BMJ Open Prognostic factors for chronic postsurgical pain after lung or pleural surgery: a protocol for a systematic review and meta-analysis

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ABSTRACT

Introduction Chronic post-surgical pain (CPSP) after lung or pleural surgery is a common complication and associated with a decrease in quality of life, long-term use of pain medication and substantial economic costs. An abundant number of primary prognostic factor studies are published each year, but findings are often inconsistent, methods heterogeneous and the methodological quality questionable. Systematic reviews and meta-analyses are therefore needed to summarise the evidence.

Methods and analysis The reporting of this protocol adheres to the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) checklist. We will include retrospective and prospective studies with a follow-up of at least 3 months reporting patientrelated factors and surgery-related factors for any adult population. Randomised controlled trials will be included if they report on prognostic factors for CPSP after lung or pleural surgery. We will exclude case series, case reports, literature reviews, studies that do not report results for lung or pleural surgery separately and studies that modified the treatment or prognostic factor based on pain during the observation period. MEDLINE, Scopus, Web of Science, Embase, Cochrane, CINAHL, Google Scholar and relevant literature reviews will be searched. Independent pairs of two reviewers will assess studies in two stages based on the PICOTS criteria. We will use the Quality in Prognostic Studies tool for the quality assessment and the CHARMS-PF checklist for the data extraction of the included studies. The analyses will all be conducted separately for each identified prognostic factor. We will analyse adjusted and unadjusted estimated measures separately. When possible, evidence will be summarised with a meta-analysis and otherwise narratively. We will quantify heterogeneity by calculating the Q and I² statistics. The heterogeneity will be further explored with meta-regression and subgroup analyses based on clinical knowledge. The quality of the evidence obtained will be evaluated according to the Grades of Recommendation Assessment, Development and Evaluation guideline 28. Ethics and dissemination Ethical approval will not be necessary, as all data are already in the public domain. Results will be published in a peer-reviewed scientific

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Strengths and limitations of this study

- ► This systematic review and meta-analysis will be the first to systematically identify all prognostic factors for chronic post-surgical pain after lung or pleural surgery and to summarise the evidence.
- To ensure methodological quality, this systematic review and meta-analysis will be conducted following the PROGnosis RESearch Strategy guide for prognostic factor meta-analyses.
- Heterogeneity in the methods, the study populations and the reported outcomes of the included studies together with unexplained heterogeneity, will result in some level of uncertainty in our conclusions.

INTRODUCTION

Lung or pleural surgery is performed for a variety of diseases or injuries, such as lung cancer, cancer of the pleura, lung emphysema, lung transplantation and abscess after trauma or pleurodesis for recurrent pneumothorces. The thorax can be surgically accessed with a regular thoracotomy or with less invasive video-assisted thoracic surgery (VATS). Thoracic surgery is associated with chronic post-surgical pain (CPSP), which is classified as any pain related to the surgery and persisting for 3months or longer after surgery.^{1 2} CPSP often starts as a hard to control and acute post-surgical pain which later transitions into a persisting chronic pain.³ The pain is regularly localised at the chest wall and related to the area of surgery, but it can also be referred to a different area. It commonly increases with movement and often has a neuropathic component. 4 5 CPSP has been observed in as many as 57% and 47% of the patients 3 and 6 months after thoracic surgery, respectively.⁶ Hence, surgery has the highest incidence of CPSP among all types of surgery.³⁷ VATS is assumed



to be less painful compared with a regular thoracotomy because it is less invasive, however, incidence and severity of CPSP have been reported to be similar. CPSP after thoracic surgery has been associated with a lower overall quality of life, 9-13 and chronic pain is associated with an increased utilisation of healthcare, increased absenteeism and decreased work-related effectiveness. 14-16 The direct health-related costs of chronic pain have been reported to be US\$11846 annually, 17 and the indirect work-related costs have been reported to be US\$29617 annually. 17 The burden of CPSP for cancer survivors is also increasingly recognised, given the progress that has been made in cancer treatment. 18 Furthermore, CPSP often results in the long-term use of pain medication, particularly opioids, which contributes to overuse, misuse and addiction of opioids, 19-21 and thoracic surgery as an independent factor has also been associated with prolonged postoperative opioid use.²² Thus, CPSP has significant health and economic related consequences and is a problematic complication. Evidence for prognostic factors can contribute to improved clinical decision-making and individualised risk prediction by healthcare providers. A prognostic factor is defined as any variable affecting the risk of a particular health outcome and should be evaluated in a representative sample of patients assembled at the same time point in the course of their disease. 23 24 It can also contribute to the development of treatment strategies by identifying modifiable prognostic factors as targets.²⁵ This systematic review and meta-analysis will focus on all relevant reported prognostic factors for CPSP after lung or pleural surgery. There are two main categories we are interested in: Patient-related factors and surgery-related factors. A great number of primary prognostic factor studies are being published each year, however, they are often methodologically poor, their findings inconsistent and the methods heterogeneous.²³ Therefore, systematic reviews and meta-analyses are needed to summarise the evidence. 23 26 Other systematic reviews have been done regarding the incidence, severity and therapeutic interventions of chronic pain after thoracic surgery. 6 27 28 Another review has been done regarding the pathogenic mechanisms and strategies for prevention of chronic pain after thoracotomy.²⁹ To our knowledge, a systematic review and meta-analysis regarding prognostic factors for CPSP after lung or pleural surgery has not yet been performed.

