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Toward Identifying Moderators of Associations Between Presurgery Emotional Distress and Postoperative Pain Outcomes: A Meta-Analysis of Longitudinal Studies

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Abstract: Presurgery emotional distress has had variable associations with outcomes of surgery in past narrative reviews. This meta-analysis was designed to evaluate the overall strengths of relations between presurgical emotional distress and key postsurgical pain outcomes (ie, pain intensity, analgesic use, functional impairment) and to identify moderators that might explain effect size heterogeneity between studies. PubMed, Web of Science, PsychINFO, Google Scholar, and Science Direct databases were searched to identify studies subjected to meta-analysis. Forty-seven studies of 6,207 patients met all 10 inclusion criteria. High presurgery emotional distress levels were associated with significantly more postsurgical pain, analgesic use, and impairment after surgery, with small to medium average effect sizes. Moderator analyses for relations between distress and pain intensity indicated effect sizes were larger in studies that assessed catastrophizing, anxiety, and/or depression than other types of emotional distress as well as those with lower rather than higher quality scores. Associations between presurgery distress and postoperative impairment were moderated by type of surgery. Heterogeneity in these relations was reduced or no longer significant after statistically controlling for moderators. Moderator analyses also supported the role of presurgery emotional distress as a risk factor for, rather than simply a correlate of, elevations in postoperative pain and disability.

Perspective:* *This meta-analysis indicates presurgery emotional distress has significant associations with postoperative outcomes but specific methodological factors and sample characteristics contribute to effect size variability in the literature. Considering emotional distress within presurgical assessment protocols may aid in identifying vulnerable patients who can benefit from interventions targeting distress reductions.

Key words: *Meta-analysis, postoperative pain, emotional distress, catastrophizing, pain intensity, functional impairment.*

Although pain is the most frequent complaint reported within 24 hours after surgery,[9] 10%–50% of surgery patients develop chronic postsurgical pain (CPSP) that persists for at least 2 months after surgery.[36,41] In light of such data, researchers have attempted to identify factors that increase risk for poorer postoperative functioning. Preoperative emotional distress is widely assumed to be a possible psychosocial vulnerability factor yet reviewers have drawn highly disparate conclusions about its effect. For example, Munafò and Stevenson[48] reported that preoperative anxiety reliably predicts acute postoperative

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pain. Another early review contended neither depression nor anxiety were preoperative predictors of CPSP[56] in contrast to Hinrichs-Rocker and colleagues[24] who asserted preoperative elevations in depression and stress predict increased risk for CPSP whereas the data are inconclusive for other types of emotional distress, including anxiety. Still other authors[27,36,42,78] have concluded elevations in preoperative anxiety, catastrophizing, and other forms of emotional distress predict higher rates of acute postoperative pain, analgesic use, and/or CPSP.

Together, past reviews suggest overall associations between presurgery emotional distress and postoperative outcomes are highly variable but clearly imply subtype(s) of emotional distress assessed and surgery to follow-up assessment intervals are potentially important moderators that contribute to discrepant effect sizes between individual studies and reviews. Type of surgery[24,78] and demographic characteristics such as sample age and sex composition[27] have also been discussed as key influences on variable strengths of relation between presurgery distress and postoperative outcomes within this literature. For example, an important review of retrospective and prospective research concluded that depressed or anxious patients are more susceptible to CPSP after undergoing complex rather than circumscribed surgeries.[24] Because of its potential implications, this contention should be followed-up on the basis of a larger number of effect sizes and studies that are strictly longitudinal.

Typically, past reviews were narrative or qualitative in nature and examined a broad array of influences aside from emotional distress. Hence, because explicit tests of possible moderators were undertaken only rarely, little is known about factors that account for comparatively strong or weak links between presurgery distress and postoperative outcomes. Meta-analysis, a variant of traditional narrative reviews that draws conclusions from analyses of specific effect sizes of relevant studies instead of expert judgments or general "vote-counting" analyses (eg, proportion of total studies having significant results), might clarify average strengths of relation between presurgery distress and postoperative functioning. Furthermore, meta-analysis can explicitly test moderators hypothesized to influence effect size heterogeneity between studies.

On the basis of this overview, a meta-analysis of longitudinal surgery studies was performed to determine overall associations between presurgery emotional distress and specific postoperative pain outcomes (ie, pain intensity, analgesic use, functional impairment) and identify factors that moderate these associations. We hypothesized presurgery emotional distress would have modest, significant positive average correlations with each outcome but also anticipated high levels of effect size heterogeneity, given the lack of consensus between past reviews. Hence, we also assessed the extent to which effect size differences between studies for each outcome were moderated by specific methodological influences (ie, type of emotional distress, surgery to follow-up assessment interval, and statistical control of presurgery responses on outcome measures within analyses) as well as type of surgery, sample age, and sex composition.

Literature Search Methods

Search Strategy

To identify relevant studies, PubMed, Web of Science, PsychINFO, Google Scholar, and Science Direct database searches were performed from August, 1995 to September, 2015. Search terms were "surgery" or "post-operative" or "post-surgical" and "pain" or "impairment" or "functioning" or "dysfunction" or "analgesic" or "medication," and "emotion" or "emotional" or "affect" or "affective" or "distress" or "depression" or "anxiety" or "fear" or "phobia" or "phobic" or "stress" or "catastrophizing" or "optimism" or "well-being" or "mental health." All searches used the broad search field, "anywhere" to identify citations. Reference lists of previous reviews of postoperative pain and articles identified from database searches were also reviewed to increase the pool of eligible studies.

Selection Criteria

Abstracts of all possibly eligible studies were independently screened by the first 2 authors (T.J., P.T.) to exclude articles in which the content was not germane. Subsequently, full-text versions of potentially relevant articles were retrieved and reviewed to determine if they met the following 10 selection criteria:

1. In contrast to the inclusion of cross-sectional and prospective evidence in some past reviews, this meta-analysis was restricted to longitudinal studies that included presurgery and postsurgery assessments. When more than 1 follow-up assessment was indicated, the longest follow-up interval with available effect size information was used in analyses.
2. A minimum sample n of 30 patients was required because results of very small prospective studies are often unreliable.[77]
3. Samples were comprised of adult human patients with mean ages of 18 years or older.
4. Within included studies, patients had undergone a discrete surgical intervention. Research involving dental procedures (eg, tooth extraction) or surgeries designed to provide ongoing pain relief (eg, implants providing deep brain stimulation) were excluded.
5. Included studies assessed at least 1 association between presurgery emotional distress and a salient postoperative outcome (ie, pain intensity, analgesic use, and/or functional impairment). Presumably, different types of emotional distress overlap with each other, yet there is utility in determining whether certain forms are more or less critical to postoperative outcomes. Therefore, emotional distress indices included narrowly defined measures of anxiety, fear, and depression, general indices of negative affect/psychological distress

that subsumed various aversive mood states (eg, anger, fear, anxiety, guilt), and general measures of low positive affect or reduced general well-being more typically characterized by sadness and lethargy.[84] Catastrophizing, which has been characterized as a facet of depression or anxiety,[71,78] as well as appraisal and/or coping,[28,81] was included because item content in associated measures reflects cognitive–affective facets of emotional distress (eg, helplessness, rumination/worry). Studies that evaluated other traits having conceptual or empirical associations with emotional status (eg, hardiness, resilience) and complex forms of emotional distress (ie, post-traumatic stress disorder) were excluded.

