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Persistent Use of Prescription Opioids Following Lumbar Spine Surgery: Observational Study with Prospectively Collected Data from Two Norwegian Nationwide Registries

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Min Abstract

Among 32886 study participants, 2754 (8.4%) met the criteria for persistent opioid use the second year after surgery. Our study suggests that patients with or at risk of developing persistent opioid should be identified and provided counseling and support to taper off opioid treatment.

Abstract

Study Design: Prospective pharmacoepidemiological study

Objective: To investigate the use of prescription opioids two years following degenerative lumbar spine surgery.

Summary of Background Data: There are limited data providing details to evaluate patterns of opioid use. The number of patients is often limited and data on opioid use following some of the most common surgical procedures are lacking.

Methods: Data from the Norwegian Registry for Spine Surgery and the Norwegian Prescription Database were linked on an individual level. The primary outcome measure was persistent opioid use the second year after surgery. Functional disability was measured with the Oswestry disability index (ODI). Study participants were operated between 2007 and 2017.

Results: Among 32886 study participants, 2754 (8.4%) met criteria for persistent opioid use the second year after surgery. Among persistent opioid users in the second year after surgery, 64% met the criteria for persistent opioid use the year preceding surgery. Persistent opioid use the year preceding surgery (OR 31.10, 95% CI 26.9-36.0, P = .001), use of high doses of benzodiazepines (OR 1.62, 95% CI 1.30-2.04, P = .001), and use of high doses of z-hypnotics (OR 1.90, 95% CI 1.58-2.22, P = .001) the year before surgery were associated with increased risk of persistent opioid use the second year after surgery. A higher ODI score at one year was observed in persistent opioid users compared to non-persistent users (41.5 vs 18.8 points) and there was a significant difference in ODI change (-13.7 points). Patients with persistent opioid use in the year preceding surgery were less likely to achieve a minimal clinically important ODI change at one year compared to non-persistent users (37.7% vs 52.6%, P = .001).

Conclusion: Patients with or at risk of developing persistent opioid should be identified and provided counseling and support to taper off opioid treatment.

Key Words: back pain; Lumbar spine surgery; microdecompression; pain related disability; persistent opioid use; pharmacoepidemiology; epidemiology

Level of Evidence: 2

Introduction

Despite uncertainties concerning long-term efficacy, prescription opioid use is common and has increased rapidly for lumbar spine disorders.[1,2] Complications related to opioid abuse and overdoses have risen in parallel, both in this patient population and in the general population.[3-5] The obvious goals of lumbar spine surgery are to reduce pain and improve functioning. For patients on prescription opioids a related aim is to reduce or eliminate opioid use. The risk of lasting or new-onset persistent opioid use after spine surgery is increasingly recognized[6], and previous studies have described wide variations in long-term prevalence of prescription opioid use after spinal surgery with rates varying from 26 to 52%.[2,7-9] Further, studies show a high prevalence of co-medication with benzodiazepines and benzodiazepine-related hypnotics (z-hypnotics) in patients with persistent opioid use for chronic non-malignant pain.[5,10,11] This tendency is alarming because benzodiazepines increase the risk of fatal opioid overdoses.[5,12]

There are important gaps in knowledge regarding patterns of opioid use after lumbar spine surgery. Studies providing point prevalence rates lack the nuanced, granular detail to evaluate the contextual and temporal patterns of opioid use. The number of patients is often limited and data on opioid use following some of the most common surgical procedures are lacking. Further, the lack of patient reported outcome measures (PROMs) hinders contextualizing opioid use within the framework of physical and psychosocial recovery.

The aim of this study was to investigate the use of prescription opioids in the two years following lumbar spine surgery by linking prospectively collected data from two Norwegian nationwide registries.

Material and methods

Data from the Norwegian Registry for Spine Surgery (NORspine) and the Norwegian Prescription Database (NorPD) were linked on an individual level. The Regional Committee for Medical Research Ethics approved the study, and all participants provided written informed consent. Patients were eligible if they had degenerative lumbar spine disease and underwent either microdiscectomy, decompressive surgery or fusion surgery between 2007 and 2017.

