Supplementary material

Methods

Inclusion and exclusion criteria

The participants recruited for the study were adult patients healthy enough to undergo minor day surgery, classified as ASA-I-II defined in line with the American Society of Anesthesiologists' Physical Status Classification System[1]. Very few patients invited to participate declined (n<10, exact number was not recorded). Excessive anxiety or a language barrier were criteria for not inviting otherwise eligible patients to take part in the study (small minority, number not recorded).

Surgery categories

The surgical categories consisted of colorectal (e.g., haemorrhoid resection, anal fissures), gynaecological (e.g., hysteroscopy, conisation, dilatation and curettage, minor abdominal (e.g., open and laparoscopic herniotomy, laparoscopic cholecystectomy), otorhinolaryngology (adenectomy, tonsillectomy, septum operations), minor orthopaedics (arthroscopy, arthrodesis) and other surgeries.

Perioperative pain management

Preoperative pain management: As part of the standard procedure at Kongsberg hospital patients were instructed to take 2 g acetaminophen (1.5 <70 kg) at home before surgery. If no contraindications were present, e.g. history of gastric or duodenal ulcer, significant gastroesophageal reflux disease (GERD), or kidney disease, patients also received an NSAID (500mg naproxen, 20mg esomeprazol and 12mg dexamethasone).

Intraoperative pain management: Regarding intraoperative pain management, all patients received a Target Controlled Infusion (TCI) of Propofol (Schneiders model - effect site control (4-6µg/ml) at the induction. Patients received Remifentanil (Mintos model - effect

site concentration 5 ng/ml) or 5 mg oxycodone as a pre-anesthetic opioid in the three to five minutes before propofol induction. If the patient had not fallen asleep within 2 - 3 min, propofol was increased to 8.0 µg/ml. Patients received either a laryngeal mask or were intubated. For intubation, patients received either Rocuronium 0.6 mg/kg or Mivacurium 0.2mg/kg. To maintain the anesthesia, propofol was administered in the range of 3 - 5 µg/ml and remifentanil to 2 - 4 ng/ml for all patients, but with individual adjustments. Intraoperatively, in some cases fentanyl was given on a case-by-case basis. No regional anesthesia was used, but infiltration of the wounds with local anesthesia was conducted in some patients.

Recovery room pain management: The overall goal of pain management in the recovery room was for patients to reach a pain score below 3 points on a numeric rating scale. If the patient scored above 3 points on the pain scale or the pain left them unable to relax, patients received 5 mg oxycodone per oral + 2.5 mg oxycodone iv up to 4 times (total 10 mg iv). If the patient remained in pain, the anesthetist was contacted for further treatment.

Subjective ratings

Pain

Patients rated pain intensity and pain interference at three time points: weeks before surgery (average pain last week), morning of surgery (pain right now) and during the acute recovery phase after discharge from the hospital (pain right now). Pain was rated on a numeric rating scale (NRS) from 0 to 10 with the ankers ‘no pain’ to ‘worst imaginable pain’ for pain intensity and ‘no interference’ to ‘worst interference’ for pain interference. They also indicated the duration of pain before surgery in months and years, and pain coping as well as analgeisc effect and associated pain relief after surgery on a NRS (0-10, ‘coping very badly’ to ‘coping very well’; ‘no pain relief’ to ‘full pain relief’).

Nervousness

Nervousness was measured at several time points. Patients indicated their nervousness about surgery in the weeks before surgery, state nervousness on the day of surgery, and their nervousness about recovery during the post-surgery phone interview on a NRS (0-10, 'not nervous' to 'very nervous').

Feeling good & feeling anxious in the operating room

Ratings of how good and anxious patients felt on the surgery table before and one minute after opioid injection were collected verbally on a NRS (0-10, 'not good/anxious' to 'very good/anxious').

Patient satisfaction

Patients were asked to indicate treatment satisfaction as a binary outcome variable (yes/no) at the post-surgery interview.

