Preoperative Anxiety and Catastrophizing A Systematic Review and Meta-analysis of the Association With Chronic Postsurgical Pain

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A Systematic Review and Meta-analysis of the Association With Chronic Postsurgical Pain

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Objectives: Anxiety and pain catastrophizing predict acute postoperative pain. However, it is not well established whether they also predict chronic postsurgical pain (CPSP). The aim of this systematic review and meta-analysis was to investigate whether high levels of preoperative anxiety or pain catastrophizing are associated with an increased risk of CPSP.

Methods: Electronic search databases included PubMed and PsychINFO. Additional literature was obtained by reference tracking and expert consultation. Studies from 1958 until October 2010, investigating the association between preoperative anxiety or pain catastrophizing and CPSP in adult surgery patients, were assessed. The primary outcome was the presence of pain at least 3 months postoperatively.

Results: Twenty-nine studies were included; 14 instruments were used to assess anxiety or pain catastrophizing. Sixteen studies (55%) reported a statistically significant association between anxiety or pain catastrophizing and CPSP. The proportion of studies reporting a statistically significant association was 67% for studies of musculoskeletal surgery and 36% for other types of surgery. There was no association with study quality, but larger studies were more likely to report a statistically significant relationship. The overall pooled odds ratio, on the basis of 15 studies, ranged from 1.55 (95% confidence interval, 1.10-2.20) to 2.10 (95% confidence interval, 1.49-2.95). Pain catastrophizing might be of higher predictive utility compared with general anxiety or more specific pain-related anxiety.

Discussion: There is evidence that anxiety and catastrophizing play a role in the development of CPSP. We recommend that anxiety measures should be incorporated in future studies investigating the prediction and transition from acute to chronic postoperative pain.

Key Words: anxiety, catastrophizing, risk factor, postsurgical, chronic pain

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Postoperative pain is of major concern after surgery because of the impact on postoperative recovery, quality of life, and the risk of acute postoperative pain (APP) in the first postoperative days progressing to become chronic postsurgical pain (CPSP).[1] Many studies report unacceptably high levels of APP after surgery.[2–5] Predictive factors for APP include factors such as younger age and prior pain experience, in addition to psychological factors.[2,6,7] In particular, the influence of preoperative anxiety on APP is well established.[6,8–10] Both state anxiety, a temporary condition experienced in a specific situation, and trait anxiety, a general tendency to perceive situations as threatening, can play a role in the experience of postoperative pain.[11] Another psychological factor that has been found to be predictive of APP is pain catastrophizing.[12–14] Pain catastrophizing, defined as the tendency to magnify the threat value of pain and to feel helpless in the context of pain, is highly correlated with both state and trait anxiety and with more specific pain-related fears.[15–17]

The question we seek to answer in this systematic review is whether preoperative anxiety and catastrophizing also predict chronic pain after surgery. Since the early 1990s, there has been a growth in clinical and epidemiological research investigating the prevalence, predictors, and burden of CPSP: the potential long-term impact on quality of life and the societal and economic burden from CPSP has been well reported.[18–20] Chronic pain is defined by the IASP as pain persisting beyond the normal time of healing, generally after 3 months.[21] More specifically, for CPSP, Macrae refers to pain that develops after a surgical procedure; is present for at least 2 months; no other cause for the pain can be identified; and is not the result of a continuing, preexisting problem.[22] Prevalence estimates for CPSP have ranged from 10% to 50% depending on the specific study, methodology, timing of follow-up, and type of surgical procedure.[18,23] The role of psychological factors in the development of CPSP has been suggested[23,24] but is not as well established as in the case of APP.

One of the most recent systematic reviews targeting the role of psychosocial predictors of CPSP in patients undergoing various types of surgery was performed by Hinrichs-Rocker et al.[25] Depression, psychological vulnerability, and stress were identified as psychological factors showing a likely correlation to CPSP. For many other psychological factors, including anxiety, the results were inconclusive. However, since the publication of this review, which included papers published up to 2006, several new studies have examined preoperative anxiety and/or pain catastrophizing in relation to CPSP. To our knowledge, no formal meta-analysis has been conducted using data from multiple primary studies. Therefore, it is timely to conduct an updated review and meta-analysis that specifically focuses on the predictive value of anxiety and pain catastrophizing for CPSP after different types of surgeries.

For the purpose of this review, we consider all studies that have included either a measure of general (state or trait) anxiety, specific pain-related anxiety, or pain catastrophizing. According to the fear-avoidance model of chronic pain, pain catastrophizing elicits pain-related anxiety, and both are considered major determinants of pain persistence after an acute injury.[26] In addition, a hierarchical model of general and specific anxieties has been proposed in which both pain catastrophizing and pain-related anxiety are seen as pain-specific constructs that are subsumed under the higher order construct of trait anxiety.[27] A high global anxiety disposition is hypothesized to lead to pain-related anxieties in acute pain situations, for example during surgery. Because it may also be speculated that more proximal constructs (ie, pain-specific anxieties) have higher predictive value than more distal constructs (ie, global trait or state anxiety), in addition to pooling the results of all classes of predictors together, we will also examine the role of global anxiety, pain-specific anxiety, and pain catastrophizing separately.

An additional question is whether an association between anxiety and pain catastrophizing would be more evident in patients undergoing surgery involving the musculoskeletal system, that is lumbar, hip, knee, and shoulder surgery. The fear-avoidance model of chronic pain was originally developed to explain the persistence of nonspecific musculoskeletal pain. A key role is assigned to avoidance of physical activity: fear-induced avoidance results in decreased physical fitness, which in turn fuels the cycle of increased disability and pain.[26] Persistent avoidance might therefore be especially detrimental in the recovery from musculoskeletal surgery. Moreover, musculoskeletal surgery patients may be more likely to have chronic or ongoing preoperative pain that could be the primary indication for surgery, and preexisting pain is in itself a determinant of CPSP.[24,28]

Two systematic reviews have specifically focused on psychological predictors of outcome after lumbar surgery. Den Boer et al[29] found evidence that, in addition to somatization and passive avoidance coping strategies, preoperative anxiety may predict unfavorable outcomes (including pain) after lumbar surgery. More recently, Celestin et al[30] performed a systematic review of psychosocial variables as predictors of outcomes (including pain) after lumbar surgery and spinal cord stimulation. The results suggest a possible association between preoperative levels of anxiety, depression, coping, somatization, hypochondriasis, and poor outcome (including pain) after lumbar procedures. Thus, the evidence that preoperative anxiety and pain catastrophizing are predictive of persistent pain in patients undergoing lumbar surgery seems to be more consistent than for other types of surgery. Whether this also holds for other surgeries involving the musculoskeletal system remains to be determined.

The aim of this systematic review was to summarize current evidence concerning the hypothesis that high levels of preoperative anxiety or pain catastrophizing are associated with an increased risk of CPSP. The outcome in this review will be limited to intensity and/or presence of pain or a composite score including pain presence/intensity at 3 months or longer after surgery. Furthermore, we will investigate whether the hypothesized association between anxiety and CPSP is consistent between studies of musculoskeletal surgery and the other types of surgery.

MATERIALS AND METHODS

Search Strategy and Study Selection

Studies considered eligible for inclusion within the review were observational cohort studies, case-control studies, and RCTs of adult surgical patients undergoing all types of surgery except dental surgery. Studies published in English, German, French, and Dutch were eligible for inclusion. Only studies in which anxiety data were collected before surgery and pain data were collected after surgery were included.

Bibliographic searches were conducted on PubMed (National Center for Biotechnology Information, NCBI, Bethesda) and PsychINFO (EBSCO Publishing, Ipswich) databases for literature published between 1958 and October 2010. Search strategies were initially developed and piloted using MEDLINE but a higher return rate was obtained using PubMed. Final search strategies used a combination of Medical Subject Heading (MeSH) and text words: ((presurgical or preoperative) AND ("Fear"[Mesh] OR "Anxiety"[Mesh] OR "Anxiety Disorders"[Mesh], fear or anxiety or coping or catastrophizing or psychosocial)) AND ("Pain, Postoperative"[Mesh], pain or acute pain or chronic pain or persistent pain) AND (postoperative or postsurgical). Electronic searches were limited to studies of adults. Additional searches were carried out by reference tracking and expert consultation. The search was performed by M.P. (psychologist) and M.T. (epidemiologist). The abstracts retrieved from electronic and hand searching were assessed independently. Subsequently, all studies describing surgical patients not having dental surgery, with an assessment of preoperative psychosocial state and postoperative measurement of pain at least 3 months after surgery, were selected for full-text reading. If any aspect of the abstract was unclear, the full text was obtained and assessed. There was no use of conference abstracts. To enable meta-analysis, all authors of publications that did not include data suitable for the calculation of pooled odds ratios (OR) were contacted for additional data to contribute to the review.

Outcomes and Predictors

The primary outcome was pain assessed at least 3 months after surgery. In addition, multidimensional outcome measures were included if they incorporated a pain component or measure. Predictors related to preoperative anxiety were eligible for inclusion if they assessed concepts of anxiety, surgical fear, or pain catastrophizing. If multidimensional instruments were used preoperatively or postoperatively, these had to include and report at least 1 relevant subscale.