Data collection by NORspine

NORspine is a comprehensive registry for quality control and research, and currently includes all centers performing spinal surgery in Norway.[13,14] On admission for surgery the patients completed a self-administered questionnaire, including PROMS and questions about personal characteristics. 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.

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.[10] NorPD contains information on all prescription drugs, reimbursed or not, that are dispensed 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).[15] OMEQs describe an equianalgesic dose of an opioid compared to oral morphine. The value can be counted from DDD quantities included in the NorPD data with equianalgesic conversion factors.[15] All prescription opioids (ATC: N02A) were included with the exception of those used primarily in opioid maintenance therapy (methadone, buprenorphine 8 mg, buprenorphine/naloxone combination) and opioids only used by anesthesiologists in hospitals (alfentanil, remifentanil, and sulfentanil). 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 and acetaminophen/paracetamol were also included, but small quantities of these drugs are available without prescription and not captured by NorPD.

Primary outcome

The primary outcome measure, persistent opioid use, was defined as the use of >180 DDD or >4500 OMEQ for 365 days and dispensing of prescriptions in 3/4 quarters of the year.[16] This is an established “wide” definition that has been used in several previous studies and clinically corresponds to using opioids most days of the week.[15,17] In sensitivity analyses, two additional definitions of persistent opioid use were used: (1) the intermediate definition corresponding to daily opioid use and (2) the strict definition that corresponds to using opioids around the clock all days.[16]

Secondary outcome measures

Functional outcome at one year following surgery was measured with the Oswestry disability index (ODI) version 2.0. The ODI is scored 0-100, with increasing values reflecting more disability. We used 10 points as the minimal clinically important change (MCIC).[18] Changes in quality of life were measured with EQ-5D (EuroQol Research Foundation). Changes in low back pain and leg pain measured with 0-10 numeric rating scales (NRS).

Statistical analysis

Statistical analyses were performed with SPSS version 26.0. The statistical significance level was defined as $P \leq 0.05$. Changes in ODI, EQ-5D, and NRS from baseline to one-year were examined with paired sample T-test and mixed linear models. For the mixed linear models, the fixed effect was time, and the random effect was patient identification number. 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 second year after surgery, and co-medication with opioids and benzodiazepines or z-hypnotics in patients with persistent opioid use the second year after surgery. Concomitant use was defined as high doses (DDD >100) of either benzodiazepines or z-hypnotics the year before surgery and the second year after surgery respectively. Mixed linear model analyses were used for handling missing data of PROMs.[19] 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.

User involvement

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

Results

Baseline characteristics are presented in table 1. A total of 32886 patients were included in the study, and data from NorPD were available for all patients. The mean age at baseline was 54.7 (±15.8) years and 47.0% were women. In total, 23678 (72.0%) completed one-year NORspine follow-up with PROMs. There were minor differences in baseline characteristics between responders and non-responders including female sex (49.1% vs 43.4%, P = .001), smokers (23.1% vs 28.8%, P = .001), life partner (75.4% vs 71.4%, P = .001), working at time of surgery (17.1% vs 20.1%, P = .001), age (56.8 vs 51.1 years, P = .001), and ODI (43.3 vs 42.5 points, P = .001).

Prescription opioid use in the second year after surgery

A total of 2754 (8.4%) patients were defined as persistent opioid users the second year after surgery, and among these 1763/2754 patients (64%) also met the criteria for persistent opioid use the year preceding surgery. Concomitant use with high doses of benzodiazepines or z-hypnotics was observed in 1247/2754 (45.3%) among persistent opioid users the second year after surgery. Among the proportion of patients who did not meet the criteria for persistent

use of opioids the year before surgery, 991 patients (3.3%) developed persistent use the second year after surgery. Furthermore, there was a reduction in DDD of opioids among persistent users the second year after surgery compared to one year prior to surgery (56.7 DDD to 44.2 DDD, mean difference -12.5 DDD, 95% CI -14.0 to -10.9, P = .001). During the same time period mean OMEQ increased from 1553 to 1690 (difference 137 OMEQ, 95% CI 4.5 to 270.4, P= 0.043). In patients who underwent fusion surgery, a higher proportion were persistent opioid users at two years compared with those who did not undergo fusion surgery (14.0% vs. 7.4%, P = .001). The prevalence of persistent opioid use during the observation period according to the wide, intermediate, and strict definitions is presented in figure 1.