Long-term follow-up questionnaire data

We measured catastrophic thinking around pain (*Pain Catastrophizing Scale*, PCS)[2,3], pain (*Brief Pain Inventory*, BPI)[4], depression and anxiety (*Hospital Anxiety and Depression Scale,* HADS)[5], occurrence of traumatic experiences during childhood (*Childhood Trauma Questionnaire – short form*, CTQ-SF)[6,7], subjective perception of socio-economic status during child- and adulthood (*MacArthur Scale of Subjective Social Status*)[8], potential substance abuse (*Alcohol Use Disorders Identification Test*, AUDIT[9] and *Drug Use Disorders Identification Test*, DUDIT)[10], life satisfaction (*Life Satisfaction Questionnaire*, LISAT-11)[11], hedonic experience (*Snaith Hamilton Pleasure Scale*, SHAPS)[12], and mindfulness relating to thoughts, experiences and actions in day-to-day life (*Five Facet Mindfulness Questionnaire*, FFMQ-15)[13]. All questionnaires were administered online and in Norwegian.

Results

Comparison of patients who did and did not use rescue opioids during acute recovery

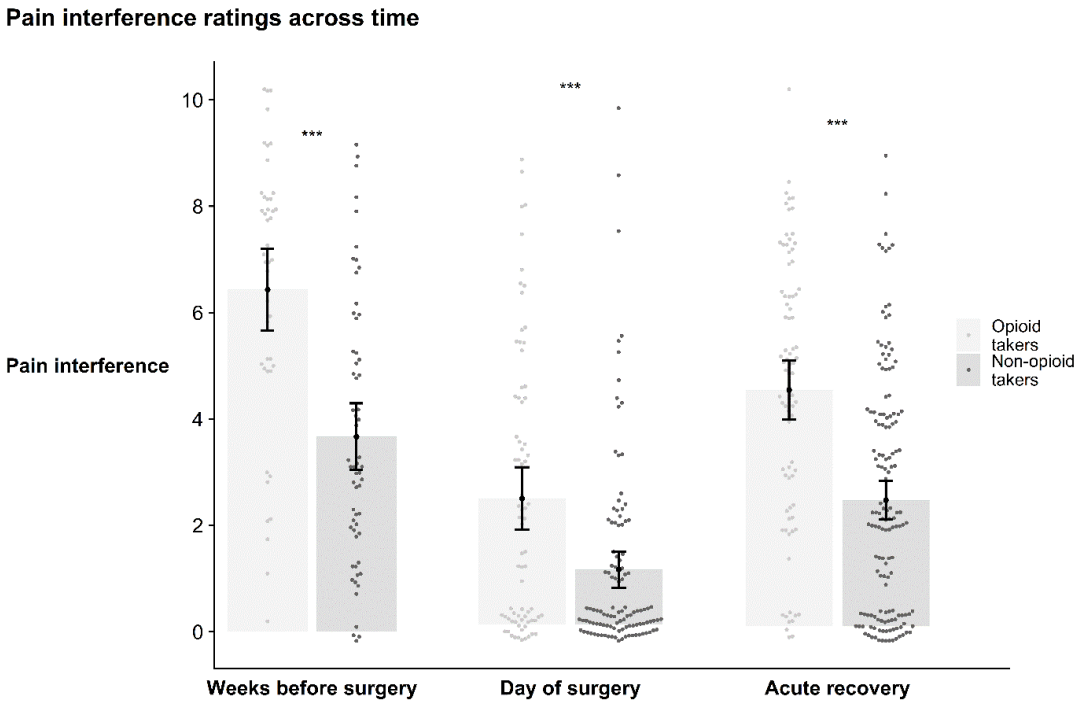
An overview of pain and mood ratings can be found in **Table 2**.

Pain interference

For pain interference, the non-parametric repeated measures ANOVA revealed a significant main effect of group (N=228; opioid takers vs. non-takers; $F(1) = 62.1$, $p < 0.0001$) and time (weeks before surgery, day of surgery, acute recovery; $F(2.0) = 99.2$, $p < 0.0001$). No significant group*time interaction effect was found ($F(2.0) = 1.2$, $p = 0.32$). Opioid takers self-reported higher pain interference weeks before surgery, on the day of surgery and during acute recovery (see supplementary **Figure 6** and **Table 2**).