OBJECTIVES

Our main goal is to carry out a systematic overview of the evidence regarding prognostic factors for CPSP after lung or pleural surgery. Our objectives are to identify, describe and appraise all studies reporting prognostic factors for CPSP after lung or pleural surgery, and summarise the evidence for each prognostic factor, either quantitatively with a meta-analysis or qualitatively by describing the evidence as a narrative, as appropriate.

criteria Any population of adult participants (18 years or older) who have had any type of Population lung or pleural surgery. Index Pre-identified prognostic factors: prognostic Preoperative pain, postoperative pain, factors pain catastrophising score, age, gender, body mass index, diabetes mellitus, exercise tolerance, malignant diseases, chemotherapy, radiation therapy, surgery duration, anaesthesia technique and surgical technique. Any newly identified prognostic factors will also be considered. Because we will systematically identify Comparator prognostic all prognostic factors and summarise the factors evidence, no comparator prognostic factors are involved. Chronic post-surgical pain as outcome. Outcome

Summary table of the PICOTS used as selection

METHODS AND ANALYSIS

Timing

Setting

Table 1

The reporting of this protocol adheres to the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) checklist. 30 31 It has been registered at the International Prospective Register of Systematic Reviews. For the project design we used guidance from the PROGnosis RESearch Strategy group, and specifically the guide for systematic reviews and meta-analyses for prognostic factor studies. 26 The results of the systematic review will be reported following the PRISMA checklist. 32

Follow-up of 3 months or more.

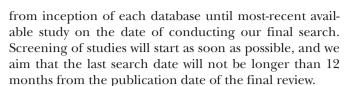
Any healthcare setting.

Study eligibility

We will include retrospective and prospective studies naming and evaluating a prognostic factor relating to chronic pain following lung or pleural surgery with at least 3 months of follow-up. Randomised controlled trials will be included if they report on prognostic factors for chronic pain after lung or pleural surgery. Case series, case studies, literature reviews, studies that do not report results for lung or pleural surgery separately and studies that modified the treatment or prognostic factor based on pain during the observation period will be excluded. We will use the PICOTS system as selection criteria for studies with the appropriate study type. (table 1). The PICOTS system is an updated modification for prognostic studies of the traditional PICO system, incorporating 'timing (T)' and 'setting (S)'. 33 34 Timing includes at what time points the prognostic factors are being measured and setting includes the intended setting, such as primary or secondary care.²⁶

Search strategy

We will search key health and medical databases (MEDLINE, Scopus, Web of Science, Embase, Cochrane, CINAHL and Google Scholar) for peer-reviewed literature



The systematic search will be built by an experienced information scientist and will be adapted to fit each information source.³⁵ The reporting and retrieval of prognostic factors is generally known to be poor, with no specialised filters available. Hence a broad search will be employed using the most recent prognostic strategies, offering a high sensitivity at the cost of a lower specificity.36 We will use no restrictions on language, study status or time of publication. If translation is necessary, we will ask a colleague who is fluent in that language to translate. When this is not possible, we will use the Cochrane task exchange service or Google Translate.³⁷ The search strategy is included in online supplemental file 1, with the adaptations for each database. Because of potential limitations of the electronic search strategy, we will supplement our search with reference searches of relevant literature studies.

Study screening

Independent pairs of two reviewers will assess studies in two stages based on the inclusion and exclusion criteria. They will screen studies in stage one on title and abstract and in stage two on the full text. Differences will be resolved through either a consensus meeting or consultation of a third reviewer in both selection phases. We will use the PRISMA flowchart to display the study selection process, including the exclusion reasons of non-eligible studies.³² Studies retrieved from the searches will be stored and screened in EndNote V.X9.38 The excluded studies will be stored in EndNote subgroups for each exclusion reason. The data that will be extracted from eligible studies will be stored and managed in Microsoft Excel V.16.43.

Data extraction

For the data collection process we will use the standardised CHARMS-PF checklist, 26 which is based on the CHARMS checklist,³⁴ but adjusted for prognostic factor studies. It has nine domains, covering everything needed to reliably pool data: source of data, participants, outcomes to be predicted, prognostic factors, sample size, missing data, analysis, results and interpretation and discussion. Specific attention will be paid to the following data items: Reported factors of prognostic interest, definition and measurement of outcomes, adjusted and unadjusted outcomes, adjustment factors, regression methods and timing. When multiple follow-up time points are available, we will use a time point of at least 3 months that is closest to 3 months. If only the mean follow-up or the range of follow-up is reported, it needs to be at least 3 months. Any additional information deemed necessary will be added in a bespoke Excel data extraction file. If information in a study is missing or unclear, the primary study authors will be contacted with the request to provide additional information. We will consider the study with the biggest sample size or the most recent, as appropriate, as the most relevant one when there are multiple publications with the same or overlapping participant data.

