Rethinking the definition of chronic postsurgical pain: composites of patient-reported pain-related outcomes vs pain intensities alone

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Abstract

Chronic postsurgical pain (CPSP) is defined by pain intensity and pain-related functional interference. This study included measures of function in a composite score of patient-reported outcomes (PROs) to investigate the incidence of CPSP. Registry data were analyzed for PROs 1 day and 12 months postoperatively. Based on pain intensity and pain-related interference with function, patients were allocated to the groups “CPSPF” (at least moderate pain with interference), “mixed” (milder symptoms), and “no CPSPF”. The incidence of CPSPF was compared with CPSP rates referring to published data. Variables associated with the PRO-12 score (composite PROs at 12 months; numeric rating scale 0-10) were analyzed by linear regression analysis. Of 2319 patients, 8.6%, 32.5%, and 58.9% were allocated to the groups CPSPF, mixed, and no CPSPF, respectively. Exclusion of patients whose pain scores did not increase compared with the preoperative status, resulted in a 3.3% incidence. Of the patients without pre-existing pain, 4.1% had CPSPF. Previously published pain cutoffs of numeric rating scale >0, ≥3, or ≥4, used to define CPSP, produced rates of 37.5%, 9.7%, and 5.7%. Pre-existing chronic pain, preoperative opioid medication, and type of surgery were associated with the PRO-12 score (all P < 0.05). Opioid doses and PROs 24 hours postoperatively improved the fit of the regression model. A more comprehensive assessment of pain and interference resulted in lower CPSPF rates than previously reported. Although inclusion of CPSP in the ICD-11 is a welcome step, evaluation of pain characteristics would be helpful in differentiation between CPSPF and continuation of pre-existing chronic pain.

Keywords: CPSP, ICD-11 code, Pain-related affective interference, Pain-related functional interference, Pre-existing chronic pain, Risk factors

1. Introduction

Chronic postsurgical pain (CPSP) is a common and serious clinical problem resulting in impaired postoperative long-term outcome and reduced quality of life.⁹ This pain is localized in the surgical field or a referred area, develops or increases in intensity, and persists beyond the normal healing period.⁵,³²,⁴² After mixed surgical procedures, 3% to 85% of patients develop CPSP, with 2% to 25% suffering from severe CPSP.³¹ Pain should be of at least 3 months’ duration, and other possible causes for the pain should be ruled out.⁵,³¹,³₂ However, diagnosis should not be based entirely on pain intensity—as was the case in most of the investigations published in the past—but requires pain that negatively affects quality of life.⁵,³₂ To contribute to identification, diagnosis, and therapy, CPSP is now included in the International Classification of Diseases (ICD-11).³² Pain severity is one of the newly defined chronic pain specifiers and encompasses 3 dimensions: pain intensity, pain-related distress, and pain-related interference with activities of daily living.²⁴ Thus, the updated definition provides a more global measure of the impact of the complex phenomenon pain on health-related quality of life.²⁵,⁴²

In this analysis, we assessed CPSP using both pain scores and pain-related functional interference in the activities of daily living, which were combined in a composite score of patient-reported outcomes. This more comprehensively reflects how much a subject is impaired by pain in his function (ability to work, to perform leisure activities, or housework as well as in his mood and enjoyment of life) compared with a single measure which may not adequately describe the patients’ pain experience.¹⁶ The new term “CPSPF” was used to underline the additional consideration of pain-related impaired function. We assumed that CPSPF rates would differ from rates previously described for CPSP. Using data...
from a European cohort retrieved from the registry PAIN OUT, CPSPF rates were compared with CPSP rates, which were calculated by applying pain intensity scores with various cutoffs, as reported in previous publications.

Predictive factors for CPSP have been studied before, but no data are available for variables associated with a composite patient-reported outcome measure encompassing pain intensity as well as pain-related physical and affective interference 12 months after surgery. Thus, as a second aim, we investigated factors associated with a composite of patient-reported outcomes at 12 months.