Data Extraction and Critical Appraisal

Extracted data of the selected studies were tabulated, reporting author, publication date, country, study design, follow-up duration, type of surgery, sample size, outcome measure(s), predictor(s), effect, and type of statistics used. Study quality was assessed using an 8-item checklist (scores 0 to 8). The quality items were based on the Critical Appraisal Checklist for Cohort/Case Control appraisal of the Joanna Briggs institute[31] and the checklist for measuring study quality developed by Downs and Black,[32] which were adapted for use (Appendix). Unblinded quality assessment was performed independently by M.T. and V.T. (MSc in Medicine). Interrater agreement on the total score was assessed using the weighted quadratic κ[33]; interrater agreement per item was assessed using the κ statistic. In cases of divergent scoring, a consensus meeting with a third rater (M.L.P.) led to the final judgment. Chi-square tests were used for a sensitivity analysis on study quality with regard to the proportion of studies reporting statistically significant results, type of surgery (musculoskeletal surgery vs. remaining types of surgery), and publication date (before/after 2008). The publication of the STROBE statement,[34] providing guidelines for the reporting of observational studies, was the reason for selecting 2008 as the cutoff for publication date as a proxy quality indicator. The weighted quadratic κ was calculated using kappapls.exe software [Software developed by A.G. Kessels, MD, MSc, Department of Clinical Epidemiology and Medical Technology Assessment (KEMTA), MUMC+, Maastricht, The Netherlands]. The κ statistic and χ^2 tests were performed using the Statistical Package for the Social Sciences (SPSS version 18, Chicago, IL). Meta-analysis was performed using STATA version 11.2 (Stata Corp., College Station, TX).

Because of heterogeneity in the reported data, initial pooling of the results of all 29 included studies was restricted to vote counting and descriptive analysis. At the study level, the total number of studies reporting any statistically significant positive association between preoperative anxiety or catastrophizing and CPSP is reported. At the predictor level, the number of studies reporting any statistically significant positive association between a specific predictor and any of the pain-related outcomes, versus the total number of studies using that predictor, is reported.

Second, a random-effects meta-analysis was performed on a subset of 15 studies that provided data to allow the calculation of pooled OR. Published data (9 references) and unpublished data, which were provided at request by 6 authors, were used. If raw data were provided, patients were classified as having CPSP yes/no and preoperative anxiety or catastrophizing yes/no by a median split. Because of the nonparametric distribution, statistical pooling was performed using log-transformed ORs. Subsequently, the results were converted by taking the exponential of the log OR. Because of the heterogeneity in predictor and outcome measures, the random-effects model was chosen. Where a study presented more than one predictor/outcome combination, we divided the results into a maximum effect scenario (highest OR) and a minimum effect scenario (lowest OR) to avoid overrepresentation of studies reporting more than 1 outcome.

RESULTS

The process of study selection is presented in the flow chart (Figure 1). A total of 71 articles from 512 references were obtained and critically appraised; of these, 29 studies were considered eligible for inclusion in the review (N = 6628 patients). Musculoskeletal surgery was performed in 18 studies (n = 4963 patients) and 11 studies concerned other types of surgery (n = 1665). All studies were either performed in the United States (11) or western Europe (18). One study was a nested cohort study within an RCT; all other studies were observational cohort studies. Data on the selected studies are presented in Table 1.

Quality of Evidence

Overall, the quality of studies was relatively high. The quality scores of the selected studies were 5 (10%),[19,40,45] 6 (42%),[36,38,39,44,46–48,52,54,55,60,61] 7 (17%),[37,43,49,53,58] or 8 (31%),[1,28,35,42,50,51,56,57,62] respectively (Table 1). Agreement

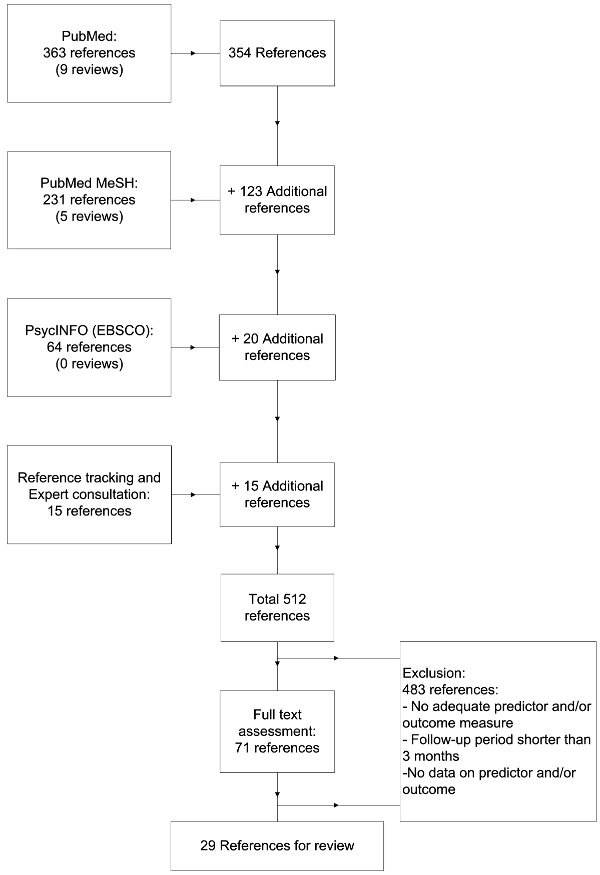

FIGURE 1. Flow chart study selection.

between the 2 raters was substantial: the weighted quadratic κ was 0.67 [SD 0.14; 95% confidence interval (CI), 0.40-0.95). The κ scores per item ranged from 0.35 to 1.00. The lowest values were 0.35 for the item “withdrawal described” and 0.44 for the item “sample representative.” A sensitivity analysis revealed that the quality of the selected studies was not affected by publication date (before/after 2008; χ^2 0.94, *df* 3, $P = 0.82$) or by categorization of surgery (musculoskeletal vs. remaining types of surgery; χ^2 1.25, *df* 3, $P = 0.74$). With regard to the relationship between study quality and the reported effects of the predictors, no statistically significant differences were found (studies reporting any significant predictor vs. no significant predictor; χ^2 1.57, *df* 3, $P = 0.67$).

Retrospective studies were excluded. In one of the included studies, selection bias could have played a role. Preoperative anxiety was based on assessment of the ICD-9 anxiety code in the patient file. The author stated that this might have led to underreporting of anxiety. For 6 of the 29 included studies, it was not possible to determine whether the study population was representative of the whole surgical population (eg, single surgical center or only patients of 1 surgeon included). A further 16 (55%) studies had a sample size of <100 participants. Attrition was $>30\%$ or could not be determined in 2 studies. Confounding variables were adjusted by multivariate analyses in 16 studies; in the remaining studies, bivariate analysis was used or the correction method used to adjust for confounding was unclear.

TABLE 1. Study Characteristics

References Country	Design	Follow-up (mo)	Surgery	N	Chronic PostSurgical Pain	Predictor(s): Anxiety, Pain Catastrophizing	Effect	Study Quality	Included in Meta-analysis
Various types of surgery									
Aasvang et al[35] Denmark Germany	Observational cohort	6	Inguinal hernia	464	AAS (pain-related impairment)	PCS: global score	0	8	+
						HADS: anxiety subscale	0		
Brandsborg et al[36] Denmark	Observational cohort	4	Hysterectomy	90	Pelvic Pain affecting daily life	CSQ: catastrophizing subscale	0	6	+
Ene et al[37] Sweden	Observational cohort	3	Prostatectomy	155	1 VAS worst pain intensity (0-100) 2 SF-36 bodily pain (0-100)	HADS: anxiety subscale	1 + 2 +	7	0
Gerbershagen et al[38] Germany	Observational cohort	**3**, 6	Nephrectomy	35	CPSP 3 of 4 criteria Macrae (2001)	HADS: anxiety subscale	+, 0	6	+
Gerbershagen et al[39] Germany	Observational cohort	**3**, 6	Prostatectomy	84	CPSP 3 of 4 criteria Macrae (2001)	HADS: anxiety subscale	0	6	+
Hickey et al[40] Ireland	Observational cohort	3	Breast	28	Report of any breast surgery-related pain	HADS: anxiety subscale	0	5	+
						VAS (0-100): Anxiety	0		
Katz et al[19,41] Canada	Cohort nested in RCT	18	Thoracotomy	30	VRS pain intensity (0-10)	STAI: state anxiety	0	5	0
						STAI: trait anxiety	0		
Peters et al[1] The Netherlands	Observational cohort	6	Various types	625	Report of increased or new pain due to surgery	Surgical Fear (long-term)	+	8	+
						PCS	0		
Peters et al[42] The Netherlands	Observational cohort	**6**, **12**	Various types	401#	SF-36 bodily pain (0-100)	Surgical Fear (long-term)	0	8	+
						PCS	0		
Poleshuck et al[43] USA	Observational cohort	3	Lump- or Mastectomy	95	Report of any breast surgery-related pain	STAI: state anxiety	0	7	0
Richardson et al[44] United Kingdom	Observational cohort	6	Lower limb amputation	59	PPQ (phantom limb pain)	CSQ: catastrophizing subscale	+, 0	6	+
Musculoskeletal surgery									
Boer den et al[28] The Netherlands	Observational cohort	6	Lumbar disc	277	VAS Back and leg pain intensity (0-100)	TSK (TSK-AV, 13 items)	0	8	0
Brander et al[45]	Observational cohort	(1), 3, 6, **12**	Knee replacement	116	VAS knee pain intensity (0-100)	STAI: trait anxiety	+	5	0
Brander et al[46] USA	Observational cohort	60	Knee replacement	83#	VAS knee pain intensity (0-100)	STAI: trait anxiety	0	6	0