Risk of bias in individual studies

The quality of included studies will be assessed by two independent reviewers with the Quality in Prognostic Studies tool.³⁹ This tool contains six domains: Study participation, study attrition, prognostic factor measurement, outcome measurement, study covariates and statistical analysis and reporting. Each domain is rated as low, moderate or high risk of bias. If information in a study is missing or unclear, the authors will be contacted with the request to provide additional information. Differences between the two reviewers will be resolved through either a consensus meeting or consultation of a third reviewer.

Data synthesis

The characteristics of the identified prognostic factors will be summarised in a table. For the quantitative synthesis we will obtain ORs, risk ratios (RRs) and HRs as measures of association as reported in each included study. The mean difference will also be considered as an appropriate measure of association for continuous prognostic factors. Adjusted and unadjusted estimates for each factor will be considered and analysed separately. The OR, RR and HR will also be considered separately. A meta-analysis will be performed for each prognostic factor when reported by at least five studies with similar measures of association. 26 40 In cases where either the measure (OR, RR or HR), or its SE are not reported, where possible we will estimate them from any available data in the included study, such as confidence intervals, Kaplan-Meier curves, logrank test p values or other as appropriate. $^{41-44}$ We will explore any differences between the reported and estimated measures through a sensitivity analysis. We will also include a sensitivity analysis when there is heterogeneity between studies in how chronic pain is defined. For pooling the data, we will use the DerSimonian and Laird random effects model to account for expected between study heterogeneity. 45 46 We will include a 95% prediction interval in addition to the 95% CI for the pooled measures. 46 Heterogeneity between studies will be assessed for each meta-analysis by visually inspecting forest plots and by calculating the Q statistic and the I² statistic.⁴⁷ We will perform a univariable meta-regression for each continuous prognostic factor reported by 10 or more studies. All analyses will be performed with the metafor package in the latest version of R and RStudio. When quantitative synthesis is not possible, we will summarise the evidence narratively.

Subgroup analyses

We will perform subgroup analyses where possible to further explore the heterogeneity. Based on clinical knowledge, the following subgroups will be investigated: Malignant diseases, regional anaesthesia (particularly



intercostal infiltration, single shot and continuous blocks and duration), neuropathic pain and surgical technique (particularly VATS or no VATS).

Publication bias

Funnel plots will be used to assess potential publication bias for factors of prognostic interest that are reported by 10 or more studies. ⁴⁸ Funnel plots suffer from low power and this is more problematic for observational studies (as are studies of prognosis) where there is additionally increased heterogeneity. To statistically test the asymmetry of the funnel plots we will use the Harbord test, ⁴⁹ and any findings will be interpreted with caution.

Rating of evidence

The evidence and inferences will be evaluated according to the Grades of Recommendation Assessment, Development, and Evaluation (GRADE) guidelines (GRADE guideline 28) for assessing the evidence from prognostic factors. ⁵⁰ It contains five domains: Risk of bias, inconsistency, imprecision, indirectness and publication bias.

Contributors PRDC designed and wrote the protocol in close collaboration with SEH. MH and PMS provided the idea of the topic. MT and SEH contributed to the design of the statistical methods. CSG contributed to finding the a priori prognostic factors. MH and MK coordinated the whole process. All authors read, provided feedback and approved the final manuscript.

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REFERENCES

- 1 Schug SA, Lavand'homme P, Barke A, et al. The IASP classification of chronic pain for ICD-11: chronic postsurgical or posttraumatic pain. *Pain* 2019;160:45–52.
- 2 Treede R-D, Rief W, Barke A, et al. A classification of chronic pain for ICD-11. Pain 2015;156:1003-7.
- 3 Glare P, Aubrey KR, Myles PS. Transition from acute to chronic pain after surgery. *Lancet* 2019;393:1537–46.

