National Institute for Health and Care Excellence

Final

Chronic pain (primary and secondary) in over 16s: assessment of all chronic pain and management of chronic primary pain

[A] Evidence reviews for factors that may be barriers to successfully managing chronic pain (chronic primary pain and chronic secondary pain)

NICE guideline NG193

Prognostic evidence review underpinning recommendations 1.1.1 to 1.1.23 and the research recommendation in the NICE guideline

April 2021

These evidence reviews were developed by the National Guideline Centre based at the Royal College of Physicians

Disclaimer

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and, where appropriate, their carer or guardian.

Local commissioners and providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

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1 Introduction

Over the past forty years, a ‘biopsychosocial approach’ has been used to categorise, explore and understand contextual factors in health. This model suggests that health and illness will have a biological, psychological and social dimension.

Those factors that are associated with pain triggers, pain perception, the persistence of pain and likely prognosis for pain and function are well described in the literature. However, the factors that are associated with the successful management of chronic pain are less well described. This review sets out to inform the Guideline Committee’s assessment of biological, psychological and social factors that influence the successful management of chronic pain. These factors may be modifiable by the person with chronic pain, or the approach to managing the pain could be modified to take account of these factors.

It is important to have an understanding of the many factors that may have an impact on the experience of chronic pain. It may help identify those who need additional help to access appropriate care and support for chronic pain. It will inform discussions between people with chronic pain and their healthcare professionals and could inform commissioners and service providers in meeting the needs of people with chronic pain.

2 Biological factors

2.1 Review question: What biological factors may be barriers to successfully managing chronic pain?

2.2 PICO table

For full details see the review protocol in Appendix A:.

Table 1: PICO characteristics of review question

Population	People, aged 16 years and over, with chronic pain. *Pain that persists or recurs for longer than 3 months.*
Prognostic variables under consideration	• Physical activity at baseline • Presence or absence of comorbid physical condition • Polypharmacy • Pain diagnosis
Confounding factors	Studies not accounting for at least 2 key confounders (prognostic factors plus number of pain sites, smoking, age and gender) in a multivariable analysis are excluded.
Outcomes	CRITICAL: • Health related quality of life (including meaningful activity) • Pain reduction (any validated scale)
Study design	Prospective and retrospective cohort studies Case control studies if no cohort studies are identified

2.3 Clinical evidence

2.3.1 Included studies

Seven studies were included in the review[94, 171, 521, 226, 355, 552, 559]; these are summarised in Table 2 below. Evidence from these studies is summarised in the clinical evidence summary tables below (Table 3, Table 4 and

Table 5).

Outcomes were reported as adjusted odds ratios and beta coefficients. Beta coefficient values represent the change in the dependent variable (outcome) for every one unit change in the independent variable (prognostic factor). A unit change in an independent variable could represent an incremental change on a scale, for example a five point increase in body mass index, or it could represent a change in prognostic category, for example underweight, normal weight, overweight, obese.

2.3.2 Excluded studies

See the excluded studies list in Appendix I.

2.3.3 Summary of clinical studies included in the evidence review

Table 2: Summary of studies included in the evidence review

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments
Chester 2018 [94] Prospective cohort	N=804 people with musculoskeletal shoulder pain (n followed up out of total 1030). Number of events: NA (continuous outcome). Duration of pain (mean, SD: 14 (28) months.	Multivariable linear regression: variables with statistically significant relationship with the outcome at the 10% level in simple linear regression models were entered in to multivariable model.	• Presence or absence of comorbid physical condition (number of additional health problems) • Physical activity at baseline (most strenuous exercise).	Confounders/other prognostic variables included in the review protocol: • Number of additional health problems • Frequency of pain medication • Most strenuous exercise. Other confounders adjusted for: • Reported pan intensity (severity of shoulder pain at rest, 0-10 numeric rating scale) at baseline • Comorbid psychiatric disorder (anxiety and depression in the last 7 days, unclear how measured) • Coping style (Pain self-efficacy questionnaire) • Patient expectation of change • Difference between passive and active abduction	Shoulder pain and disability index (time point not reported).	Outcome indirectness: includes disability elements Outcomes for prognostic variables were adjusted for other prognostic variables listed in the review protocol i.e. comorbid physical condition adjusted for frequency of pain medication and physical activity

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments
				• Change during scapular facilitation • Duration of symptoms • Paraesthesia • Employment status.		
Forssell 2017 [171] Prospective cohort	N=263 temporo-mandibular disorder pain in the previous month (n followed up out of total 399 enrolled) Number of events: 71 respondents reported clinically significant pain at 1 year Duration of pain (median, quartile range): time since onset 3 (1-10) years	Multivariable logistic regression analysis: all variables with p<0.1 in univariate models entered in to multivariable model.	• Presence or absence of comorbid physical condition (number of other pain conditions)	Confounders/other prognostic variables included in the review protocol: • Number of other pain conditions • Age (included in regression model but not significant) • Gender (included in regression model but not significant). Other confounders adjusted for: • Reported pain intensity (characteristic pain intensity measured by the Research Diagnostic Criteria for Temporomandibular Disorders questionnaire) • Comorbid psychiatric disorder (depression and somatization with pain items measured by the Symptom Checklist-90 Revised)	Clinically significant pain (Graded Chronic Pain Scale grade 1, 2 3 and 4) at 1 years	

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments
				• Coping style (catastrophizing measured by ruminative thoughts from Pain Catastrophising Scale; confidence in ability to control pain or to decrease pain measured by the Coping Strategies Questionnaire) • Time since onset • Pain-related disability • Number of disability days • Functional jaw limitations • SCL-90 somatization no pain • Sleep dysfunction • Pain-related worry • Anxiety (NRS) • Tension and stress • Perceived risk of chronicity • Number of healthcare visits • Pain intensity/dysfunction of other pains • General health • RAND-36 physical function subscale .		

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments
Helminen 2016 [226] Secondary analysis of an RCT (CBT intervention vs control).	N=111 patients with radiologically diagnosed knee osteoarthritis and associated pain symptoms Number of events: NA (continuous outcomes) Duration of pain (mean, SD): 7.8 (7) years	Multivariate linear mixed model	• Physical activity at baseline (exercise times per week).	Confounders/other prognostic variables included in the review protocol: • Age • Gender • Number of comorbidities. Other confounders adjusted for: • Coping style (Pain self-efficacy questionnaire; Tampa scale of kinesiophobia; Pain catastrophizing scale) • Comorbid psychiatric disorder (Beck depression inventory; Beck anxiety inventory) • Disease severity • Educational level • Body mass index • Work status • Marital status • Life satisfaction • Sense of coherence • Group randomisation • Time.	Pain subscale (0-100mm) of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) at 12 months. SF36 Finnish version physical and mental component summary scores.	
McIntosh 2011 [355]	N=2777 chronic low back pain patients	Multivariable logistic regression analysis	• Presence or absence of comorbid physical condition (comorbidity)	Confounders/other prognostic variables included in the review protocol	2 point change in VAS 0-10 pain intensity	

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments
Prospective cohort (rehabilitation programme)	Duration of pain (mean): 5.8 months			• Age • Gender	(time point not reported).	
Tseli 2020 [521]	N=2876 people with persistent back pain (n followed up out of total 6449 participating in a rehabilitation programme) Number of events: not reported Duration of pain (mean (SD)): 106.2 (107.7) months	Multivariable logistic regression analysis	• Pain diagnosis (widespread pain)	Confounders/other prognostic variables included in the review protocol: • Gender • Age • Number of pain sites Other confounders adjusted for: • Education level • Country of origin • Employment status • Beliefs of restored health • Pain intensity • Multidimensional pain inventory – pain interference • Multidimensional pain inventory – life control • Multidimensional pain inventory – overall activity • Multidimensional pain inventory – social support	Quality of life (difference of ≥3 on SF36 physical component) at 12 months after completion of the 10 week programme.	Indirect outcome: results for this prognostic factor only reported for physical component, not mental component.

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments
				• Hospital anxiety and depression scale – anxiety • Hospital anxiety and depression scale – depression • SF36 mental component • SF36 physical component • Pain duration • EQ5D		
Velly 2011 [552] Prospective cohort	N=480 people with a diagnosis of any temporomandibular joint disorder pain (n followed up out of total 570 enrolled) Number of events: NA (continuous outcome pain intensity) Duration of pain: not reported	Multivariable linear regression analysis	• Pain diagnosis (widespread pain)	Confounders/other prognostic variables included in the review protocol: • Widespread pain • Age • Gender. Other confounders adjusted for: • Reported pain intensity (0-100 numeric rating scale) • Comorbid psychiatric disorder (Beck Depression Inventory) • Coping style (catastrophizing measured by the Coping strategies questionnaire).	Pain intensity (0-100 numeric rating scale) at 18 months	

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments
Verkerk 2015 [559] Prospective cohort (multidisciplinary treatment)	N=1564 for 5 month outcomes, n=960 for 12 month outcomes chronic non-specific low back pain patients not recovering after primary/ secondary care (n followed up out of total 1760 enrolled). Number of events (30% improvement in pain intensity): 862 at 5 months, 578 at 12 months Duration of pain (mean, SD): 7.7 (8.8) years.	Multivariable logistic regression analysis	• Presence or absence of comorbid physical condition (comorbidity).	Confounders/other prognostic variables included in the review protocol: • Age • Gender. Other confounders adjusted for: • Reported pain intensity (visual analogue scale 0-100) at baseline • Comorbid psychiatric disorder (Symptom Checklist-90 item 9 – psychoneurosis) • Coping style (Tampa scale for kinesiophobia) • Education • Marital status • B200 isostation extension.	30% improvement in pain intensity at 12 months.	

Where studies have confounders / prognostic variables related to the protocol defined factors, these have been included in the absence of more direct data. The study definition is provided in this table for transparency.

See Appendix D: for full evidence tables.

2.3.4 Quality assessment of clinical studies included in the evidence review

Table 3: Clinical evidence summary: physical activity at baseline

Risk factor and outcome (population)	No. of studies	Effect (95% CI)	Imprecision	GRADE Quality
Most strenuous exercise (mild versus none) for predicting pain reduction (Shoulder pain and disability index at 6 months)	1	Adjusted ß coefficient −5.53 (−10.32 to −0.74)	None	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, indirectness
Most strenuous exercise (moderate versus none) for predicting pain reduction (Shoulder pain and disability index at 6 months)	1	Adjusted ß coefficient -8.98 (−13.86 to −4.11)	None	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, indirectness
Most strenuous exercise (strenuous versus none) for predicting pain reduction (Shoulder pain and disability index at 6 months)	1	Adjusted ß coefficient −6.82 (−12.17 to −1.47)	None	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, indirectness
Exercise (2 or more/week or 1 or less/week): for predicting pain reduction (Pain subscale (0-100mm) of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) at 12 months)	1	Adjusted ß coefficient 0.32 (-6.29 to 6.92)	Serious	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision
Exercise (2 or more/week or 1 or less/week) for predicting quality of life (SF36 Finnish version physical component summary scores at 12 months)	1	Adjusted ß coefficient 2.07 (-1.38 to 5.51)	Serious	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision
Exercise (2 or more/week or 1 or less/week) for predicting quality of life (SF36 Finnish version mental component summary scores at 12 months)	1	Adjusted ß coefficient 2.42 (-1.15 to 6)	Serious	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 or 2 increments because the majority of the evidence had indirect outcomes
3 Downgraded by one increment if the confidence interval crossed the null line

Table 4: Clinical evidence summary: presence or absence of comorbid physical condition

Risk factor and outcome (population)	No. of studies	Effect (95% CI)	Imprecision	GRADE Quality
Number of other conditions 0 versus >1) for predicting clinically significant pain (Graded Chronic Pain Scale grade 1, 2 3 and 4) at 12 months	1	Adjusted OR: 1.3 (0.86 to 1.96)	Serious	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision
Number of additional health problems (one versus none) for predicting shoulder pain and disability index at 6 months	1	Adjusted ß coefficient 3.52 (0.3 to 6.75)	None	⊕⊕⊖⊖ LOW1 due to risk of bias
Number of additional health problems (two versus none) for predicting shoulder pain and disability index at 6 months	1	Adjusted ß coefficient 6.62 (1.48 to 9.75)	None	⊕⊕⊖⊖ LOW1 due to risk of bias
Presence or absence of comorbid physical condition(s): for predicting 2 point change in VAS 0-10 pain intensity (Low back pain)	1	Adjusted OR 1.013 (0.963 to 1.065)	Serious	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision
Presence or absence of comorbid physical condition (co-morbidity yes/no for predicting 30% improvement in pain intensity at 12 months	1	Adjusted OR 0.76 (0.52 to 1.11)	Serious	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by one increment if the confidence interval crossed the null line

Table 5: Clinical evidence summary: Pain diagnosis

Risk factor and outcome (population)	No. of studies	Effect (95% CI)	Imprecision	GRADE Quality
Pain diagnosis (widespread pain yes/no) for predicting pain intensity (0-100)	1	Adjusted ß coefficient 2.88 (-0.83 to 6.58)	Serious	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision
Pain diagnosis (widespread pain compared to 0-2 regions) for predicting quality of life (difference of ≥3 on SF36 physical component)	1	Adjusted OR 0.69 (0.45-1.06)	Serious	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by one increment if the confidence interval crossed the null line
3 Downgraded by one increment for outcome indirectness

See Appendix F: for full GRADE tables.

2.4 Economic evidence

2.4.1 Included studies

No health economic studies were included.

2.4.2 Excluded studies

No relevant health economic studies were excluded due to assessment of limited applicability or methodological limitations.

See also the health economic study selection flow chart in Appendix G:.

2.5 Evidence statements

2.5.1 Clinical evidence statements

Physical activity at baseline

- Very low quality evidence from 1 study with a total of 804 participants showed that more strenuous physical activity at baseline predicted lower pain intensity at 6 months, but very low quality evidence from one study with a total of 111 participants showed that higher frequency physical activity at baseline did not predict pain intensity at 12 months.
- Very low quality evidence from one study with a total of 111 participants showed that physical activity at baseline did not predict quality of life at 12 months.

Presence or absence of comorbid physical condition

- Low quality evidence from 1 study with a total of 804 participants showed that presence of comorbid physical conditions predicted greater pain intensity at 6 months, but very low quality evidence from 3 studies with a total of 4000 participants showed that comorbid physical conditions did not predict pain intensity at 12 months.

Pain diagnosis

- Very low quality evidence from 1 study with a total of 480 participants showed that type of pain diagnosis (widespread pain) did not predict pain intensity at 18 months.
- Very low quality evidence from 1 study with a total of 2876 participants showed that type of pain diagnosis (widespread pain) did not predict change in quality of life at 12 months.