The multivariable analysis demonstrated that persistent opioid use one year before surgery (OR 31.10, 95% CI 26.9 to 36.0, P = .001), a higher ODI score one year after surgery (1.06, 95% CI 1.05 to 1.06, P = .001), and previous surgery in the same level (OR 1.20, 95% CI 1.01 to 1.41, P=0.033) were independent predictors associated with persistent opioid use in the second year after surgery (table 2). Both high doses of benzodiazepines (OR 1.62, 95% CI 1.30 to 2.04, P = .001) and high doses of z-hypnotics (OR 1.90, 95% CI 1.58 to 2.22, P = .001) the year before surgery were associated with increased risk of persistent opioid use the second year after surgery.

Among patients with persistent opioid use the second year after surgery the prevalence of concomitant use with both high doses of benzodiazepines and z-hypnotics was 10.3% (figure 2). Predictors of co-medication with high doses of benzodiazepines and/or z-hypnotics in patients with persistent opioid use two years following surgery are presented in supplementary table 1, http://links.lww.com/BRS/B828 (see Supplemental Digital Content 1, http://links.lww.com/BRS/B827). The strongest predictors for concomitant use were preoperative persistent use of prescription opioids and preoperative use of high doses of benzodiazepines and/or z-hypnotics.

Preoperative analgesic use

The prevalence of persistent opioid use in the year preceding surgery was 8.7% (figure 1). The non-opioid analgesics with highest periodic prevalence during the last three months before surgery were NSAIDS (43.9%) and paracetamol/acetaminophen (30.7%) with mean DDD 27.9 (± 49.2) and 14.0 (± 28.3), respectively. Predictors associated with persistent use of prescription opioids the year preceding surgery are presented in supplementary table 2, http://links.lww.com/BRS/B828 (see Supplemental Digital Content 2), previous surgery in the same level, and surgery in more than one level was associated with persistent use. Preoperative use of high doses of benzodiazepines or high doses of z-hypnotics were independent factors associated with persistent use of prescription opioids the year preceding surgery.

PROMs

There were large and clinically important improvements in all PROMs for the total study population. Mixed linear model analyses showed similar results for all PROMs. For all patients included in the study, the mean change in ODI one year after surgery was -22.1 (95% CI -22.3 to -21.8, P = .001). The mean change in EQ-5D at one year represents a clinically important change with an effect size of 1.23 (Cohen's d). Changes in PROMs for persistent opioid users and non-persistent users one year after surgery are presented in table 3. A higher ODI score at one year was observed in persistent opioid users compared to non-persistent users (41.5 vs 18.8 points) and there was both a statistically and clinically significant difference in mean change of ODI (-13.7 points, 95% CI -14.7 to -12.7, P = .001). Patients with persistent opioid use in the year preceding surgery, were less likely to achieve a MCIC at one year (37.7% vs 52.6%, P = .001) As shown in supplementary table 3, http://links.lww.com/BRS/B828 (see Supplemental Digital Content 1, http://links.lww.com/BRS/B827), persistent preoperative use of opioids, previous spine surgery in the same level, and preoperative use of high doses of benzodiazepines or Z-hypnotics were negative predictors for achieving a MCIC.

Discussion

This pharmacoepidemiologic study shows that 8.4% of patients who underwent surgery for degenerative lumbar spine conditions were persistent opioid users the second year after surgery. The majority of patients with persistent opioid use before surgery were unable to discontinue persistent opioid use. Persistent preoperative opioid use was also associated with inferior PROMs one year after surgery. It appears that surgery must be accompanied by other interventions to help patients reduce opioid consumption.