(*continued*)

TABLE 1. (*continued*)

References Country	Design	Follow-up (mo)	Surgery	N	Chronic PostSurgical Pain	Predictor(s): Anxiety, Pain Catastrophizing	Effect	Study Quality	Included in Meta-analysis
Edwards et al[47] USA	Observational cohort	(1), 3, 6, **12**	Knee replacement	43	1 VAS overall pain severity (0-100) 2 VAS night-time pain severity (0-100)	CSQ: catastrophizing subscale	1 0 2 +	6	+
Forsythe et al[48] Canada	Observational cohort	3, 12, **24**	Knee arthroplasty	55	1 Pain Rating Index (MPQ, 0-3) 2 VAS pain intensity (0-10)	PCS: total score	1 + 2 0	6	0
George et al[49] USA	Observational cohort	3-5	Shoulder	59	BPI (NRS 0-10) Shoulder pain intensity	PCS: total score	+	7	+
						STAI: trait anxiety	0		
						FPQ	0		
						TSK (TSK-11)	0		
Graver et al[50] Norway	Observational cohort	6, **12**	Lumbar disc	122	1 Clinical Overall Score (VAS highest pain intensity + clinical/ neurological examination + ODI + analgesics) 2 VAS back pain intensity (0-100) 3 VAS leg pain intensity (0-100)	HADS: anxiety subscale	1 + 2 0 3 +	8	0
Groot de et al[51] The Netherlands	Observational cohort	3	Lumbar surgery	126	VAS (0-100) 1 Back pain (intensity × frequency) 2 Leg pain (intensity × frequency)	STAI: state anxiety	1 + 2 0	8	0
Harden et al[52] USA	Observational cohort	(1), **3**, **6**	Knee arthroplasty	77	IASP criteria CRPS	STAI: trait anxiety	0	6	0
Johansson et al[53] Sweden	Observational cohort	12	Lumbar disc	59	1 VAS back pain intensity (0-100) 2 VAS leg pain intensity (0-100)	CSQ: catastrophizing subscale	1 0 2 0	7	+
						TSK (TSK, 12 items)	1 0 2 0		
Kjellby-Wendt et al[54] Sweden	Observational cohort	3, **12**, 24	Lumbar disc	50	Discontent/ content (0-5)	STAI: state anxiety	+	6	0
						STAI: trait anxiety	+		
Lavernia et al[55] USA	Observational cohort	60	Knee or Hip arthroplasty	331	1 WOMAC pain 2 SF-36 bodily pain (0-100)	PPSS: total score	1 + 2 +	6	0

(*continued*)

TABLE 1. (*continued*)

References Country	Design	Follow-up (mo)	Surgery	N	Chronic PostSurgical Pain	Predictor(s): Anxiety, Pain Catastrophizing	Effect	Study Quality	Included in Meta-analysis
Riddle et al[56] USA	Observational cohort	6	Knee arthroplasty	140	WOMAC pain 1 Improve 2 Minimal relevant change	TSK (TSK-11)	1 0 2 0	8	+
						PCS: total score	1 + 2 +		
Rosenberger et al[57] USA	Observational cohort	12	Arthroscopic Knee surgery	180	MPI: 1 Knee pain severity 2 Knee pain interference	Surgery Stress Scale	1 + 2 0	8	+
Schade et al[58,59] Switzerland	Observational cohort	24	Lumbar disc	46	1 Pain relief 2 Surgical outcome score (pain relief, work, pain medication, limit activities)	Psychological general well-being Index: anxiety subscale	1 0 2 0	7	0
Singh et al[60] USA	Observational cohort	24 and/or 60	Revision total hip arthroplasty	3123	MKHQ	ICD-9 code anxiety	0	6	+
Sorensen et al[61] Denmark	Observational cohort	6	Lumbar disc	57	Poor outcome: (VAS pain, pain chart score, poor health)	MMPI: panic-fear subscale	+	6	+
Trief et al[62] USA	Observational cohort	6, **12**	Lumbar surgery	102	DPQ: 1 Change back pain 2 Change leg pain	STAI: trait anxiety	1 0 2 +	8	0
						MSPQ: somatic anxiety	1 + 2 0		

Follow-up: in case of multiple follow-up measurements, the bold number indicates the period assessed in this review.
N: #numbers do not account for the total review population number due to overlap with another study on the same population.
Effect: +, significant positive association; 0, nonsignificant association. For multivariate analysis, if applicable, on the basis of published data. If both + and 0 association are reported for 1 predictor, this is due to different types of analysis. For more details on predictors and statistical analysis: see Table 2.
Study Quality: range 0 to 8.
AAS indicates Activity Assessment Scale; BPI, Brief Pain Inventory; CPSP, Chronic Postsurgical Pain; CRPS, Complex Regional Pain Syndrome; CSQ, Coping Strategies Questionnaire; DPQ, Dallas Pain Questionnaire; FPQ, Fear of Pain Questionnaire; HADS, Hospital Anxiety and Depression Scale; MKHQ, Mayo Knee & Hip Questionnaire; MMPI, Minnesota Multiphasic Personality Inventory; MPI, Multidimensional Pain Inventory; MPQ, McGill Pain Questionnaire; MSPQ, Modified Symptom Perception Questionnaire; ODI, Oswestry Disability Index; PASS, Pain Anxiety Symptoms Scale; PCS, Pain Catastrophizing Scale; PPQ, Phantom Phenomena Questionnaire; STAI, State-Trait Anxiety Inventory; TSK, Tampa Scale of Kinesiophobia; VAS, Visual Analog Scale; VRS, Verbal Rating Scale; WOMAC, Western Ontario MacMaster Osteoarthritis Index.

Measurement of Predictors and Outcomes

A total of 14 different instruments were used to assess psychological predictors: (in alphabetical order) Coping Strategies Questionnaire (CSQ, subscale pain catastrophizing); Fear of Pain Questionnaire (FPQ III); Hospital Anxiety and Depression Scale (HADS, subscale anxiety); ICD-9 code anxiety; Minnesota Multiple Personality Inventory [MMPI, subscale panic-fear (PF)]; Modified Somatic Perception Questionnaire (MSPQ, subscale somatic anxiety); Pain and Anxiety Symptoms Scale (PASS); Pain Catastrophizing Scale (PCS); Psychological general well-being index (subscale anxiety); State-Trait Anxiety Inventory (STAI); Surgery Stress Scale; Surgical Fear Questionnaire; Tampa Scale of Kinesiophobia (TSK); the Visual Analogue Scale (VAS anxiety).

A total of 21 different instruments were used to capture pain-related outcomes: Activity Assessment Scale (AAS, pain-related impairment); Brief Pain Inventory [BPI; the pain intensity Numerical Rating Scale (NRS) scores]; Clinical Overall Score (COS; an aggregate measure of pain intensity by VAS, clinical examination, the Oswestry Disability Index, and analgesic use); CPSP presence (Macrae criteria); Dallas Pain Questionnaire (back pain, leg pain); International Association for the Study of Pain (IASP) criteria for Complex Regional Pain Syndrome (CRPS); Mayo Knee and Hip Questionnaire; McGill Pain Questionnaire (MPQ, pain rating index); Pain intensity/change by Likert or Visual Analogue Scale (VAS) or Verbal Rating Scale (VRS); Pain relief (VAS); Pelvic pain affecting daily life (Likert); Phantom Phenomena Questionnaire (intensity by VAS, presence yes/no); Poor outcome [aggregate score of pain intensity (VAS), pain chart score, poor health]; Presence of any breast surgery-related pain (yes/no); Retrospective report of increased or new pain due to surgery; Satisfaction with surgical treatment (content/discontent); SF-36 (subscale bodily pain); Surgical outcome score (aggregate score of pain relief, return to work, medication use, limitation of physical activities); Western Ontario and McMaster Universities (WOMAC) Osteoarthritis index; and West-Haven Yale Multidimensional Pain Inventory (MPI).

Predictors of Chronic Pain After Surgery

In 16 of the 29 studies (55%), preoperative anxiety or pain catastrophizing was significantly associated with higher rates of CPSP. In all cases, higher levels of anxiety or pain catastrophizing predicted worse outcome. However, in 12 out of these 16 studies using multiple predictor or outcome measures, a significant association was not uniformly found across all measures or analyses. Reported effect sizes varied across studies, but were generally small to moderate (all correlations <0.5; ORs ranged from 1.90 to 6.04). Thirteen studies did not find any association between preoperative anxiety or pain catastrophizing and CPSP (Tables 1 and 2).

Table 3 shows the number of studies that reported a statistically significant effect of a specific predictor on any pain-related outcome. To obtain more homogeneity in the predictors assessed, we divided them into 3 groups: general anxiety measures, pain-related anxiety measures, and pain catastrophizing. Remarkably, pain-related anxiety seems to be less predictive compared with the general anxiety measures and pain catastrophizing, respectively. This seems to be mainly due to an absence of association for the TSK.