- 4 Guastella V, Mick G, Soriano C, et al. A prospective study of neuropathic pain induced by thoracotomy: incidence, clinical description, and diagnosis. Pain 2011;152:74–81.
- 5 Haroutiunian S, Nikolajsen L, Finnerup NB, et al. The neuropathic component in persistent postsurgical pain: a systematic literature review. *Pain* 2013;154:95–102.
- 6 Bayman EO, Brennan TJ. Incidence and severity of chronic pain at 3 and 6 months after thoracotomy: meta-analysis. *J Pain* 2014;15:887–97.
- 7 Cregg R, Anwar S, Farquhar-Smith P. Persistent postsurgical pain. Curr Opin Support Palliat Care 2013;7:144–52.
- 8 Bayman EO, Parekh KR, Keech J, et al. A prospective study of chronic pain after thoracic surgery. *Anesthesiology* 2017;126:938–51.
- 9 Kinney MAO, Hooten WM, Cassivi SD, et al. Chronic postthoracotomy pain and health-related quality of life. Ann Thorac Surg 2012;93:1242–7.
- 10 Kar P, Sudheshna KD, Padmaja D, et al. Chronic pain following thoracotomy for lung surgeries: It's risk factors, prevalence, and impact on quality of life - A retrospective study. *Indian J Anaesth* 2019;63:368–74.
- 11 Peng Z, Li H, Zhang C, et al. A retrospective study of chronic postsurgical pain following thoracic surgery: prevalence, risk factors, incidence of neuropathic component, and impact on qualify of life. PLoS One 2014;9:e90014.
- 12 Fiorelli S, Cioffi L, Menna C, et al. Chronic pain after lung resection: risk factors, neuropathic pain, and quality of life. J Pain Symptom Manage 2020;60:326–35.
- 13 Loxe SC, de Mello LS, Camara L, et al. Chronic pain after lung transplantation and its impact on quality of life: a 4-year follow-up. Transplant Proc 2020;52:1388–93.
- 4 Blyth FM, March LM, Brnabic AJM, et al. Chronic pain and frequent use of health care. *Pain* 2004;111:51–8.
- 15 Blyth FM, March LM, Nicholas MK, et al. Chronic pain, work performance and litigation. *Pain* 2003;103:41–7.
- 16 van Leeuwen MT, Blyth FM, March LM, et al. Chronic pain and reduced work effectiveness: the hidden cost to Australian employers. Eur J Pain 2006;10:161–6.
- 17 Parsons B, Schaefer C, Mann R, et al. Economic and humanistic burden of post-trauma and post-surgical neuropathic pain among adults in the United States. J Pain Res 2013;6:459–69.
- 18 Brown MR, Ramirez JD, Farquhar-Smith P. Pain in cancer survivors. Br J Pain 2014;8:139–53.
- 19 Huang A, Azam A, Segal S, et al. Chronic postsurgical pain and persistent opioid use following surgery: the need for a transitional pain service. Pain Manag 2016;6:435–43.
- 20 Baker DW. History of the joint Commission's pain standards: lessons for today's prescription opioid epidemic. *JAMA* 2017;317:1117–8.
- 21 Manchikanti L, Fellows B, Ailinani H, et al. Therapeutic use, abuse, and nonmedical use of opioids: a ten-year perspective. Pain Physician 2010;13:401–35.
- 22 Clarke H, Soneji N, Ko DT, et al. Rates and risk factors for prolonged opioid use after major surgery: population based cohort study. BMJ 2014;348:g1251.
- 23 Altman DG. Systematic reviews of evaluations of prognostic variables. *BMJ* 2001;323:224–8.
- 24 Riley RD, Hayden JA, Steyerberg EW, et al. Prognosis research strategy (progress) 2: prognostic factor research. PLoS Med 2013;10:e1001380.
- 25 Hemingway H, Croft P, Perel P, et al. Prognosis research strategy (progress) 1: a framework for researching clinical outcomes. BMJ 2013:346:e5595.
- 26 Riley RD, Moons KGM, Snell KIE, et al. A guide to systematic review and meta-analysis of prognostic factor studies. BMJ 2019;364:k4597.
- 27 Guimarães-Pereira L, Reis P, Abelha F, et al. Persistent postoperative pain after cardiac surgery: a systematic review with meta-analysis regarding incidence and pain intensity. Pain 2017;158:1869–85.
- 28 Humble SR, Dalton AJ, Li L. A systematic review of therapeutic interventions to reduce acute and chronic post-surgical pain after amputation, thoracotomy or mastectomy. *Eur J Pain* 2015;19:451–65.
- 29 Wildgaard K, Ravn J, Kehlet H. Chronic post-thoracotomy pain: a critical review of pathogenic mechanisms and strategies for prevention. *Eur J Cardiothorac Surg* 2009;36:170–80.
- 30 Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev 2015;4:1.
- 31 Shamseer L, Moher D, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ 2015;350:g7647.



- 32 Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med 2009;6:e1000097.
- 33 Debray TPA, Damen JAAG, Snell KIE, et al. A guide to systematic review and meta-analysis of prediction model performance. BMJ 2017;356:i6460.
- 34 Moons KGM, de Groot JAH, Bouwmeester W, et al. Critical appraisal and data extraction for systematic reviews of prediction modelling studies: the charms checklist. PLoS Med 2014;11:e1001744.
- 35 Bramer WM, de Jonge GB, Rethlefsen ML, et al. A systematic approach to searching: an efficient and complete method to develop literature searches. J Med Libr Assoc 2018;106:531–41.
- 36 Geersing G-J, Bouwmeester W, Zuithoff P, et al. Search filters for finding prognostic and diagnostic prediction studies in MEDLINE to enhance systematic reviews. PLoS One 2012;7:e32844.
- 37 Jackson JL, Kuriyama A, Anton A, et al. The accuracy of Google translate for Abstracting data from Non-English-Language trials for systematic reviews. Ann Intern Med 2019;171:677–9.
- 38 Bramer WM, Milic J, Mast F. Reviewing retrieved references for inclusion in systematic reviews using endnote. J Med Libr Assoc 2017;105:84–7.
- 39 Hayden JA, Côté P, Bombardier C. Evaluation of the quality of prognosis studies in systematic reviews. *Ann Intern Med* 2006;144:427–37.
- 40 Jackson D, Turner R. Power analysis for random-effects metaanalysis. Res Synth Methods 2017;8:290–302.