2.5.2 Health economic evidence statements

- No relevant economic evaluations were identified.

3 Psychological factors

3.1 Review question: What psychological factors may be barriers to successfully managing chronic pain?

3.2 PICO table

For full details see the review protocol in Appendix A:.

Table 6: PICO characteristics of review question

Population	People, aged 16 years and over, with chronic pain. *Pain that persists or recurs for longer than 3 months.*
Prognostic variable(s) under consideration	• Comorbid psychiatric disorder (including personality disorder) • Adverse childhood experience • Reported pain intensity • Substance addiction/dependence/misuse • Coping styles
Confounding factors	Studies not accounting for at least 2 key confounders (prognostic factors) in a multivariable analysis are excluded.
Outcome(s)	CRITICAL: • Health related quality of life (including meaningful activity) • Pain reduction
Study design	Prospective and retrospective cohort studies Case control studies if no cohort studies are identified Exclusions: • Non-English language studies • Studies not accounting for at least 2 key confounders (prognostic factors) in a multivariable analysis

3.3 Clinical evidence

3.3.1 Included studies

Nineteen studies were included in the review;[2, 13, 52, 94, 118, 123, 144, 145, 171, 364, 380, 411, 425, 451, 515, 538, 552, 559, 568, 585] these are summarised in **Table 7** below. Evidence from these studies is summarised in the clinical evidence summary tables below (**Table 8**, **Table 9** and **Table 10**). Outcomes were reported as adjusted odds ratios, (unstandardised) beta coefficients and standardised beta coefficients. Beta coefficient values represent the change in the dependent variable (outcome) for every one unit change in the independent variable (prognostic factor). Standardised beta coefficients use standard deviations as their units, so standardised beta coefficient values represent the number of standard deviations the dependent variable (outcome) change by for every one standard deviation change in the independent variable (prognostic factor).

No relevant clinical studies investigating the effects of adverse childhood experience or substance addiction/dependence/misuse on successful pain management were identified.

See also the study selection flow chart in Appendix C:, study evidence tables in Appendix D:, forest plots in Appendix E: and GRADE tables in Appendix F.

3.3.2 Excluded studies

See the excluded studies list in Appendix I.

3.3.3 Summary of clinical studies included in the evidence review

Table 7: Summary of studies included in the evidence review

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments
Adnan 2017 [2] Retrospective cohort	n=412 chronic low back pain patients recruited from an exercise-based rehabilitation program (from a total sample of 565 with acute and chronic pain). Number of events = 121 with favourable outcome. Duration of pain not stated (other than >14 weeks).	Logistic regression: all factors tested one at a time in a univariate logistic regression, multiple model included all statistically significant (p <0.25) variables.	• Reported pain intensity (0-10 numeric pain rating scale for back pain at baseline) • Comorbid psychiatric disorder (Beck depression index 0-63).	Other prognostic variables included in the review protocol: • Reported pain intensity (NPRS) at baseline • Comorbid psychiatric disorder (Beck depression index) • Coping styles (Tampa scale for kinesiophobia) – included in univariate analysis but not significant. Other confounders adjusted for: • Age • Disability (Oswestry disability index).	Favourable outcome: defined as 30% reduction from baseline in both the Numeric Pain Rating Scale and the Oswestry Disability Index (follow up time not reported)	Those who had other comorbidities were excluded Outcome indirectness: included disability element Outcomes for prognostic variables were adjusted for other prognostic variables listed in the review protocol i.e. pain intensity adjusted for comorbid psychiatric disorder and coping style.
Allaire 2018 [13] Prospective cohort (interdisciplinary interventions)	N=284 women referred to a centre for pelvic pain and endometriosis (n followed up out of the total sample of 525)	Logistic regression: ordinal logistic regression used to identify factors significantly associated with	• Reported pain intensity (chronic pelvic pain severity 0-10 numeric rating scale at baseline) • Coping style (pain catastrophizing scale).	Other prognostic variables included in the review protocol: • Reported pain intensity (NRS) at baseline • Comorbid psychiatric disorder (Patient health	Increase in chronic pelvic pain severity (0-10) categorised as none-mild 0-3, moderate 4-6 and severe 7-10 at 1 year	Outcomes for prognostic variables were adjusted for other prognostic variables listed in the review protocol i.e. pain intensity

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments
	Number of events= not reported Duration of pain (median, interquartile range): 13 (5.2-21) years.	the outcome (p<0.05), significant factors entered in to the multivariable ordinal logistic regression model.		questionnaire; Generalised anxiety disorder -7) – included in initial regression analysis but not significant • Coping style (Pain catastrophizing scale). Other confounders adjusted for: • Abdominal wall pain • Age • Re-referral • History of sexual assault • Surgery at center.		adjusted for comorbid psychiatric disorder and coping style.
Boonstra 2015 [52] Prospective cohort (CBT)	N=230 chronic musculoskeletal pain Number of events: NA (continuous outcome) Duration of pain (mean, SD): outpatient 4.9 (5.3), inpatient 5.9 (5.8) years.	Multiple linear regression analysis: variables with p<0.2 in univariate analyses identified as potential predictors and clustered in to blocks, variables with p values <0.2 in block analysis entered in to next model, variables with p	• Reported pain intensity (pain subscale of the SF36) at baseline.	Other prognostic variables included in the review protocol: • Coping style (active coping and helplessness composite scores measured by Coping with pain questionnaire; Tampa scale of kinesiophobia) – not significant in univariate analysis so not included in final model • Comorbid psychiatric disorder (psychological distress measured by	Pain subscale of the SF36 (time point not reported).	Study reports two other sub scales of SF36 as outcomes – not validated measures of quality of life individually.

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments
		values <0.05 entered in to final model		Symptom checklist-90 revised) – not included in final model. Other confounders adjusted for: • Work status.		
Chester 2018 [94] Prospective cohort (physiotherapy)	N=804 people with musculoskeletal shoulder pain (n followed up out of total 1030) Number of events: NA (continuous outcome) Duration of pain (mean, SD: 14 (28) months	Multivariable linear regression: variables with statistically significant relationship with the outcome at the 10% level in simple linear regression models were entered in to multivariable model.	• Reported pain intensity (severity of shoulder pain at rest, 0-10 numeric rating scale) at baseline • Comorbid psychiatric disorder (anxiety and depression in the last 7 days, unclear how measured) • Coping style (Pain self-efficacy questionnaire).	Other prognostic variables included in the review protocol: • Reported pain intensity (severity of shoulder pain at rest, 0-10 numeric rating scale) at baseline • Comorbid psychiatric disorder (anxiety and depression in the last 7 days, unclear how measured) • Coping style (Pain self-efficacy questionnaire). Other confounders adjusted for: • Patient expectation of change • Number of additional health problems • Frequency of pain medication • Most strenuous exercise	Shoulder pain and disability index (time point not reported).	Outcome indirectness: includes disability elements. Outcomes for prognostic variables were adjusted for other prognostic variables listed in the review protocol i.e. pain intensity adjusted for comorbid psychiatric disorder and coping style.

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments
				• Difference between passive and active abduction • Change during scapular facilitation • Duration of symptoms • Paraesthesia • Employment status.		
de Rooij 2013 [118] Prospective cohort (multidisciplinary intervention)	N=120 with chronic widespread pain (n followed up out of a total of 138 who entered the study) Number of events = not applicable (continuous outcome) Duration of pain: not reported	Multiple linear regression: explorative univariate regression analysis identified potential predictors for the multivariate analysis (p<0.2).	• Reported pain intensity (numeric rating scale 0-10 at baseline).	Other prognostic variables included in the review protocol: • Comorbid psychiatric disorder (Hospital anxiety and depression scale, anxiety subscale). Depression (Beck depression inventory) and psychological functioning (symptom checklist 90) included in univariate analysis but not significant • Coping style (General self-efficacy scale, Tampa scale for kinesiophobia, avoidance behaviour measured by Pain coping inventory and catastrophizing measured by Coping scale questionnaire) – included in univariate	Pain intensity (numeric rating scale 0-10) at 6 months.	

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments
				analysis but not significant. Other confounders adjusted for: • Personal control (illness perception questionnaire) • Consequence (illness perception questionnaire) • Fatigue (fibromyalgia impact questionnaire) • Gender • Education.		
Demarchi 2019 [123] Prospective cohort	N=92 with chronic non-specific low back pain (n followed up out of total 102 enrolled) Number of events: not applicable (continuous outcome) Duration of pain (median, interquartile rage): 24 (6-60) months.	Multivariate linear regression: univariate regression analysis identified potential predictors for the multivariate analysis (p<0.25).	• Reported pain intensity at baseline (0-10 numeric rating scale) • Comorbid psychiatric disorder (Beck depression inventory).	Other prognostic variables included in the review protocol: • Reported pain intensity (0-10 numeric rating scale) at baseline • Comorbid psychiatric disorder (Beck depression inventory) • Coping style (fear of movement measured by Tampa scale for Kinesiophobia). Other confounders adjusted for: • Age	Pain intensity (NRS 0-10) at 6 months.	Outcomes for prognostic variables were adjusted for other prognostic variables listed in the review protocol i.e. pain intensity adjusted for comorbid psychiatric disorder and coping style.

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments
				• Disability (Roland Morris disability questionnaire) • Sex • BMI • Perceived physical overload.		
Dunn 2011 [144] Prospective cohort	N=389 with low back pain (n followed up out of total 776 consenting to follow up) Number of events: 17.7% had chronic pain grade IV at 12 months Duration of pain: 2/5 had pain for ≥3 years, among those with <3 years 1/3 reported that pain had started in the previous 3 months.	Cox regression: factors that had a statistically significant association with outcome were then adjusted for potential confounders.	• Reported pain intensity at baseline (mean of 3 0-10 numeric rating scales for least, usual and current low back pain intensity; scores of ≥5 defined as high) • Comorbid psychiatric disorder (probable cases of anxiety/depression defined as scores of ≥11 on the Hospital anxiety and depression scale) • Coping style (catastrophising measured by the Coping strategies questionnaire; fear-avoidance beliefs measured by Tampa scale for kinesiophobia).	Other prognostic variables included in the review protocol: • Reported pain intensity at baseline (mean of 3 0-10 numeric rating scales for least, usual and current low back pain intensity; scores of ≥5 defined as high) • Comorbid psychiatric disorder (probable cases of anxiety/depression defined as scores of ≥11 on the Hospital anxiety and depression scale) • Coping style (catastrophising measured by the Coping strategies questionnaire; fear-avoidance beliefs measured by Tampa scale for kinesiophobia)	Chronic pain grade IV (highly disabling and severely limiting low back pain) at 12 months	Outcomes for prognostic variables were adjusted for other prognostic variables listed in the review protocol i.e. pain intensity adjusted for comorbid psychiatric disorder and coping style.

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments
				Other confounders adjusted for: • Less education • Unemployment • Dissatisfaction with work status • Work absence • Long duration • High functional disability • Leg pain • Distal leg pain • Upper body pain • Bothersomeness • Poor self-rated health • Low vitality.		
Dybowski 2018 [145] Prospective cohort	N=109 people with chronic pelvic pain syndrome (n followed out of total 211 enrolled) Number of events: 44 patients reported a clinically perceptible change of 6 or more points in the NIH-CPSI	Ordinary least squares linear regression	• Reported pain intensity (National institutes of health chronic prostatitis symptom index pain scale) at baseline • Comorbid psychiatric disorder (Patient health questionnaire anxiety and depression scale) • Coping style (pain catastrophizing scale).	Other prognostic variables included in the review protocol: • Reported pain intensity (National institutes of health chronic prostatitis symptom index pain scale) at baseline • Comorbid psychiatric disorder (Patient health questionnaire anxiety and depression scale) • Coping style (pain catastrophizing scale).	Pain symptoms and quality of life measured by National institutes of health chronic prostatitis symptom index (modified version with female homologs) at 11 months.	Outcomes for prognostic variables were adjusted for other prognostic variables listed in the review protocol i.e. pain intensity adjusted for comorbid psychiatric disorder and coping style.

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments
	from baseline to follow up Duration of pain (mean, SD): 5.7 (6.9) years.			Other confounders adjusted for: • Age • Sex • Pain duration • NIH-CPSI urinary symptoms • NIH-CPSI quality of life • Health anxiety • Social support.		
Forssell 2017 [171] Prospective cohort	N=263 temporo-mandibular disorder pain in the previous month (n followed up out of total 399 enrolled) Number of events: 71 respondents reported clinically significant pain at 1 year Duration of pain (median, quartile range): time since onset 3 (1-10) years.	Multivariable logistic regression analysis: all variables with p<0.1 in univariate models entered in to multivariable model.	• Reported pain intensity at baseline (characteristic pain intensity measured by the Research Diagnostic Criteria for Temporomandibular Disorders questionnaire) • Comorbid psychiatric disorder (depression and somatization with pain items measured by the Symptom Checklist-90 Revised) • Coping style (catastrophizing measured by ruminative thoughts from Pain Catastrophising Scale; confidence in ability to control pain or to decrease pain	Other prognostic variables included in the review protocol: • Reported pain intensity at baseline (characteristic pain intensity measured by the Research Diagnostic Criteria for Temporomandibular Disorders questionnaire) • Comorbid psychiatric disorder (depression and somatization with pain items measured by the Symptom Checklist-90 Revised) • Coping style (catastrophizing measured by ruminative thoughts from Pain Catastrophising Scale;	Clinically significant pain (Graded Chronic Pain Scale grade 1, 2 3 and 4) at 1 year.	Outcomes for prognostic variables were adjusted for other prognostic variables listed in the review protocol i.e. pain intensity adjusted for comorbid psychiatric disorder and coping style.

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments
			measured by the Coping Strategies Questionnaire).	confidence in ability to control pain or to decrease pain measured by the Coping Strategies Questionnaire). Other confounders adjusted for: • Time since onset • Pain-related disability • Number of disability days • Functional jaw limitations • SCL-90 somatization no pain • Sleep dysfunction • Pain-related worry • Anxiety (NRS) • Tension and stress • Perceived risk of chronicity • Number of healthcare visits • Number of other pain conditions • Pain intensity/dysfunction of other pains • General health • RAND-36 physical function subscale.		