State measures on the surgery table

The acute effects of opioid injection on the operating table are reported in Eikemo et al.[14]. Here, we compared these effects between opioid-takers and non-takers. When patients were asked to rate how good they felt right before and 1 minute after opioid induction on the surgery table, there was a significant main effect of time (N=227; before vs. after opioid injection, $F(1)=7.4$, $p=0.007$), but not of group (opioid-takers vs. non-takers, $F(1)=0.57$, $p=0.45$) nor a significant interaction effect ($F(1)=0.04$, $p=0.84$). After opioid injection, both patient subgroups reported feeling on average slightly less good (opioid-takers: pre: 7.2±2.1 vs. post: 6.7±2.3; non-takers: pre: 7.4±1.9 vs. post: 7.0±2.3; mean±SD). For ratings of feeling anxious on the surgery table, a non-parametric rmANOVA revealed a significant main effect of time (N=227; $F(1)=13.0$, $p<0.001$), but no significant effect of group ($F(1)=3.2$, $p=0.08$) nor a significant interaction effect ($F(1)=1.2$, $p=0.27$). Both opioid-takers and non-takers reported somewhat lower anxiety after opioid induction on the surgery table (opioid-takers: pre: 3.8±2.9 vs. post: 3.2±2.8; non-takers: pre: 2.9±2.7 vs. post: 2.6±2.6).



Supplementary Figure 6: Pain interference ratings for opioid takers and non-takers. Opioid-takers reported significantly higher pain interference before surgery and during acute recovery compared to non-takers. Groupwise means, 95% confidence intervals, dots depict individual numeric ratings indicated via questionnaire (weeks before surgery and day of surgery) and verbally via phone interview (acute recovery). Numeric ratings were always given as discrete numbers on a scale from 0 to 10. Error bars represent 95% confidence intervals. *** = $p \leq .001$.

Effect of intraoperative opioid on recovery room- and at home opioid use

More patients receiving oxycodone in the minutes before propofol induction received opioid analgesics vs. non-opioid analgesics in the recovery room (N=269; oxycodone: 51%; remifentanil: 35%; χ^2 = 13(2), p=.002). Rescue opioid use at home was not affected by intraoperative opioid choice (opioid takers: oxycodone 24%; remifentanil 20%; χ^2 = 0.6(2), p=0.73).

Supplementary Table 2. Overview of subjective ratings

	Full sample	Opioid takers	Non-opioid takers	*p*
Pain intensity (mean, SD)				
Weeks before surgery	3.7 (2.4)	4.8 (2.5)	3.0 (2.1)	**< 0.001**[b]
On day of surgery	1.4 (2.0)	2.2 (2.3)	1.0 (1.7)	**< 0.001**[c]
Post-surgery Day 1 or 2	3.2 (2.3)	4.5 (2.2)	2.5 (2.1)	**< 0.001**[c]
Long-term follow up: Pain right now	1.2 (1.8)	1.6 (1.9)	1.0 (1.8)	0.06[c]
Long-term follow up: Worst pain 24h	2.0 (2.3)	2.5 (2.5)	1.8 (2.3)	0.2[c]
Pain interference (mean, Sd)				
Weeks before surgery	5.0 (2.8)	6.4 (2.6)	3.7 (2.5)	**< 0.001**[b]
On day of surgery	1.4 (2.0)	2.2 (2.4)	0.9 (1.7)	**< 0.001**[c]
Post-surgery Day 1 or 2	3.1 (2.5)	4.4 (2.5)	2.3 (2.2)	**< 0.001**[c]
Pain relief acute recovery (mean, SD)	7.0 (2.5)	6.8 (2.3)	7.1 (2.6)	0.2[c]
Pain coping acute recovery (mean, SD)	8.5 (1.7)	7.9 (2.0)	8.9 (1.5)	**<0.001**[c]
Nervousness				
Nervousness before surgery	3.3 (3.0)	4.1 (3.3)	2.7 (2.8)	**0.002**[c]
Nervousness day of surgery	4.0 (3.0)	4.5 (3.3)	3.5 (2.8)	0.04[c]
Nervousness about recovery	1.6 (2.2)	2.1 (2.6)	1.4 (1.9)	0.1[c]

Notes. Overview of subjective ratings for full sample (N=270) and the two subgroups reached for the acute recovery interview (N=228). Overview of pain intensity and interference at three different time points, before surgery, on day of surgery and during acute recovery. In addition, pain intensity ratings were collected in the longterm-follow up phase (N=218). Pain relief and pain coping were collected during acute recovery. Nervousness ratings were collected before surgery, on the day of surgery and during acute recovery. Numeric ratings were always given as discrete numbers on a scale from 0 to 10. Groupwise means indicated for non-missing data. Percentage of missing data for group comparisons of pain intensity: weeks before surgery: 57%, day of surgery: 14%, long-term follow up: 44%; and of pain interference: weeks before surgery: 54%, day of surgery: 17%; pain relief: 8%; pain coping: 1%; Nervousness before surgery: 12%, day of surgery: 3%. SD= standard deviation. b= Welch's t-test, c= Wilcoxon sum of ranks test.