2. Methods

2.1. Data source

The data for this analysis were retrieved from the PAIN OUT registry, a multinational, multicenter project originally funded by the European Commission’s Seventh Framework program, designed to improve perioperative pain management (ClinicalTrials.gov: NCT02083835). Participating hospitals obtained ethics approval and patient consent according to their local requirements. Details of the PAIN OUT registry have been previously published (www.pain-out.eu).44 In brief, patient characteristics, medical history, anesthesia-related and surgery-related data, and analgesics administered perioperatively were collected by trained surveyors not involved in patient care, to avoid bias. They entered the data into a password-secured web-based registry.

Patient-reported outcomes (PROs) were evaluated using the validated International Pain Outcome Questionnaire on the first postoperative day (www.pain-out.eu).30 Pain, as well as pain-related physical and affective interference, was quantified by the patients using a numeric rating scale (NRS 0-10; 0: no pain/no interference; 10: pain as bad as you can imagine or interferes completely). Patients’ perception of care was assessed with yes or no answers or percentage scales.

Twelve months after surgery, existence of pain, pain-related interference in daily activities, and analgesic treatment were assessed using the questions originating from the Brief Pain Inventory short form (BPI), either filled in electronically by the patient or filled out by a surveyor during a telephone interview.6,12

2.2. Cohort analyzed in this study

A proposal for data analysis with the end points CPSPF and patient-reported pain-related outcomes was submitted to the PAIN OUT publication board. Approval from the Ethics Committee of Bern University Hospital was obtained for analysis of registry data (KEK 2020-02699). Anonymized data of patients who had participated in the 12-month follow-up between 2012 and September 2020 after general surgery, orthopedic surgery or traumatology, gynecological or obstetric surgery, and neurosurgery (spine surgery only) were made available by the PAIN OUT consortium. This article adheres to the applicable STROBE or RECORD guidelines.

2.3. Patient-reported outcomes and composite scores

For the first day after surgery, the following PROs retrieved from the patient questionnaires were analyzed and summarized as composite scores (Supplemental Digital Content Table S1, available at http://links.lww.com/PAIN/B623): Pain Composite Score (PCS-1: worst pain, least pain, and % time in severe pain) and Pain Interference Total Score at day 1 (PITS-1; pain-related interference with activities in bed, taking a deep breath or coughing, and with sleep, pain-related anxiety and helplessness). The PRO-1 score is the mean of PCS-1 and PITS-1, thus summarizing pain intensities and pain-related PROs.

For the time point 12 months after surgery, composite scores were calculated from measures of the BPI as outlined in Supplemental Digital Contents Figure S1 (available at http://links.lww.com/PAIN/B623). The 4 questions on pain intensity (least, worst, average, and current pain) were averaged to create the Pain Composite Score (PCS-12). On the basis of this score, patients were allocated to the groups pain free (PCS-12; NRS = 0), mild pain (NRS <3), moderate pain (NRS 3 to <6), and severe pain (NRS ≥6). In the same manner, pain-related functional interference was calculated from the 7 questions of the BPI addressing physical and affective interference as well as pain-related interference with sleep, thus summarizing the reactive dimensions of pain.8,20 These measures were combined in the Pain Interference Total Score (PITS-12). Patients were allocated to no, mild, moderate, and severe functional interference according to the optimal cut points described by Shi et al. (moderate interference NRS 2-5) and previously used to evaluate functional interference in patients with CPSP.33,35 Finally, the 11 measures of pain intensity and pain-related interference were combined to a composite score of patient-reported outcomes PRO-12 (Supplemental Figure S1, available at http://links.lww.com/PAIN/B623).

2.4. Definitions of CPSPF

Taking into account pain intensity (PCS-12) and pain-related functional interference in daily activities (PITS-12), patients were allocated to 3 CPSPF groups. (1) No CPSPF group: Patients with neither pain nor pain-related functional interference. (2) Mixed group: Patients with only mild symptoms (PCS-12 or PITS-12 ≥0) not meeting the criteria for the CPSPF group, and patients reporting functional interference without any pain. (3) CPSPF group: Patients with a PRO-12 ≥3 with at least moderate pain and at least mild pain-related interference. Using these 3 criteria, CPSPF rates were calculated for the whole cohort, as well as for patients with and without any pre-existing chronic pain. Furthermore, we applied the ICD-11 requirement of an increase in pain intensity at 12 months compared with the preoperative situation.