- 41 Trivella M, Altman DG. Systematic reviews of prognostic factor studies: thesis (D Phil). 2005. University of Oxford, 2005.
- 42 Tierney JF, Stewart LA, Ghersi D, et al. Practical methods for incorporating summary time-to-event data into meta-analysis. *Trials* 2007;8:16.
- 43 Altman DG, McShane LM, Sauerbrei W, et al. Reporting recommendations for tumor marker prognostic studies (REMARK): explanation and elaboration. BMC Med 2012;10:51.
- 44 Parmar MK, Torri V, Stewart L. Extracting summary statistics to perform meta-analyses of the published literature for survival endpoints. Stat Med 1998;17:2815–34.
- 45 DerSimonian R, Laird N. Meta-Analysis in clinical trials. Control Clin Trials 1986;7:177–88.
- 46 Riley RD, Higgins JPT, Deeks JJ. Interpretation of random effects meta-analyses. *BMJ* 2011;342:d549.
- 47 Higgins JPT, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. BMJ 2003;327:557–60.
- 48 Sterne JA, Egger M, Smith GD. Systematic reviews in health care: investigating and dealing with publication and other biases in metaanalysis. BMJ 2001;323:101–5.
- 49 Harbord RM, Egger M, Sterne JAC. A modified test for small-study effects in meta-analyses of controlled trials with binary endpoints. Stat Med 2006;25:3443–57.
- 50 Foroutan F, Guyatt G, Zuk V, et al. Grade guidelines 28: use of grade for the assessment of evidence about prognostic factors: rating certainty in identification of groups of patients with different absolute risks. J Clin Epidemiol 2020;121:62–70.

Supplement 1

Embase

('chronic pain'/exp OR (((chronic* OR constant* OR continu* OR persist* OR longterm OR long-term OR longstanding OR long-standing OR longlasting OR long-lasting OR phantom) NEAR/6 (pain* OR discomfort* OR complaint*)):ti,ab,kw)) AND ('postoperative pain'/exp OR (((postoperative OR posttreatment OR postsurg*) NEAR/6 (pain* OR analgesi*)) OR ((post OR after OR follow*) NEAR/3 (surg* OR operat* OR treat* OR resect* OR transplant*) NEAR/6 (pain* OR analgesi*)) OR ((post* NEAR/1 pain*)) OR pain-relief-after OR ((post-extraction OR postextraction OR amputat* OR mediastinoscopy OR sternotomy OR thoracoplasty OR thoracoscopy OR thoracostomy OR thoracotomy OR thoracocentesis OR thymectomy OR tracheostomy OR tracheotomy OR bronchoscopy OR pneumonolysis OR pneumonectomy OR esophagectomy OR oesophagectomy OR postmediastinoscop* OR poststernotom* OR postthoracoplast* OR postthoracoscop* OR postthoracostom* OR postthoracotom* OR postthoracocentesis OR postthymectom* OR posttracheostom* OR posttracheotom* OR postbronchoscop* OR postpneumonolysis OR postpneumonectom* OR postesophagectom* OR postoesophagectom* OR postlobectom*) NEAR/6 (pain* OR discomfort OR analgesi*))):ti,ab,kw) AND (('thorax surgery'/exp NOT 'heart surgery'/exp) OR 'lung tumor'/exp/dm_su OR (((thora* OR lung OR pulmonary OR esophag* OR oesophag* OR trachea* OR rib OR thym* OR chest OR pleura*) NEAR/6 (surg* OR operat* OR resect*)) OR mediastinoscop* OR sternotom* OR thoracoplast* OR thoracoscop* OR thoracostom* OR thoracotom* OR thoracocentesis OR thymectom* OR tracheostom* OR tracheotom* OR bronchoscop* OR pneumonolysis OR pneumonectom* OR esophagectom* OR oesophagectom* OR lobectom* OR postmediastinoscop* OR poststernotom* OR postthoracoplast* OR postthoracoscop* OR postthoracostom* OR postthoracotom* OR postthoracocentesis OR postthymectom* OR posttracheostom* OR posttracheotom* OR postbronchoscop* OR postpneumonolysis OR postpneumonectom* OR postesophagectom* OR postoesophagectom* OR postlobectom* OR ((lung OR pulmonary OR thym*) NEAR/6 (transplant* OR graft*)) OR ((esophag* OR oesophag*) NEAR/6 (anastom* OR transect* OR dilat* OR reconstruct*))):ti,ab,kw) NOT [conference abstract]/lim NOT ([animals]/lim NOT [humans]/lim)