It might be surprising that 3.3% of those patients who were not persistent opioid users before spinal surgery met criteria of persistent opioid use the second year after surgery. One obvious explanation is that in some patients the history of their back pain and opioid use was too short to meet criteria of persistent opioid use preoperatively even though they had been using high doses. Another possible explanation is that surgery and use of opioids in the postoperative phase may lead to persistent opioid use, especially in subjects with major surgery, poor surgical outcome, and predisposing risk factors for addiction. Previous studies have shown that there is a risk of long-term use irrespective of preoperative opioid consumption.[20]

The escalating use of therapeutic opioids over the past two decades has rendered long-term opioid use a public concern.[21] The proportion of persistent opioid users following spine surgery is more than eightfold compared to the general Norwegian population.[15] Part of the reason might be a discrepancy in age, as the mean age in the study population was higher compared to the general population. Moreover, patients who undergo spine surgery are more likely to be exposed for opioids.[22] The observed increase in OMEQ in the second year following surgery, might reflect a worrying trend with use of more potent opioids.[23]

As reported previously, preoperative persistent opioid use was the strongest predictor for sustained opioid use.[20,24] In a recent trial involving patients with sciatica lasting more than

four months due to lumbar disc herniation, surgery was superior to nonsurgical care with respect to pain intensity at six months.[25] Patients with persistent pain and clear corresponding image findings should be considered for surgical intervention before they develop persistent opioid use, and better timing of surgical treatment may influence postoperative prescription opioid use. Previous surgery in the same level was also identified as a strong predictor for persistent prescription opioid use at two years. Previous spine surgery has previously been identified as a predictor for deterioration in pain and disability.[26] Patients with other relevant comorbidity had an increased risk of persistent use one year prior to surgery. This may indicate that opioids intended for pain also are being used for other indications for which long-term opioid treatment is not recommended.[27-29]

The proportion of patients with persistent opioid use is substantially lower than reported in US studies.[2,24,30] The explanation is probably multifaceted and may include a more restrictive prescription practice among Norwegian physicians and important differences in patient selection, surgical strategies, prevalence of substance abuse disorders, access to health care, and health care organization.

Our study shows that 45.3% of persistent opioid users received co-medication with high doses of either benzodiazepines or z-hypnotics the second year after surgery. Similar results have been reported in previous studies with a growing use of opioids in combination with benzodiazepines for patients with back pain and chronic pain.[31,32] Such co-medication is in conflict with existing guidelines for treatment of chronic pain,[33] and the combination of these drugs is likely to increase the risk of developing problematic opioid use and risk of fatal opioid overdoses.[34]

Considerable disparities were observed in PROMs between non-opioid users and persistent opioid users, with the latter reporting worse preoperative scores and less improvement. Neurosurgeons are faced with the challenge of optimizing postoperative pain management and limiting opioid use after surgery. Caution should be exercised regardless of previous opioid exposure. Patients with persistent opioid use prior to surgery should be provided support to taper off opioid treatment. Tapering of opioids should start after the acute postoperative pain has resolved and should involve primary care physicians.

Registry data can help monitor opioid use and effects of interventions to reduce persistent postoperative opioid use. Although awareness has increased in both 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. We would strongly encourage clinical trials where patients with or at risk of opioid abuse are provided counseling.

Strengths and limitations

Strengths of our study include a large sample size, use of prospectively collected data, and a long observation period. The heterogenous study population recruited from everyday clinical

practice ensures high external validity. A weakness of studies based on prescription databases is that it is not known whether drugs are actually used by the recipient. 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.[35]

Conclusion

In this study, 8.4% of patients who underwent lumbar spine surgery were persistent opioid users the second year after surgery. The prevalence of persistent opioid users remained almost unchanged from the year preceding surgery to the end of follow-up at two years.