2.5. Aim of this study

The aim of this study was first to calculate PRO-12 scores (primary end point) encompassing pain and pain-related interference after surgery. On the basis of PRO-12 scores, the incidence of CPSPF was generated and then compared with CPSP rates based on previously published definitions of CPSP. The cutoffs used in the past were pain NRS ≥0 (group CPSP-0), ≥3 (group CPSP-3), or ≥4 (group CPSP-4). Because in previous trials these cutoffs referred to pain at rest, pain with movement, average pain, or type of pain was not specified, we used the PCS-12 to define CPSP for this comparison.

The second aim of this study was to investigate variables already assessable preoperatively which are associated with PRO-12 or CPSPF group. In a further step, we additionally entered perioperative variables to evaluate whether the regression model could be improved.

2.6. Analysis of data

During the process of data cleaning, only hospitals providing at least 50 cases with complete perioperative process data and
filled-in patient questionnaires were included in the analysis. Part of the anonymized data set made available for this statistical analysis has been used in the past for other projects derived from this registry.\textsuperscript{12,35} Because time of enrollment was long, we introduced a variable considering an early study period (2012-2015) and a more recent period (2016-2020).

2.7. Statistics
The definition of CPSPF was more stringent than those used in the past, which referred to pain scores alone. Based on a previous investigation,\textsuperscript{35} we estimated the CPSPF rate at approximately 10%. Thus, a cohort of roughly 2000 patients would result in a representative cohort of 200 patients reporting CPSPF.

Categorical data were presented as absolute numbers and percentage of patients, continuous data by mean and 95% confidence intervals (CI) of the mean or mean ± SD (standard deviation), and NRS scores by median with interquartile range. The χ² test was applied to test relationships between categorical variables. Two-sided independent samples t test or analysis of variance was used to compare the mean values of normally distributed data between 2 or more than 2 groups, respectively. Ordinal data were compared by the 2-sided Mann–Whitney U test or Kruskal–Wallis test.

A multivariable linear regression model was fitted for the PRO-12 score as a dependent variable with risk factors for CPSP known before surgery (patients’ demographics and history and type of surgery). Estimated regression coefficients b with 95% CI were reported to assess the influence of the independent variables. The results were compared with a model with risk factors known before surgery and additional perioperative data (anesthesia-related variables and PROs retrieved from the first postoperative day). The coefficient of determination R² and the Bayesian information criterion (BIC) is provided for both models (BIC\textsubscript{pre} and BIC\textsubscript{pen}), and the likelihood ratio test was performed for model selection.

In a sensitivity analysis, an ordinal regression model was fitted, with CPSPF as a dependent 3-stage variable (No CPSP, Mixed group, and CPSPF) and the preoperative and perioperative factors as independent variables. Estimated odds ratios with 95% confidence intervals (OR [95% CI]) were reported, and goodness of fit of the regression model was assessed by Nagelkerke’s R².

Additional subanalyses were performed separately for patients undergoing general, orthopedic, gynecological or obstetric surgery, and neurosurgery (spine surgery only), as well as for patients from one single hospital, using the model including preoperative and perioperative variables. Statistical analyses were performed using IBM SPSS Statistics 25.0 (Corp, Armonk, NY).

3. Results
3.1. Study cohort and incidence of CPSPF
Data of 5237 patients were obtained from PAIN OUT. After exclusion of patients not responding to the 12-month questionnaire and patients with incomplete data sets, 2319 cases were analyzed (Fig. 1). Considering pain and pain-related interference 12 months after surgery, 8.6% of patients were allocated to the CPSPF group, 32.5% to the Mixed group, and 58.9% to the No CPSPF group. In the heterogeneous Mixed group, 61.3% of the patients reported pain as the leading symptom (PCS-12 > PITS-12) and 37.5% reported higher scores for functional interference than for pain (PITS-12 > PCS-12). Composite PRO-12 scores amounted to 4.8 (4.6; 5.0), 1.2 (1.1; 1.2), and 0.0 (0; 0) for the groups CPSPF, Mixed, and No CPSPF, respectively.