Medline

(Chronic Pain/ OR (((chronic* OR constant* OR continu* OR persist* OR longterm OR long-term OR longstanding OR long-standing OR longlasting OR long-lasting OR phantom) ADJ6 (pain* OR discomfort* OR complaint*)).ti,ab,kf)) AND (Pain, Postoperative/ OR (((postoperative OR posttreatment OR postsurg*) ADJ6 (pain* OR analgesi*)) OR ((post OR after OR follow*) ADJ3 (surg* OR operat* OR treat* OR resect* OR transplant*) ADJ6 (pain* OR analgesi*)) OR ((post* ADJ1 pain*)) OR pain-relief-after OR ((post-extraction OR postextraction OR amputat* OR mediastinoscopy OR sternotomy OR thoracoplasty OR thoracoscopy OR thoracostomy OR thoracotomy OR pneumonolysis OR pneumonectomy OR esophagectomy OR oesophagectomy OR postmediastinoscop* OR poststernotom* OR postthoracoplast* OR postthoracoscop* OR postthoracostom* OR postthoracotom* OR postthoracocentesis OR postthymectom* OR postthoracostom* OR posttracheotom* OR postbronchoscop* OR postpneumonolysis OR postpneumonectom* OR postesophagectom* OR postoesophagectom* OR postlobectom*) ADJ6 (pain* OR discomfort OR analgesi*))).ti,ab,kf) AND (Thoracic Surgery/ OR (exp Thoracic Surgical Procedures/ NOT exp Cardiac Surgical Procedures/) OR

Lung Neoplasms/su OR (((thora* OR lung OR pulmonary OR esophag* OR oesophag* OR trachea* OR rib OR thym* OR chest OR pleura*) ADJ6 (surg* OR operat* OR resect*)) OR mediastinoscop* OR sternotom* OR thoracoplast* OR thoracoscop* OR thoracostom* OR thoracotom* OR thoracocentesis OR thymectom* OR tracheostom* OR tracheotom* OR bronchoscop* OR pneumonolysis OR pneumonectom* OR esophagectom* OR oesophagectom* OR lobectom* OR postmediastinoscop* OR poststernotom* OR postthoracoplast* OR postthoracoscop* OR postthoracostom* OR postthoracocentesis OR postthymectom* OR posttracheostom* OR posttracheotom* OR postbronchoscop* OR postpneumonolysis OR postpneumonectom* OR postesophagectom* OR postoesophagectom* OR postlobectom* OR ((lung OR pulmonary OR thym*) ADJ6 (transplant* OR graft*)) OR ((esophag* OR oesophag*) ADJ6 (anastom* OR transect* OR dilat* OR reconstruct*))).ti,ab,kf) NOT (exp animals/ NOT humans/)

Web of Science

TS=(((((chronic* OR constant* OR continu* OR persist* OR longterm OR long-term OR longstanding OR long-standing OR longlasting OR long-lasting OR phantom) NEAR/5 (pain* OR discomfort* OR complaint*)))) AND ((((postoperative OR posttreatment OR postsurg*) NEAR/5 (pain* OR analgesi*)) OR ((post OR after OR follow*) NEAR/2 (surg* OR operat* OR treat* OR resect* OR transplant*) NEAR/5 (pain* OR analgesi*)) OR ((post* NEAR/1 pain*)) OR pain-relief-after OR ((post-extraction OR postextraction OR amputat* OR mediastinoscopy OR sternotomy OR thoracoplasty OR thoracoscopy OR thoracostomy OR thoracotomy OR thoracocentesis OR thymectomy OR tracheostomy OR tracheotomy OR bronchoscopy OR pneumonolysis OR pneumonectomy OR esophagectomy OR oesophagectomy OR postmediastinoscop* OR poststernotom* OR postthoracoplast* OR postthoracoscop* OR postthoracostom* OR postthoracotom* OR postthoracocentesis OR postthymectom* OR posttracheostom* OR posttracheotom* OR postbronchoscop* OR postpneumonolysis OR postpneumonectom* OR postesophagectom* OR postoesophagectom* OR postlobectom*) NEAR/5 (pain* OR discomfort OR analgesi*)))) AND ((((thora* OR lung OR pulmonary OR esophag* OR oesophag* OR trachea* OR rib OR thym* OR chest OR pleura*) NEAR/5 (surg* OR operat* OR resect*)) OR mediastinoscop* OR sternotom* OR thoracoplast* OR thoracoscop* OR thoracostom* OR thoracotom* OR thoracocentesis OR thymectom* OR tracheostom* OR tracheotom* OR bronchoscop* OR pneumonolysis OR pneumonectom* OR esophagectom* OR oesophagectom* OR lobectom* OR postmediastinoscop* OR poststernotom* OR postthoracoplast* OR postthoracoscop* OR postthoracostom* OR postthoracotom* OR postthoracocentesis OR postthymectom* OR posttracheostom* OR posttracheotom* OR postbronchoscop* OR postpneumonolysis OR postpneumonectom* OR postesophagectom* OR postoesophagectom* OR postlobectom* OR ((lung OR pulmonary OR thym*) NEAR/5 (transplant* OR graft*)) OR ((esophag* OR oesophag*) NEAR/5 (anastom* OR transect* OR dilat* OR reconstruct*))))) AND DT=(article)

