0.25)	0.23 (0.21 to 0.24)	<.001
VAS	46.9 (22.5)	71.0 (28.4)	-24.1 (-24.5 to 23.7)	38.7 (20.9)	54.3 (22.4)	-15.6 (-16.8 to -14.3)	12.2 (11.5 to 13.0)	<.001
NRS Back pain	6.3 (2.3)	3.3 (3.2)	3.0 (2.9 to 3.0)	7.5 (2.3)	5.2 (2.7)	2.3 (2.1 to 2.4)	-1.6 (-1.6 to -1.5)	<.001
NRS Leg pain	6.6 (2.5)	2.8 (3.4)	3.8 (3.7 to 3.8)	7.2 (2.9)	4.5 (2.8)	2.7 (2.0 to 2.2)	-1.1 (-1.2 to -1.0)	<.001

Abbreviations: ODI, Oswestry Disability Index; VAS, Visual Analog Scale; NRS, Numeric Rating Scale; EQ5D, EuroQoL 5L - health-related quality of life