Pre-existing chronic pain for at least 3 months before surgery was frequently reported in patients undergoing orthopedic surgery (68.6%) and neurosurgery (spine surgery) (76.0%). It was more common in the CPSPF group compared with the other 2 groups (P <0.001, Fig. 1). Regarding location, 15.9% of the patients suffered from pre-existing pain at the surgical site, 54.6% reported pain elsewhere, and 29.4% had pain at both locations (Supplemental Fig. S2, available at http://links.lww.com/PAIN/B623). Patients’ characteristics and clinical data are summarized in Table 1. The incidence of CPSPF was highest after neurosurgical (31.9%), orthopedic back or spine surgery (19.4%), and total knee arthroplasty (19.1%).

CPSPF rates did not vary between the early and more recent study phase (8.5% vs 8.8%; $P = 0.06$). The proportion of patients in the Mixed group was higher in the early period (38.2% vs 24.3%; $P <0.001$). However, different hospitals contributed data to the 2 study periods, and the types of surgery were not always comparable.

3.2. Chronic postsurgical pain rates using different definitions of chronic postsurgical pain
Considering the ICD-11 requirement that pain intensity should have increased after surgery compared with the preoperative status, only 3.3% of the patients could be categorized as having CPSPF (presented in Fig. 2 as CPSPF ICD-11). Applying previously published cutoffs to the present cohort, incidence rates for CPSP amounted to 37.5% using a PCS-12 cutoff of NRS >0. With a cutoff of NRS ≥3 or ≥4, CPSPF rates declined (Fig. 2). A comparison of these results with CPSP rates reported by other working groups is also presented in Figure 2. Distribution of patients according to their CPSPF group vs different cutoffs to define CPSP is shown in Supplemental Figure S3 (available at http://links.lww.com/PAIN/B623).

![Figure 1: Flowchart with number (%) of patients. Definition of CPSPF considers not only pain but also pain-related functional interference assessed with a questionnaire 12 months (M12) after surgery. CPSPF-CSPF defined by chronic postsurgical pain and pain-related interference of function.](http://links.lww.com/PAIN/B623)
Of the patients without any pre-existing chronic pain, 322 reported pain at 12 months; 55 of those had CPSPF (4.1% of the whole cohort). In patients with pre-existing pain, CPSPF rates were significantly higher, with the incidence amounting to 22.2% in patients with pain at the surgical site and elsewhere (Supplemental Fig. S2, available at http://links.lww.com/PAIN/B623). In most of the patients with pre-existing chronic pain, pain intensity had declined at 12 months, with 50.5% being completely pain free.

3.3. Opioids

A small percentage of the patients (5.6%) took opioids before hospital admission, with the highest rates in patients undergoing orthopedic surgery (10.6%) or spine surgery in the neurosurgical department (19.5%). Of the CPSPF groups, the highest proportion of patients with preoperative opioids were those having CPSPF at 12 months (Table 1; \( P < 0.001 \)). At the end of surgery, 570 patients (27.0%) received opioids to prevent pain immediately after emergence from anesthesia. These opioids were more frequently administered to patients developing CPSPF later on (40.2%) than to patients in the Mixed group (33.7%) or the No CPSPF group (21.3%; \( P < 0.001 \)).

During their stay in the PACU and on the ward, more patients in the CPSPF group received opioids (91.0%) than patients in the Mixed (77.5%) and No CPSPF groups (70.8%; \( P < 0.001 \)). Twelve months after surgery, opioids were taken more frequently by the CPSPF group (23.4%; Mixed: 2.9%, No CPSPF: 1.1%; \( P < 0.001 \)).

3.4. Patient-reported outcome on the first postoperative day

PRO measures evaluated on the first postoperative day differed between CPSPF groups (Fig. 3). Greater pain intensity in the CPSPF group was accompanied by increased pain-related interference with activities and increased affective interference.