6. Included studies treated emotional distress measure(s) as predictors rather than dependent/outcome measures.
7. Regarding pain intensity as an outcome, only studies that used continuous subjective intensity measures or continuous measures recoded into groups (eg, median splits) were included for analyses. Conversely, research using less sensitive, dichotomously-coded (0 vs 1) categorical indices such as "presence of pain" (no or yes) or "presence of moderate to severe pain" (no or yes) was excluded because variable pain experiences (eg, "no pain" and "mild pain" or "moderate" and "severe" pain) were poorly differentiated and could receive identical ratings. For impairment as an outcome, studies that evaluated self-reported disability or interference in the domains of physical, work, household, social/recreational, and/or self-care were considered for evaluation. Finally, studies that assessed patient-controlled or staff-administered opioid use for pain (eg, morphine, tramadol, meperidine, fentanyl) within the first week after surgery were included to evaluate post-operative analgesic consumption. Studies examining self-report ratings of post-surgery analgesic use, relief or satisfaction with analgesics were excluded from analyses.
8. Evaluation of and evidence for the reliability and validity of all emotional distress and outcome measures was either documented or available. Studies based on author-created measures that had not undergone psychometric evaluations were excluded.
9. Only articles from peer-reviewed, English-language journals were retained. Reviews and studies that reported results on the basis of secondary analyses of data in other articles were excluded.
10. After other published meta-analyses,[17,29] articles were included when sufficient data for effect size calculation were presented in a transparent way within the published article. Authors of potentially relevant papers published within the most recent 3 years were also contacted for effect size information. The decision to limit additional time and resources needed for data requests to 3 years followed from our own recent experience with meta-analysis, past evidence that positive responses to raw data requests decrease by 17% for each year that passes after publication,[82] and poor response rates found, even within 1 year after publication.[86]

T.J. and P.T. reviewed papers for inclusion in the meta-analysis. Disagreements were resolved through discussion and consensus.

Search Results

Figure 1 indicates that 7,604 potentially relevant studies were found. After removing duplicates and articles that failed to meet all 10 inclusion criteria, 47 longitudinal surgery studies comprising 6,207 patients were retained for analyses. The rate of inter-rater agreement for study inclusion within the meta-analysis was $\kappa = .84$.

Coding Study Characteristics

For each included study, data were extracted for first author last name, publication year, country of data collection, mean sample age, sex composition, type(s) of surgery, and time from surgery to follow-up assessment. As well, the first 2 authors (T.J. and P.T.) independently reviewed presurgery emotional status measures used and coded them within the categories of anxiety, fear, catastrophizing, depression, and general negative affect/emotional distress. Measures of positive affect/well-being were also included but directions of their associations with outcomes were reversed when necessary to reflect relations of low rather than high well-being levels with postoperative functioning. Outcome measures were also reviewed by T.J. and P.T. and were classified within 1 of 3 broader categories (ie, pain intensity, analgesic use, functional impairment) described previously. Inter-rater agreement rates were 100% from the classification of emotional distress and outcome measures.

Quality Assessments

T.J. and P.T. independently assessed the quality of included studies on the basis of criteria used in other recent pain meta-analyses[13,28]: 1) representative sampling (ie, random sample or unselected sample of consecutive patients), 2) inclusion of emotional distress measures with published reliability/validity support, 3) inclusion of outcome measures with published reliability/validity support, 4) sufficient statistical power (ie, sample N's at least 10 times the number of predictors), 5) description of missing data (eg, outcomes of people who withdrew early), 6) adjustment for confounding influences (ie, statistical control of baseline responses on outcome measures in analyses), 7) sample size larger than 100, and 8) adequate report of sample demographic characteristics (ie, age, sex, and at least 1 socioeconomic status measure of education, type of employment/job category, and/or income) to facilitate external validity evaluation. Studies were rated as not

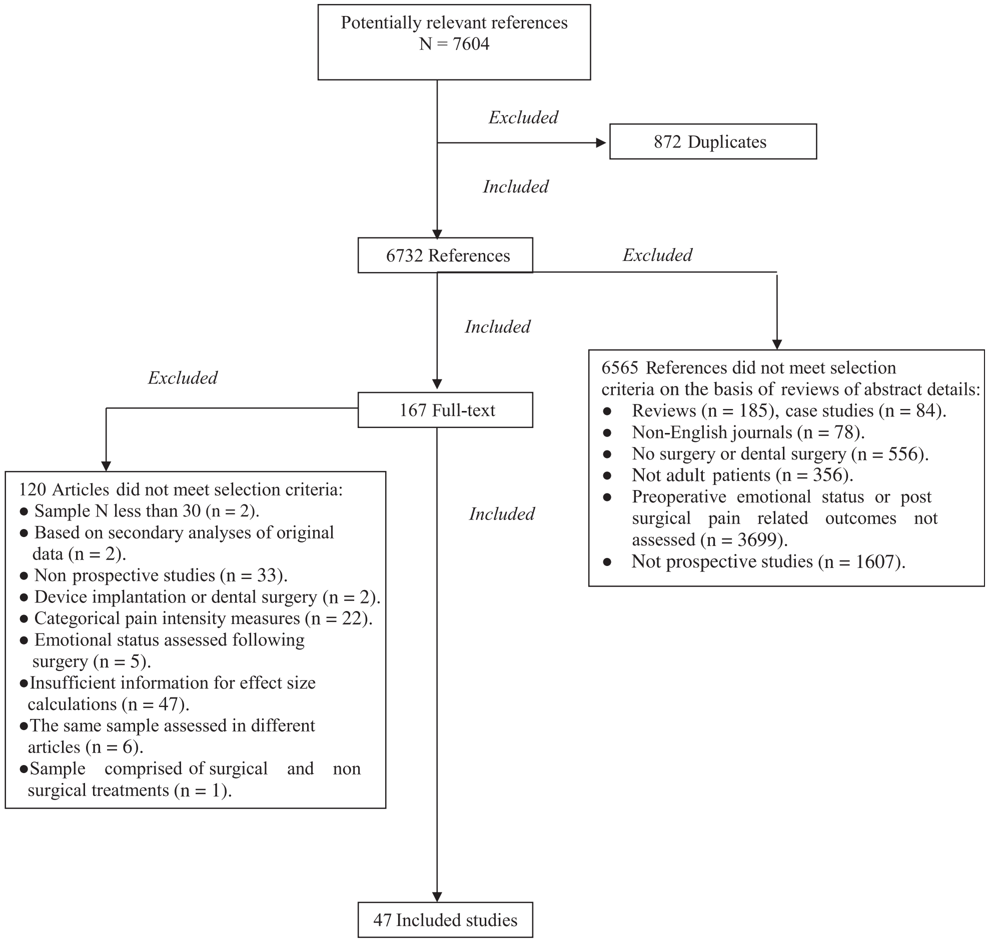

Figure 1. Outline of study selection process.

adequate (0), adequate (1), or (?) unclear on each criterion. The inter-rater agreement level on quality ratings was acceptable at κ = .80. After reaching a consensus on each rating, total quality score for each study was calculated by summing ratings on these criteria.