Next, we assessed whether there were differences in outcome between studies addressing musculoskeletal surgery versus other types of surgery. There was a trend showing an increased proportion of statistically significant predictors in studies of musculoskeletal surgery (67%) compared with the studies investigating other types of surgery (36%, χ^2 2.54, *df* 1, $P=0.11$). Stratification for sample size is shown in Table 4. The proportion of studies revealing statistically significant predictors was 69% for studies with >100 participants compared with 44% for the smaller studies (χ^2 1.88, *df* 1, $P=0.17$). The proportion of statistically significant predictors was similar for the higher quality studies (scores 7 to 8) (57%) compared with studies with intermediate quality scores 5 to 6 (53%, χ^2 0.04, *df* 1, $P=0.84$). The length of postoperative follow-up, 3 to 12 months compared with 12 months or more, did not yield a significantly different proportion of studies reporting a significant association between predictor and outcome (respectively, 53% and 57%, χ^2 0.04, *df* 1, $P=0.84$). For studies using bivariate versus multivariate analysis, the proportions were 62% and 50%, respectively (χ^2 0.39, *df* 1, $P=0.53$).

For the meta-analysis, pooled ORs were calculated on the basis of 15 studies including 5046 patients. Five studies made use of multivariate analysis[1,35,49,56,60] and 10 were based on bivariate analysis.[36,38–40,42,44,47,53,57,61] Table 5 presents pooled ORs with their CI and a measure for between-study variation (heterogeneity). Overall, anxiety and catastrophizing seemed to be significant predictors of CPSP. Depending on the (sub)group and the maximum or the minimum effect scenario, pooled ORs varied between 1.11 (95% CI, 0.82-1.50) and 2.71 (95% CI, 1.40-5.24), with a total OR of 2.1 (95% CI, 1.49-2.95) for the maximum effect scenario and 1.55 (95% CI, 1.10-2.20) for the minimum effect scenario. Because the OR of 1 study [49] included an interaction effect of catastrophizing with the COMT gene, the analysis was repeated excluding these data. Although ORs were reduced slightly, the direction of the effects did not change, except for the magnitude of the total OR, minimum effect scenario: 1.32 (95% CI, 0.98 to 1.77). The pooled ORs confirmed the trend from the vote counting procedure that pain-related anxiety measures were less predictive for CPSP than either pain catastrophizing or pain-related anxiety. Moreover, the ORs also suggest the relative superiority of pain catastrophizing as a predictor. Finally, the trend showing that anxiety and catastrophizing are most predictive for CPSP in musculoskeletal surgery was confirmed by the pooled ORs according to the maximum effect scenario but not by the minimum effect scenario.

DISCUSSION

This systematic review identified 29 studies that examined the relationship between preoperative psychological factors and the risk of persistent, chronic pain after surgery. In 16 out of 29 studies (55%), at least one of the measures of preoperative anxiety or pain catastrophizing showed a significant positive association with CPSP. The remaining 13 studies (45%) failed to detect a relationship between anxiety or pain catastrophizing and CPSP. No studies reported a reversed association, that is a decreased risk of CPSP with high levels of anxiety or lower levels of anxiety predicting CPSP. Overall effect sizes on the basis of 15 studies varied between pooled OR 1.55 (95% CI, 1.10-2.20, minimum effect scenario) and pooled OR 2.10 (95% CI, 1.49-2.95, maximum effect scenario).

Previous systematic reviews by Huber and Lautenbacher,[8] which included 6 empirical papers, and Hinrichs-Rocker et al,[25] which included 7 empirical papers examining the relationship between preoperative anxiety and CPSP, both concluded that there is inconclusive evidence for a predictive relationship. Our systematic review was more comprehensive in that we were able to identify no less than 29 empirical papers investigating the relationship between preoperative anxiety or pain catastrophizing and CPSP. Moreover, we were able to perform a meta-analysis. Although there was no consistent relationship between anxiety or pain catastrophizing and CPSP among the 29 papers, a small majority of studies demonstrated a statistically significant positive association, with no study reporting a reversed effect. It is noteworthy that the results were not related to overall study quality, but that studies with larger sample sizes more often yielded significant relationships. The meta-analysis on a subset of the papers provided additional evidence for an association between preoperative anxiety or catastrophizing and CPSP, yielding effect sizes (pooled ORs) varying between 1.55 and 2.10. Therefore, we propose that there is at least moderate evidence that preoperative anxiety and pain catastrophizing play a role in the development of chronic pain after surgery.

A secondary aim of this review was to examine whether the association between anxiety and pain catastrophizing is more evident in patients undergoing musculoskeletal surgery compared with other types of surgery. Our results show that the proportion of studies showing a significant association was indeed larger and the maximum effect ORs were higher for the subgroup of musculoskeletal surgery patients. It is important to note that CPSP in these patients may be a continuation of preexisting pain instead of new onset pain after surgery as in the definition proposed by Macrae.[22] Thus, it may be speculated that anxiety and pain

TABLE 2. Outcome Measures, Predictors, and Statistics

Study	Chronic PostSurgical Pain	Anxiety, Pain Catastrophizing Other Psychosocial Predictors	Effect	Statistics	Other Predictors
Various types of surgery					
Aasvang et al[35]	AAS (pain-related impairment): ≥ 8,3%	PCS: global score	0	Multivar. Log. regression: OR (95% CI) 1.78 (0.81-3.91), NS	Age, BMI, work/leisure intensity, **preoperative AAS**, pain intensity, other frequent pain, warmth detection, heat detection, 47°C pain scores, open vs. laparoscopy, pain score days 7 and 30
		HADS: anxiety subscale	0	Multivar. Log. regression: OR (95% CI) 1.78 (0.85-3.72), NS	
		Other psychosocial predictor:		Multivar. Log. regression:	
		HADS: depression subscale	0	OR (95% CI) 1.31 (0.43-4.03), NS	
Brandsborg et al[36]	Pelvic pain affecting daily life: some/lot/very much	CSQ: catastrophizing subscale	0	χ^2: NS (no data shown)	Age, preoperative pelvic pain, **preoperative pain elsewhere**, previous pelvic surgery, Uterine Fibroid Symptom Score, indication for surgery, type of hysterectomy, type of anesthesia, weight of uterus, acute postoperative pain, pain at 3 wk
		Other psychosocial predictors:		χ^2	
		CSQ: a Re-interpreting pain sensations subscale	a +	a $P = 0.018$	
		b Coping self-statements subscale	b +	b $P = 0.022$	
		c Control of pain subscale	c +	c $P = 0.023$	
		d SF-36: mental health subscale	d 0	Mann-Whitney U test: d NS (no data shown)	
Ene et al[37]	1 VAS worst pain intensity: (0-100) 2 SF-36 bodily pain: (0-100)	HADS: anxiety subscale	1 + 2 +	Correlation 1 $r = 0.26$, $P < 0.01$ 2 r no data shown, $P < 0.01$	Age, marital status, education, employment, time on waiting list, ASA, pain treatment, SF-36, acute postoperative pain
		Other psychosocial predictors :		Correlation:	
		a HADS: depression subscale	1a +	1a $r = 0.31$, $P < 0.01$	
		b SF-36: mental health subscale	2a +	2a r no data shown, $P < 0.01$	
				1b, 2b No data shown	
Gerbershagen et al[38]	CPSP 3 of 4 criteria Macrae (2001)	HADS: anxiety subscale	+, 0	Mann-Whitney U test: CPSP+ 9.00 ± 2.45 CPSP− 6.92 ± 3.64 (mean ± SD), $P = 0.025$ Fisher exact test:	Age, race, education, employment status, marital status, type of insurance, disability/retirement claims, sick leave, Weighted Illness Check List, **preoperative pain**, preoperative pain

(*continued*)

TABLE 2. (*continued*)

Study	Chronic PostSurgical Pain	Anxiety, Pain Catastrophizing Other Psychosocial Predictors	Effect	Statistics	Other Predictors
				CPSP+ 70% CPSP− 84% (cutoff, % score ≤10), NS	disability, MPSS, CPGQ, NPS, ASA, BMI, type/duration of surgery, tumor stage, type of anesthesia, blood loss, complications, acute postoperative pain, SF-12 physical health subscale
		Other psychosocial predictors :		Mann-Whitney test:	
		a HADS: depression subscale	0	a CPSP+ 3.90 ± 3.69 CPSP− 3.12 ± 3.56 (mean ± SD), NS	
		b SF-12: mental health subscale	0	b CPSP+ 45.74 ± 9.17 CPSP− 48.09 ± 10.83, NS	
		c HWBQ-7 Well-Being	0	c CPSP+ 24.70 ± 8.20 CPSP− 27.80 ± 8.00, NS	
		d SCL-8 psychosomatic dysfunction	0	d CPSP+ 10.88 ± 2.65 CPSP− 9.82 ± 3.08, NS	
Gerbershagen et al[39]	CPSP 3 of 4 criteria Macrae (2001)	HADS: anxiety subscale	0	Mann-Whitney test: CPSP+ 9.58 ± 3.50 CPSP− 7.99 ± 3.38 (mean ± SD), NS Fisher exact test: CPSP+ 58% CPSP− 78% (cutoff, % score ≤10), NS	Age, race, education, employment status, marital status, type of insurance, disability/retirement claims, sick leave, Weighted Illness Check List, **preoperative pain**, MPSS, CPGQ, NPS, ASA, BMI, PSA level, duration of surgery, tumor stage, type of anesthesia, blood loss, complications, acute postoperative pain, SF-12 physical health subscale
		Other psychosocial predictors:		Mann-Whitney U test:	
		a HADS: depression subscale	0	a CPSP+ 6.00 ± 4.11 CPSP− 4.31 ± 3.48 (mean ± SD), NS	
		b SF-12: mental health subscale	+	b CPSP+ 41.79 ± 10.17 CPSP− 49.15 ± 10.46, $P = 0.019$	
		c HWBQ-7 Well-Being	0	c CPSP+ 20.75 ± 9.95 CPSP− 25.47 ± 8.54, NS	
		d SCL-8 psychosomatic dysfunction	+	d CPSP+ 4.33 ± 3.14 CPSP− 2.56 ± 3.36, $P = 0.031$	