### Table 1

**Patient characteristics and clinical data according to the CPSPF groups.**

|                  | All patients | No CPSPF | Mixed CPSPF | CPSPF | \( P \) |
|------------------|--------------|----------|-------------|-------|--------|
| **All patients** |              |          |             |       |        |
| Female patients  | 2319         | 1365     | 754         | 200   | 0.002  |
| Male patients    | 862          | 470      | 302         | 90    |        |
| Age (years)      | 51.5±15.2    | 51.6±15.3| 51.1±15.2   | 52.9±14.1 | 0.300  |
| BMI (kg/m\(^2\)) | 28.9±7.9     | 29.8±8.5 | 27.4±6.4    | 28.7±6.9 | <0.001 |
| Patients with comorbidities† | 1514 (65.9) | 916 (67.4) | 448 (60.5) | 150 (75.8) | <0.001 |
| Number of comorbidities | 1.2±1.2     | 1.2±1.2  | 1.0±1.2     | 1.4±1.3 | <0.001 |
| Pre-existing pain‡ | 959 (41.4)  | 453 (33.2) | 361 (48.1) | 145 (72.5) | <0.001 |
| Pain scores of all patients‡ | NRS 0.0 (0.0/4.0) | 0.0 (0.0/4.0) | 0.0 (0.0/6.0) | 6.0 (0.0/8.0) | <0.001 |
| Patients with pain only | NRS 6.0 (4.0/8.0) | 6.0 (4.0/8.0) | 6.0 (4.0/7.0) | 7.0 (5.0/8.0) | <0.001 |
| Opioids before surgery | n (%) 129 (5.6) | 48 (3.5) | 40 (5.3) | 41 (20.5) | <0.001 |
| Duration of surgery | Min 147.7±90.8 | 142.0±91.7 | 153.9±91.3 | 164.5±79.7 | 0.002 |

**Surgical group**

- General surgery: 837, 603 (72.0), 200 (23.9), 34 (4.1)
- Orthopedic surgery: 651, 257 (39.5), 290 (44.5), 104 (16.0)
- Gynecology: 629, 397 (63.1), 198 (31.5), 34 (5.4) <0.001
- Neurosurgery (spine surgery): 129, 57 (44.2), 47 (36.4), 25 (19.4)
- Others: 73, 51 (69.9), 19 (26.0), 3 (4.1)

**Regional analgesia§** n (%) 632 (27.5), 359 (26.4), 223 (30.2), 50 (25.0%) 0.127

Data presented as n (%), mean±SD, or median (IQR).

* \( x^2 \) test, ANOVA, or Kruskal–Wallis test.
† Patients with at least 1 comorbidity, refers to 2298 patients.
‡ Refers to 2316 patients (3 missing data in the mixed group) with data regarding pre-existing pain before surgery for at least 3 months.
§ Regional analgesia includes neuraxial anesthesia and peripheral nerve blocks performed intraoperatively only, postoperatively, or during both time intervals (n = 2296).
BMI, body mass index.

Figure 2. Percent of patients with CPSPF and CPSP in the present cohort applying different definitions of CPSP. For comparison, some results of previous studies are displayed. CPSPF ICD-11: Patients meeting the ICD-11 requirement that pain intensity at the site of surgery had increased compared with the preoperative situation. CPSP-0, CPSP-3, and CPSP-4 (orange bars): application of the cutoff NRS \( >0 \), NRS \( \geq 3 \), or NRS \( \geq 4 \) to this cohort. Time after surgery is indicated after the author’s name (i.g. 3M: 3 months). a: mixed surgical group; b: trauma/orthopedic surgery; c: breast cancer surgery; d: gynecological surgery; e: thoracic or cardiac surgery; f: outpatient surgery. NRS, numeric rating scale.
3.5. Variables associated with CPSPF

The multivariable linear regression model, including variables assessable preoperatively, revealed that pre-existing opioid medication increased PRO-12 score on average by nearly 1 point (β = 1.04 [95% CI: 0.77; 1.30] and scheduled spine surgery by 0.63 [0.26; 0.99] points (Table 2). Pre-existing chronic pain for at least 3 months before admission, orthopedic surgery, and younger age were also associated with increasing PRO-12.

The second model—which also included perioperative variables—contains some additional explanatory factors (Fig. 4). If opioids were given for postoperative pain management, this was associated with a marginal increase in PRO-12 (for PACU: 0.16 [0.03; 0.30]) and the administration of nonopioid analgesics with a decrease of PRO-12 (−0.24 [−0.39; −0.09]). Further variables associated with an increase of PRO-12 were “desire for more pain treatment” and an increase in PRO-1 score. Proportion of variance explained by the most relevant variables PRO-1 and opioid medication before admission were 6.3% and 5.4%. Goodness of fit of this model was judged as moderate (R² = 0.16) with lower BIC (BICperi = 7657) than the model using only information available preoperatively (BICpre = 7965), indicating stronger evidence for the model with perioperative data. The likelihood ratio test also confirmed the better fit of the perioperative model (χ² = 73.5, degrees of freedom = 9, P < 0.001).