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Key points:

- Among 32886 study participants, 2754 (8.4%) met criteria for persistent opioid use the second year after surgery.
- Persistent opioid use the year preceding surgery the year before surgery were associated with increased risk of persistent opioid use the second year after surgery.
- A higher ODI score at one year was observed in persistent opioid users compared to non-persistent users (41.5 vs 18.8 points).
- Patients with persistent opioid use in the year preceding surgery were less likely to achieve a minimal clinically important ODI change at one year compared to non-persistent users.

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Figure legends

Figure 1. The proportion of patients with persistent use of prescription opioids in relation to time of surgery. The wide definition displayed in green, intermediate in orange and the strict definition displayed in red.

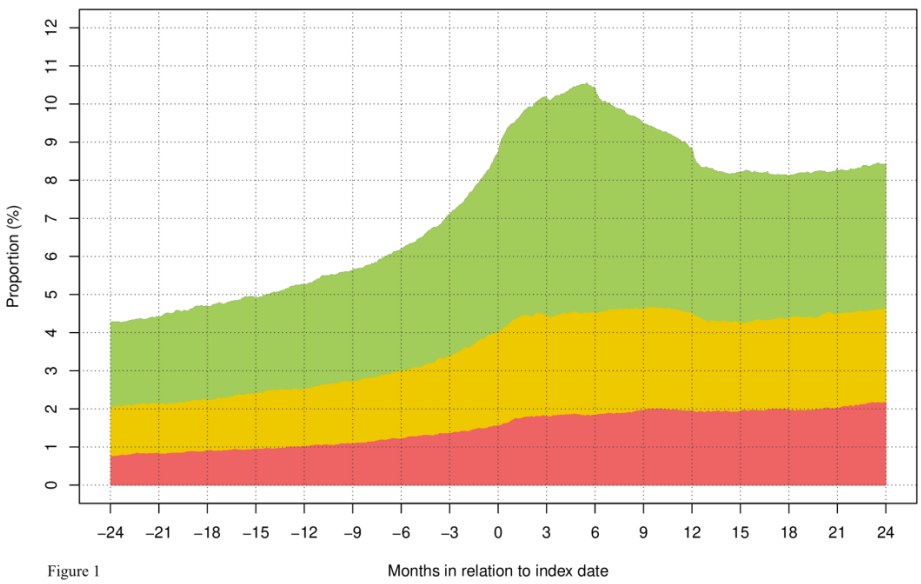

Figure 2. Persistent prescription opioid use in the second year following spine surgery and concomitant use with high doses of benzodiazepines (>100 defined daily doses) and/or z-hypnotics (>100 defined daily doses).

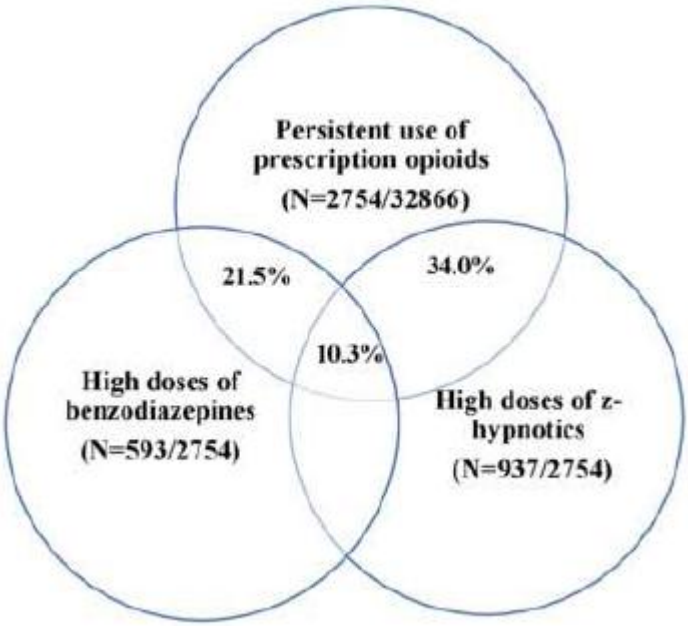

Table 1. Personal characteristics, surgical treatments, complications, and events for the total study population (n= 32886)