(*continued*)

TABLE 2. (*continued*)

Study	Chronic PostSurgical Pain	Anxiety, Pain Catastrophizing Other Psychosocial Predictors	Effect	Statistics	Other Predictors
Hickey et al[40]	Report of any breast surgery-related pain	HADS: anxiety subscale	0	Mann-Whitney U test: CPSP+ 8.0 (4.0-16) CPSP− 6.0 (0-13) (median min-max), NS	Age, height, weight, BMI, preoperative pain, Quantitative Sensory Testing, menstrual status, type of surgery, adjunctive therapy, type of anesthesia, **acute postoperative pain**
		VAS (0-100): Anxiety	0	Mann-Whitney U test: CPSP+ 36.0 (12.0-100) CPSP− 34.5 (2.0-100), NS	
		Other psychosocial predictors :		Mann-Whitney test:	
		HADS:			
		a Depression subscale	0	a CPSP+ 3.5 (1.0-14) CPSP− 3.0 (1.0-14), NS	
		b Total score	0	b CPSP+ 11.0 (5.0-25) CPSP− 8.0 (0.0-27), NS	
Katz et al[19,41]	VRS pain intensity (0-10): Score > 0	STAI: state anxiety	0	Student *t* test: CPSP+ 44.3 ± 6.8 CPSP− 37.1 ± 9.8 (mean ± SD), NS	Age, sex, weight, pain threshold to pressure, diagnosis, type/duration of surgery, type of anesthesia, blood loss, morphine use, **acute postoperative pain**
		STAI: trait anxiety	0	Student *t* test: CPSP+ 36.3 ± 10.0 CPSP− 39.6 ± 10.5, NS	
		Other psychosocial predictor:		Student *t* test:	
		BDI	0	CPSP+ 5.6 ± 4.8 CPSP− 8.3 ± 4.6, NS	
Peters et al[1]	Report of increased or new pain due to surgery	Surgical fear (long term)	+	Multivar. Log. regression: OR (95% CI) 1.90 (1.08-3.33), $P = 0.03$	Age, height, weight, BMI, sex, education, SF-36, ASA, preoperative pain, type/duration of surgery, anatomic region of surgery, type of anesthesia, postoperative pain therapy, **acute postoperative pain**
		PCS	0	Multivar. Log. Regression: NS	
		Other psychosocial predictors:		Multivar. Log. Regression:	
		a BIS	0	a No data shown	
		b LOT	0	b NS	
		c GSES	0	c No data shown	
		d SF-36: mental health subscale	0	d No data shown	
Peters et al[42]	SF-36 bodily pain: (0-100)	Surgical fear (long term)	0	Multivar. Lin. regression: NS	Age, height, weight, BMI, sex, education, SF-36, ASA, **preoperative pain**, type/duration of surgery, anatomic region of surgery, type of anesthesia, postoperative pain therapy, acute postoperative pain

(*continued*)

TABLE 2. (*continued*)

Study	Chronic PostSurgical Pain	Anxiety, Pain Catastrophizing Other Psychosocial Predictors	Effect	Statistics	Other Predictors
		PCS	0	Multivar. Lin. regression: NS	
		Other psychosocial predictors:		Multivar. Lin. regression:	
		a LOT	0	NS	
		b SF-36: mental health subscale	0	NS	
Poleshuck et al[43]	Report of any breast surgery-related pain	STAI: state anxiety	0	Multivar. Log. regression: NS Student *t* test: CPSP+ 35.5 ± 12.6 CPSP− 33.7 ± 12.8 (mean ± SD), NS	**Age**, race, education, marital status, preoperative pain, history of breast cancer, malignant/benign tumor, type of surgery, adjunctive therapy, acute postoperative pain, postoperative analgesic use
		Other psychosocial predictors:		Multivar. Log. regression: a-e NS Student *t* test	
		a BDI	0	a CPSP+ 6.3 ± 5.8 CPSP− 4.6 ± 5.7, NS	
		b HDARS	0	b CPSP+ 5.7 ± 4.5 CPSP− 4.5 ± 5.1, NS	
		c FACT-E	0	c CPSP+ 17.3 ± 4.3 CPSP− 18.8 ± 4.7, NS	
		d IBQ	0	d CPSP+ 0.9 ± 1.1 CPSP− 0.7 ± 1.0, NS	
		e SAS	0	e CPSP+ 2.4 ± 0.5 CPSP− 2.4 ± 2.0, NS	
Richardson et al[44]	Phantom phenomena questionnaire (phantom limb pain): 1 Presence 2 Intensity: (0-100)	CSQ : catastrophizing subscale	1 + 2 0	Fisher exact test: 1 OR (95% CI) 3.28 (1.71-14.91), $P = 0.02$ 2 No data shown Student *t* test: 1 *t* 2.53, *df* 50, $P = 0.02$ 2 No data shown	Age, peripheral vascular disease history, type of surgery, preoperative pain
		Other psychosocial predictors: CSQ:		Fisher exact test:	
		a Total score	1a +	1a OR (95% CI) 12.76 (6.58-57.86), $P = 0.02$	
		b Passive coping subscale	1b +	1b OR (95% CI) 4.60 (6.50-25.00), $P = 0.001$	
		c Praying/hoping subscale	1c +	1c OR (95% CI) 2.86 (1.68-13.18), $P = 0.01$ Student *t* test:	
		d Active coping subscale	1d 0	1d *t* 1.45, *df* 50, NS	
			2 0	2 No data shown	

(*continued*)

TABLE 2. (*continued*)

Study	Chronic PostSurgical Pain	Anxiety, Pain Catastrophizing Other Psychosocial Predictors	Effect	Statistics	Other Predictors
Musculoskeletal surgery					
Boer den et al[28]	VAS back and leg pain intensity: (0-100)	TSK-AV, 13 items	0	Multivar. Lin. regression: B (SE) 0.04 (0.03), NS	Age, sex, education, preoperative pain, duration of complaints, RDQ, neurological deficits, analgesic use, acute postoperative pain
		Other psychosocial predictors:		Multivar. Lin. regression:	
		a PCI	0	a B (SE) 0.04 (0.06), NS	
		b Negative outcome expectancies	+	b B (SE) 0.39 (0.11), $P < 0.001$	
Brander et al[45]	VAS knee pain intensity: (0-100)	STAI: trait anxiety	+	Correlation: $r = 0.38$, $P < 0.01$;	Age, sex, race, BMI, education, preoperative pain, preoperative radiograph, type of surgery, complications, postoperative pain
		Other psychosocial predictors:		Correlation:	
		a BDI	+	a $r = 0.43$, $P < 0.05$;	
		b PSS	0	b $r = -0.06$, NS	
Brander et al[46]	VAS knee pain intensity: (0-100):	STAI: trait anxiety	0	Linear regression: t -0.05, NS	Age, sex, race, BMI, education, preoperative pain, preoperative radiograph, type of surgery, complications, postoperative pain
		Other psychosocial predictor:		Linear regression:	
		BDI	0	t -0.74, NS	
Edwards et al[47]	1 VAS overall pain severity: (0-100) 2 VAS night-time pain severity: (0-100)	CSQ: catastrophizing subscale	1 0 2 +	Repeated measures 1 B (SE) 2.1 (2.2), t 0.9, NS 2 B (SE) 5.1 (2.5), t 2.0, $P = 0.04$	Age, sex, race, postoperative pain
		Other psychosocial predictor: CES-D	1 + 2 0	Repeated measures: 1 B (SE) 0.67 (0.30), t 2.2, $P = 0.03$ 2 B (SE) 0.40 (0.33), t 1.2, NS	
Forsythe et al[48]	1 Pain Rating Index (MPQ, 0-3): Score > 0 2 VAS pain intensity (0-10): Score > 0	PCS: total score	1 + 2 0	ROC curve: 1 AUC 0.713, $P = 0.028$ Mann-Whitney U test: 1 CPSP+ 11.4 ± 9.8 CPSP− 4.9 ± 3.5 (mean ± SD), $P = 0.028$ 2 CPSP+ 10.4 ± 9.6 CPSP− 7.5 ± 6.0, NS	Age, comorbidity, preoperative pain, type of anesthesia

(*continued*)

TABLE 2. (*continued*)