Characteristics of Studies Included in the Meta-Analysis

Characteristics of included studies are summarized in Table 1. Reflecting emotional status as a salient focus within the current literature on predictors of postoperative functioning, 57.4% of included articles had been published between 2010 and 2015. On average, samples included 154 patients (range of N = 34–916), were middle-aged (mean = 52.93 years, SD 13.36, range = 18.5–70.9 years), and had proportionately more women (mean = 63.37%, SD 32.89%, range = 0–100%) than men. The most common interventions were spine/lumbar surgery (n = 8), knee arthroplasty (n = 8), breast cancer (n = 7), and chest malformation correction (n = 3) whereas 16 other procedures were documented in the remaining studies.

Twenty-seven studies included measures of anxiety or fear, 18 studies assessed depression, 19 evaluated catastrophizing, 18 assessed general distress or negative affect, and 8 included measures of general positive affect/well-being. Regarding outcome measures, post-operative pain intensity was assessed in more samples (n = 40) than either analgesic use (n = 11) or impairment (n = 12). Post-operative pain intensity was assessed an average of 103.49 days after surgery (SD 176.80). In 24 studies that evaluated acute postoperative pain, pain intensity was examined an average of 5.62 days after surgery (SD 7.57, range = 1–30 days). In 18 studies of CPSP, including 2 that had also examined acute postoperative pain, pain intensity was evaluated an average of 247.41 days after surgery (SD 207.46, range = 61–910). For studies of postoperative analgesic use, assessments continued for an average of 2.48 days after surgery (SD 2.11, range = 1–7). Studies of postoperative impairment evaluated this outcome an average of 378.17 days after surgery (SD 284.17). Only 1 impairment effect size was reported within the first 60 days after surgery (12 days) whereas the average effect size for those assessed at least 2 months after surgery was 411.45 days (SD 272.40, range = 61–930).

Finally, included studies had average quality scores of 5.40 (SD 1.56, range = 2–8). Final quality ratings for each included study are presented in Supplemental Table 1.

Table 1. Overview of Studies Included in Meta-Analysis on Associations Between Emotional Distress and Postoperative Outcomes

							Outcome Measure		
Reference	Country	Sample	Mean Age, Y	Surgery Type	Postsurgery Assessment*	Distress Index	Pain Intensity Measure	Impairment Measure	AC
Aasvang et al[1]	Denmark, Germany	442 M	55.2	IH	180	HADS(A), HADS(D)‡, PCS	—	AAS	—
Abbott et al[2]	Sweden	66 F, 41 M	50.6	LUM	910	CSQ(C), TSK, SF-36(MH)	VAS	ODI	—
Archer et al[4]	US	82 F, 59 M	59.1	Spine	90	PHQ-9, TSK	BPI(P)	BPI(I), ODI	—
Brander et al[6]	US	64 F, 52 M	66	KA	365	BDI, PSS, STAI(tot)	VAS	—	—
Bruce et al[7]	Scotland	293 F	59.1	BC	270	STAI, HADS, PCS, PANAS (P, N), LOT	BPI	—	—
Cohen et al[11]	Canada	71 F	45	ABDM	1.5, 28	MHI, PSS	MPQ(PRI-T)	—	Y
De Cosmo et al[15]	Italy	49 F, 31 M	45.3	CC	1	SAS, SRQ-D	VAS	—	Y
de Groot et al[16]	The Netherlands	58 F, 68 M	44	LUM	90	STAI(tot)	VAS	—	—
Ene et al[19]	Sweden	140 M	63.1	RP	90	HADS(A), HADS(D)	VAS	—	—
Granot and Ferber[20]	Israel	19 F, 19 M	52	VAR	1.5	PCS, STAI(S), STAI(T)	VAS	—	Y
Graver et al[21]	Norway	56 F, 66 M	40.8	LUM	365	HADS(A), HADS(D)	VAS	OLBDQ	—
Grosen et al[22]	Denmark	42 M	19	CCM	3.5, 180	BDI, STAI(tot)	NRS	—	Y
Johansson et al[30]	Sweden	24 F, 35 M	19	CCM	365	TSK	—	EQ-5D	—
Kain et al[31]	US	53 F	42.5	HYST	7	PSS, STAI(S), STAI(T)	VAS	—	—
Katz et al[34]	US	117 F, 82 M	68.6	Spine	730	RHIS-D	—	WC	—
Katz et al[32]	US	86 F	58.2	BC	30	BDI, HDARS (A, D), STAI(tot), FACT-E	NRS	—	—
Kaunisto et al[35]†	Finland	916 F	57	BC	1	STAI(T)	NRS	—	Y
Khan et al[37]	UK	10 F, 54 M	65.7	CARD	2	HADS(A), HADS(D)	VRS	—	—
Kremer et al[38]	Israel	17 F, 31 M	61.9	THOR	5	PCS	NPS	—	—
Lautenbacher et al[39]	Germany	54 M	18.5	CCM	7	STAI(tot), PCS, CES-D	NRS	—	Y
Lunn et al[40]	Denmark	50 F, 47 M	66	KA	1	PCS	VAS	—	—
Masselin-Dubois et al[43]	France	58 F, 31 M	69	KA	90	BDI, PCS, STAI(S), STAI(T)	BPI(P)	—	—
Meretoja et al[44]†	Finland	860 F	57.3	BC	365	STAI(S), STAI(T), BDI	NRS	—	—
Montgomery et al[46]	US	101 F	49.4	BC	7	SV-POMS(TA)	BPI(P)	—	—
Miaskowski et al[45]	US	398 F	54.9	BC	180	STAI(S), STAI(T), CES-D	NRS	—	—
Noiseux et al[50]	US	125 F, 90 M	61.7	KA	180	STAI	NRS	—	—
Özalp et al[52]	Turkey	99 F	43	BC	1	STAI(tot), BDI	NRS	—	Y
Pan et al[53]	US	34 F	—	CD	1	STAI(tot)	VAS	—	Y
Papaioannou et al[54]	Greece	36 F, 25 M	50.5	LUM	2	HADS(A), HADS(D), PCS	VRS	—	Y
Pavlin et al[55]	Canada	21 F, 27 M	31	ACL	7	PCS	VAS	—	—
Peters et al[57]	Netherlands	216 F, 185 M	54	VAR	365	SFQ (LT), PCS	—	SF-36(Ph)	—
Petrovic et al[58]	Serbia	42 F, 48 M	66.7	HA	2	HADRS (A,D)	NRS	—	—
Pinto et al[59]†	Portugal	195 F	51	HYST	2	CSQ(C), HADS(D)	BPI(SF)	—	—
Pinto et al[61]†	Portugal	186 F	51	HYST	120	HADS(A), SFQ	BPI(SF)	—	—
Pinto et al[60]	Portugal	83 F, 41 M	65.2	HA, KA	2	HADS(A), HADS(D), LOT-R, CSQ(C)	BPI(P), BPI(SF)	—	—
Pinto et al[62]	Portugal	179 F,73 M	—	HYST,MJA	2	HADS(A), HADS(D), CSQ(C), LOT-R	NRS	—	—
Powell et al[63]	UK	115 M	61.5	IH	120	LOT	MPQ(WPI)	—	—
Raichle et al[64]	US	21 F, 48 M	43.9	AMPT	5	NVAA	NRS	—	Y
Rosenberger et al[65]	US	79 F, 101 M	48.2	AKS	365	CES-D, LOT-R, SSS	MPI(P)	MPI(I)	—