Demographics (n=32886)		N (%) or Mean (SD)
Age, years		54.7 ± 15.8
Female		15455 (47.0%)
Married or partner		24320 (74.0%)
Current tobacco smoker		8285 (25.2%)
Education >12 years		10974 (33.4%)
Body Mass Index		27.13 ± 4.4
ASA Grade >2		3854 (11.7%)
Comorbidity		13755 (41.8%)
Back pain >1 year		17589 (53.5%)
Radiculopathy >1 year		16997 (51.7%)
Previous spine surgery		7117 (21.6%)
Previous surgery in the same level		4708 (14.3%)
Cauda equina syndrome		233 (0.7%)
Emergency surgery		3228 (9.8%)
Dispensed prescriptions of non-opioid analgesics three months preceding surgery		
	NSAIDS	14435 (43.9%)
	Gabapentinoids	3108 (9.5%)
	Paracetamol/acetaminophen	10089 (30.7%)
Surgical treatments, complications, and events		
Microdiscectomy		15790 (48.0%)
Decompression only		12314 (37.4%)
Fusion		4685 (14.2%)
Levels of surgery >1		6166 (18.7%)
Level of surgery		
	L2-L3	1952 (5.9%)
	L3-L4	7146 (21.7)
	L4-L5	18998 (57.8%)

	L5-S1	1192 (3.6%)
Perioperative complications		1192 (3.6%)
	Unintentional durotomy	972 (3.0%)
	Nerve injury	68 (0.2%)
	Blood replacement or postoperative hematoma	90 (0.3%)
	Cardiovascular complications	15 (0.04%)
	Respiratory complications	9 (0.03%)
	Anaphylactic reaction	17 (0.1%)
	Wrong-level surgery	51 (0.2%)
Patient reported complications after hospital discharge (<3 months)		2494 (7.6%)
	Wound infection	25 (0.1%)
	Urinary tract infection	959 (2.9%)
	Pneumonia	203 (0.6%)
	Pulmonary embolism	52 (0.2%)
	Deep venous thrombosis	46 (0.1%)
	Micturition problems	778 (2.4%)

Abbreviations: ASA, American Society of Anesthesiologists; NSAIDS, Non-Steroidal Anti-Inflammatory Drugs

Table 2. Predictors of persistent use of opioids second year after surgery (n=32886)

Demographics	Univariable			Multivariable		
	OR	95% CI	P-Value	OR	95% CI	P-Value
Age	1.00	1.00-1.01	.001	0.98	0.98-0.99	.001
Female	1.59	1.47-1.72	.001	1.707	0.93-1.23	.318
Partner	1.00	0.99-1.00	.265			
Current tobacco smoker	1.00	1.00-1.00	.043	1.00	0.99-0.1.00	.410
Education >12 years	1.00	1.00-1.00	.222			
Body Mass Index	1.02	1.01-1.03	.001	1.00	0.99-1.01	.938
Working	1.00	1.00-1.00	.638			
ASA >2	1.00	1.00-1.00	.940			
Comorbidity	2.01	1.86-2.18	.001	1.10	0.95-1.28	.197
Preoperative mean ODI	1.03	1.03-1.03	.001	0.99	0.99-1.00	.639
Postoperative mean ODI	1.06	1.06-1.06	.001	1.06	1.05-1.06	.001
Preoperative back pain >1 year	1.00	1.00-1.00	.837			
Preoperative leg pain >1 year	1.00	1.00-1.00	.999			
Previous lumbar spine surgery	1.00	1.00-1.00	.980			
Previous surgery in the same level	2.55	2.32-2.78	.001	1.20	1.01-1.41	.033
Emergency Surgery	1.00	1.00-1.00	.283			
Levels of surgery >1	1.44	1.32-1.58	.001	1.00	0.83-1.21	.975
Microdiscectomy	0.46	0.43-0.50	.001	1.54	0.50-4.75	.454
Decompression only	1.36	1.26-1.47	.001	2.16	0.70-6.65	.181
Fusion	2.04	1.85-2.35	.001	2.20	0.71-6.77	.171
Spine level of surgery:						
L2-L3	1.65	1.44-1.90	.001	1.10	0.85-1.41	.483
L3-L4	1.33	1.21-1.45	.001	1.01	0.84-1.22	.884