Study	Chronic PostSurgical Pain	Anxiety, Pain Catastrophizing Other Psychosocial Predictors	Effect	Statistics	Other Predictors
		Other psychosocial predictors:		ROC curve: 1a AUC 0.696, $P = 0.044$	
		PCS: a Rumination subscale	1 +	Mann-Whitney U test: 1a CPSP+ 5.6 ± 3.7 CPSP− 3.3 ± 2.1, $P = 0.043$	
		b Magnification subscale	1 0	1b CPSP+ 1.8 ± 2.5 CPSP− 0.4 ± 0.7, NS	
		c Helplessness subscale	1 0	1c CPSP+ 3.9 ± 5.2 CPSP− 1.3 ± 1.5, NS	
			2a-c 0	2a CPSP+ 5.2 ± 3.6 CPSP− 4.4 ± 2.9, NS 2b CPSP+ 1.4 ± 2.3 CPSP− 1.5 ± 2.3, NS 2c CPSP+ 3.7 ± 5.1 CPSP− 1.6 ± 1.8, NS	
George et al[49]	BPI Shoulder pain intensity (NRS 0-10): Score > 4	PCS: total score	+	Multivar. hierarch. regression: PCS NS; PCS × COMT-diplotype interaction Relative risk 6.8 (95% CI 2.8-16.7)	Age, sex, race, medication use, marital status, employment status, preoperative pain, COMT gene
		STAI: trait anxiety	0	Multivar. hierarch. regression: NS	
		FPQ	0	Multivar. hierarch. regression: NS	
		TSK-11	0	Multivar. hierarch. Regression: NS	
Graver et al[50]	1 Clinical Overall Score (VAS highest pain intensity + clinical/ neurological examination + ODI + analgesics): Score ≥ 250	HADS: anxiety subscale	1 + 2 0 3 +	Multivar. Log. Regression: 1 F 2.19, R^2 0.09, $P = 0.02$ Correlation: 2 $r = 0.17$, NS 3 $r = 0.28$, $P = 0.002$	Age, sex, height, weight, BMI, duration of complaints, sick leave, tobacco use, cholesterol, triglycerides, γ-glutamyl transpeptidase, plasminogen activator inhibitor 1, euglobulin clot lysis time
	2 VAS back pain intensity: (0-100)	Other psychosocial predictors:		Multivar. Log. regression:	
		a HADS: depression subscale	1 0	1a F 1.49, R^2 0.04, NS	
		b MSPQ	1 +	1b F 2.36, R^2 0.10, $P = 0.01$	
	3 VAS leg pain intensity: (0-100)	VPMI: c Active coping subscale	1 0	1c F 1.57, R^2 0.05, NS	
		d Passive coping subscale	1 0	1d F 1.69, R^2 0.06, NS	
		e Inappropriate Symptoms	1 0	1e F 1.60, R^2 0.05, NS	

(*continued*)

TABLE 2. (*continued*)

Study	Chronic PostSurgical Pain	Anxiety, Pain Catastrophizing Other Psychosocial Predictors	Effect	Statistics	Other Predictors
		f Nonorganic Signs	1 0	1f F 1.67, R^2 0.05, NS	
				Correlation:	
			2, 3a 0	2a $r = 0.01$, NS 3a $r = 0.13$, NS	
			2, 3b +	2b $r = 0.24$, $P = 0.007$ 3b $r = 0.30$, $P = 0.001$	
			2, 3c 0	2c $r = -0.03$, NS 3c $r = -0.02$, NS	
			2, 3d 0 +	2d $r = 0.15$, NS 3d $r = 0.30$, $P = 0.001$	
			2, 3e 0 +	2e $r = 0.13$, NS 3e $r = 0.19$, $P = 0.04$	
			2, 3f 0 +	2f $r = 0.06$, NS 3f $r = 0.19$, $P = 0.03$	
Groot de et al[51]	VAS (0-100): 1 Back pain (intensity × frequency) 2 Leg pain (intensity × frequency)	STAI: state anxiety	1 + 2 0	Correlation: 1 $r = 0.35$, $P < 0.01$ 2 $r = 0.05$, NS	Age, sex, overweight, severity of disorder, diagnosis, prior lumbar surgery, expected recovery, duration of surgery, number of analgesics, types of analgesics, fatigue, preoperative back/leg pain, pain during activities
		Other psychosocial predictors: TMSI:			
		a Monitoring	0	Correlation: 1a $r = 0.16$, NS; 2a $r = -0.04$, NS	
		b Specific monitoring	0	1b $r = 0.05$, NS; 2b $r = 0.03$ NS	
		c Blunting	1 0, 2 +	1c $r = 0.05$, NS; 2c $r = 0.22$ $P < 0.05$	
		d Specific blunting	0	1d $r = -0.01$, NS; 2d $r = 0.05$ NS	
Harden et al[52]	IASP criteria CRPS	STAI: trait anxiety	0	Point-biserial correlation: NS	Age, sex, race, education, CRPS characteristics, **preoperative pain**
		Other psychosocial predictor: BDI	0	Point-biserial correlation: NS	
Johansson et al[53]	1 VAS back pain intensity (0-100): Residual back pain	CSQ: catastrophizing subscale	1 0 2 0	Multivar. Log. regression: 1, 2: NS	Age, sex, education, physical activity level, work load, sick leave, preoperative leg/back pain, duration of complaints, disability, **expectations on work return**, quality of life, level of disc herniation, neurological signs, rehabilitation group
	2 VAS leg pain intensity (0-100): Residual leg pain	TSK, 12 items	1 0 2 0	Multivar. Log. regression: 1, 2: NS	
		Other psychosocial predictor: CSQ: self-statement subscale	1 0 2 0	Multivar. Log. regression: 1, 2: NS	

(*continued*)

TABLE 2. (*continued*)

Study	Chronic PostSurgical Pain	Anxiety, Pain Catastrophizing Other Psychosocial Predictors	Effect	Statistics	Other Predictors
Kjellby-Wendt et al[54]	Discontent/ content (0-5): ≤3 discontent	STAI: state anxiety	+	Discriminant analysis: STAI + BDI + Pain-VAS correctly classified 78% of discontent, 76% of content patients Student *t* test: CPSP + 48.3 ± 8.2 CPSP − 38.4 ± 11.1 (mean ± SD), $P = 0.017$	Age, sex, preoperative pain, duration of complaints
		STAI: trait anxiety	+	Discriminant analysis: STAI + BDI + Pain-VAS correctly classified 78% of discontent, 76% of content patients Student *t* test: CPSP + 42.6 ± 13.9 CPSP − 33.9 ± 12.6, $P = 0.035$	
		Other psychosocial predictor:		Student *t* test:	
		BDI	+	CPSP + 11.3 ± 8.1 CPSP − 6.4 ± 5.3, $P = 0.022$	
Lavernia et al[55]	1 WOMAC pain 2 SF-36 bodily pain:(0-100)	PASS: total score	Blacks 1 +	Correlation: Blacks: 1 $r = 0.382$, $P \leq 0.05$	Age, sex, stratification for blacks and whites
			2 0	2 $r = -0.280$, NS	
			Whites 1 0	Whites: 1 $r = 0.074$, NS	
			2 +	2 $r = -0.212$, $P \leq 0.01$	
Riddle et al[56]	WOMAC pain: 1 Improve < 50% 2 Minimal relevant change ≤ 4	TSK-11	1 0	Multivar. Log. regression:	Age, sex, race, BMI, education, marital status, Rheumatoid arthritis score, comorbidity, preoperative pain
			2 0	1 NS 2 F 3.19, OR (95% CI) 0.92 (0.85-1.01), NS	
		PCS: total score	1 +	Multivar. Log. regression:	
			2 +	1 F 5.47, OR (95% CI) 2.67 (1.2-6.1), $P = 0.02$ 2 F 8.29, OR (95% CI) 6.04 (1.75-20.81), $P = 0.005$	
				Multivar. Log. regression:	

(*continued*)

TABLE 2. (*continued*)

Study	Chronic PostSurgical Pain	Anxiety, Pain Catastrophizing Other Psychosocial Predictors	Effect	Statistics	Other Predictors
		Other psychosocial predictors:			
		a PHQ-8 depression	0	1a-e NS	
		PRIME-MD:		2a-e NS	
		b Generalized anxiety disorder subscale	0		
		c Panic disorder subscale	0		
		d ASES	0		
		e SF-36 mental health subscale	0		
Rosenberger et al[57]	WHYMPI: 1 Knee pain severity:(log-transformed) 2 Knee pain interference: (log-transformed)	Surgery Stress Scale	1 +	Multivar. Log. regression:	Age, sex, height, weight, BMI, **preoperative pain**, osteoarthritis
			2 0	1 F 5.26, standardized B 0.176, $P<0.05$ 2 NS Correlation: 1 $r=0.29$, $P<0.001$ 2 $r=0.15$, NS	
		Other psychosocial predictors:		Multivar. Log. regression:	
		a CES-D	0	1a NS	
		b LOT-Revised		2a NS	
			1 +	1b F 11.23, standardized B -0.210, $P<0.01$	
			2 0	2b NS	
Schade et al[58,59]	1 VAS pain relief:(0-100)	Psychological general well-being Index Anxiety subscale	1 0	Multivar. regression:	Age, sex, height, weight, BMI, marital status, preoperative recreational activities, preoperative pain, duration complaints, disability, sick leave, physical examination, tobacco use, extent of neural compromise/herniation/disc generation
			2 0	1, 2 NS	
	2 Surgical outcome score (pain relief, work, pain medication, limit activities): (poor, fair, good, excellent)	Other psychosocial predictors:		Multivar. regression:	
		PGWI:			
		a Depression subscale	1 0, 2 +	1a-e NS	
		b Self-control subscale	0	2a B -0.46, t -4.26, $P<0.001$	

(*continued*)

TABLE 2. (*continued*)