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments
Michaelson 2004 [364] Prospective cohort (multimodal programme)	N=235 patients with chronic low back (n=149) and neck (n=106) pain (n followed up out of total 315 enrolled) Number of events: not reported Duration of pain (mean, SD): 106 (91) months	Logistic regression: models built by adding one variable at a time with the criteria of keeping/removing variable as a result of the corresponding p value.	• Reported pain intensity at baseline (average pain intensity over the last 7 days 0-100mm visual analogue scale) • Coping style (Optimism index)	Other prognostic variables included in the review protocol: • Reported pain intensity at baseline (average pain intensity over the last 7 days 0-100mm visual analogue scale) • Coping style (Optimism index) • Comorbid psychiatric disorder (somatic and psychosomatic complaints measured by a 29-item questionnaire on general health) – excluded from model as not significant. Other confounders adjusted for: • Multidimensional pain inventory pain severity • Multidimensional pain inventory affective distress • Sociability index • Endurance index • Age	Reduced pain (reduction in pain intensity ≥25mm on a 0-100mm visual analogue scale from baseline) at 12 months.	Psychiatric diagnoses excluded Outcomes for prognostic variables were adjusted for other prognostic variables listed in the review protocol i.e. pain intensity adjusted for comorbid psychiatric disorder and coping style.
Naliboff 2017 [380]	N=397 interstitial cystitis/bladder pain syndrome	Exploratory multivariable stepwise	• Reported pain intensity (pain severity) at baseline	Other prognostic variables included in the review protocol:	Improvement in pain severity (functional clustering	

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments
Prospective cohort	or chronic prostatitis/ chronic pelvic pain syndrome Number of events: 87 were classified as improved Duration of pain (mean, SD): males 8.1 (10.9), females 9.1 (10.3) years	ordinal logistic regression		• Comorbid psychiatric disorder (Hospital Anxiety and Depression scale) – included in univariate analysis but not significant • Coping style (catastrophizing measured by Coping strategies questionnaire) – included in univariate analysis but not significant. Other confounders adjusted for: • Age • SF12 physical component.	procedure applied to biweekly severity scores to classify overall symptom trajectory as worsening, stable or improving) (time point not reported).	
Rabey 2017 [425] Prospective cohort	N=266 people with axial chronic low back pain (n followed up out of total 294 enrolled) Number of events: NA (continuous outcome pain intensity) Duration of pain (median,	Multivariable regression models: variables with univariate associations (p<0.1) were considered candidate variables and selected for final multivariable regression models using a	• Reported pain intensity (11-point numeric rating scale) at baseline	Other prognostic variables included in the review protocol: • Comorbid psychiatric disorder (Depression Anxiety Stress Scale DASS-21) – included in univariate analysis but not significant • Coping style (Fear avoidance beliefs questionnaire; Pain Catastrophising scale; Pain self-efficacy questionnaire; Chronic	Pain intensity (numeric rating scale 0-10) at 1 year	

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments
	interquartile range): 120 (42-240) months	backwards stepwise method combined with purposeful selection of covariates, variables significant at p<0.05 were included in the final multivariable models.		pain acceptance questionnaire Avoidance endurance questionnaire) – included in univariable analysis but not significant. Other confounders adjusted for: • Exercise as intervention • Years in education • Multidimensional pain inventory punishing subscale score.		
Rollman 2013 [451] Prospective cohort	N=100 patients with temporo-mandibular disorder pain (n followed up out of total 129 enrolled) Number of events: 50 patients had improved at 6 months Duration of pain: 0-3 months 9%, 3-6 months 20%, 6-12 months 14%, 1-3 years 25%, 3-	Multiple logistic regression analysis: predictors with at least moderate association with improvement (p≤0.1) in univariate analysis were entered in to multiple regression analysis, then the variable with the weakest association was removed until all variables	• Coping style (pain coping measured by the Pain coping and cognition list).	Other prognostic variables included in the review protocol: • Reported pain intensity at baseline (Characteristic pain intensity, part of the graded chronic pain scale) – included in univariate analysis but not significant • Comorbid psychiatric disorder (depression, anxiety and somatisation measured by the Symptom checklist-90) – included in univariate analysis but not significant.	Improvement (based on the question: 'did the pain in your face that you reported half a year ago…': 'completely disappear', 'largely decrease', 'slightly decrease', 'remain the same', 'increase slightly' or 'increase a lot?' Those reporting 'completely disappear' or 'largely	

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments
	10 years 15%, >10 years 17%	showed a p≤0.05.		Other confounders adjusted for: • Pain duration • Number of care practitioners for TMD-pain complaints • Hindrance on function.	decrease' were classified as improved) at 6 months.	
Trinderup 2018 [515] Secondary analysis of an RCT(12 week work-orientated multidisciplinary intervention vs. usual multidisciplinary care)	N=284 chronic low back pain (n followed up out of 559 enrolled) Number of events: 191/363 responders had an unsuccessful outcome Duration of pain <12 months, n (%): 273 (51.41)	Secondary analysis of an RCT (12 week work-orientated multidisciplinary intervention vs. usual multidisciplinary care). Multiple logistic regression analyses: univariate regression analysis identified potential predictors for the multivariate analysis (p<0.2)	• Reported pain intensity at baseline (Back pain questionnaire included 3 separate 11-point numeric rating scales comprising pain at the moment, worst pain within the last 2 weeks and average pain within the last 2 weeks: high/low 0-30) • Coping style (High fear-avoidance beliefs about work measured by Fear Avoidance Beliefs Questionnaire: low, 0–29; high, 30–42)	Other prognostic variables included in the review protocol: • Reported pain intensity at baseline (Back pain questionnaire included 3 separate 11-point numeric rating scales comprising pain at the moment, worst pain within the last 2 weeks and average pain within the last 2 weeks: high/low 0-30) • Coping style (High fear-avoidance beliefs about work measured by Fear Avoidance Beliefs Questionnaire: low, 0–29; high, 30–42) • Comorbid psychiatric disorder (Depression (Symptom Checklist-90-Revised); Anxiety (Symptom Checklist-90-Revised))	Unsuccessful outcome (reduction of less than 6 points on the Numeric Pain Rating Scale) at 12 months.	Outcomes for prognostic variables were adjusted for other prognostic variables listed in the review protocol i.e. pain intensity adjusted for comorbid psychiatric disorder and coping style.

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments
				Other confounders adjusted for: • Smoking • Disability (Roland Morris Disability Questionnaire) • Sex • Age • BMI • Education • Alcohol consumption • Physical activity level • Sick leave • Duration of sick leave • Employment • Compensation case • Physical job demands • Physical health • Mental health • Age at first episode of pain • Family history of low back pain • Fear avoidance beliefs physical activity • Group intervention.		
van der Hulst 2008 [538] Secondary analysis of an	N=163 non-specific chronic low back pain Number of events: NA	Multivariate linear regression analysis	• Reported pain intensity (visual analogue scale 0-10) at baseline • Comorbid psychiatric disorder (Symptom	Other prognostic variables included in the review protocol: • Reported pain intensity (visual analogue scale 0-10) at baseline	Difference in SF36 mental and physical component scale scores from baseline to	Outcomes for prognostic variables were adjusted for other prognostic variables listed in

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments
RCT (back rehabilitation programme vs. waiting list)	(continuous outcome) Duration of pain (median, range): rehab programme 72 (380), waiting list 48 (559) months		checklist questionnaire-90 depression subscale) • Coping style (Tampa scale of kinesiophobia; Multidimensional pain inventory classification adaptive coper, average, anomalous/ dysfunction, distressed).	• Comorbid psychiatric disorder (Symptom checklist questionnaire-90 depression subscale) • Coping style (Tampa scale of kinesiophobia). Other confounders adjusted for: • Treatment • Work status • Multidimensional pain inventory • Sick leave.	4 weeks after treatment.	the review protocol i.e. pain intensity adjusted for comorbid psychiatric disorder and coping style.
Velly 2011 [552] Prospective cohort	N=480 people with a diagnosis of any temporo-mandibular joint disorder pain (n followed up out of total 570 enrolled) Number of events: NA (continuous outcome pain intensity) Duration of pain: not reported	Multivariable linear regression analysis	• Reported pain intensity (0-100 numeric rating scale) at baseline • Comorbid psychiatric disorder (Beck Depression Inventory) • Coping style (catastrophizing measured by the Coping strategies questionnaire).	Other prognostic variables included in the review protocol: • Reported pain intensity (0-100 numeric rating scale) at baseline • Comorbid psychiatric disorder (Beck Depression Inventory) • Coping style (catastrophizing measured by the Coping strategies questionnaire). Other confounders adjusted for: • Widespread pain	Pain intensity (0-100 numeric rating scale) at 18 months.	Those with 'primary psychiatric disease' (uncontrolled schizophrenia, psychoses, or other serious disorders that interfere with ability to consent and participate) or who consumed >3 alcoholic drinks per day were excluded Outcomes for prognostic variables were adjusted for other

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments
				• Age • Gender.		prognostic variables listed in the review protocol i.e. pain intensity adjusted for comorbid psychiatric disorder and coping style.
Verkerk 2015 [559] Prospective cohort (multidisciplinary treatment)	N=1564 for 5 month outcomes, n=960 for 12 month outcomes chronic non-specific low back pain patients not recovering after primary/ secondary care (n followed up out of total 1760 enrolled) Number of events (30% improvement in pain intensity): 862 at 5 months, 578 at 12 months Duration of pain (mean, SD): 7.7 (8.8) years	Multivariable logistic regression analysis	• Reported pain intensity (visual analogue scale 0-100) at baseline • Comorbid psychiatric disorder (Symptom Checklist-90 item 9 – psychoneurosis) • Coping style (Tampa scale for kinesiophobia).	Other prognostic variables included in the review protocol: • Reported pain intensity (visual analogue scale 0-100) at baseline • Comorbid psychiatric disorder (Symptom Checklist-90 item 9 – psychoneurosis) • Coping style (Tampa scale for kinesiophobia) Other confounders adjusted for: • Age • Gender • Education • Marital status • B200 isostation extension.	30% improvement in pain intensity at 5 months (SCL-90) and 12 months (pain intensity and kinesiophobia).	Outcomes for prognostic variables were adjusted for other prognostic variables listed in the review protocol i.e. pain intensity adjusted for comorbid psychiatric disorder and coping style.

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments
Weiner 2013 [568] Secondary analysis of an RCT (periosteal stimulation therapy vs. control; all arms included in analysis).	N=190 people with knee osteoarthritis Number of events: NA (continuous outcome) Duration of pain (mean, SD): PST + PST 5.7 (6.4), PST + control 6.2 (6.8), control 7.2 (8.3) years	Linear mixed models and generalised estimating equations	• Reported pain intensity (Western Ontario and McMaster Universities Osteoarthritis Index pain scale) at baseline • Comorbid psychiatric disorder (Centre for Epidemiological studies- depression) • Coping style (catastrophizing measured by coping strategies questionnaire; pain, function and other symptoms self-efficacy measured by Arthritis self-efficacy scale).	Other prognostic variables included in the review protocol: • Reported pain intensity (Western Ontario and McMaster Universities Osteoarthritis Index pain scale) at baseline • Comorbid psychiatric disorder (Centre for Epidemiological studies- depression) • Coping style (catastrophizing measured by coping strategies questionnaire; pain, function and other symptoms self-efficacy measured by Arthritis self-efficacy scale). Other confounders adjusted for: • Age • Sex • Race • Body mass index • WOMAC difficulty performing daily activities • WOMAC stiffness • Short physical performance battery	Western Ontario and McMaster Universities Osteoarthritis Index at 9 months (6 months after end of treatment).	Outcomes for prognostic variables were adjusted for other prognostic variables listed in the review protocol i.e. pain intensity adjusted for comorbid psychiatric disorder and coping style.

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments
				• Duration of pain • Kellgren-Lawrence score.		
Wong 2015 [585] Prospective cohort	N=184 at 3 months and 178 at 6 months chronic non-malignant musculoskeletal pain (n followed up out of total 226 enrolled) Number of events: Duration of pain (mean, SD): 7.19 (6.15) years	Multivariate linear mixed effects model.	• Reported pain intensity (measured by Chronic pain grade questionnaire pain intensity scale) at baseline • Comorbid psychiatric disorder (Hospital anxiety and depression scale depression sub scale) • Coping style (rumination, magnification and helplessness measured by the Pain catastrophizing scale; Tampa scale for Kinesiophobia).	Other prognostic variables included in the review protocol: • Pain intensity at baseline (measured by Chronic pain grade questionnaire pain intensity scale) • Comorbid psychiatric disorder (Hospital anxiety and depression scale depression sub scale) • Coping style (rumination, magnification and helplessness measured by the Pain catastrophizing scale; Tampa scale for Kinesiophobia). Other confounders adjusted for: • Time • Age • Sex • Marital status • Education • Occupation • Religion	Medical Outcomes study 12-item short form health survey (QoL-physical and QoL-mental component scores) at 6 months.	Outcomes for prognostic variables were adjusted for other prognostic variables listed in the review protocol i.e. pain intensity adjusted for comorbid psychiatric disorder and coping style.

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments
				• Family monthly income • Number of pain sites • Pain duration • Medical adherence • Treatment satisfaction.		

Where studies have confounders / prognostic variables related to the protocol defined factors, these have been included in the absence of more direct data. The study definition is provided in this table for transparency.

See Appendix D: for full evidence tables.