Table 1. Continued

							Outcome Measure		
Reference	Country	Sample	Mean Age, Y	Surgery Type	Postsurgery Assessment*	Distress Index	Pain Intensity Measure	Impairment Measure	AC
Roth et al[66]	Canada	28 F, 32 M	70.9	KA	2	SPOMS, PCS	MPQ(SF)	—	—
Rudin et al[67]	Sweden	59 F	—	LTL	5	STAI(S), STAI(T), HADS(A), HADS(D)	VAS	—	—
Seebach et al[68]	US	82 F, 59 M	59.1	Spine	61	PHQ-9, PANAS (P, N)	BPI(P)	ODI, SF-12(Ph)	—
Sinikallio et al[69]	Finland	57 F, 42 M	61.7	Spine	730	BDI	—	ODI	—
Strulov et al[70]	Israel	45 F	32.8	CD	2	PCS	VAS	—	Y
Sullivan et al[72]	Canada	73 F, 47 M	67	KA	365	PCS, PHQ-9, TSK	WOMAC(P)	WOMAC(F)	—
Vranceanu et al[83]	US	69 F, 51 M	61	Hand	12	PASS, PCS, PHQ-9	NRS	DASH	—
Weissman-Fogel et al[85]	Israel	35 F, 49 M	61.6	THOR	5	PCS	NPS	—	—

Abbreviations: AC, assessment of postoperative opioid analgesic consumption; F, females; M, males.

Surgery type abbreviations: AMPT, amputation; ABDM, abdominal; ACDF, anterior cervical decompression/fusion; ACL, anterior cruciate ligament; AKS, arthroscopic knee surgery; BC, breast cancer; CARD, cardiac; CC, cholecystectomy; CCM, chest malformation correction; CD, Cesarean delivery; HA, hip arthroplasty; HYST, hysterectomy; IH, inguinal herniotomy; KA, knee arthroplasty; LTLP, laparoscopic tubal ligation; LUM, lumbar surgery; MJA, major joint arthroplasty; RP, radical prostatectomy; THOR, thoracotomy; VAR, various surgical procedures.

Emotional distress measure abbreviations: Anxiety: HADS(A), Hospital Anxiety Depression Scale(Anxiety); HDARS, Hamilton Depression and Anxiety Rating Scales; NVAA, Numerical Visual Analog of Anxiety; PASS, Pain Anxiety Sensitivity Scale; SAS, Self-Rating Anxiety Scale; STAI(tot, S, T), State-Trait Anxiety Inventory(total, State, Trait).

Fear: SFQ (LT), Surgical Fear Questionnaire (Long-Term Fear); TSK, Tampa Scale of Kinesiophobia.

Catastrophizing: CSQ(C), Coping Strategies Questionnaire(Catastrophizing); PCS, Pain Catastrophizing Scale.

Depression: BDI, Beck Depression Inventory; CES-D, Center for Epidemiological Studies Depression Scale; HADS(D), Hospital Anxiety Depression Scale(Depression); HDARS, Hamilton Depression and Anxiety Rating Scales; RHIS-D, Rand Health Insurance Study - Depression; SRQ-D, Self-Rating Questionnaire for Depression.

Positive affect/well-being: LOT-R, Life Orientation Test-Revised; MHI, Mental Health Inventory; PANAS, Positive and Negative Affect Schedule-Positive Affect; PHQ-9, 9-Item Patient Health Questionnaire; SF-36(MH), Med Outcomes Study Short-Form General Health Survey (Mental Health).

Negative affect/general distress: DRAM, Distress Risk Assessment Method; PANAS, Positive and Negative Affect Schedule-Negative Affect; SV-POMS(TA), Profile of Mood States (Tension-Anxiety); PSS, Perceived Stress Scale; SSS, Surgery Stress Scale; FACT-E, Functional Assessment of Cancer Treatment-Emotional Scale; SPOMS, Shortened Version of Profile of Mood States.

Pain intensity measure abbreviations: BPI(P,SF), Brief Pain Inventory(Pain, Short Form); MPI(P), West Haven-Yale Multidimensional Pain Inventory (Pain); MPQ(PRI-T,WPI,SF), McGill Pain Questionnaire (Pain Rating Index, Worst Pain Intensity, Short Form); NPS, Numerical Pain Scale; NRS, Numerical Rating Scale; VAS, Visual Analogue Scale; VRS, Verbal Rating Scale; WOMAC(P), Western Ontario and McMaster University Osteoarthritis Index (Pain).

Impairment measure abbreviations: AAS, Activity Assessment Scale; BPI(I), Brief Pain Inventory (Interference); DASH, Disability of Arm, Shoulder, Hand Questionnaire; EQ-5D, Eur Quality of Life Questionnaire-5 Dimensions; MPI(I), West Haven-Yale Multidimensional Pain Inventory (Interference); NDI, Neck Disability Index; ODI, Oswestry Disability Index; OLBDQ, Oswestry Low Back Disability Questionnaire; SF-12(Ph), 12-Item Short-Form Health Survey (Physical Functioning); SF-36(Ph), Med Outcomes Study Short-Form General Health Survey (Physical functioning); WC, self-reported walking capacity; WOMAC(F), Western Ontario and McMaster University Osteoarthritis Index (Function).

*Days from surgery completion to follow-up assessment.

†Articles from 1) Pinto et al[59,61] and 2) Kaunisto et al[35] and Meretoja et al[44] used the same sample but assessed different emotional distress measures or outcome measures at different follow-up intervals. Effect size information from each article was retained but overlapping sample n's were counted only once in calculating the total sample size for the meta-analysis.

‡Meta-analysis (Cosco et al[12], Norton et al[51]) of HADS factor structures have concluded the scale best reflects general distress rather than distinct anxiety and depression dimensions. Effect sizes on the basis of HADS subscales have been treated as general distress measures in this meta-analysis. However, overall effect sizes for anxiety, depression, and general distress changed only modestly if HADS(A) and HADS(D) subscale scores were included in the calculation of mean anxiety and depression effect sizes rather than mean general distress effect sizes.