Sensitivity analysis using an ordinal regression model with the CPSPF group as dependent variable confirmed the results of the linear regression model (Supplemental Table S2, available at http://links.lww.com/PAIN/B623). The subanalyses performed for the 4 different surgical disciplines and data of one single institution underline the relevance of pre-existing chronic pain and opioid medication before admission and PRO-1 (Supplemental Tables S3 A-E, available at http://links.lww.com/PAIN/B623). Receiving regional analgesia was a protective factor in gynecological and obstetric patients, resulting in a decrease of −0.4 (−0.6; −0.1) in PRO-12 at 12 months.

4. Discussion

In a European cohort of 2319 patients, chronic postsurgical pain was studied using the new ICD-11 definition. The results showed lower rates than published before, in part because of inclusion of pain-related functional interference and in part because of restrictions on cases presenting with an increase of pain intensity compared with the preoperative status.

In the 1990s, Kehlet et al. underlined that low pain intensity could no longer be the only goal of pain management; thus, they promoted the early return to functional recovery. This fundamental change in approach gained additional proponents when it became clear that striving for pain intensities below a distinct cutoff was in part the reason for increased prescription of opioids, resulting in the opioid crisis. To the best of our knowledge, this is the first large-scale study assessing CPSPF rates in a mixed surgical cohort by using measures to capture the multidimensional pain characteristics.

4.1. Defining chronic postsurgical pain using pain scores alone

Evaluation of CPSP in the past clearly relied on pain scores and focused on unidimensional measures. Pain was often assessed at rest or as average pain, reflecting a defined period of time (1 day up to 3 months). Sometimes, details of pain assessment were not even specified. Applying published cutoffs in the present cohort and adding results of other working groups uncovers striking differences in CPSPF rates (Fig. 2).

However, even if more extensive questionnaires were to be used taking into account pain severity as a combination of pain intensity, pain-related distress, and functional interference, we still have to question whether we need cutoffs to define CPSP and if yes, which cutoff is clinically meaningful from the patients’ point of view. Development of standardized, validated assessment tools is a further crucial step to identify meaningful PROs reflecting pain severity and pain-related functional interference at long term after surgery. This study suggests an approach that could serve as a basis for further discussion.

4.2. Alternative tools for assessment of chronic postsurgical pain

Enhanced restoration of function after abdominal surgery—helping the patient to breath, cough, and move easily—has been described as one central aspect of pain relief. More sophisticated, complementary measures have been proposed but evaluating them requires additional resources and tools. The Initiative of Methods, Measurement, and Pain Assessment in Clinical Trials recommended measurement of the outcome domains of physical and emotional functioning, side effects, and satisfaction. The BPI has been suggested as one option;
however, other questionnaires on quality of life can be used.\textsuperscript{4,10,21}
Certainly, introducing some surgery-specific items is advisable because interference after joint replacement differs from
interference after hernia repair or thoracotomy.\textsuperscript{11,21,43}

4.3. Time as a factor
Chronic postsurgical pain develops or increases in intensity after a
surgical procedure and persists more than 3 months after the
surgery.\textsuperscript{31} Previous investigations were aimed at periods ranging
from 2 months up to several years.\textsuperscript{13,17} After most types of surgery,
rates of moderate-to-severe CPSP decreased over time. In a
European study, rates declined from 16.0% at 6 months to 11.8%
at 12 months.\textsuperscript{12} In patients with breast cancer, the incidence of any
permanent pain 1 and 2 years after surgery decreased from 67% to
45%.\textsuperscript{13} However, as indicated by the ICD-11, some patients may
suffer from pain after an asymptomatic time interval.\textsuperscript{13,25,27,42}

4.4. Continuing pre-existing pain vs chronic
postsurgical pain
Another challenge is distinguishing CPSP from continuing pre-
existing pain.\textsuperscript{22} This issue has rarely been addressed\textsuperscript{11,21,22,40}
and might have contributed to higher CPSP rates reported
previously. In the present trial, only 3.3% of the cohort remained in
the CPSPF group when an increase of pain intensity compared
with the preoperative status was required. This decline is certainly
because of the high proportion of patients with long-term
presurgical pain, a lot of them presenting for joint replacement
and spine surgery.