3.3.4 Quality assessment of clinical studies included in the evidence review

Table 8: Clinical evidence summary: reported pain intensity at baseline

Risk factor and outcome	No. of studies	Effect (95% CI)	Imprecision	GRADE Quality
Reported back pain intensity (0-10) at baseline for predicting 30% reduction from baseline in NRS and ODI (time point not reported)	1	Adjusted OR 1.19 (1.06 to 1.33)	No serious imprecision	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, indirectness
Reported chronic pelvic pain severity (0-10) at baseline for predicting increase in chronic pelvic pain severity at 1 year	1	Adjusted OR 1.19 (1.09 to 1.3)	No serious imprecision	⊕⊕⊖⊖ LOW1 due to risk of bias
Reported pain intensity (pain subscale of the SF36) at baseline for predicting change in SF36 pain sub scale (time point not reported)	1	unstandardized ß coefficient -1.36 (-1.5 to -1.22)	No serious imprecision	⊕⊕⊖⊖ LOW1 due to risk of bias
Reported pain intensity (shoulder pain at rest, 0-10) at baseline for predicting Shoulder pain and disability index score at 6 months	1	β coefficient 1.89 (1.26 to 2.51)	No serious imprecision	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, indirectness
Reported pain intensity (0-10) at baseline for predicting pain intensity (numeric rating scale 0-10) at 6 months	1	B (unstandardized regression coefficient) -0.53 (-0.67 to -0.39)	No serious imprecision	⊕⊕⊕⊖ MODERATE1

Risk factor and outcome	No. of studies	Effect (95% CI)	Imprecision	GRADE Quality
				due to risk of bias
Reported pain intensity (0-10) at baseline for predicting pain intensity (numeric rating scale 0-10) at 6 months	1	ß coefficient 0.14 (95% CI -0.2-0.49)	Serious imprecision	⊕⊕⊖⊖ LOW1,3 due to risk of bias, imprecision
Reported pain intensity (0-10; scores of ≥5 defined as high) at baseline for predicting Chronic pain grade IV at 12 months	1	Adjusted RR 4.13 (1.73 to 9.86)	No serious imprecision	⊕⊕⊖⊖ LOW1 due to risk of bias
Reported pain intensity (National institutes of health chronic prostatitis symptom index pain scale) at baseline for predicting pain symptoms measured by National institutes of health chronic prostatitis symptom index at 11 months	1	unstandardized regression coefficient B 0.38 (0.13 to 0.64)	No serious imprecision	⊕⊕⊖⊖ LOW1 due to risk of bias
Reported pain intensity (National institutes of health chronic prostatitis symptom index pain scale) at baseline for predicting quality of life measured by National institutes of health chronic prostatitis symptom index at 11 months	1	unstandardized regression coefficient B -0.11 (-0.29 to 0.07)	Serious imprecision	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision
Reported pain intensity (Research Diagnostic Criteria for Temporomandibular Disorders questionnaire) at baseline for predicting clinically significant pain (Graded chronic pain scale 1,2,3,4) at 12 months	1	Adjusted OR 1.1 (0.84 to 1.44)	Serious imprecision	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision
Reported low back pain intensity (0-100mm VAS) at baseline for predicting ≥25mm reduction from baseline at 12 months	1	Adjusted OR 1.06 (1.03 to 1.09)	No serious imprecision	⊕⊕⊖⊖ LOW1 due to risk of bias
Reported neck pain intensity (0-100mm VAS) at baseline for predicting ≥25mm reduction from baseline at 12 months	1	Adjusted OR 1.05 (1.01 to 1.09)	No serious imprecision	⊕⊕⊖⊖ LOW1 due to risk of bias
Reported pain intensity (pain severity) at baseline for predicting improvement in pain severity (time point not reported)	1	Adjusted OR 1.18 (1.12 to 1.25)	No serious imprecision	⊕⊕⊖⊖ LOW1 due to risk of bias
Reported pain intensity (0-10) at baseline for predicting pain intensity (0-10) at 12 months	1	unstandardized coefficient 0.32 (0.19 to 0.45)	No serious imprecision	⊕⊕⊕⊖ MODERATE1 due to risk of bias

Risk factor and outcome	No. of studies	Effect (95% CI)	Imprecision	GRADE Quality
Reported pain intensity (Low score on Back pain questionnaire) at baseline for predicting pain intensity (unsuccessful outcome: reduction of less than 6 points) at 12 months	1	Adjusted OR 1.14 (1.08-1.2)	No serious imprecision	⊕⊕⊖⊖ LOW1 due to risk of bias
Reported pain intensity (0-10) at baseline for predicting difference in SF36 physical component scale scores from baseline at 4 weeks post treatment	1	unstandardized ß coefficient 0.2 (-0.53 to 0.93)	Serious imprecision	⊕⊕⊖⊖ LOW1,3 due to risk of bias, imprecision
Reported pain intensity (0-10) at baseline for predicting difference in SF36 mental component scale scores from baseline at 4 weeks post treatment	1	unstandardized ß coefficient -0.13 (-2.45 to 2.37)	Serious imprecision	⊕⊕⊖⊖ LOW1,3 due to risk of bias, imprecision
Reported pain intensity (0-100) at baseline for predicting pain intensity (0-100) at 18 months	1	ß coefficient 0.39 (0.31 to 0.46)	No serious imprecision	⊕⊕⊖⊖ LOW1 due to risk of bias
Reported pain intensity (0-100) at baseline for predicting 30% improvement in pain intensity from baseline at 12 months	1	Adjusted OR 1.01 (1 to 1.02)	No serious imprecision	⊕⊕⊖⊖ LOW1 due to risk of bias
Reported pain intensity (Western Ontario and McMaster Universities Osteoarthritis Index pain scale) at baseline for predicting Western Ontario and McMaster Universities Osteoarthritis Index at 9 months	1	ß coefficient -0.68 (-0.81 to -0.55)	No serious imprecision	⊕⊕⊖⊖ LOW1 due to risk of bias
Reported pain intensity (Chronic pain grade questionnaire pain intensity scale) at baseline for predicting Medical Outcomes study 12-item short form health survey (QoL-physical component score) at 6 months	1	standardised ß coefficient 0.03 (-0.07 to 0.13)	Serious imprecision	⊕⊕⊖⊖ LOW1,3 due to risk of bias, imprecision
Reported pain intensity (Chronic pain grade questionnaire pain intensity scale) at baseline for predicting Medical Outcomes study 12-item short form health survey (QoL-mental component score) at 6 months	1	standardised ß coefficient 0.12 (0.02 to 0.23)	No serious imprecision	⊕⊕⊕⊖ MODERATE1 due to risk of bias

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 or 2 increments because the majority of the evidence had indirect outcomes
3 Downgraded by 1 increment if the confidence interval crossed the null line

Table 9: Clinical evidence summary: comorbid psychiatric disorder

Risk factor and outcome	No. of studies	Effect (95% CI)	Imprecision	GRADE Quality
Beck depression index (incremental increase) for predicting 30% reduction from baseline in NRS and ODI (time point not reported)	1	Adjusted OR 0.96 (0.9 to 0.97)	No serious imprecision	⊕⊕⊖⊖ LOW1,2 due to risk of bias, indirectness
Moderate anxiety/depression in the last 7 days (unclear how measured) at baseline for predicting Shoulder pain and disability index at 6 months	1	ß coefficient 2.19 (-0.99 to 5.37)	Serious imprecision	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision
Extreme anxiety/depression in the last 7 days (unclear how measured) at baseline for predicting Shoulder pain and disability index	1	ß coefficient 12.02 (1.49 to 22.56)	No serious imprecision	⊕⊕⊖⊖ LOW1 due to risk of bias
Beck Depression Inventory at baseline for predicting pain intensity (NRS 0-10) at 6 months	1	ß coefficient 0.09 (95% CI 0.02-0.16)	No serious imprecision	⊕⊕⊕⊖ MODERATE1 due to risk of bias
Probable cases of anxiety (≥11 on the Hospital anxiety and depression scale) for predicting Chronic pain grade IV at 12 months	1	Adjusted RR 1.84 (1.05 to 3.22)	No serious imprecision	⊕⊕⊖⊖ LOW1 due to risk of bias
Probable cases of depression (≥11 on the Hospital anxiety and depression scale) for predicting Chronic pain grade IV at 12 months	1	Adjusted RR 1.53 (0.9 to 2.6)	Serious imprecision	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision
Patient health questionnaire anxiety and depression scale for predicting pain symptoms measured by National institutes of health chronic prostatitis symptom index at 11 months	1	Unstandardized regression coefficient B 0.14 (0.04 to 0.24)	No serious imprecision	⊕⊕⊖⊖ LOW1 due to risk of bias
Patient health questionnaire anxiety and depression scale for predicting quality of life measured by National institutes of health chronic prostatitis symptom index at 11 months	1	Unstandardized regression coefficient B 0.09 (0.01 to 0.17)	No serious imprecision	⊕⊕⊖⊖ LOW1 due to risk of bias
Depression (Symptom Checklist-90 Revised) for predicting clinically significant pain (Graded chronic pain scale 1,2,3,4) at 12 months	1	Adjusted OR 0.36 (0.11 to 1.18)	Serious imprecision	⊕⊖⊖⊖ VERY LOW1,3

Risk factor and outcome	No. of studies	Effect (95% CI)	Imprecision	GRADE Quality
				due to risk of bias, imprecision
Somatization (Symptom Checklist-90 Revised) for predicting clinically significant pain (Graded chronic pain scale 1,2,3,4) at 12 months	1	Adjusted OR 0.21 (0.02 to 2.21)	Serious imprecision	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision
Somatic and psychosomatic complaints (more vs. fewer) measured by a 29-item questionnaire on general health for predicting ≥25mm pain reduction on 0-100mm VAS from baseline at 12 months	1	Adjusted OR 0.92 (0.87 to 0.97)	No serious imprecision	⊕⊕⊖⊖ LOW1 due to risk of bias
Symptom checklist questionnaire-90 depression subscale for predicting difference in SF36 physical component scale scores from baseline at 4 weeks post treatment	1	Unstandardized ß coefficient 0.03 (-0.17 to 0.23)	Serious imprecision	⊕⊕⊖⊖ LOW1,3 due to risk of bias, imprecision
Symptom checklist questionnaire-90 depression subscale for predicting difference in SF36 mental component scale scores from baseline at 4 weeks post treatment	1	Unstandardized ß coefficient 0.35 (0.1 to 0.61)	No serious imprecision	⊕⊕⊕⊖ MODERATE1 due to risk of bias
Beck Depression Inventory for predicting pain intensity (0-100 numeric rating scale) at 18 months	1	ß coefficient 1.1 (-0.81 to -3)	No serious imprecision	⊕⊕⊖⊖ LOW1 due to risk of bias
Symptom Checklist-90 item 9 – psychoneurosis for predicting 30% improvement in pain intensity from baseline at 5 months	1	Adjusted OR 0.99 (0.98 to 1)	No serious imprecision	⊕⊕⊖⊖ LOW[1] due to risk of bias
Centre for Epidemiological studies- depression for predicting Western Ontario and McMaster Universities Osteoarthritis Index at 9 months	1	ß coefficient 0.017 (-0.04 to 0.08)	Serious imprecision	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision
Hospital anxiety and depression scale depression sub scale for predicting Medical Outcomes study 12-item short form health survey (QoL-mental component score) at 6 months	1	Standardised ß coefficient -0.14 (-0.27 to 0)	No serious imprecision	⊕⊕⊕⊖ MODERATE1 due to risk of bias
Hospital anxiety and depression scale depression sub scale Medical Outcomes study 12-item short form health survey (QoL-physical component score) at 6 months	1	Standardised ß coefficient -0.11 (-0.24 to 0.02)	Serious imprecision	⊕⊕⊖⊖ LOW1,3 due to risk of bias, imprecision

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 or 2 increments because the majority of the evidence had indirect outcomes
3 Downgraded by one increment if the confidence interval crossed the null line

Table 10: Clinical evidence summary: coping style

Outcome	Number of studies	Effect (95% CI)	Imprecision	GRADE Quality
Pain catastrophizing scale (every 5 point increase) for predicting increase in chronic pelvic pain severity at 12 months	1	Adjusted OR 1.1 (1 to 1.21)	No serious imprecision	⊕⊕⊖⊖ LOW1 due to risk of bias
Pain self-efficacy questionnaire for predicting Shoulder pain and disability index at 6 months	1	β coefficient -0.36 (-0.5 to -0.22)	No serious imprecision	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, indirectness
Catastrophising (coping strategies questionnaire) for predicting Chronic pain grade IV at 12 months	1	Adjusted RR 1.46 (0.83 to 2.57)	Serious imprecision	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision
Tampa scale of kinesiophobia for predicting Chronic pain grade IV at 12 months	1	Adjusted RR 1.08 (0.66 to 1.77)	Serious imprecision	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision
Pain catastrophizing scale for predicting pain symptoms measured by National institutes of health chronic prostatitis symptom index at 11 months	1	unstandardized regression coefficient 0.02 (-0.06 to 0.1)	Serious imprecision	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision
Pain catastrophizing scale for predicting quality of life measured by National institutes of health chronic prostatitis symptom index at 11 months	1	unstandardized regression coefficient 0.05 (-0.01 to 0.11)	Serious imprecision	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision
Ruminative thoughts (each unit change on Pain Catastrophising Scale) for predicting clinically significant pain (Graded chronic pain scale 1,2,3,4) at 12 months	1	Adjusted OR 1.06 (0.94 to 1.2)	Serious imprecision	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision
Confidence in ability to control pain (each unit change on Coping strategies questionnaire) for predicting clinically significant pain (Graded chronic pain scale 1,2,3,4)	1	Adjusted OR 0.73 (0.52 to 1.02)	Serious imprecision	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision
Confidence in ability to decrease pain (each unit change on Coping strategies questionnaire) for predicting clinically significant pain (Graded chronic pain scale 1,2,3,4)	1	Adjusted OR 0.95 (0.66 to 1.37)	Serious imprecision	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision

Outcome	Number of studies	Effect (95% CI)	Imprecision	GRADE Quality
Optimism index for predicting ≥25mm reduction on 0-100mm VAS from baseline at 12 months	1	Adjusted OR 2.95 (1.26 to 6.91)	No serious imprecision	⊕⊕⊖⊖ LOW1 due to risk of bias
Pain coping (Pain coping and cognition list) for predicting improvement at 6 months	1	Adjusted OR 1.28 (0.76 to 2.16)	Serious imprecision	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision
High fear-avoidance beliefs about work measured by Fear Avoidance Beliefs Questionnaire (low, 0–29; high, 30–42) for predicting pain intensity (unsuccessful outcome: reduction of less than 6 points) at 12 months	1	Adjusted OR 1.04 (1.01-1.08)	No serious imprecision	⊕⊕⊖⊖ LOW1 due to risk of bias
Tampa scale of kinesiophobia for predicting difference in SF36 physical component scale scores from baseline at 4 weeks post treatment	1	unstandardized ß coefficient -0.05 (-0.27 to 0.17)	Serious imprecision	⊕⊕⊖⊖ LOW1,3 due to risk of bias, imprecision
Multidimensional pain inventory classification (adaptive coper/average/anomalous or dysfunction/distressed) for predicting difference in SF36 physical component scale scores from baseline at 4 weeks post treatment	1	unstandardized ß coefficient 1.54 (-1.42 to 4.5)	Serious imprecision	⊕⊕⊖⊖ LOW1,3 due to risk of bias, imprecision
Tampa scale of kinesiophobia for predicting difference in SF36 mental component scale scores from baseline at 4 weeks post treatment	1	unstandardized ß coefficient 0.1 (-0.14 to 0.34)	Serious imprecision	⊕⊕⊖⊖ LOW1,3 due to risk of bias, imprecision
Multidimensional pain inventory classification (adaptive coper/average/anomalous or dysfunction/distressed) for predicting difference in SF36 mental component scale scores from baseline at 4 weeks post treatment	1	unstandardized ß coefficient -0.78 (-4.09 to 2.53)	Serious imprecision	⊕⊕⊖⊖ LOW1,3 due to risk of bias, imprecision
Catastrophizing (Coping strategies questionnaire) for predicting change in pain intensity (NRS 0-10) from baseline at 18 months	1	ß coefficient 3.79 (2.09 to 5.49)	No serious imprecision	⊕⊕⊖⊖ LOW1 due to risk of bias
Tampa scale for kinesiophobia for predicting 30% improvement in pain intensity from baseline at 12 months	1	Adjusted OR 0.97 (0.95 to 0.99)	No serious imprecision	⊕⊕⊖⊖ LOW1 due to risk of bias