Effect Size Computations

Comprehensive Meta-Analysis version 2.0[5] was used for analyses. Wherever possible, measures of univariate statistics such as correlation coefficients and analysis of variance were selected to represent individual effect sizes. Studies that reported effect sizes only on the basis of partial correlations or coefficients within multivariate regression models were also retained. However, such effect sizes may be attenuated (eg, because of overlaps with other predictors) or, less typically, magnified (eg, as a result of error variance suppression) compared with those obtained from univariate analyses. Therefore, average effect sizes for each outcome were also calculated after excluding results on the basis of partial correlation/multiple regression analyses and presented in the text. When assessing relations between multiple emotional distress measures and an outcome or associations of 1 distress index with more than 1 measure of the same outcome within a single study, effect sizes for each association were calculated individually and then averaged to provide 1 overall effect size for that study following other meta-analyses.[28,47] Each effect size was weighted by the inverse of the study's variance. The Cochran Q test was used to evaluate heterogeneity in the effect size distribution for each outcome. Overall effect sizes were on the basis of bivariate correlation coefficients and calculated using random effects models as recommended by Hoffman et al.[25] Following Cohen,[10] correlation coefficient effect sizes of r = .10, r = .30, and r = .50 were interpreted as small, medium, and large, respectively.

Moderator Analyses

I^2 values represented total heterogeneity. I^2 values of 25%, 50%, and 75% were low, moderate, and high, respectively.[23] When Q values (ie, weighted square deviations) reflected significant differences between included individual effect sizes, moderator analyses were conducted to identify possible sources of variability. Moderating effects of sample age, sex (ie, percentage of women in each sample), and overall study quality score were assessed using the method of moments procedure, an approach appropriate for the evaluation of continuous moderators.[79] A method of moments analysis also evaluated the moderating effect of total days between surgery and follow-up on relations between presurgery distress and analgesic use during the first week after surgery.

Subgroup analyses were used to assess effects of categorical moderators including 1) type of emotional distress (ie, anxiety, fear, catastrophizing, depression, general negative affect/distress, low general positive affect/well-being), 2) type of surgery (head/neck, back, thoracic, abdominal, extremity, or "other" drawn from studies that included multiple surgery sites) using a simplified grouping of anatomical sites on the basis of Peters et al,[57] and 3) surgery to follow-up assessment interval (for pain intensity and impairment only) based on Macrae's[41] definition of CPSP duration (ie, <2 months vs ≥2 months). For analgesic use, patient- versus staff-controlled analgesia was assessed. Finally, moderating effects of analysis approach was examined in assessing relations of presurgery distress with postoperative pain intensity and impairment (ie, no control vs control of presurgery responses on outcome measures); these analyses clarified the status of presurgery distress as a correlate and risk factor for poorer postoperative functioning. Q_{within} and $Q_{residual}$ were reported as indicators of heterogeneity remaining after controlling for effects of moderators in subgroup and method of moments analyses, respectively.

Evaluation of Publication Bias

The trim and fill method[18] was used to assess possible publication bias by inspecting effect size funnel plots for asymmetrical distributions around average effect sizes. Typically, larger samples (top of an effect size plot) provide more accurate effect size estimates; the spread should increase symmetrically with smaller samples toward the bottom of a plot. Hence, when there is no evidence of publication bias, plots resemble an inverted funnel. Bias against the publication of studies having nonsignificant effects is suggested by funnel plots that include fewer effects sizes on the left than the right side of the mean effect size for a given outcome. This method provides estimates of the nature and number of studies missing from an entire effect size distribution.

Results

Overall Relations Between Presurgery Emotional Distress and Postsurgical Outcomes

Overall effect sizes for relations between presurgery emotional distress and postsurgical outcomes were small to medium and highly significant (Table 2). Specifically, patients who reported elevations in presurgery distress were more likely than less distressed cohorts to experience elevations in pain, analgesic use, and functional impairment after surgery. Omitting studies with effect sizes represented by odds ratio, standard regression, or partial correlation coefficients, overall effect sizes were slightly higher in 34 studies (N = 4,099) of distress–pain intensity relations (r = .27, $P < .001$, 95% confidence interval [CI] = .21–.32), 10 studies (N = 629) of distress–analgesic use relations (r = .29, $P < .001$, 95% CI = .13–.44), and 8 studies (N = 1,349) of distress–impairment relations (r = .19, $P < .001$, 95% CI = .14–.24). Table 2 also indicates heterogeneity levels were high across analyses of overall effect sizes.

As an alternate frame of reference for evaluating strengths of distress–outcome relations, average effect sizes were also calculated for study subsets that had assessed relations of presurgery pain intensity with each outcome. On average, associations of preoperative pain intensity with postoperative pain intensity (N = 20, r = .23, $P < .001$, 95% CI = .16–.30) and impairment (N = 7, r = .14, $P > .05$, 95% CI = .00–.30) were similar to

Table 2. Overall Effect Sizes and Heterogeneity Tests for Associations Between Presurgery Emotional Distress and Postsurgical Outcomes

			95% CI		Heterogeneity		
Outcome	Total Samples	Effect Size, Point Estimate	Lower Limit	Upper Limit	Q	Degrees of Freedom	I^2
Pain intensity	40	.25*	.20	.29	322.04*	39	87.89%
Analgesic use	11	.26†	.10	.41	125.30*	10	92.02%
Functional impairment	12	.15*	.09	.20	59.14*	11	81.40%

*$P < .001$.
†$P < .01$.

those observed for preoperative emotional distress in Table 2. The average effect size for presurgery pain intensity and postoperative analgesic use was noticeably weaker than that found for presurgery distress but was based on only 2 effect sizes (r = .15, $P > .05$, 95% CI = −.15 to .41).

Moderators of Associations Between Presurgery Emotional Distress and Postoperative Pain Intensity

Overall distress–pain relations were not moderated by sample age (slope = −.00094, $P = .680$) or sex composition (slope = −.00040, $P = .621$). However, the moderator analysis for study quality (slope = −.04841, $P < .001$) indicated effect sizes were larger for studies having lower rather than higher quality scores. Effect size heterogeneity was no longer significant after controlling for study quality ($Q_{residual} = 42.39$, $P = .287$).