Long-term follow-up

Consistent with the acute post-surgery data, patients reported low concern about recovery after being released from the hospital (N=218; mean±SD: 2.2±1.2; Likert scale 1-6) and very high satisfaction with treatment at the hospital (N=218; mean±SD: 5.6±0.9; Likert scale 1-6). Sixty-nine percent of patients reported to have received support from close others during the acute recovery period. One person preferred not to disclose information on support and 67 of 218 (30.7%) patients reported to not have received support during acute recovery. Out of the patients who reported no support during recovery, 27 indicated that they did not need any support and 2 patients that they would have needed support but did not receive any. None of the other 38 patients who reported no support commented on their need of support.

Supplementary Table 3. Overview of long-term follow-up questionnaire outcomes.

	OPIOID TAKERS N=67	**NON-OPIOID TAKERS** N=119	***p***
CTQ total			
Mean (SD)	38.2 (10.4)	36.4 (8.4)	0.7[c]
Median (min - max)	34.0 (28-49)	34.0 (29-67)	
AUDIT total (N=			
Mean (SD)	4.9 (2.7)	3.7 (2.5)	0.2[c]
Median (min - max)	4 (1-14)	3 (0-12)	
DUDIT total			
Mean (SD)	0.6 (1.7)	0.07 (0.4)	0.6[c]
Median (min - max)	0 (0-8)	0 (0-3)	
BPI intensity total			
Mean (SD)	1.5 (1.7)	1.2 (0.3)	0.2[c]
Median (min - max)	1 (0-5)	0 (0-9)	
PCS total			
Mean (SD)	7.3 (7.9)	5.2 (6.4)	0.1[c]
Median (min - max)	5 (0-27)	3 (0-26)	
HADS total			
Mean (SD)	8.3 (6.0)	6.4 (4.4)	0.1[c]
Median (min - max)	8.0 (0-24)	6.0 (0-21)	
LISAT total			
Mean (SD)	4.4 (1.0)	4.8 (0.7)	0.09[b]
Median (min - max)	4.6 (1-5.8)	4.9 (2.9-6)	
SES childhood			
Mean (SD)	5.7 (1.6)	5.6 (1.6)	0.7[b]
Median (min - max)	5.5 (2-10)	6 (2-9)	
SES now			
Mean (SD)	6.8 (1.4)	7.1 (1.1)	0.4[c]
Median (min - max)	7 (4-10)	7 (4-10)	
SHAPS total			
Mean (SD)	0.9 (1.5)	0.8 (1.9)	0.6[b]
Median (min - max)	0 (0-6)	0 (0-14)	
FFMQ total			
Mean (SD)	2.6 (0.5)	2.5 (0.5)	1.0[b]
Median (min - max)	2.6 (1.5-3-3)	2.6 (1.3-3-5)	

Note: Total scores of all questionnaires were calculated for opioid takers and non-takers in the follow-up subsample. Out of 218 patients who took part in the long-term follow-up part of the study, data on opioid use during acute recovery was available in N=186 patients. The two groups did not differ significantly on any of the measures. Groupwise means and medians indicated, reflecting non-missing data. Percentage of missing data for N=186 in CTQ: 40%; AUDIT: 44%; DUDIT: 40%; BPI: 32%; PCS: 37%; HADS: 34%; LISAT: 40%; SESyoung: 35%; SESnow: 34%; SHAPS: 35%; FFMQ: 41%. SD= standard deviation. b= Welch's t-test, c= Wilcoxon sum of ranks test.

Supplementary Table 4. Results from multimodel inference.