L4-L5	0.99	0.92-1.08	.937			
L5-S1	0.985	0.91-1.07	.726			
Perioperative complications	1.16	0.96-1.42	.131			
Complications within three months	1.00	1.00-1.00	.001	1.00	1.00-1.00	.440
Preoperative persistent opioid use	46.91	42.51-51.76	.001	31.10	26.9-36.0	.001
Benzodiazepines in high doses one year before surgery	9.03	8.04-10.13	.001	1.62	1.30-2.04	.001
Z-hypnotics in high doses one year before surgery	4.50	4.10-4.91	.001	1.90	1.58-2.22	.001

Abbreviations: ASA, American Society of Anesthesiologists; ODI, Oswestry Disability Index.

Table 3. Outcome variables at baseline and one year after surgery

Non-persistent opioid users n= 21799				Persistent users n= 2754				
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)	18.8 (16.7)	-23.1 (-23.4 to -22.8)	50.9 (14.7)	41.5 (18.1)	-9.4 (-10.2 to -8.6)	13.7 (12.7 to 14.7)	.001
EQ-5D	0.34 (0.34)	0.70 (0.28)	0.36 (0.36 to 0.37)	0.15 (29.0)	0.31 (0.35)	0.16 (0.01 to 0.14)	-0.20 (-0.22 to -0.18)	.001
VAS	47.3 (21.1)	72.0 (21.7)	24.7 (24.2 to 25.1)	39.1 (20.1)	46.5 (22.5)	7.35 (6.0 to 8.7)	-17.3 (-18.8 to -15.8)	.001
NRS Back pain	6.30 (2.3)	3.2 (2.7)	-3.1 (-3.1 to -3.0)	7.5 (1.8)	6.1 (2.5)	-1.4 (-1.5 to -1.3)	1.7 (1.5 to 1.8)	.001
NRS Leg pain	6.6 (2.3)	2.8 (2.7)	-3.8 (-3.9 to -3.8)	7.1 (2.3)	5.4 (2.9)	-1.8 (-1.9 to -1.6)	2.1 (1.9 to 2.3)	.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)	18.9 (20.5)	-23.4 (-23.6 to -23.1)	51.2 (59.4)	41.5 (71.4)	-9.6 (-10.5 to -8.7)	-13.8 (-14.7 to -12.8)	.001
EQ-5D	0.33 (0.36)	0.70 (0.36)	-0.37 (-0.37 to -0.36)	0.15 (1.25)	0.31 (1.25)	-0.17 (-0.18 to -0.15)	-0.20 (-0.22 to -0.18)	.001
VAS	46.9 (22.5)	71.6 (27.7)	-24.7 (-25.1 to -24.3)	38.6 (74.6)	46.2 (29.0)	-7.6 (-8.9 to -6.3)	-17.1 (-18.4 to -15.8)	.001
NRS Back pain	6.3 (2.4)	3.2 (3.2)	3.1 (3.1 to 3.1)	7.5 (7.9)	6.1 (11.3)	1.4 (1.3 to 1.5)	1.7 (1.6 to 1.8)	.001
NRS Leg pain	6.6 (2.5)	2.8 (3.4)	3.8 (3.8 to 3.9)	7.1 (8.1)	5.4 (12.0)	1.7 (1.6 to 1.9)	2.1 (1.9 to 2.2)	.001

Abbreviations: ODI, Oswestry Disability Index; VAS, Visual Analog Scale; NRS, Numeric Rating Scale.