Study	Chronic PostSurgical Pain	Anxiety, Pain Catastrophizing Other Psychosocial Predictors	Effect	Statistics	Other Predictors
		c Well-being subscale	0	2b-e NS	
		d General health subscale	0		
		e Vitality subscale	0	1f, 2f NS	
		f Sum index occupational mental stress	0	1g B −0.39, t −2.42, $P<0.01$	
		g Social support	1+, 2 0	2g NS	
Singh et al[60]	MKHQ: moderate or severe pain	ICD-9 code anxiety	1 0 2 0	Multivar. Log. regression: 1 OR (95% CI) 0.5 (0.2-1.0), NS 2 OR (95% CI) 0.8 (0.3-1.9), NS	Age, sex, BMI, comorbidity, ASA, diagnosis, distance from medical center
	1 After 2 y	Other psychosocial predictor:	1 +	Multivar. Log. regression: 1 OR (95% CI) 1.6 (1.0-2.5), $P=0.04$	
	2 After 5 y	ICD-9 code depression	2 0	2 OR (95% CI) 1.7 (1.0-2.9), NS	
Sorensen et al[61]	Poor outcome (VAS ≥ 50, pain chart ≥ 2, poor health)	MMPI: panic-fear subscale	+	Student t test: t 2.5, $P=0.02$	Age, sex, marital status, education, preoperative pain, duration of complaints/current attack, work load, employment status, sick leave, social support, life events, myelographic findings, surgical findings, previous therapy, acute postoperative pain
		Other psychosocial predictors: MMPI:		Student t test:	
		a Hypochondria subscale	+	a t 2.7, $P=0.01$	
		b Depression subscale	+	b t 3.1, $P=0.005$	
		c Hysteria subscale	+	c t 3.3, $P=0.005$	
		d Psychopathia subscale	0	d t 1.3, NS	
		e Masculine subscale	0	e t 1.9, NS	
		f Feminine subscale	0	f t 1.6, NS	
		g Paranoia subscale	0	g t 1.4, NS	
		h Psychasthenia subscale	+	h t 2.2, $P=0.05$	
		i Schizophrenia subscale	0	i t 1.5, NS	
		j Hypomania subscale	0	j t 1.3, NS	
		k Socially introvert/extrovert subscale	0	k t 0.2, NS	

(*continued*)

TABLE 2. (*continued*)

Study	Chronic PostSurgical Pain	Anxiety, Pain Catastrophizing Other Psychosocial Predictors	Effect	Statistics	Other Predictors
		l Admission of symptoms subscale	+	l t 2.7, P = 0.01	
		m Alexithymia subscale	0	m t 0.6, NS	
Trief et al[62]	DPQ: Little or much better 1 Change back pain 2 Change leg pain	STAI: trait anxiety	1 0	ANOVA 1 CPSP+ 44.3 ± 10.4 CPSP− 40.3 ± 12.6 (mean ± SD), F 2.20, NS	Age, sex, race, marital status, education, employment status, duration of pain, previous therapy, legal action pending, receiving disability payments
			2 +	2 CPSP+ 46.0 ± SD CPSP− 40.3 ± 12.1, F 4.33, $P<0.05$	
		MSPQ: somatic anxiety	1 +	ANOVA 1 CPSP+ 10.4 ± 6.7 CPSP− 7.0 ± 4.7, F 7.28, $P<0.01$	
			2 0	2 CPSP+ 9.9 ± 5.2 CPSP− 7.8 ± 6.0, F 2.51, NS	
		Other psychosocial predictors:		ANOVA	
		a SDS	1 +	1a CPSP+ 28.4 ± 11.0 CPSP-− 23.5 ± 11.3, F 3.71, $P<0.05$	
			2 +	2a CPSP+ 30.2 ± 9.4 CPSP− 23.5 ± 11.8, F 6.64, $P<0.01$	
		b CMHS	1 0	1b CPSP+ 17.7 ± 7.1 CPSP− 16.0 ± 8.1 F 0.92, NS	
			2 0	2b CPSP+ 18.7 ± 6.9 CPSP− 15.8 ± 8.0, F 2.59, NS	

CPSP: if no cutoff values or criteria are mentioned, outcomes were analyzed as a continuous measure.

In case one of the predictors other than anxiety, pain catastrophizing, or remaining psychosocial predictors was the most significant or powerful predictor overall, it is printed in **bold**.

Effect: + significant positive association, 0 nonsignificant association. For multivariate analysis if applicable, on the basis of published data.

Chronic PostSurgical Pain: AAS indicates Activity Assessment Scale; BPI, Brief Pain Inventory; CPSP, Chronic PostSurgical Pain; CRPS, Complex Regional Pain Syndrome; DPQ, Dallas Pain Questionnaire; IASP, the International Association for the Study of Pain; MKHQ, Mayo Knee and Hip Questionnaire; MPQ, McGill Pain Questionnaire; NRS, Numerical Rating Scale; ODI, Oswestry Disability Index; SF-36, The Short-From 36 Health Survey; VAS, Visual Analogue Scale; VRS, Verbal Rating Scale; WOMAC, Western Ontario and McMaster Universities osteoarthritis index; WHYMPI, West-Haven Yale Multidimensional Pain Inventory.

Predictors: ASA indicates the American Society of Anesthesiologists physical status classification; ASES, Arthritis Self-Efficacy Scale; BDI, Beck Depression Inventory; BIS, Behavioral Inhibition Scale; BMI, Body Mass Index; CES-D, Center for Epidemiological Studies Depression Scale; CMHS, Cook-Medley Hostility Scale; COMT, catechol-*O*-methyltransferase; CPGQ, Chronic Pain Grading Questionnaire; CSQ, Coping Strategies Questionnaire; FACT-E, Functional Assessment of Cancer Treatment-Emotional Scale; FPQ, Fear of Pain Questionnaire; GSES, General Self-Efficacy Scale; HADS, Hospital Anxiety and Depression Scale; HDARS, Hamilton Depression and Anxiety Rating Scale; HWBQ-7, Habitual Well-Being Questionnaire; IBQ, Illness Behavior Questionnaire Disease conviction Scale; ICD-9, International Classification of Diseases, ninth revision; LOT, Life Orientation Test; MMPI, Minnesota Multiple Personality Inventory; MPSS, Mainz Pain Staging System; MSPQ, Modified Somatic Perception Questionnaire; NPS, Neuropathic Pain Scale; PASS, Pain and Anxiety Symptoms Scale; PCI, Pain-Coping Inventory; PCS, Pain Catastrophizing Scale; PGWI, Psychological general well-being Index; PHQ-8, Patient Health Questionnaire; PRIME-MD, Primary Care Evaluation of Mental Disorders; PSA, Prostate Specific Antigen; PSS, Perceived Stress Scale; RDQ, Roland Disability Questionnaire; SAS, Somatosensory Amplification Scale; SCL-8, Symptom Checklist; SDS, Zung Self-Rating Depression Scale; SF-12/36, The Short-From 12/36 Health Survey; STAI, State-Trait Anxiety Inventory; TMSI, Threatening Medical Situation Inventory; TSK, Tampa Scale of Kinesiophobia; VPMI, Vanderbilt Pain Management Inventory.

Statistics: CI indicates confidence interval; CPSP−, group without chronic postsurgical pain; CPSP+, group with chronic postsurgical pain; NS, nonsignificant; OR, odds ratio.

TABLE 3. Predictors: Statistical Significance Per Total Studies

References	Predictor	Significant Effect (Total Studies)
Anxiety general		
Aasvang and colleagues[35,37–40,50]	HADS (subscale anxiety)	3 (6)
Katz and colleagues[19,45,46,49,52,54,62]	STAI (trait)	3 (7)
Katz and colleagues[19,43,51,54]	STAI (state)	2 (4)
Singh and Lewallen[60]	ICD-9	0 (1)
Schade et al[58]	Psychological well-being (subscale anxiety)	0 (1)
Trief et al[62]	MSPQ (subscale anxiety)	1 (1)
Sorensen et al[61]	MMPI (panic-fear scale)	1 (1)
Hickey et al[40]	VAS (anxiety)	0 (1)
	Sub total	10 (22)
Anxiety pain related		
den Boer and colleagues[28,49,53,56]	TSK	0 (4)
Lavernia et al[55]	PASS (total)	1 (1)
Peters et al[1,42]	Surgical fear	1 (2)
Rosenberger et al[57]	Surgery stress scale	1 (1)
George et al[49]	Fear of pain questionnaire	0 (1)
	Sub total	3 (9)
Catastrophizing		
Peters and colleagues[1,35,42,48,49,56]	PCS	3 (6)
Brandsborg and colleagues[36,44,47,53]	CSQ	2 (4)
	Sub total	5 (10)
	Total	18 (41)

Any statistically significant effect (one or more times counts for one) of each predictor per study versus total number of studies using that predictor.
CSQ indicates Coping Strategies Questionnaire; HADS, Hospital Anxiety and Depression Scale; ICD-9, International Classification of Diseases, ninth revision; MMPI, Minnesota Multiple Personality Inventory; MSPQ, Modified Symptom Perception Questionnaire; PASS, Pain Anxiety Symptoms Scale; PCS, Pain Catastrophizing Scale; STAI, State-Trait Anxiety Inventory; TSK, Tampa Scale of Kinesiophobia; VAS, Visual Analog Scale.

catastrophizing play a more prominent role in nonrecovery from (often longstanding) pain than inciting new pain.