Data set and predictor	Model-averaged OR [95% CI]	Model-averaged B (SE)	z	p_z	Importance
Complete cases (n = 118)					
Sex: Women	1.23 [0.54, 2.80]	0.21 (0.42)	0.49	0.62	0.37
Age (years)	0.99 [0.97, 1.02]	-0.01 (0.01)	-0.41	0.68	0.33
BMI	1.02 [0.95, 1.10]	0.02 (0.04)	0.59	0.55	0.43
Pervious opioid use: Yes	1.35 [0.52, 3.48]	0.30 (0.48)	0.62	0.53	0.44
Tobacco use: Yes	1.08 [0.54, 2.15]	0.08 (0.35)	0.22	0.82	0.27
Chronic pain: Yes	0.99 [0.52, 1.89]	-0.01 (0.33)	-0.03	0.98	0.27
Pain weeks before surgery (0-10)	1.11 [0.86, 1.43]	0.11 (0.13)	0.82	0.41	0.56
Nervousness weeks before surgery (0-10)	1.02 [0.92, 1.13]	0.02 (0.05)	0.35	0.73	0.31
Operation cat.: Minor gynecological	0.96 [0.60, 1.56]	-0.04 (0.24)	-0.15	0.88	0.08
Operation cat.: Colorectal	1.01 [0.69, 1.47]	0.01 (0.19)	0.05	0.96	0.08
Operation cat.: Minor Orthopedics	1.02 [0.59, 1.77]	0.02 (0.28)	0.08	0.93	0.08
Operation cat.: Other	0.87 [0.26, 2.91]	-0.13 (0.61)	-0.22	0.83	0.08
Operation cat.: Otorhinolaryngology	3.76 [0.00, Inf]	1.32 (401.54)	0.00	1.00	0.08
Opioid admin. in recovery room (freq.)	2.89 [1.70, 4.93]	1.06 (0.27)	3.91	**< 0.0001**	1.00
Pain day of surgery (0-10)	1.10 [0.81, 1.50]	0.09 (0.16)	0.59	0.55	0.44
All cases after imputation (n = 228)					
Sex: Women	1.18 [0.64, 2.16]	0.16 (0.31)	0.52	0.60	0.40
Age (years)	0.99 [0.96, 1.02]	-0.01 (0.01)	-0.83	0.41	0.56
BMI	1.03 [0.96, 1.11]	0.03 (0.04)	0.79	0.43	0.55
Pervious opioid use: Yes	1.36 [0.62, 2.95]	0.30 (0.40)	0.77	0.44	0.53
Tobacco use: Yes	1.08 [0.63, 1.86]	0.07 (0.28)	0.27	0.79	0.29
Chronic pain: Yes	1.02 [0.50, 2.08]	0.02 (0.36)	0.06	0.95	0.34
Pain weeks before surgery (0-10)	1.23 [0.98, 1.54]	0.21 (0.11)	1.79	0.07	0.88
Nervousness weeks before surgery (0-10)	1.04 [0.92, 1.17]	0.04 (0.06)	0.67	0.50	0.48
Operation cat.: Minor gynecological	1.00 [0.90, 1.11]	0.00 (0.06)	-0.03	0.98	0.01
Operation cat.: Colorectal	1.00 [0.90, 1.11]	0.00 (0.05)	0.00	1.00	0.01
Operation cat.: Minor Orthopedics	1.00 [0.89, 1.12]	0.00 (0.06)	-0.03	0.98	0.01
Operation cat.: Other	1.00 [0.86, 1.16]	0.00 (0.07)	0.01	0.99	0.01
Operation cat.: Otorhinolaryngology	1.01 [0.76, 1.34]	0.01 (0.14)	0.06	0.95	0.01
Opioid admin. in recovery room (freq.)	2.68 [1.86, 3.86]	0.99 (0.19)	5.30	**< 0.0001**	1.00
Pain day of surgery (0-10)	1.06 [0.86, 1.31]	0.06 (0.11)	0.54	0.59	0.43

Note. As reference category, we used *Men* for the predictor *Sex*, *No* for the predictors *Tobacco use* and *Chronic pain*, and. *Minor abdominal surgery* for the predictor *Operation category*. Odds ratios > 1 indicate increased risk of opioid use after surgery while odds ratios < 1 indicate reduced risk of opioid use after surgery. All p-values are from two-tailed z-tests. The importance of each predictor was calculated as the sum of Akaike weights for models containing the predictor. Models containing predictors of high importance tend to perform better at predicting opioid use after surgery compared to models not containing these predictors.

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