In a population-based study, 18% of patients reported
moderate-to-severe pain at the surgical site 3 to 36 months after
surgery.\textsuperscript{22} If all patients who had the same kind of pain before
surgery were excluded, 10.5% were allocated to CPSP. If
patients with any pain before surgery were excluded, 6.2% were
left with CPSP. Apart from pain intensity, CPSP was frequently
not a continuum of pre-existing pain for other reasons. Of the
patients with CPSP and with preoperative pain at the surgical site,
74.1% reported a change of “kind of pain” compared with
preoperative pain.\textsuperscript{22} A change in characteristics of pain, sensory
disturbance and the location or spatial distribution compared with
presurgery are further diagnostic criteria.\textsuperscript{11,27,39,42} However,
these are not considered in the ICD-12. Because the questionnaires do not consider character-
istics and temporal patterns of pain, we could not further classify
subjects. For the future, a more detailed evaluation of patients’
history including physical examinations before and after surgery
would be helpful.\textsuperscript{11,21,27}

4.5. Incidence of chronic postsurgical pain and CPSPF
The results—including a large variance in the incidence of CPSP
depending on different definitions—confirm the previous find-
ings.\textsuperscript{12,31} It is likely that a considerable number of patients who were
categorized in the past as having CPSP would not meet the
current definition because their chronic pain did not increase in
intensity compared with preoperative pain or was not related to
surgery because questionnaires did not capture this information,
and thorough preoperative and postoperative evaluation was not
performed.

The Mixed group comprised patients with milder symptoms,
with some pain, but no or marginal interference, or with (nearly) no
pain and at least moderate interference. Based on these results, it
is not possible to determine which of these patients are in need of
or would benefit from a multimodal therapeutic approach.
However, regardless of whether their pain is categorized as
CPSPF, mixed, or a continuation of pre-existing chronic pain,
patients should be offered treatment.

It seems appropriate to provide some information before
discharge to patients at risk, such as whom to consult if pain-
related problems associated with surgery continue or arise.
Patients with pain as the leading symptom need other therapeutic
strategies than patients suffering from impaired function in whom
pain plays a minor role. Reasonable options could be consultation
of a multidisciplinary team of pain experts, for example, within the
setting of a transitional pain service, offering a multidimensional
assessment and providing an interdisciplinary treatment

| Variables | Regression coefficient | 95% CI          | P    |
|-----------|------------------------|-----------------|------|
| Sex: female vs male (reference) | 0.018 | −0.125; 0.160 | 0.808 |
| Age | −0.006 | −0.016; 0.001 | 0.009 |
| Weight | −0.001 | −0.004; 0.001 | 0.312 |
| Pre-existing chronic pain: yes vs no (reference) | 0.455 | 0.322; 0.589 | <0.001 |
| Opioids before admission: yes vs no (reference) | 1.035 | 0.768; 1.302 | <0.001 |
| Type of surgery: general surgery (reference) | 0.551 | 0.384; 0.719 | <0.001 |
| Orthopedic surgery | 0.194 | 0.025; 0.362 | 0.024 |
| Neurosurgery (spine surgery) | 0.031 | −0.417; 0.479 | 0.891 |
| Others | −0.090 | −0.446; 0.266 | 0.619 |
| Spine surgery*: yes vs no (reference) | 0.625 | 0.264; 0.986 | 0.001 |
| Number of comorbidities | 0.046 | −0.021; 0.114 | 0.180 |
| Cancer: yes vs no (reference) | 0.028 | −0.154; 0.210 | 0.765 |
| Smoking: yes vs no (reference) | 0.116 | −0.057; 0.289 | 0.190 |
| Alcohol: yes vs no (reference) | 0.063 | −0.303; 0.428 | 0.737 |
| Substance abuse: yes vs no (reference) | −0.208 | −0.690; 0.275 | 0.399 |

Dependent variable is patient-reported pain-related outcome 12 months after surgery (PRO-12 score). n = 2238; R²: 0.128.