Subgroup analyses of hypothesized categorical moderators (Table 3) identified emotional distress subtype as a significant moderator; effect sizes were noticeably larger and highly significant for studies that assessed catastrophizing, and to a lesser extent, anxiety and depression before surgery although effect sizes were weak and not significant for presurgery fear indices. Heterogeneity was reduced but highly significant after controlling for distress subtype ($Q_{within} = 285.57$, $P < .001$). Surgery to follow-up interval did not moderate relations of presurgery distress with postoperative pain intensity; significant average effect sizes were observed whether pain intensity was assessed less or more than 2 months after surgery. For analysis approach, the average effect size for studies that did not statistically control for presurgery pain intensity was substantially larger than that of studies that controlled for presurgery pain intensity. However, the latter effect size was also significant. Heterogeneity was modestly reduced but significant after

Table 3. Effects of Categorical Moderators on Associations Between Emotional Distress and Pain Intensity

				95% CI		Heterogeneity	
Moderator	Moderator Subgroups	Total Effects	Effect Size, Point Estimate	Lower Limit	Upper Limit	Q-Between	Degrees of Freedom
Emotional distress subtype‡	Anxiety	19	.27*	.21	.33	30.65*	5
	Fear	4	.06	−.03	.15		
	Catastrophizing	17	.37*	.28	.45		
	Depression	16	.27*	.20	.34		
	Low well-being/positive affect	8	.15†	.03	.26		
	General distress/negative affect	16	.19†	.14	.25		
Type of surgery	Abdominal	10	.30*	.16	.43	7.86	4
	Back	7	.21†	.07	.34		
	Thorax	11	.26*	.20	.29		
	Extremity	11	.26*	.19	.32		
	Other	1	.17*	.11	.23		
Follow-up assessment§	<2 Months after surgery	24	.25*	.17	.31	.60	1
	≥2 Months after surgery	18	.20*	.11	.29		
Longitudinal analysis§	Baseline pain controlled	13	.10*	.06	.14	17.90*	1
	Baseline pain uncontrolled	29	.27*	.20	.34		

*$P < .001$.
†$P < .01$.
‡Total effect sizes for emotional distress subtype exceed the total studies because multiple distress and/or outcome measures were used in some studies. These were averaged for each emotional distress subtype within each study.
§Total effect sizes for follow-up assessment and longitudinal analysis exceed the total number studies because of multiple time point assessments in Pinto et al[55,61] and Kaunisto et al[35]/Meretoja et al[44]. Each time point was treated independently in subgroup analysis.

Table 4. Categorical Moderators of Associations Between Emotional Distress and Analgesic Use

			95% CI			Heterogeneity	
Moderator	Moderator Subgroups	Total Effects§	Point Estimate	Lower Limit	Upper Limit	Q-Between	Degrees of Freedom
Emotional Distress	Anxiety	9	.23*	.01	.43	1.13	4
	Catastrophizing	4	.31*	.03	.54		
	Depression	5	.30*	.02	.55		
	Low well-being/positive affect	1	.20*	.14	.48		
	General distress/negative affect	1	.32*	.01	.38		
Type of Surgery	Abdominal	5	.36†	.17	.52	1.91	3
	Back	1	.21‡	.06	.34		
	Thorax	4	.17	−.16	.47		
	Extremity	1	.25*	.01	.46		
Analgesic Administration	Patient-controlled	8	.30‡	.10	.47	2.36	2
	Staff-administered	3	.16	−.17	.45		

*$P < .05$.
†$P < .001$.
‡$P < .01$.
§Total effect sizes for emotional distress subtype exceed the total studies because multiple distress and/or outcome measures were used in some studies. These were averaged for each emotional distress subtype within each study.

controlling for analysis approach (Q_{within} = 302.31, $P < .001$). Distress–intensity effect sizes were not moderated by type of surgery (Table 3).

Moderators of Associations Between Presurgery Emotional Distress and Postoperative Analgesic Use

For continuous moderators of relations between presurgery distress and analgesic use within the first week after surgery, nonsignificant effects were found for age (slope = .00820, P = .309), sex composition (slope = .00210, P = .397), follow-up interval (slope = −.06247, P = .196), and study quality (slope = −.04847, P = .564). Furthermore, distress–analgesic use relations were not moderated by emotional distress subtype although medium average effect sizes emerged for catastrophizing, depression, and negative affect/general distress (Table 4). Surgery type was not a moderator on the basis of the small number of included effects although the mean effect size for abdominal surgery was noticeably higher than effect sizes for back or thoracic surgery. Finally, analgesic administration (patient- vs staff-controlled) did not moderate relations of presurgery distress with postoperative analgesic use. However, the average effect size for studies on the basis of patient-

Table 5. Categorical Moderators of Associations Between Emotional Distress and Functional Impairment

			95% CI			Heterogeneity	
Moderator	Moderator Subgroups	Total Effects	Point Estimate	Lower Limit	Upper Limit	Q-Between	Degrees of Freedom
Emotional distress subtype§	Anxiety	1	.15*	−.03	.32	8.80	5
	Fear	5	.13†	.03	.22		
	Catastrophizing	4	.24‡	.15	.33		
	Depression	7	.17‡	.05	.29		
	Low well-being/positive affect	3	.05	−.04	.15		
	General distress/negative affect	4	.11*	.03	.20		
Type of surgery	Back	6	.08†	.02	.14	7.35†	2
	Extremity	2	.21‡	.19	.31		
	Other	4	.20‡	.12	.27		
Follow-up	<2 Months after surgery	1	.26*	.08	.43	1.78	1
Assessment	≥2 Months after surgery	11	.13‡	.08	.19		
Longitudinal analysis	Baseline pain controlled	6	.12*	.03	.20	.78	1
	Baseline pain uncontrolled	6	.16‡	.12	.20		

*$P < .01$.
†$P < .05$.
‡$P < .001$.
§Total effect sizes for emotional distress subtype exceed the total studies because multiple distress and/or outcome measures were used in some studies. These were averaged for each emotional distress subtype within each study.

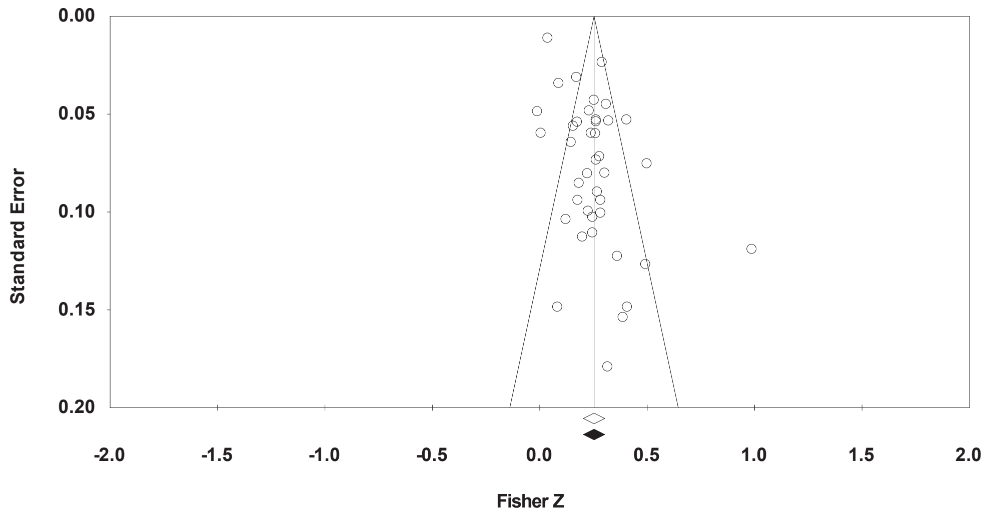

Figure 2. Funnel plot of emotional distress and pain intensity association.

controlled analgesic use (r = .30) was substantially stronger than the effect size for staff-administered analgesics (Table 4).