Outcome	Number of studies	Effect (95% CI)	Imprecision	GRADE Quality
Catastrophizing (coping strategies questionnaire) for predicting Western Ontario and McMaster Universities Osteoarthritis Index at 9 months	1	ß coefficient -0.01 (-0.08 to 0.06)	Serious imprecision	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision
Pain self-efficacy (Arthritis self-efficacy scale) for predicting Western Ontario and McMaster Universities Osteoarthritis Index at 9 months	1	ß coefficient 0.02 (-0.3 to 0.29)	Serious imprecision	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision
Rumination (Pain catastrophizing scale) for predicting Medical Outcomes study 12-item short form health survey (QoL-physical component score) at 6 months	1	standardised ß coefficient 0.03 (-0.08 to 0.14)	Serious imprecision	⊕⊕⊖⊖ LOW1,3 due to risk of bias, imprecision
Magnification (Pain catastrophizing scale) for predicting Medical Outcomes study 12-item short form health survey (QoL-physical component score) at 6 months	1	standardised ß coefficient 0 (-0.13 to 0.12)	Serious imprecision	⊕⊕⊖⊖ LOW1,3 due to risk of bias, imprecision
Helplessness (Pain catastrophizing scale) for predicting Medical Outcomes study 12-item short form health survey (QoL-physical component score) at 6 months	1	standardised ß coefficient 0.09 (-0.03 to 0.22)	Serious imprecision	⊕⊕⊖⊖ LOW1,3 due to risk of bias, imprecision
Tampa scale of kinesiophobia for predicting Medical Outcomes study 12-item short form health survey (QoL-physical component score) at 6 months	1	standardised ß coefficient -0.18 (-0.29 to -0.07)	No serious imprecision	⊕⊕⊕⊖ MODERATE1 due to risk of bias
Rumination (Pain catastrophizing scale) for predicting Medical Outcomes study 12-item short form health survey (QoL-mental component score) at 6 months	1	standardised ß coefficient -0.03 (-0.27 to 0)	No serious imprecision	⊕⊕⊕⊖ MODERATE1 due to risk of bias
Magnification (Pain catastrophizing scale) for predicting Medical Outcomes study 12-item short form health survey (QoL-mental component score) at 6 months	1	standardised ß coefficient 0 (-0.15 to 0.09)	Serious imprecision	⊕⊕⊖⊖ LOW1,3 due to risk of bias, imprecision
Helplessness (Pain catastrophizing scale) for predicting for predicting Medical Outcomes study 12-item short form health survey (QoL-mental component score) at 6 months	1	standardised ß coefficient -0.01 (-0.13 to 0.14)	Serious imprecision	⊕⊕⊖⊖ LOW1,3 due to risk of bias, imprecision
Tampa scale of kinesiophobia for predicting Medical Outcomes study 12-item short form health survey (QoL-mental component score) at 6 months	1	standardised ß coefficient 0.1 (-0.02 to 0.21)	Serious imprecision	⊕⊕⊖⊖ LOW1,3 due to risk of bias, imprecision

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

2 Downgraded by 1 or 2 increments because the majority of the evidence had indirect outcomes

3 Downgraded by 1 increment if the confidence interval crossed the null line

See Appendix F: for full GRADE tables.

3.4 Economic evidence

3.4.1 Included studies

No health economic studies were included.

3.4.2 Excluded studies

No relevant health economic studies were excluded due to assessment of limited applicability or methodological limitations.

See also the health economic study selection flow chart in Appendix G:.

3.5 Evidence statements

3.5.1 Clinical evidence statements

Reported pain intensity at baseline

- Moderate to very low quality evidence from 9 studies with a total of 3006 participants showed that higher reported pain intensity at baseline predicted greater pain reduction at 6 to 12 months.
- Moderate to very low quality evidence from 6 studies with a total of 2332 participants showed that higher reported pain intensity at baseline predicted higher pain intensity at 6 to 18 months, but low to very low quality evidence from 2 studies with a total of 355 participants showed that reported pain intensity at baseline did not predict pain intensity at 6 to 12 months.
- Moderate quality evidence from one study with a total of 178 participants showed that higher reported pain intensity at baseline predicted better quality of life at 6 months, but low to very low quality evidence from 3 studies with a total of 450 participants showed that pain intensity at baseline did not predict quality of life at 11 weeks to 11 months.

Comorbid psychiatric disorder

- Low quality evidence from 3 studies with a total of 2082 participants showed that comorbid psychiatric disorder predicted less pain reduction at 5 to 12 months, but very low quality evidence from one study with a total of 190 participants showed that comorbid psychiatric disorder did not predict pain reduction at 9 months.
- Moderate to low quality evidence from 5 studies with a total of 1874 participants showed that comorbid psychiatric disorder predicted higher pain intensity at 6 to 18 months, but very low quality evidence from 2 studies with a total of 1067 participants showed that comorbid psychiatric disorder did not predict pain intensity at 6 to 12 months.
- Moderate to low quality evidence from 2 studies with a total of 287 participants showed that comorbid psychiatric disorder predicted worse quality of life at follow up, but low quality evidence from 2 studies with a total of 341 participants showed that comorbid psychiatric disorder did not predict quality of life at follow up and moderate quality evidence from one study with a total of 163 participants showed that comorbid psychiatric disorder predicted better quality of life at 11 weeks.

Coping style

- Low quality evidence from 3 studies with a total of 1724 participants showed that coping style predicted higher and less reduction in pain intensity at 12 to 18 months, but very low quality evidence from 5 studies with a total of 1051 participants showed that coping style did not predict pain reduction or intensity at 6 to 12 months and low to very low quality

evidence from 2 studies with a total of 910 participants showed that coping style predicted better pain reduction and lower pain intensity at 6 to 12 months.

- Moderate quality evidence from one study with a total of 178 participants showed that coping style predicted worse quality of life at 6 months, but low to very low quality evidence from 3 studies with a total of 450 participants showed that coping style did not predict quality of life at 11 weeks to 11 months.

3.5.2 Health economic evidence statements

- No relevant economic evaluations were identified.

4 Social factors

4.1 Review question: What social factors may be barriers to successfully managing chronic pain?

4.2 PICO table

For full details see the review protocol in Appendix A:.

Table 11: PICO characteristics of review question

Population	People, aged 16 years and over, with chronic pain. *Pain that persists or recurs for longer than 3 months.*
Prognostic variable(s) under consideration	• Social and work participation • Isolation (social and/or geographical) • Caring responsibilities • Ongoing litigation/compensation claims • Financial concerns
Confounding factors	Studies not accounting for at least 2 key confounders (prognostic factors) in a multivariable analysis are excluded.
Outcome(s)	CRITICAL • Quality of life • Pain
Study design	Cohort studies Case-controls if no cohort studies identified

4.3 Clinical evidence

4.3.1 Included studies

No included evidence.

4.3.2 Excluded studies

See the excluded studies list in Appendix I.

4.3.3 Summary of clinical studies included in the evidence review

No included evidence.

4.3.4 Quality assessment of clinical studies included in the evidence review

No included evidence.

See Appendix F: for full GRADE tables.

4.4 Economic evidence

4.4.1 Included studies

No health economic studies were included.

4.4.2 Excluded studies

No relevant health economic studies were excluded due to assessment of limited applicability or methodological limitations.

See also the health economic study selection flow chart in Appendix G:.

4.5 Evidence statements

4.5.1 Clinical evidence statements

No included evidence.

4.5.2 Health economic evidence statements

- No relevant economic evaluations were identified.

5 The committee's discussion of the evidence

5.1 Interpreting the evidence

5.1.1 The outcomes that matter most

The committee considered health related quality of life and pain reduction to be critical outcomes for measuring successful or unsuccessful pain management. Other outcomes such as pain self-efficacy and psychological distress that were reported in the management reviews were instead considered to be potential prognostic or confounding factors.

Evidence was identified for both critical outcomes in the reviews of psychological and biological factors. No evidence was identified for the review of social factors.

5.1.2 The quality of the evidence

The evidence for psychological factors ranged from moderate to very low quality, although the majority of the evidence was of low to very low quality. The evidence for biological factors ranged from low to very low quality. The main reasons for downgrading of evidence were risk of bias, indirectness and imprecision (discussed in more detail below).

Outcomes that included measures of both pain intensity and disability were considered to be indirect. In addition, some studies outlined the intervention or management strategy which participants had undergone, whilst others did not specify this, or stated that participants had access to usual care for the duration of the studies. The committee noted it was therefore difficult to interpret the evidence when the predictive value of each risk factor could vary depending on the management strategy or intervention in place.

All of the outcomes were at least at high risk of bias because none of the studies adjusted for all of the confounding factors identified by the committee. Therefore, the committee could not be sure that any association between the prognostic factors and the outcomes were not due to the effect of other confounding factors.

Some evidence was at high risk of study participation bias, due to the exclusion of people who had potential prognostic factors. The committee considered that, particularly within studies that included a treatment programme, it is likely that participants were selected/referred based on the absence of the prognostic factors, but that this would not have necessarily been reported in the exclusion criteria. Therefore the evidence may underestimate the true effect of the prognostic factors. This was of particular concern to the psychological factors review.

Other sources of bias included study attrition and poor definition of the prognostic factors. The lack of clarity in the studies around the cut-offs or increments used to define high and low scores on some continuous measures, for example, made the evidence difficult to interpret. The committee considered that the majority of the evidence for comorbid psychiatric disorders was based on scores on continuous scales rather than clinical diagnosis. Changes in depression scale scores for example did not necessarily represent a change in diagnostic status of depression.

The committee discussed concerns around the use of the Tampa scale for kinesiophobia. Although it has shown good internal consistency, the committee were aware of some literature that suggests correlations with other relevant psychometric measures are weak to moderate. Therefore, the scale potentially provides a measure of kinesiophobia and nothing more. For this reason, the committee placed less weight on evidence for the predictive value of coping style that was measured using this scale.

The committee could not draw conclusions from imprecise estimates of association, as there was uncertainty about the direction of effect. This was of particular relevance to coping styles, physical activity, physical comorbidity and pain diagnosis as potential prognostic factors.

Meta-analysis was not appropriate due to differences in the study methodologies, confounding factors included in the multivariable analyses and measures used to assess the outcomes.

5.1.3 Predictive value of psychological, biological and social factors

Psychological factors

Overall, evidence for the predictive value of reported pain intensity at baseline for pain management outcomes showed that higher pain intensity at baseline was predictive of a greater reduction in pain, but higher pain intensity at follow up. This was in line with the expectations of the committee that those with higher pain intensity have more room for improvement, but that the reduction would be unlikely to surpass those who start with less pain. There was less evidence for quality of life, but overall it showed that pain intensity at baseline was not predictive of quality of life outcomes.

The majority of the evidence showed that comorbid psychiatric disorders (anxiety, depression, psychoneurosis, somatic and psychosomatic complaints) predicted more intense pain and poorer quality of life outcomes. However, the limitations of the evidence, particularly those regarding the selection of participants and the methods used to measure the prognostic factor, which were mostly continuous scales rather than clinical diagnosis, were considered too great to allow conclusions to be drawn.

There was some evidence to suggest catastrophizing and kinesiophobia were associated with unsuccessful chronic pain management. However, there was more evidence to suggest that there was no association. There was very low quality evidence from a single study to suggest that pain self-efficacy predicts successful pain management and low quality evidence from a single study to suggest that optimism predicts successful pain management.

No evidence was identified for the prognostic value of adverse childhood experience or substance addiction/dependence/misuse.

The committee considered that there was insufficient evidence of high enough quality and certainty to conclude that any psychological factors are predictive of successful pain management, or upon which to base any recommendations. There was variation in prognostic value across outcomes and studies, meaning that the committee could not conclude that any factors were barriers to successful management, nor could they predict people's likely response to treatment based on individual factors. Rather, they concluded that there was an association between some factors and outcomes, but it was inconsistent across the review.

Biological factors

There was evidence to suggest that more strenuous physical activity at baseline predicts better pain outcome, however this was of very low quality and based on one study. There was also evidence showing no association between frequency of physical activity and pain or quality of life.

There was evidence to suggest that having a comorbid physical condition predicts worse pain outcome, however this was of low quality and based on one study and there was also evidence showing no association between comorbidity and pain.

Very low quality evidence from one study showed that pain diagnosis (having widespread pain) was not predictive of pain intensity in a population with temporomandibular disorder pain. Another study also reported that pain diagnosis (having widespread pain) was not predictive of a change in quality of life, this was also rated as very low quality evidence.

No evidence was identified for the predictive value of polypharmacy.

The committee concluded that there was insufficient evidence with certainty to suggest that any biological factors are predictive of successful pain management or not, or upon which to base any recommendations.

Social factors

No evidence was identified.

Overall

Due to the lack of evidence with high quality and certainty to inform recommendations, the committee agreed that a research recommendation to identify the factors that may best enable stratification of treatment for people with chronic pain would be of benefit.

5.2 Cost effectiveness and resource use

No economic evidence was identified for this question.

The purpose of these reviews were to identify the factors that are associated with changes in quality of life or reduction in pain, in order to highlight factors that clinicians should be mindful of when carrying out a comprehensive assessment of a person with chronic pain. A comprehensive biopsychosocial approach could enhance treatment impact as it is more tailored to an individual's biological, psychological, and social factors. A more comprehensive assessment is likely to involve more staff time, and any resulting positive impact from treatment is likely to improve the cost effectiveness of treatment.

The committee agreed that overall the body of clinical evidence was insufficient to suggest a strong association between particular factors and outcomes. It was also difficult to interpret what any association between factors and outcomes would mean in terms of how this would guide treatment choices.

Therefore, the committee decided to make some consensus recommendations regarding how psychological, biological and social factors in general should be considered in assessing barriers to management of chronic pain, and developing care plans with consideration of these factors in mind.

Considering psychological, biological and social factors in an assessment, and developing a care plan should be part of best practice, although where this might not be the case, then

resources such as staff time may be involved in order to fully implement these recommendations.

5.3 Other factors the committee took into account

The committee were aware of a body of epidemiological evidence showing associations between social factors such as compensation claims and social isolation and chronic pain. These studies were not included in this review because they reported risk factors for the development of chronic pain in non-chronic pain populations (rather than factors predicting success of management in people with existing chronic pain), or did not conduct relevant multivariable analysis.

It was the experience of the lay members on the committee that although comprehensive biopsychosocial assessments are considered best practice, they are not usually carried out. The committee agreed that a comprehensive biopsychosocial approach should extend beyond initial assessment to ongoing management.

The committee were mindful of the potential for assessment of biopsychosocial factors to be used as a way to rule out some treatments for people with potential risk factors for unsuccessful pain management. The committee agreed that assessments should only be used to inform treatment decisions by clinicians working with individuals, taking all factors into account, and that such discretion is essential to successful pain management.