Cochrane

((((chronic* OR constant* OR continu* OR persist* OR longterm OR long NEXT term OR longstanding OR long NEXT standing OR longlasting OR long NEXT lasting OR phantom) NEAR/6 (pain* OR discomfort* OR complaint*)):ti,ab)) AND ((((postoperative OR posttreatment OR postsurg*) NEAR/6 (pain* OR analgesi*)) OR ((post OR after OR follow*) NEAR/3 (surg* OR operat* OR treat* OR resect* OR transplant*) NEAR/6 (pain* OR analgesi*)) OR ((post* NEAR/1 pain*)) OR pain NEXT relief NEXT after OR ((post NEXT extraction OR postextraction OR amputat* OR mediastinoscopy OR sternotomy OR thoracoplasty OR thoracoscopy OR t

OR tracheostomy OR tracheotomy OR bronchoscopy OR pneumonolysis OR pneumonectomy OR esophagectomy OR oesophagectomy OR postmediastinoscop* OR poststernotom* OR postthoracoplast* OR postthoracoscop* OR postthoracostom* OR postthoracotom* OR postthoracocentesis OR postthymectom* OR posttracheostom* OR posttracheotom* OR postbronchoscop* OR postpneumonolysis OR postpneumonectom* OR postesophagectom* OR postoesophagectom* OR postlobectom*) NEAR/6 (pain* OR discomfort OR analgesi*))):ti,ab) AND ((((thora* OR lung OR pulmonary OR esophag* OR oesophag* OR trachea* OR rib OR thym* OR chest OR pleura*) NEAR/6 (surg* OR operat* OR resect*)) OR mediastinoscop* OR sternotom* OR thoracoplast* OR thoracoscop* OR thoracostom* OR thoracotom* OR thoracocentesis OR thymectom* OR tracheostom* OR tracheotom* OR bronchoscop* OR pneumonolysis OR pneumonectom* OR esophagectom* OR oesophagectom* OR lobectom* OR postmediastinoscop* OR poststernotom* OR postthoracoplast* OR postthoracoscop* OR postthoracostom* OR postthoracotom* OR postthoracocentesis OR postthymectom* OR posttracheostom* OR posttracheotom* OR postbronchoscop* OR postpneumonolysis OR postpneumonectom* OR postesophagectom* OR postoesophagectom* OR postlobectom* OR ((lung OR pulmonary OR thym*) NEAR/6 (transplant* OR graft*)) OR ((esophag* OR oesophag*) NEAR/6 (anastom* OR transect* OR dilat* OR reconstruct*))):ti,ab)

CINAHL

(MH Chronic Pain OR TI(((chronic* OR constant* OR continu* OR persist* OR longterm OR long-term OR longstanding OR long-standing OR longlasting OR long-lasting OR phantom) N5 (pain* OR discomfort* OR complaint*))) OR AB(((chronic* OR constant* OR continu* OR persist* OR longterm OR long-term OR longstanding OR long-standing OR longlasting OR long-lasting OR phantom) N5 (pain* OR discomfort* OR complaint*)))) AND (MH Postoperative Pain OR TI(((postoperative OR posttreatment OR postsurg*) N5 (pain* OR analgesi*)) OR ((post OR after OR follow*) N2 (surg* OR operat* OR treat* OR resect* OR transplant*) N5 (pain* OR analgesi*)) OR ((post* N1 pain*)) OR pain-relief-after OR ((post-extraction OR postextraction OR amputat* OR mediastinoscopy OR sternotomy OR thoracoplasty OR thoracoscopy OR thoracostomy OR thoracotomy OR thoracocentesis OR thymectomy OR tracheostomy OR tracheotomy OR bronchoscopy OR pneumonolysis OR pneumonectomy OR esophagectomy OR oesophagectomy OR postmediastinoscop* OR poststernotom* OR postthoracoplast* OR postthoracoscop* OR postthoracostom* OR postthoracotom* OR postthoracocentesis OR postthymectom* OR posttracheostom* OR posttracheotom* OR postbronchoscop* OR postpneumonolysis OR postpneumonectom* OR postesophagectom* OR postoesophagectom* OR postlobectom*) N5 (pain* OR discomfort OR analgesi*))) OR AB(((postoperative OR posttreatment OR postsurg*) N5 (pain* OR analgesi*)) OR ((post OR after OR follow*) N2 (surg* OR operat* OR treat* OR resect* OR transplant*) N5 (pain* OR analgesi*)) OR ((post* N1 pain*)) OR pain-relief-after OR ((post-extraction OR postextraction OR amputat* OR mediastinoscopy OR sternotomy OR thoracoplasty OR thoracoscopy OR thoracostomy OR thoracotomy OR thoracocentesis OR thymectomy OR tracheostomy OR tracheotomy OR bronchoscopy OR pneumonolysis OR pneumonectomy OR esophagectomy OR oesophagectomy OR postmediastinoscop* OR poststernotom* OR postthoracoplast* OR postthoracoscop* OR postthoracostom* OR postthoracotom* OR postthoracocentesis OR postthymectom* OR posttracheostom* OR posttracheotom* OR postbronchoscop* OR postpneumonolysis OR postpneumonectom* OR postesophagectom* OR postoesophagectom* OR postlobectom*) N5 (pain* OR discomfort OR analgesi*)))) AND ((MH "Thoracic Surgery+" NOT MH "Heart Surgery+") OR TI(((thora* OR lung OR pulmonary OR esophag* OR oesophag* OR trachea* OR rib OR thym* OR chest