Moderators of Associations Between Presurgery Emotional Distress and Postoperative Impairment

Distress–impairment effect sizes were not affected by sample age (slope = −.00032, P = .936), sex composition (slope = −.00037, P = .837), or study quality (slope = −.05314, P = .127). Regarding categorical moderators (Table 5), distress subtype did not have a significant effect on distress–impairment associations; effect sizes were strongest when catastrophizing was assessed and weakest when low general positive affect/well-being was examined. For surgery type, the mean distress–impairment effect size was significantly smaller for back surgery samples than other surgery subgroups. Controlling for surgery type reduced heterogeneity substantially, although the effect remained significant (Q_{within} = 23.72, P < .005). Neither surgery to follow-up interval nor longitudinal analysis approach moderated distress–impairment effect sizes. However, for the latter, significant effect sizes were evident both for "uncontrolled" studies and those that statistically controlled for presurgery impairment. Hence, elevations in presurgery distress predicted more impairment after surgery, independent of initial impairment levels.

Effects of Publication Bias

Trim and fill analyses indicated the spread of effect sizes for studies of distress–pain intensity relations was approximately symmetrical around the obtained mean; no studies were estimated to be missing from the distribution (Figure 2). Conversely, 1 study with a larger than average effect size was estimated to be missing from the distribution of effect sizes for distress and analgesic use (Figure 3). Its inclusion would result in an average effect size increase from .26 (95% CI = .10–.41) to .29 (95% CI = .13–.43). Furthermore, 2 studies with smaller than

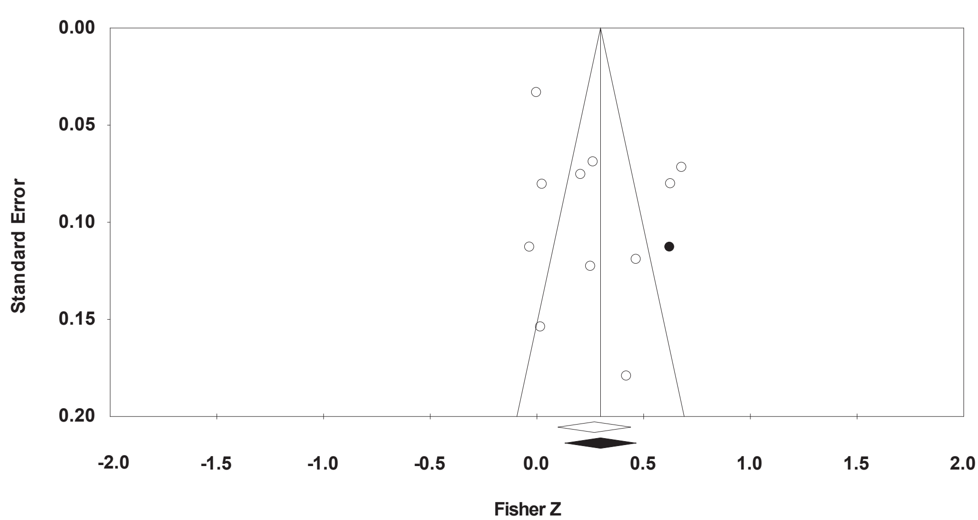

Figure 3. Funnel plot of emotional distress and analgesia use association.

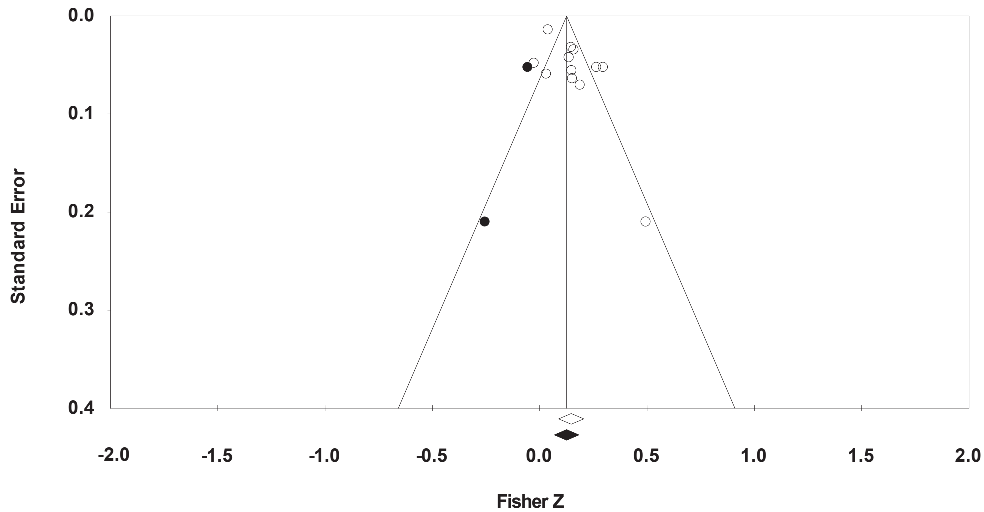

Figure 4. Funnel plot of emotional distress and dysfunction association.

average effects were estimated to be missing from the distress–impairment effect size distribution (Figure 4). Their inclusion would result in a modest decrease from the observed value of .15 (95% CI = .088–.203) to an adjusted value of .13 (95% CI = .068–.181).

Discussion

Overall results of this meta-analysis indicated patients who experience more emotional distress before surgery tend to experience higher levels of pain intensity, analgesic use, and functional impairment after surgery. Average effect sizes were small to medium and highly significant for each outcome. These findings dovetail with conclusions of select past reviews examining links of specific types of emotional distress including anxiety,[48,78] depression,[24] and catastrophizing[33,78] with postoperative functioning. Notably, the average association between presurgery distress and postoperative pain intensity represented by included studies was comparable with that of presurgery pain intensity, which has been cited as a robust influence on postoperative pain and functional outcomes across surgery types and time frames.[33,36,49]

Moderator analyses indicated effect sizes for postoperative pain intensity varied as a function of emotional distress subtype assessed before surgery; catastrophizing had particularly strong associations with pain intensity and the largest average effect size of any distress subtype with impairment. As such, features of pain catastrophizing including rumination about pain, helplessness in managing pain, and anticipation or magnification of pain before surgery correspond to poorer recovery courses. Notwithstanding debates about catastrophizing as a facet of other forms of distress,[71,78] appraisal,[28,80,81] or coping,[73–75] results suggest evaluations of adapted single- and multiple-session interventions to reduce catastrophizing[14,81] before or shortly after surgery are an important agenda for ongoing research.