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Appendices

Appendix A: Review protocols

Review protocol for biological factors

ID	Field	Content
0.	PROSPERO registration number	CRD42019126876
1.	Review title	What biological factors may be barriers to successfully managing chronic pain?
2.	Review question	What biological factors may be barriers to successfully managing chronic pain?
3.	Objective	To determine the prognostic value of biological factors for pain management.
4.	Searches	The following databases will be searched: • Embase • MEDLINE Searches will be restricted by: • English language • Human studies • Letters and comments are excluded. Other searches:

		• Inclusion lists of relevant systematic reviews will be checked by the reviewer. The searches may be re-run 6 weeks before final committee meeting and further studies retrieved for inclusion if relevant. The full search strategies will be published in the final review.
5.	Condition or domain being studied	Chronic pain - pain that persists or recurs for longer than 3 months.
6.	Population	People, aged 16 years and over, with chronic pain.
7.	Intervention/Exposure/Test	Exposures/prognostic factors: -physical activity at baseline -presence or absence of comorbid physical condition -poly-pharmacy -pain diagnosis
8.	Comparator/Reference standard/Confounding factors	Not applicable
9.	Types of study to be included	Prospective and retrospective cohort studies. Case control studies if no cohort studies are identified. Exclusions:

		- studies not accounting for at least 2 key confounders (prognostic factors plus number of pain sites, smoking, age and gender) in a multivariable analysis.
10.	Other exclusion criteria	Non-English language studies. Conference abstracts will be excluded as it is expected there will be sufficient full text published studies available.
11.	Context	-
12.	Primary outcomes (critical outcomes)	Critical outcomes: - Health related quality of life (including meaningful activity), measured using a validated scale e.g. EQ-5D, SF36, SF12 - Pain reduction, as reported by the studies Studies must report at least one of these outcomes in order to be included in the review.
13.	Secondary outcomes (important outcomes)	None
14.	Data extraction (selection and coding)	EndNote will be used for reference management, sifting, citations and bibliographies. All references identified by the searches and from other sources will be screened for inclusion. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4).
15.	Risk of bias (quality) assessment	Risk of bias will be assessed using the QUIPs checklist. 10% of all evidence reviews are quality assured by a senior research fellow. This includes checking: • papers were included /excluded appropriately • a sample of the data extractions • correct methods are used to synthesise data

		• a sample of the risk of bias assessments Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary.			
16.	Strategy for data synthesis	Pairwise meta-analyses performed using Cochrane Review Manager (RevMan5) depending on the appropriateness of the data. GRADEpro will be used to assess the quality of evidence for each outcome. If meta-analysis is not possible, data will be presented as individual values in adapted GRADE profile tables.			
17.	Analysis of sub-groups	None			
18.	Type and method of review	☐	Intervention		
		☐	Diagnostic		
		☒	Prognostic		
		☐	Qualitative		
		☐	Epidemiologic		
		☐	Service Delivery		
		☐	Other (please specify)		
19.	Language	English			
20.	Country	England			
21.	Anticipated or actual start date	11/02/2019			
22.	Anticipated completion date	19/08/2020			
23.	Stage of review at time of this submission	Review stage		Started	Completed
		Preliminary searches		☑	☑

		Piloting of the study selection process	☑	☑
		Formal screening of search results against eligibility criteria	☐	☐
		Data extraction	☐	☐
		Risk of bias (quality) assessment	☐	☐
		Data analysis	☐	☐
24.	Named contact	5a. Named contact National Guideline Centre 5b Named contact e-mail Chronicpain@nice.org.uk 5e Organisational affiliation of the review National Institute for Health and Care Excellence (NICE) and the National Guideline Centre		
25.	Review team members	From the National Guideline Centre: Serena Carville, Guideline Lead Maria Smyth, Senior Systematic Reviewer Rebecca Boffa, Senior Systematic Reviewer Margaret Constanti, Senior Health Economist Joseph Runicles, Information Specialist Katie Broomfield, Project Manager		

26.	Funding sources/sponsor	This systematic review is being completed by the National Guideline Centre which receives funding from NICE.
27.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
28.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ng10069
29.	Other registration details	-
30.	Reference/URL for published protocol	https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=126876
31.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.
32.	Keywords	-
33.	Details of existing review of same topic by same authors	-

34.	Current review status	☒	Ongoing
		☐	Completed but not published
		☐	Completed and published
		☐	Completed, published and being updated
		☐	Discontinued
35.	Additional information	None	
36.	Details of final publication	www.nice.org.uk	

Review protocol for psychological factors

ID	Field	Content
0.	PROSPERO registration number	CRD42019126565
1.	Review title	What psychological factors may be barriers to successfully managing chronic pain?
2.	Review question	What psychological factors may be barriers to successfully managing chronic pain?
3.	Objective	To determine the prognostic value of psychological factors for pain management.
4.	Searches	The following databases will be searched: • Embase • MEDLINE

		• PsycINFO Searches will be restricted by: • English language • Human studies • Letters and comments are excluded. Other searches: • Inclusion lists of relevant systematic reviews will be checked by the reviewer. The searches may be re-run 6 weeks before final committee meeting and further studies retrieved for inclusion if relevant. The full search strategies will be published in the final review.
5.	Condition or domain being studied	Chronic pain - pain that persists or recurs for longer than 3 months.
6.	Population	People, aged 16 years and over, with chronic pain.
7.	Intervention/Exposure/Test	Exposures/prognostic factors: -comorbid psychiatric disorder (including personality disorder) -adverse childhood experience -reported pain intensity -substance addiction/dependence/misuse -coping styles

8.	Comparator/Reference standard/Confounding factors	Not applicable
9.	Types of study to be included	Prospective and retrospective cohort studies. Case control studies if no cohort studies are identified. Exclusions: - studies not accounting for at least 2 key confounders (prognostic factors) in a multivariable analysis.
10.	Other exclusion criteria	Non-English language studies. Conference abstracts will be excluded as it is expected there will be sufficient full text published studies available.
11.	Context	-
12.	Primary outcomes (critical outcomes)	Critical outcomes: - Health related quality of life (including meaningful activity), measured using a validated scale e.g. EQ-5D, SF36, SF12 - Pain reduction, as reported by the studies Studies must report at least one of these outcomes in order to be included in the review.
13.	Secondary outcomes (important outcomes)	None
14.	Data extraction (selection and coding)	EndNote will be used for reference management, sifting, citations and bibliographies. All references identified by the searches and from other sources will be screened for inclusion. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4).
15.	Risk of bias (quality) assessment	Risk of bias will be assessed using the QUIPs checklist.

		10% of all evidence reviews are quality assured by a senior research fellow. This includes checking: • papers were included /excluded appropriately • a sample of the data extractions • correct methods are used to synthesise data • a sample of the risk of bias assessments Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary.	
16.	Strategy for data synthesis	Pairwise meta-analyses performed using Cochrane Review Manager (RevMan5) depending on the appropriateness of the data. GRADEpro will be used to assess the quality of evidence for each outcome. If meta-analysis is not possible, data will be presented as individual values in adapted GRADE profile tables.	
17.	Analysis of sub-groups	None	
18.	Type and method of review	☐	Intervention
		☐	Diagnostic
		☒	Prognostic
		☐	Qualitative
		☐	Epidemiologic
		☐	Service Delivery
		☐	Other (please specify)
19.	Language	English	
20.	Country	England	

21.	Anticipated or actual start date	14/01/2019		
22.	Anticipated completion date	19/08/2020		
23.	Stage of review at time of this submission	Review stage	Started	Completed
		Preliminary searches	☑	☑
		Piloting of the study selection process	☑	☑
		Formal screening of search results against eligibility criteria	☐	☐
		Data extraction	☐	☐
		Risk of bias (quality) assessment	☐	☐
		Data analysis	☐	☐
24.	Named contact	5a. Named contact National Guideline Centre 5b Named contact e-mail Chronicpain@nice.org.uk 5e Organisational affiliation of the review National Institute for Health and Care Excellence (NICE) and the National Guideline Centre		
25.	Review team members	From the National Guideline Centre: Serena Carville, Guideline lead Maria Smyth, Senior Systematic Reviewer		

		Rebecca Boffa, Senior Systematic Reviewer Margaret Constanti, Senior Health Economist Joseph Runicles, Information Specialist Katie Broomfield, Project Manager
26.	Funding sources/sponsor	This systematic review is being completed by the National Guideline Centre which receives funding from NICE.
27.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
28.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ng10069
29.	Other registration details	-
30.	Reference/URL for published protocol	https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=126565
31.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as:

		• notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.	
32.	Keywords	-	
33.	Details of existing review of same topic by same authors	-	
34.	Current review status	☒	Ongoing
		☐	Completed but not published
		☐	Completed and published
		☐	Completed, published and being updated
		☐	Discontinued
35.	Additional information	None	
36.	Details of final publication	www.nice.org.uk	

Review protocol for social factors

ID	Field	Content
0.	PROSPERO registration number	CRD42019128371
1.	Review title	What social factors may be barriers to successfully managing chronic pain?
2.	Review question	What social factors may be barriers to successfully managing chronic pain?
3.	Objective	To determine the prognostic value of social factors for pain management.

4.	Searches	The following databases will be searched: • Embase • MEDLINE • SPP (Social Policy and Practice) • The Kings Fund Library Database • ASSIA (Applied Social Sciences Index and Abstracts) Searches will be restricted by: • English language • Human studies • Letters and comments are excluded. Other searches: • Inclusion lists of relevant systematic reviews will be checked by the reviewer. The searches may be re-run 6 weeks before final committee meeting and further studies retrieved for inclusion if relevant. The full search strategies will be published in the final review.
5.	Condition or domain being studied	Chronic pain - pain that persists or recurs for longer than 3 months.
6.	Population	People, aged 16 years and over, with chronic pain.
7.	Intervention/Exposure/Test	Exposures/prognostic factors:

		• social and work participation • isolation (social and/or geographical) • caring responsibilities • ongoing litigation/compensation claims • financial concerns
8.	Comparator/Reference standard/Confounding factors	Not applicable
9.	Types of study to be included	Prospective and retrospective cohort studies. Case control studies if no cohort studies are identified. Exclusions: - studies not accounting for at least 2 key confounders (prognostic factors) in a multivariable analysis.
10.	Other exclusion criteria	Non-English language studies. Conference abstracts will be excluded as it is expected there will be sufficient full text published studies available.
11.	Context	-
12.	Primary outcomes (critical outcomes)	Critical outcomes: - Health related quality of life (including meaningful activity), measured using a validated scale e.g. EQ-5D, SF36, SF12 - Pain reduction, as reported by the studies Studies must report at least one of these outcomes in order to be included in the review.
13.	Secondary outcomes (important outcomes)	None
14.	Data extraction (selection and coding)	EndNote will be used for reference management, sifting, citations and bibliographies. All references identified by the searches and from other sources will be screened for inclusion. 10% of the abstracts will be reviewed by two

		reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4).	
15.	Risk of bias (quality) assessment	Risk of bias will be assessed using the QUIPs checklist. 10% of all evidence reviews are quality assured by a senior research fellow. This includes checking: • papers were included /excluded appropriately • a sample of the data extractions • correct methods are used to synthesise data • a sample of the risk of bias assessments Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary.	
16.	Strategy for data synthesis	Pairwise meta-analyses performed using Cochrane Review Manager (RevMan5) depending on the appropriateness of the data. GRADEpro will be used to assess the quality of evidence for each outcome. If meta-analysis is not possible, data will be presented as individual values in adapted GRADE profile tables.	
17.	Analysis of sub-groups	None	
18.	Type and method of review	☐	Intervention
		☐	Diagnostic
		☒	Prognostic
		☐	Qualitative
		☐	Epidemiologic
		☐	Service Delivery

		☐	Other (please specify)
19.	Language	English	
20.	Country	England	
21.	Anticipated or actual start date	30/01/2019	
22.	Anticipated completion date	19/08/2020	
23.	Stage of review at time of this submission	Review stage	Started / Completed
		Preliminary searches	☑ / ☑
		Piloting of the study selection process	☑ / ☑
		Formal screening of search results against eligibility criteria	☐ / ☐
		Data extraction	☐ / ☐
		Risk of bias (quality) assessment	☐ / ☐
		Data analysis	☐ / ☐
24.	Named contact	5a. Named contact National Guideline Centre 5b Named contact e-mail Chronicpain@nice.org.uk 5e Organisational affiliation of the review	

		National Institute for Health and Care Excellence (NICE) and the National Guideline Centre
25.	Review team members	From the National Guideline Centre: Serena Carville, Guideline lead Maria Smyth, Senior Systematic Reviewer Rebecca Boffa, Senior Systematic Reviewer Margaret Constanti, Senior Health Economist Joseph Runicles, Information Specialist Katie Broomfield, Project Manager
26.	Funding sources/sponsor	This systematic review is being completed by the National Guideline Centre which receives funding from NICE.
27.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
28.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ng10069
29.	Other registration details	-

30.	Reference/URL for published protocol	https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=128371	
31.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.	
32.	Keywords	-	
33.	Details of existing review of same topic by same authors	-	
34.	Current review status	☒	Ongoing
		☐	Completed but not published
		☐	Completed and published
		☐	Completed, published and being updated
		☐	Discontinued
35.	Additional information	None	
36.	Details of final publication	www.nice.org.uk	

Table 12: Health economic review protocol

Review question	All questions – health economic evidence
Objectives	To identify health economic studies relevant to any of the review questions.
Search criteria	• Populations, interventions and comparators must be as specified in the clinical review protocol above. • Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.
Search strategy	A health economic study search will be undertaken using population-specific terms and a health economic study filter – see appendix B below.
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2002. Abstract-only studies and studies from non-OECD countries or the USA will also be excluded. Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual (2014).[381] **Inclusion and exclusion criteria** • If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. A health economic evidence table will be completed and it will be included in the health economic evidence profile. • If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded then a health economic evidence table will not be completed and it will not be included in the health economic evidence profile. • If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included. **Where there is discretion** The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of applicability or methodological limitations will be listed with explanation in the excluded health economic studies appendix below. The health economist will be guided by the following hierarchies. *Setting:* • UK NHS (most applicable). • OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden).

	• OECD countries with predominantly private health insurance systems (for example, Switzerland). • Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations. *Health economic study type:* • Cost–utility analysis (most applicable). • Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis). • Comparative cost analysis. • Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations. *Year of analysis:* • The more recent the study, the more applicable it will be. • Studies published in 2002 or later but that depend on unit costs and resource data entirely or predominantly from before 2002 will be rated as 'Not applicable'. • Studies published before 2002 will be excluded before being assessed for applicability and methodological limitations. *Quality and relevance of effectiveness data used in the health economic analysis:* • The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

Appendix B: Literature search strategies

These literature search strategies were used for the following reviews;

- B.1 What biological factors may be barriers to successfully managing chronic pain?
- B.2 What psychological factors may be barriers to successfully managing chronic pain?
- B.3 What social factors may be barriers to successfully managing chronic pain?