We also compared the predictive utility of instruments assessing different anxiety-related concepts. We categorized the anxiety measures into 3 main groups: general anxiety, pain-related anxiety, and (pain) catastrophizing. There did not seem to be an overall superior predictive value of 1 of the 3 groups. However, on the basis of our meta-analysis, catastrophizing was the most consistent predictor. Studies by George et al[49] and Riddle et al[56] reported that when anxiety and pain catastrophizing were entered into a regression model simultaneously, only pain catastrophizing was an independent predictor of CPSP. However, the opposite effect was found by Peters et al,[1] who reported that anxiety instead of pain catastrophizing remained a significant independent predictor after multivariate analysis. Although anxiety and pain catastrophizing are presumed to measure 2 separate constructs (ie, an affective reaction vs. beliefs about pain), they are considerably correlated. Therefore, when entering them simultaneously in one analysis, one may take precedence over the other because of shared explained variance.

TABLE 4. Predictors: Statistical Significance and Sample Size

Sample Size	Significant Studies (Total Studies)
$N \leq 100$	7 (16)
$N > 100$	9 (13)
Total	16 (29)

Studies reporting any statistically significant effect versus total number of studies per sample size.

One striking finding was the absence of the predictive utility of the TSK across studies. This instrument was developed to capture fear of movement in patients with chronic musculoskeletal pain and not specifically for surgical patients. Although the TSK was used in studies of knee, shoulder, and lumbar surgery, it was not independently predictive of CPSP. It may be proposed that fear of movement is more predictive of pain-related disability or activity-related outcomes than for pain per se. However, 3 of the 4 studies using the TSK also included a disability questionnaire, and only 1 study found that preoperative TSK scores were predictive of continued disability.[28]

Concerning the quality of evidence, several remarks can be made. First, the quality scores of the included articles were generally high, ranging from a total score of between 5 and 8 on a 0 to 8 scale. Study quality had no effect on the results. Second, in general, for predictors and outcome measures, validated or at least well-described measures were used. All studies used a prospective design. Third, the main bias in the review process was related to the heterogeneity in the measurement and reporting of predictors, outcome measures, and in statistical analyses, making comparison of results difficult. Therefore, the pooled results should be interpreted with caution. The postoperative follow-up interval also varied between studies but was at least 3 months for every included study. Fourth, the quality of evidence could have been improved, particularly if larger study samples were used, allowing correction for confounding by multivariate analysis. Fifth, there may have been an underreport of anxiety in some studies. For instance, in the study by Singh and Lewallen,[60] anxiety was based on an ICD-9 anxiety diagnosis extracted from the patient file. Moreover, 2 studies excluded patients if they

TABLE 5. Pooled Effect Sizes

(Sub-)Group	Maximum Effect Scenario: Pooled OR	95% CI	Test for Heterogeneity		Minimum Effect Scenario: Pooled OR	95% CI	Test for Heterogeneity	
General anxiety[35,38–40,60,61]	1.76	1.07-2.90	5.53 *df* 5	$P = 0.355$	1.56	0.76-3.24	11.13 *df* 5	$P = 0.049$
Anxiety pain related[1,42,53,56,57]	1.25	0.87-1.79	10.83 *df* 4	$P = 0.029$	1.11	0.82-1.50	8.19 *df* 4	$P = 0.085$
Catastrophizing [35,36,42,44,47,49,53,56]	2.37	1.32-4.28	20.94 *df* 7	$P = 0.004$	2.13	1.26-3.59	18.31 *df* 7	$P = 0.011$
Various types of surgery[1,35,36,38–40,42,44]	1.57	1.18-2.10	6.83 *df* 7	$P = 0.447$	1.57	1.13-2.16	8.06 *df* 7	$P = 0.328$
Musculoskeletal [47,49,53,56,57,60,61]	2.71	1.40-5.24	15.46 *df* 6	$P = 0.017$	1.51	0.82-2.80	28.16 *df* 6	$P < 0.001$
Total	2.10	1.49-2.95	25.37 *df* 14	$P = 0.031$	1.55	1.10-2.20	45.89 *df* 14	$P < 0.001$

Maximum effect scenario: highest OR per (sub-)group; minimum effect scenario: lowest OR per (sub-)group. Test for heterogeneity: χ^2.
95% CI indicates 95% confidence interval; OR, odds ratio.

were on current treatment with anxiolytic drugs.[45,46] Thus, a decreased prevalence of preoperative anxiety may have occurred in certain study populations, with a negative effect on the power to detect a relationship. Finally, none of the included studies incorporated an intervention aimed at reduction of preoperative anxiety or pain catastrophizing.

CONCLUSIONS

This updated systematic review and meta-analysis demonstrates that there is evidence that anxiety plays a role in the occurrence of chronic pain after surgery. Fifty-five percent of studies reported a positive association between preoperative anxiety or pain catastrophizing and CPSP and no studies reported a negative association. The meta-analysis on a subset of studies yielded pooled ORs in the range of 1.55 to 2.10 for the association between anxiety/catastrophizing and CPSP. The effect seemed to be somewhat more evident and consistent in musculoskeletal surgery, where 67% of the studies showed a significant positive association versus 36% in the remaining studies of other types of surgery. The results also suggest that the predictive value of pain catastrophizing is more consistent compared with general anxiety and pain-related fear. The TSK seems to be less appropriate for the prediction of chronic pain after surgery.

Implications for practice

It is premature to recommend widespread implementation of preoperative screening of anxiety as a predictor of CPSP. Further research is required to establish the most sensitive psychological predictors of CPSP. Then, interventions targeted toward reducing preoperative anxiety might be a next step in the prevention of CPSP.

Implications for research

There is an urgent need for larger prospective studies allowing more powerful multivariate analyses to establish which anxiety-related construct is the most important and which assessment instrument is the most suitable for predicting CPSP. Results should be clearly presented, including intercorrelation between used predictors, uniform outcome measures, and facilitating statistical pooling. A taskforce should be assembled to establish one or a strictly limited number of “standard” anxiety measures that preferably should be included in every study to facilitate future comparison of results.

APPENDIX

Checklist Quality of Observational Studies

	Checklist Quality of Observational Studies for Systematic Review	Yes	No	Unable to Determine
	Author (year)	(1)	(0)	(0)
1	Is the sample representative of patients in the population as a whole? (external validity)			
2	If any of the results were based on data dredging (retrospective), was this made clear? (internal validity/bias)			
3	Were the main predictors used accurate: reliable and valid? (internal validity/bias)			
4	Were the main outcome measures used accurate: reliable and valid? (internal validity/bias)			
5	Were the statistical tests used to assess the main outcomes appropriate? (internal validity/bias)			
6	Were the outcomes of people who withdrew described and included in the analysis? (internal validity/selection bias)			
7	Was there adequate adjustment for confounding in the analyses from which the main findings are drawn? (internal validity/confounding)			
8	Is the sample size > 100? (power)			
	Total score			

Checklist Quality of Studies for Systematic Review

	Criteria	Explanation (Based on Downs and Black[32])
1	Is the sample representative of patients in the population as a whole? (external validity)	The study must identify the source population for patients and describe how the patients were selected. Patients would be representative if they comprised the entire source population, an unselected sample of consecutive patients, or a random sample. Random sampling is only feasible where a list of all members of the relevant population exists.

(*continued*)

APPENDIX. (*continued*)

	Criteria	Explanation (Based on Downs and Black[32])
		Where a study does not report the proportion of the source population from which the patients are derived, the question should be answered as unable to determine.
2	If any of the results were based on data dredging (retrospective), was this made clear? (internal validity/bias)	Any analyses that had not been planned at the outset of the study should be clearly indicated. If no retrospective unplanned subgroup analyses were reported, then answer yes.
3	Were the main predictors used accurate: reliable and valid? (internal validity/bias)	For studies where the predictors are clearly described, the question should be answered yes. For studies which refer to other work or that demonstrates the predictors are accurate, the question should be answered as yes. For studies where validated instruments were used, the question should be answered yes. For studies using a self-developed instrument were the psychometric characteristics are clearly described, the question should be answered yes. In case of more predictors, the predictor used for the main analysis should be accurate.
4	Were the main outcome measures used accurate: reliable and valid? (internal validity/bias)	For studies where the outcome measures are clearly described, the question should be answered yes. For studies which refer to other work or that demonstrates the outcome measures are accurate, the question should be answered as yes. For studies were validated instruments were used, the question should be answered yes. For studies using a self-developed instrument were the characteristics of pain are clearly described, the question should be answered yes. In case of more outcomes, the outcome used for the main analysis should be accurate.
5	Were the statistical tests used to assess the main outcomes appropriate? (internal validity/bias)	The statistical techniques used must be appropriate to the data. For example nonparametric methods should be used for small sample sizes. Where little statistical analysis has been undertaken but where there is no evidence of bias, the question should be answered yes. If the distribution of the data (normal or not) is not described it must be assumed that the estimates used were appropriate and the question should be answered yes. N should be at least $\times 10$ the number of used predictors.
6	Were the outcomes of people who withdrew described and included in the analysis? (internal validity/selection bias)	If the numbers of patients lost to follow up are not reported, the question should be answered as unable to determine. If the proportion lost to follow up was too small to affect the main findings ($<30\%$), the question should be answered yes.
7	Was there adequate adjustment for confounding in the analyses from which the main findings are drawn? (internal validity/confounding)	In nonrandomized studies if the effect of the main confounders was not investigated or confounding was demonstrated but no adjustment was made in the final analyses the question should be answered as no.
8	Is the sample size >100 (power)	If the sample size is >100, the question should be answered yes.

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