Presurgery anxiety and depression levels also had small to medium effect sizes across outcomes, bolstering the utility of considering their inclusion with catastrophizing in presurgery assessment protocols. Conversely, fewer effect sizes reflecting fear or low positive affect/general well-being were reported and their individual effects were highly variable. For example, fear was the only presurgery distress subtype that was unrelated to postoperative pain intensity yet its association with postoperative impairment was significant. Arguably, effects of presurgery fear on postoperative pain are affected, to an extent, by fears about surgery that dissipate more quickly than other types of distress as patients survive and recover from surgeries. In contrast, the content of fear measures used in studies of impairment as an outcome reflected concerns about physical deterioration or incomplete recovery and arduousness of rehabilitation or pain as a signal for tissue damage and avoidance of activity to reduce pain and reinjury risk. In line with assumptions of the fear–avoidance perspective, those having such fears may have had reduced motivation and made fewer efforts toward increasing activity.[8,76] Consequently, these patients may have been more likely to experience elevations in impairment at 4- to 12-month follow-ups within this sample subset. However, at least some patients who reported more presurgery fear may have received information suggesting a poorer prognosis for recovery and subsequent impairment problems, reflecting prognosis information rather than fear. With this possibility, the role of presurgery fears on postoperative impairment may be elucidated more clearly by disentangling its effect from that of surgeon and patient perceptions of prognosis before surgery.

Moderator analyses for surgery to follow-up interval underscored how highly distressed patients about to undergo procedures are more likely than less distressed peers to experience elevations in pain intensity in the immediate aftermath of surgery. Effective analgesia and interventions targeting distress reductions are sensible, ethical goals for such patients during acute recovery and may help to reduce CPSP risk.[42] Nonetheless, modest, significant effect sizes for CPSP studies that assessed pain intensity an average of 9 months after surgery and impairment an average of >400 days after surgery pointed to potentially lingering effects of presurgery distress on pain chronicity. As such, ongoing support and access to aftercare resources may help highly distressed patients to negotiate the course of longer-term recovery more effectively.

Regarding patient characteristics, neither sex nor age affected relations of presurgery distress with postsurgery outcomes. This finding contradicts conclusions of 1 narrative review suggesting younger rather than older samples report more pain and use more analgesics after surgery.[27] However, the current results are more applicable than those of Ip et al[27] to middle-aged as opposed to older adults because mean ages of more than 75% of the included samples were younger than age 65 years. For type of surgery, Hinrichs-Rocker et al[24] argued previously that distressed patients are prone to CPSP after complex rather than circumscribed surgeries. On the basis of 16 studies, Theunissen et al[78] reported presurgical anxiety and catastrophizing predicted CPSP in 67% of musculoskeletal surgery studies but only 36% of studies involving other procedures, albeit this difference was not significant. Drawing upon 40 prospective samples, we found type of surgery did not moderate distress–pain intensity effect sizes. Conversely, for distress–impairment relations, a smaller overall effect size was found for spinal surgery samples than those having undergone other procedures. In line with the reviews mentioned, this finding is preliminary because it was based on a relatively small study subset. However, the result offers an alternative hypothesis for evaluation as prospective studies accumulate: presurgery emotional distress contributes to risk for impairment after more circumscribed surgeries that typically have fewer repercussions for activity level changes whereas complex procedures (eg, spinal surgery) have potentially profound effects on impairment levels[3] that override the effect of presurgery emotional status.

Study quality influenced distress–pain intensity effect sizes with larger effect sizes observed in studies having lower rather than higher quality scores. This finding likely reflects methodological soundness/rigor as an underlying feature of several quality criteria. For example, high-quality studies typically had sample N's >100 and/or increased statistical power; under such conditions, small effect sizes are more likely to garner statistically significant results than findings from smaller samples. Studies controlling for effects of presurgery pain intensity in analyses of distress–postoperative intensity relations were also scored higher than "uncontrolled" studies, even though such control typically results in attenuated effect sizes. Finally, selection criteria ensured all included studies had minimum samples sizes (N = 30), used predictor and outcome indices that had available reliability/validity support, and used continuous rather than broad, less sensitive, categorical pain intensity scales. Hence, retained studies, even those with the lowest quality scores, had methodological strengths that could reduce effects of error on distress–outcome relations.

Elaborating implications of moderator analyses for analytic approach, it was not surprising that presurgery distress had stronger relations with pain intensity and impairment when baseline responses on these outcomes were uncontrolled. Of more importance, however, average distress–outcome relations were significant within study subsets that had first statistically controlled presurgery responses on these outcomes. Corresponding effect sizes were small but supported elevations in presurgery distress as a risk factor for, and not merely a correlate of, heightened postoperative impairment, and to a lesser extent, pain intensity. Consequently, considering emotional distress within presurgical assessment protocols may aid in identifying vulnerable patients who can benefit from interventions targeting distress reductions.

Notwithstanding its possible implications, several limitations of this study warrant attention. First, findings may not generalize to children, homogeneous surgery subgroups, or unexamined outcomes such as future health care use. Hence, extensions are needed to assess overall associations of presurgery distress with postoperative functioning in these groups as well as the utilization of medical resources over extended intervals. Furthermore, because average postoperative follow-ups for CPSP studies of pain intensity and impairment did not exceed 9 and 14 months, respectively, generalizations cannot be made to longer follow-up intervals. Additional research on postoperative functioning beyond 1 year would elucidate this issue. Second, several included studies such as those that relied on stepwise regression analyses selectively reported only statistically significant effects and excluded such details for nonsignificant predictors. This practice is regrettable because it can inflate risk for type I errors and distort the scientific record to seem more robust than it is in reality. To ensure conclusions drawn about this literature are sober, we urge researcher, reviewer, and editor vigilance in ensuring all results, including nonsignificant effects, are reported transparently and in sufficient detail.

Third, although the trim and fill method permits the evaluation of publication bias, associated estimates are not always accurate. Idris[26] recommended routine use of this method in meta-analysis on the basis of its relative advantages but acknowledged the strategy is less effective in the presence of either low or severe publication bias. Furthermore, when applied to heterogeneous data sets, the trim and fill method can adjust for publication bias when none actually exists. Finally, causal effects of emotional distress were not evaluated in our study because included studies featured neither random assignment to groups nor experimental manipulations of distress levels. Examining how distress-reducing interventions influence subsequent postoperative outcomes is ethical and viable as a future research focus that can evaluate causal implications of changes in emotional status for functioning in the aftermath of surgery.

In sum, this meta-analysis indicated presurgery distress had positive overall associations, reflecting small to medium effect sizes, with postoperative pain intensity, analgesic use, and impairment. More notably, moderator analyses identified several moderators that help to explain highly variable results between studies. Emotional distress–pain intensity relations were stronger when studies included catastrophizing and, to a lesser extent, anxiety or depression as distress indices, when surgery to follow-up intervals were shorter rather than longer, when study methodologies were less rather than more rigorous, and when presurgery pain intensity levels were uncontrolled rather than controlled. Effect sizes associated with impairment varied on the basis of distress subtype and type of surgery but effects were significant only for the latter. Finally, after controlling for effects of individual moderators, effect size heterogeneity for outcomes was either reduced or no longer significant. Although these conclusions are tentative, this study provides foundations for follow-up meta-analyses as studies of this issue continue to mount.

Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.jpain.2016.04.003.

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