OR pleura*) N5 (surg* OR operat* OR resect*)) OR mediastinoscop* OR sternotom* OR thoracoplast* OR thoracoscop* OR thoracostom* OR thoracocom* OR thoracocentesis OR thymectom* OR tracheostom* OR tracheotom* OR bronchoscop* OR pneumonolysis OR pneumonectom* OR esophagectom* OR oesophagectom* OR lobectom* OR postmediastinoscop* OR poststernotom* OR postthoracoplast* OR postthoracoscop* OR postthoracostom* OR postthoracotom* OR postthoracocentesis OR postthymectom* OR posttracheostom* OR posttracheotom* OR postbronchoscop* OR postpneumonolysis OR postpneumonectom* OR postesophagectom* OR postoesophagectom* OR postlobectom* OR ((lung OR pulmonary OR thym*) N5 (transplant* OR graft*)) OR ((esophag* OR oesophag*) N5 (anastom* OR transect* OR dilat* OR reconstruct*))) OR AB(((thora* OR lung OR pulmonary OR esophag* OR oesophag* OR trachea* OR rib OR thym* OR chest OR pleura*) N5 (surg* OR operat* OR resect*)) OR mediastinoscop* OR sternotom* OR thoracoplast* OR thoracoscop* OR thoracostom* OR thoracotom* OR thoracocentesis OR thymectom* OR tracheostom* OR tracheotom* OR bronchoscop* OR pneumonolysis OR pneumonectom* OR esophagectom* OR oesophagectom* OR lobectom* OR postmediastinoscop* OR poststernotom* OR postthoracoplast* OR postthoracoscop* OR postthoracostom* OR postthoracotom* OR postthoracocentesis OR postthymectom* OR posttracheostom* OR posttracheotom* OR postbronchoscop* OR postpneumonolysis OR postpneumonectom* OR postesophagectom* OR postoesophagectom* OR postlobectom* OR ((lung OR pulmonary OR thym*) N5 (transplant* OR graft*)) OR ((esophag* OR oesophag*) N5 (anastom* OR transect* OR dilat* OR reconstruct*)))) NOT (MH animals+ NOT MH humans)

Scopus

TITLE-ABS-KEY(((((chronic* OR constant* OR continu* OR persist* OR longterm OR long-term OR longstanding OR long-standing OR longlasting OR long-lasting OR phantom) W/5 (pain* OR discomfort* OR complaint*)))) AND ((((postoperative OR posttreatment OR postsurg*) W/5 (pain* OR analgesi*)) OR ((post OR after OR follow*) W/2 (surg* OR operat* OR treat* OR resect* OR transplant*) W/5 (pain* OR analgesi*)) OR ((post* W/1 pain*)) OR pain-relief-after OR ((post-extraction OR postextraction OR amputat* OR mediastinoscopy OR sternotomy OR thoracoplasty OR thoracoscopy OR thoracostomy OR thoracotomy OR thoracocentesis OR thymectomy OR tracheostomy OR tracheotomy OR bronchoscopy OR pneumonolysis OR pneumonectomy OR esophagectomy OR oesophagectomy OR postmediastinoscop* OR poststernotom* OR postthoracoplast* OR postthoracoscop* OR postthoracostom* OR postthoracotom* OR postthoracocentesis OR postthymectom* OR posttracheostom* OR posttracheotom* OR postbronchoscop* OR postpneumonolysis OR postpneumonectom* OR postesophagectom* OR postoesophagectom* OR postlobectom*) W/5 (pain* OR discomfort OR analgesi*)))) AND ((((thora* OR lung OR pulmonary OR esophag* OR oesophag* OR trachea* OR rib OR thym* OR chest OR pleura*) W/5 (surg* OR operat* OR resect*)) OR mediastinoscop* OR sternotom* OR thoracoplast* OR thoracoscop* OR thoracostom* OR thoracotom* OR thoracocentesis OR thymectom* OR tracheostom* OR tracheotom* OR bronchoscop* OR pneumonolysis OR pneumonectom* OR esophagectom* OR oesophagectom* OR lobectom* OR postmediastinoscop* OR poststernotom* OR postthoracoplast* OR postthoracoscop* OR postthoracostom* OR postthoracotom* OR postthoracocentesis OR postthymectom* OR posttracheostom* OR posttracheotom* OR postbronchoscop* OR postpneumonolysis OR postpneumonectom* OR postesophagectom* OR postoesophagectom* OR postlobectom* OR ((lung OR pulmonary OR thym*) W/5 (transplant* OR graft*)) OR ((esophag* OR oesophag*) W/5 (anastom* OR transect* OR dilat* OR reconstruct*)))))

Google scholar

"chronic|constant|persisting|longterm|longstanding|longlasting|phantom pain"

"postoperative|postsurgical pain" "thorax|thoracic surgery|operation"