The literature searches for these reviews are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.[381]

For more information, please see the Methods Report published as part of the accompanying documents for this guideline.

B.1 Clinical search literature search strategy

Searches were constructed using the following approach:

- Population AND Prognostic/risk factor terms AND Study filter(s)

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 20 May 2020	Exclusions Observational studies
Embase (OVID)	1974 – 20 May 2020	Exclusions Observational studies

Medline (Ovid) search terms

1.	chronic pain/ or pain, intractable/
2.	((persist* or intract* or chronic or longstanding or long standing or longterm or long term or refractory or prolong* or long last* or sustain* or linger* or syndrome*) adj3 pain*).ti,ab.
3.	or/1-2
4.	letter/
5.	editorial/
6.	news/
7.	exp historical article/
8.	Anecdotes as Topic/
9.	comment/
10.	case report/
11.	(letter or comment*).ti.
12.	or/4-11
13.	randomized controlled trial/ or random*.ti,ab.
14.	12 not 13
15.	animals/ not humans/
16.	exp Animals, Laboratory/
17.	exp Animal Experimentation/
18.	exp Models, Animal/
19.	exp Rodentia/
20.	(rat or rats or mouse or mice).ti.
21.	or/14-20
22.	3 not 21
23.	limit 22 to English language
24.	Exercise/
25.	(physical* adj2 activit*).ti,ab.
26.	comorbidity/ or multimorbidity/
27.	(comorbid* or co-morbid* or multimorbid* or multi-morbid*).ti,ab.
28.	(multidisease# or multi-disease# or (multiple adj (ill* or disease? or condition? or syndrom* or disorder?))).ti,ab.
29.	((coocur* or co-ocur* or coexist* or co-exist* or multipl* or concord* or discord*) adj3 (disease? or ill* or condition? or disorder*)).ti,ab.
30.	"pain* related disabilit*".ti,ab.
31.	(pain* adj2 (site* or multisite* or spot* or intensity or intense or severity or severe or level*)).ti,ab.
32.	exp polypharmacy/
33.	(hyperpolypharmacy or polypharmacy).ti,ab.
34.	medication-related harm*.ti,ab.
35.	((medicat* or drug* or prescri*) adj2 (number* or multiple or excessive)).ti,ab.
36.	(pain* adj5 management).ti,ab.
37.	(barrier* or diagnosis*).ti,ab.
38.	36 and 37
39.	or/24-35,38
40.	Epidemiologic studies/
41.	Observational study/
42.	exp Cohort studies/
43.	(cohort adj (study or studies or analys* or data)).ti,ab.

44.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
45.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
46.	Controlled Before-After Studies/
47.	Historically Controlled Study/
48.	Interrupted Time Series Analysis/
49.	(before adj2 after adj2 (study or studies or data)).ti,ab.
50.	or/40-49
51.	exp case control study/
52.	case control*.ti,ab.
53.	or/51-52
54.	50 or 53
55.	Cross-sectional studies/
56.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
57.	or/55-56
58.	50 or 53 or 57
59.	23 and 39 and 58

Embase (Ovid) search terms

1.	chronic pain/ or intractable pain/
2.	((persist* or intract* or chronic or longstanding or long standing or longterm or long term or refractory or prolong* or long last* or sustain* or linger* or syndrome*) adj3 pain*).ti,ab.
3.	or/1-2
4.	letter.pt. or letter/
5.	note.pt.
6.	editorial.pt.
7.	case report/ or case study/
8.	(letter or comment*).ti.
9.	or/4-8
10.	randomized controlled trial/ or random*.ti,ab.
11.	9 not 10
12.	animal/ not human/
13.	nonhuman/
14.	exp Animal Experiment/
15.	exp Experimental Animal/
16.	animal model/
17.	exp Rodent/
18.	(rat or rats or mouse or mice).ti.
19.	or/11-18
20.	3 not 19
21.	limit 20 to English language
22.	*exercise/
23.	(physical* adj2 activit*).ti,ab.
24.	comorbidity/ or multimorbidity/
25.	(comorbid* or co-morbid* or multimorbid* or multi-morbid*).ti,ab.
26.	(multidisease# or multi-disease# or (multiple adj (ill* or disease? or condition? or syndrom* or disorder?))).ti,ab.

27.	((coocur* or co-ocur* or coexist* or co-exist* or multipl* or concord* or discord*) adj3 (disease? or ill* or condition? or disorder*)).ti,ab.
28.	"pain* related disabilit*".ti,ab.
29.	(pain* adj2 (site* or multisite* or spot* or intensity or intense or severity or severe or level*)).ti,ab.
30.	exp polypharmacy/
31.	(hyperpolypharmacy or polypharmacy).ti,ab.
32.	medication-related harm*.ti,ab.
33.	((medicat* or drug* or prescri*) adj2 (number* or multiple or excessive)).ti,ab.
34.	(pain* adj5 management).ti,ab.
35.	(barrier* or diagnosis*).ti,ab.
36.	34 and 35
37.	or/22-33,36
38.	Epidemiologic studies/
39.	Observational study/
40.	exp Cohort studies/
41.	(cohort adj (study or studies or analys* or data)).ti,ab.
42.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
43.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
44.	Controlled Before-After Studies/
45.	Historically Controlled Study/
46.	Interrupted Time Series Analysis/
47.	(before adj2 after adj2 (study or studies or data)).ti,ab.
48.	or/38-47
49.	exp case control study/
50.	case control*.ti,ab.
51.	or/49-50
52.	48 or 51
53.	Cross-sectional studies/
54.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
55.	or/53-54
56.	48 or 51 or 55
57.	21 and 37 and 56

B.2 Clinical search literature search strategy

Searches were constructed using the following approach:

- Population AND Prognostic/risk factor terms AND Study filter(s)

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 20 May 2020	Exclusions Systematic review studies Observational studies Prognostic studies
Embase (OVID)	1974 – 20 May 2020	Exclusions Systematic review studies Observational studies Prognostic studies

Database	Dates searched	Search filter used
The Cochrane Library (Wiley)	Cochrane Reviews to 2020 Issue 5 of 12	None
PsycINFO (ProQuest)	Inception – 20 May 2020	Observational studies

Medline (Ovid) search terms

1.	chronic pain/ or pain, intractable/
2.	((persist* or intract* or chronic or longstanding or long standing or longterm or long term or refractory or prolong* or long last* or sustain* or linger* or syndrome*) adj3 pain*).ti,ab.
3.	or/1-2
4.	letter/
5.	editorial/
6.	news/
7.	exp historical article/
8.	Anecdotes as Topic/
9.	comment/
10.	case report/
11.	(letter or comment*).ti.
12.	or/4-11
13.	randomized controlled trial/ or random*.ti,ab.
14.	12 not 13
15.	animals/ not humans/
16.	exp Animals, Laboratory/
17.	exp Animal Experimentation/
18.	exp Models, Animal/
19.	exp Rodentia/
20.	(rat or rats or mouse or mice).ti.
21.	or/14-20
22.	3 not 21
23.	limit 22 to English language
24.	exp mental disorders/
25.	((mind or anxi* or mood or neurocognitive or cognition or neurodevelopmental or neurotic or personality or sleep wake or substance or trauma* or stress or depressive or depression or communicat* or learning) adj3 disorder*).ti,ab.
26.	((axis I or axis II or axis 1 or axis 2) adj disorder*).ti,ab.
27.	((psychiatric or psychological* or mental*) adj3 (illness or ill or disorder* or factor*)).ti,ab.
28.	((development* or intellectual*) adj3 disab*).ti,ab.
29.	((substance or drug*) adj3 (abuse or misuse or addiction or dependence)).ti,ab.
30.	((adverse or negative or trauma* or abusive or abuse* or neglect*) adj2 child* adj2 (event* or experience* or life)).ti,ab.
31.	*life change events/
32.	(pain adj3 (intensity or severe or severity*)).ti,ab.
33.	(McGill adj2 pain*).ti,ab.
34.	(coping adj3 (method* or style* or strateg* or active or passive)).ti,ab.
35.	or/24-33
36.	23 and 35
37.	Meta-Analysis/

38.	exp Meta-Analysis as Topic/
39.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
40.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
41.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
42.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
43.	(search* adj4 literature).ab.
44.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
45.	cochrane.jw.
46.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
47.	or/37-46
48.	Epidemiologic studies/
49.	Observational study/
50.	exp Cohort studies/
51.	(cohort adj (study or studies or analys* or data)).ti,ab.
52.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
53.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
54.	Controlled Before-After Studies/
55.	Historically Controlled Study/
56.	Interrupted Time Series Analysis/
57.	(before adj2 after adj2 (study or studies or data)).ti,ab.
58.	or/48-57
59.	exp case control study/
60.	case control*.ti,ab.
61.	or/59-60
62.	58 or 61
63.	Cross-sectional studies/
64.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
65.	or/63-64
66.	58 or 61 or 65
67.	36 and (47 or 66)
68.	Anxiety/
69.	Depression/
70.	(anxiet* or anxious or depression or low mood).ti,ab.
71.	or/68-70
72.	prognosis/
73.	(predict* or prognos*).ti,ab.
74.	Logistic models/
75.	Disease progression/
76.	or/72-75
77.	71 and 76
78.	23 and 77
79.	67 or 78

Embase (Ovid) search terms

1.	chronic pain/ or intractable pain/
2.	((persist* or intract* or chronic or longstanding or long standing or longterm or long term or refractory or prolong* or long last* or sustain* or linger* or syndrome*) adj3 pain*).ti,ab.
3.	or/1-2
4.	letter.pt. or letter/
5.	note.pt.
6.	editorial.pt.
7.	case report/ or case study/
8.	(letter or comment*).ti.
9.	or/4-8
10.	randomized controlled trial/ or random*.ti,ab.
11.	9 not 10
12.	animal/ not human/
13.	nonhuman/
14.	exp Animal Experiment/
15.	exp Experimental Animal/
16.	animal model/
17.	exp Rodent/
18.	(rat or rats or mouse or mice).ti.
19.	or/11-18
20.	3 not 19
21.	limit 20 to English language
22.	exp *mental disease/
23.	((mind or anxi* or mood or neurocognitive or cognition or neurodevelopmental or neurotic or personality or sleep wake or substance or trauma* or stress or depressive or depression or communicat* or learning) adj3 disorder*).ti,ab.
24.	((axis I or axis II or axis 1 or axis 2) adj disorder*).ti,ab.
25.	((psychiatric or psychological* or mental*) adj3 (illness or ill or disorder* or factor*)).ti,ab.
26.	((development* or intellectual*) adj3 disab*).ti,ab.
27.	((substance or drug*) adj3 (abuse or misuse or addiction or dependence)).ti,ab.
28.	((adverse or negative or trauma* or abusive or abuse* or neglect*) adj2 child* adj2 (event* or experience* or life)).ti,ab.
29.	*life event/
30.	(pain adj3 (intensity or severe or severity*)).ti,ab.
31.	(McGill adj2 pain*).ti,ab.
32.	(coping adj3 (method* or style* or strateg* or active or passive)).ti,ab.
33.	or/22-32
34.	*anxiety/
35.	*Depression/
36.	(anxiet* or anxious or depression or low mood).ti,ab.
37.	or/34-36
38.	exp prognosis/
39.	prognostic assessment/
40.	(predict* or prognos*).ti,ab.
41.	disease course/
42.	statistical model/

43.	or/38-42
44.	systematic review/
45.	meta-analysis/
46.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
47.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
48.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
49.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
50.	(search* adj4 literature).ab.
51.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
52.	cochrane.jw.
53.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
54.	or/44-53
55.	Clinical study/
56.	Observational study/
57.	family study/
58.	longitudinal study/
59.	retrospective study/
60.	prospective study/
61.	cohort analysis/
62.	follow-up/
63.	cohort*.ti,ab.
64.	62 and 63
65.	(cohort adj (study or studies or analys* or data)).ti,ab.
66.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
67.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
68.	(before adj2 after adj2 (study or studies or data)).ti,ab.
69.	or/55-61,64-68
70.	exp case control study/
71.	case control*.ti,ab.
72.	or/70-71
73.	69 or 72
74.	cross-sectional study/
75.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
76.	or/74-75
77.	69 or 76
78.	69 or 72 or 76
79.	21 and 33
80.	79 and (54 or 78)
81.	37 and 43
82.	21 and 81
83.	80 or 82

PsycINFO (Proquest) search terms

1.	((MAINSUBJECT.EXACT.EXPLODE("Chronic Pain") OR TI,AB((persist* OR intract* OR chronic OR longstanding OR "long standing" OR longterm OR "long term" OR refractory OR prolong* OR "long last*" OR sustain* OR linger* OR syndrome*) NEAR/3 pain*)) AND (MAINSUBJECT.EXACT.EXPLODE("Mental Disorders") OR (ti,ab((mind OR mood OR anxi* OR neurocognitive OR cognition OR neurodevelopmental OR neurotic OR personality OR substance OR trauma* OR stress OR depressive OR communicat* OR learning) NEAR/3 disorder*) OR ti,ab(axis NEAR/1 disorder*) OR ti,ab((psychiatric or psychological* or mental*) near/3 (illness or ill or disorder* or factor*)) OR ti,ab((development* or intellectual*) near/3 disab*) OR ti,ab((substance or drug*) near3 (abuse or misuse or addiction or dependence)) OR ti,ab((substance OR drug*) NEAR/3 (abuse OR misuse OR addiction OR dependence)) OR ti,ab((adverse or negative or trauma* or abusive or abuse* or neglect*) near/2 child* near/2 (event* or experience* or life)) OR ti,ab(pain NEAR/3 (intensity OR severe OR severity*)) OR ti,ab(McGill near/2 pain*) OR ti,ab(coping near/3 (method* or style* or strateg* or active or passive))))) AND (su.exact.explode("longitudinal studies") or su.exact.explode("followup studies") or su.exact("time series") or su.exact("cohort analysis") or ti,ab(cohort near/1 (study or studies or analys* or data)) or ti,ab((follow-up or observational or uncontrolled or non-randomi?ed or nonrandomi?ed or epidemiologic*) near/1 (study or studies or data)) or ti,ab((longitudinal or retrospective or prospective) and (study or studies or review or analys* or cohort* or data)) or ti,ab(before near/2 after near/2 (study or studies or data)) or ti,ab(cross-sectional and (study or studies or review or analys* or cohort* or data)) or ti,ab(case-control*))