* Spine surgery either performed in the neurosurgical or orthopedic department.
Composite outcomes can reflect a more comprehensive assessment of CPSP; however, treatment approaches have to consider both pain and functional interference, to provide individualized care.

**4.6. Chronic postsurgical pain vs CPSPF: what is the difference?**

Orthopedic surgery, spine surgery, and a positive DN4 (possible neuropathic pain) are associated with pain and the most interference. These patients are frequently categorized as having CPSPF; however, some of them do not qualify for CPSP because of only mild pain. The same is true for patients with high affective interference. Subjects’ individual perception might vary considerably depending also on the preoperative status, type of surgery, and the patient’s preoperative expectations for surgical outcome.

The use of cutoffs results in precisely separated groups of patients with CPSP or no CPSP. However, reality is different, with no arbitrary lines between the groups, but a smooth transition from one group to the other. Thus, calculating incidences of CPSP or CPSPF can give an impression of the proportion of patients suffering from CPSP, but does not meet the needs of an individual subject. It is well-accepted that the multidimensional phenomenon pain should be best considered by a biopsychosocial model. The WHO specifiers with additional extension codes for pain intensity, pain-related interference, and pain-related distress provide clinically useful categories giving a more detailed picture that will improve patient management and research.

**4.7. Variables associated with CPSPF**

This analysis confirmed previously described risk factors, such as pre-existing chronic pain and opioid medication. Sex was not associated with PRO-12, probably because of the very mixed types of surgery, ranging from younger female patients undergoing laparoscopic surgery to older patients undergoing extensive orthopedic surgery.

Interestingly, not only acute postoperative pain but also pain-related physical and affective interference and administration of analgesics during the first 24-hour period after surgery were associated with PRO-12 and CPSPF and improved the regression model. This points to the usefulness of evaluating additional physical and emotional measures of acute pain, as recommended and provided by PAIN OUT. Specifically, the

![Figure 4. Multivariable linear regression analysis with PRO-12 score as dependent variable. Reference for analysis of the surgical groups is general surgery. Boxes represent regression coefficients, and whiskers are 95% CI. Exact measures are shown in the right column. * P < 0.05; ** P < 0.001; *** P < 0.001.](image-url)
time in severe pain is important from the patients’ perspec-
tive.12,35,36 Hence, this also implies a change in patient
education: Acute pain management should no longer focus on
pain scores only, but on rapid recovery of function.
It should be underlined that the administration of opioids was
associated with increased, nonopioid analgesics with decreased
PRO-12. This does not imply that opioids are the reason for
CPSP, but rather, that those patients suffering from severe acute
pain were given more opioids.

4.8. Limitations and strengths
Limitations of this analysis include the general shortcomings of
registry data (data quality and electronic questionnaires). There is
no preoperative patient assessment of functional impairment,
psychological and psychosocial variables, although these pro-
vide valuable information.1,8 Electronic questionnaires, specifi-
cally when applied within a registry project, cannot capture all
aspects of CPSP and have to be considered as a screening tool,
not as a final diagnosis.
The strengths of this investigation are the large European
cohort from clinical routine settings, a standardized documenta-
tion of process, and outcome variables with validated question-
naires addressing pain and pain-related functional physical and
affective impairment. The results do not reflect artificial study
settings, in which patient selection is rigorous, excluding
“problematic cases”, and more staff is involved.

5. Conclusions
CPSPF was identified in 8.6% of the patients using PRO
measures encompassing pain and functional interference. Using
a more stringent definition, including only patients with increased
pain scores at 12 months, 3.3% would be diagnosed with
CPSPF.

Introducing CPSP into the ICD-11 and the inclusion of pain-
related functional interference are welcome steps for clinicians,
patients, and the scientific community. However, patients with
pre-existing pain should be evaluated more extensively, both
before and after surgery. Pain characteristics and a change in
pain localization could be valuable information. We should
continue to discuss and rethink the definition of CPSP for ICD-12.

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Appendix A. Supplemental digital content
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