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Chronic Pain] explode all trees
#2.	MeSH descriptor: [Pain, Intractable] explode all trees
#3.	((persist* or intract* or chronic or longstanding or long standing or longterm or long term or refractory or prolong* or long last* or sustain* or linger* or syndrome*) near/3 pain*):ti,ab
#4.	(or #1-#3)
#5.	MeSH descriptor: [Mental Disorders] explode all trees
#6.	((mind or anxi* or mood or neurocognitive or cognition or neurodevelopmental or neurotic or personality or sleep wake or substance or trauma* or stress or depressive or depression or communicat* or learning) near/3 disorder*):ti,ab
#7.	((axis I or axis II or axis 1 or axis 2) near disorder*):ti,ab
#8.	((psychiatric or psychological* or mental*) near/3 (illness or ill or disorder* or factor*)):ti,ab
#9.	((development* or intellectual*) near/3 disab*):ti,ab
#10.	((substance or drug*) near/3 (abuse or misuse or addiction or dependence)):ti,ab
#11.	((adverse or negative or trauma* or abusive or abuse* or neglect*) near/2 child* near/2 (event* or experience* or life)):ti,ab
#12.	MeSH descriptor: [Life Change Events] explode all trees
#13.	(pain near/3 (intensity or severe or severity*)):ti,ab
#14.	(McGill near/2 pain*):ti,ab
#15.	(coping near/3 (method* or style* or strateg* or active or passive)):ti,ab
#16.	(or #5-#15)
#17.	#4 and #16
#18.	MeSH descriptor: [Depression] explode all trees
#19.	MeSH descriptor: [Anxiety] explode all trees
#20.	(anxiet* or anxious or depression or low mood):ti,ab
#21.	(or #18-#20)
#22.	#4 and #21

#23.	#17 or #22

B.3 Clinical search literature search strategy

Searches were constructed using one or more of the following approaches:

- Population AND Prognostic/risk factor terms AND Study filter(s)

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 20 May 2020	Exclusions Observational studies
Embase (OVID)	1974 – 20 May 2020	Exclusions Observational studies
Assia (Proquest)	Inception – 20 May 2020	None
SPP (Ovid)	Inception – 20 May 2020	None
King's Fund	Inception – 20 May 2020	None

Medline (Ovid) search terms

1.	chronic pain/ or pain, intractable/
2.	((persist* or intract* or chronic or longstanding or long standing or longterm or long term or refractory or prolong* or long last* or sustain* or linger* or syndrome*) adj3 pain*).ti,ab.
3.	or/1-2
4.	letter/
5.	editorial/
6.	news/
7.	exp historical article/
8.	Anecdotes as Topic/
9.	comment/
10.	case report/
11.	(letter or comment*).ti.
12.	or/4-11
13.	randomized controlled trial/ or random*.ti,ab.
14.	12 not 13
15.	animals/ not humans/
16.	exp Animals, Laboratory/
17.	exp Animal Experimentation/
18.	exp Models, Animal/
19.	exp Rodentia/
20.	(rat or rats or mouse or mice).ti.
21.	or/14-20
22.	3 not 21
23.	limit 22 to English language
24.	exp Rehabilitation, Vocational/
25.	employment, supported/ or unemployment/ or employment/
26.	return to work/
27.	(occupation* adj2 (return* or retrain* or support* or rehabilitat*)).ti,ab.
28.	(employ* adj2 (return* or retrain* or support* or rehabilitat* or insecur*)).ti,ab.
29.	(vocation* adj2 (return* or retrain* or support* or rehabilitat*)).ti,ab.
30.	(job* adj2 (return* or retrain* or support* or rehabilitat* or insecur*)).ti,ab.

31.	(work* adj2 (return* or retrain* or support* or rehabilitat* or insecur*)).ti,ab.
32.	(work* adj2 (sheltered or permitted or voluntary)).ti,ab.
33.	unemploy*.ti,ab.
34.	Social Isolation/
35.	(social adj2 (barrier* or isolate* or isolation or separat* or contact or lonely or loneliness)).ti,ab.
36.	social support/ or social work/ or social welfare/
37.	((social or work*) adj2 (participat* or circumstance* or activit* or relation*)).ti,ab.
38.	(social adj2 (wellbeing or distress or consequence* or role* or concern* or vulnerab*)).ti,ab.
39.	caregivers/
40.	(carer* or caregiver*).ti,ab.
41.	(spouse* or wife or wives or husband* or significant other* or partner* or family or families).ti,ab.
42.	(caring adj3 (dependen* or responsib*)).ti,ab.
43.	Poverty/
44.	((financ* or money or income) adj3 (unstable or instability or concern* or vulnerab* or precarious or precarity)).ti,ab.
45.	(poverty or low income or deprived or deprivation).ti,ab.
46.	((litigat* or compensat* or legal) adj3 claim*).ti,ab.
47.	or/24-46
48.	Epidemiologic studies/
49.	Observational study/
50.	exp Cohort studies/
51.	(cohort adj (study or studies or analys* or data)).ti,ab.
52.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
53.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
54.	Controlled Before-After Studies/
55.	Historically Controlled Study/
56.	Interrupted Time Series Analysis/
57.	(before adj2 after adj2 (study or studies or data)).ti,ab.
58.	or/48-57
59.	exp case control study/
60.	case control*.ti,ab.
61.	or/59-60
62.	58 or 61
63.	Cross-sectional studies/
64.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
65.	or/63-64
66.	58 or 61 or 65
67.	23 and 47 and 66

Embase (Ovid) search terms

1.	chronic pain/ or intractable pain/
2.	((persist* or intract* or chronic or longstanding or long standing or longterm or long term or refractory or prolong* or long last* or sustain* or linger* or syndrome*) adj3 pain*).ti,ab.

3.	or/1-2
4.	letter.pt. or letter/
5.	note.pt.
6.	editorial.pt.
7.	case report/ or case study/
8.	(letter or comment*).ti.
9.	or/4-8
10.	randomized controlled trial/ or random*.ti,ab.
11.	9 not 10
12.	animal/ not human/
13.	nonhuman/
14.	exp Animal Experiment/
15.	exp Experimental Animal/
16.	animal model/
17.	exp Rodent/
18.	(rat or rats or mouse or mice).ti.
19.	or/11-18
20.	3 not 19
21.	limit 20 to English language
22.	exp Rehabilitation, Vocational/
23.	Return to Work/
24.	*employment/ or employment, supported/ or *unemployment/
25.	(occupation* adj2 (return* or retrain* or support* or rehabilitat*)).ti,ab.
26.	(employ* adj2 (return* or retrain* or support* or rehabilitat* or insecur*)).ti,ab.
27.	(vocation* adj2 (return* or retrain* or support* or rehabilitat*)).ti,ab.
28.	(job* adj2 (return* or retrain* or support* or rehabilitat* or insecur*)).ti,ab.
29.	(work* adj2 (return* or retrain* or support* or rehabilitat* or insecur*)).ti,ab.
30.	(work* adj2 (sheltered or permitted or voluntary)).ti,ab.
31.	unemploy*.ti,ab.
32.	social isolation/
33.	(social adj2 (barrier* or isolate* or isolation or separat* or contact or lonely or loneliness)).ti,ab.
34.	social support/ or *social work/ or *social welfare/
35.	((social or work*) adj2 (participat* or circumstance* or activit* or relation*)).ti,ab.
36.	(social adj2 (wellbeing or distress or consequence* or role* or concern* or vulnerab*)).ti,ab.
37.	*caregiver/
38.	(carer* or caregiver*).ti,ab.
39.	(spouse* or wife or wives or husband* or significant other* or partner* or family or families).ti,ab.
40.	(caring adj3 (dependen* or responsib*)).ti,ab.
41.	poverty/
42.	((financ* or money or income) adj3 (unstable or instability or concern* or vulnerab* or precarious or precarity)).ti,ab.
43.	(poverty or low income or deprived or deprivation).ti,ab.
44.	((litigat* or compensat* or legal) adj3 claim*).ti,ab.
45.	or/22-44
46.	Epidemiologic studies/

47.	Observational study/
48.	exp Cohort studies/
49.	(cohort adj (study or studies or analys* or data)).ti,ab.
50.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
51.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
52.	Controlled Before-After Studies/
53.	Historically Controlled Study/
54.	Interrupted Time Series Analysis/
55.	(before adj2 after adj2 (study or studies or data)).ti,ab.
56.	or/46-55
57.	exp case control study/
58.	case control*.ti,ab.
59.	or/57-58
60.	56 or 59
61.	Cross-sectional studies/
62.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
63.	or/61-62
64.	56 or 59 or 63
65.	21 and 45 and 64

ASSIA (ProQuest) search terms

1.	(MAINSUBJECT.EXACT.EXPLODE("Chronic pain") OR ti,ab((persist* OR intract* OR chronic OR longstanding OR longterm OR refractory OR prolong* OR sustain* OR linger* OR syndrome*) NEAR/3 pain*)) AND (MAINSUBJECT.EXACT("Vocational rehabilitation") OR MAINSUBJECT.EXACT("Unemployment") OR (MAINSUBJECT.EXACT("Supported employment") OR MAINSUBJECT.EXACT("Employment")) OR MAINSUBJECT.EXACT("Return to work") OR ti,ab((occupation* OR employ* OR vocation* OR job* OR work*) NEAR/2 (return* OR retrain* OR support* OR rehabilitat*)) OR ti,ab(work* NEAR/2 (sheltered OR permitted OR voluntary)) OR unemploymetn OR ti.unemployment OR ti:unemployment OR ti(unemploy*) OR MAINSUBJECT.EXACT("Isolation") OR ti,ab(social NEAR/2 (barrier* OR isolate* OR isolation OR separat* OR contact OR lonely OR loneliness)) OR (MAINSUBJECT.EXACT("Social support") OR MAINSUBJECT.EXACT("Social welfare")) OR ti,ab((social OR work*) NEAR/2 (participat* OR circumstance* OR activit* OR relation*)) OR ti,ab(social NEAR/2 (wellbeing OR distress OR consequence* OR role* OR concern* OR vulnerab*)) OR ti,ab(carer* OR caregiver*) OR ti,ab(spouse* OR wife OR wives OR husband* OR "significant other*" OR partner* OR family OR families) OR ti,ab(caring near/3 (dependen* or responsib*)) OR MAINSUBJECT.EXACT("Poverty") OR ti,ab((financ* or money or income) near/3 (unstable or instability or concern* or vulnerab* or precarious or precarity)) OR ti,ab(poverty OR low income OR deprived OR deprivation) OR ti,ab((litigat* or compensat* or legal) near/3 claim*))

SPP (Ovid) search terms

1.	((persist* or intract* or chronic or longstanding or long standing or longterm or long term or refractory or prolong* or long last* or sustain* or linger* or syndrome*) adj3 pain*).ti,ab.

King's Fund search terms

1.	'chronic pain'

Appendix C: Clinical evidence selection

Figure 1: Flow chart of clinical study selection for the review of biological factors

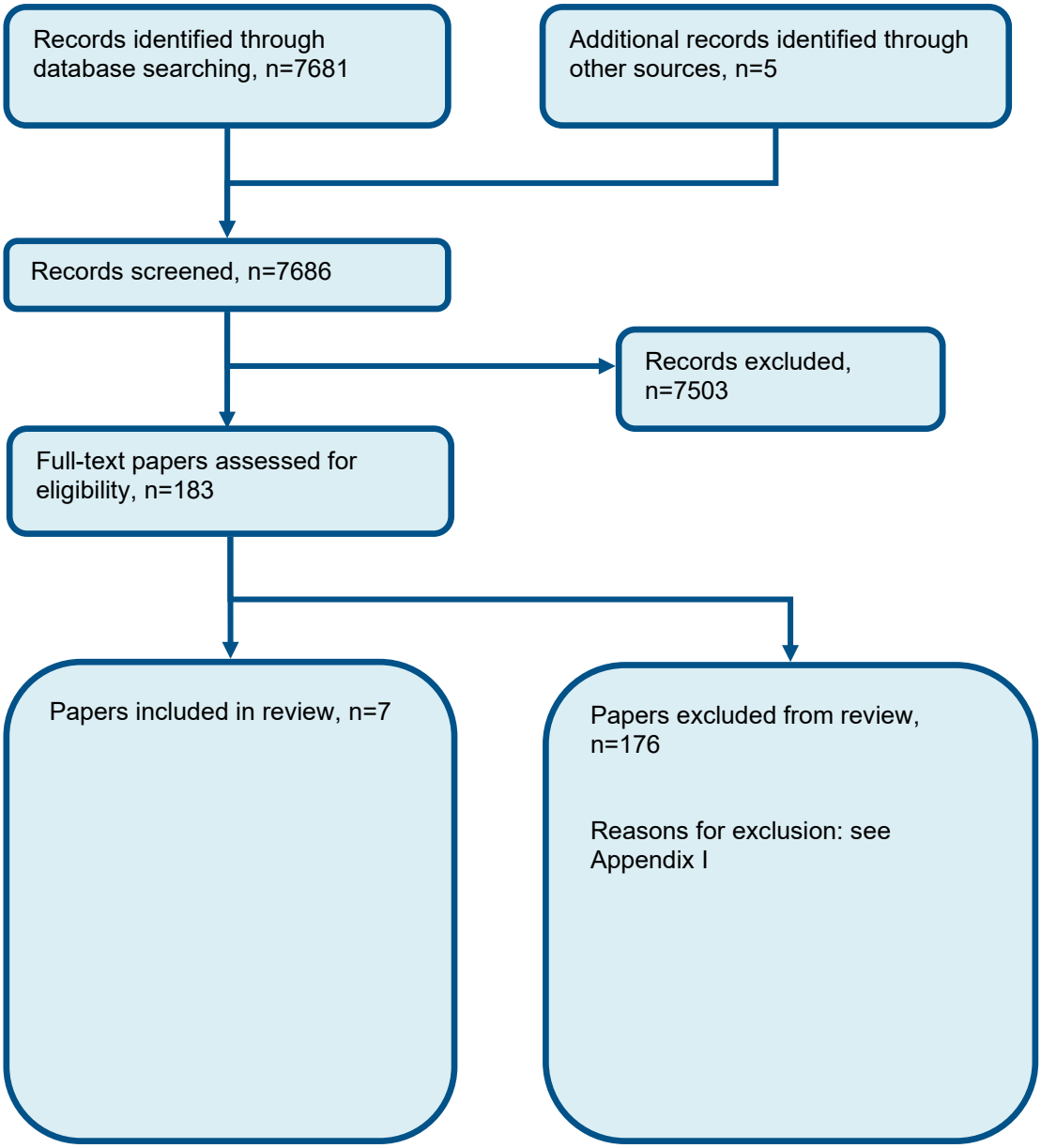


Figure 2: Flow chart of clinical study selection for the review of psychological factors

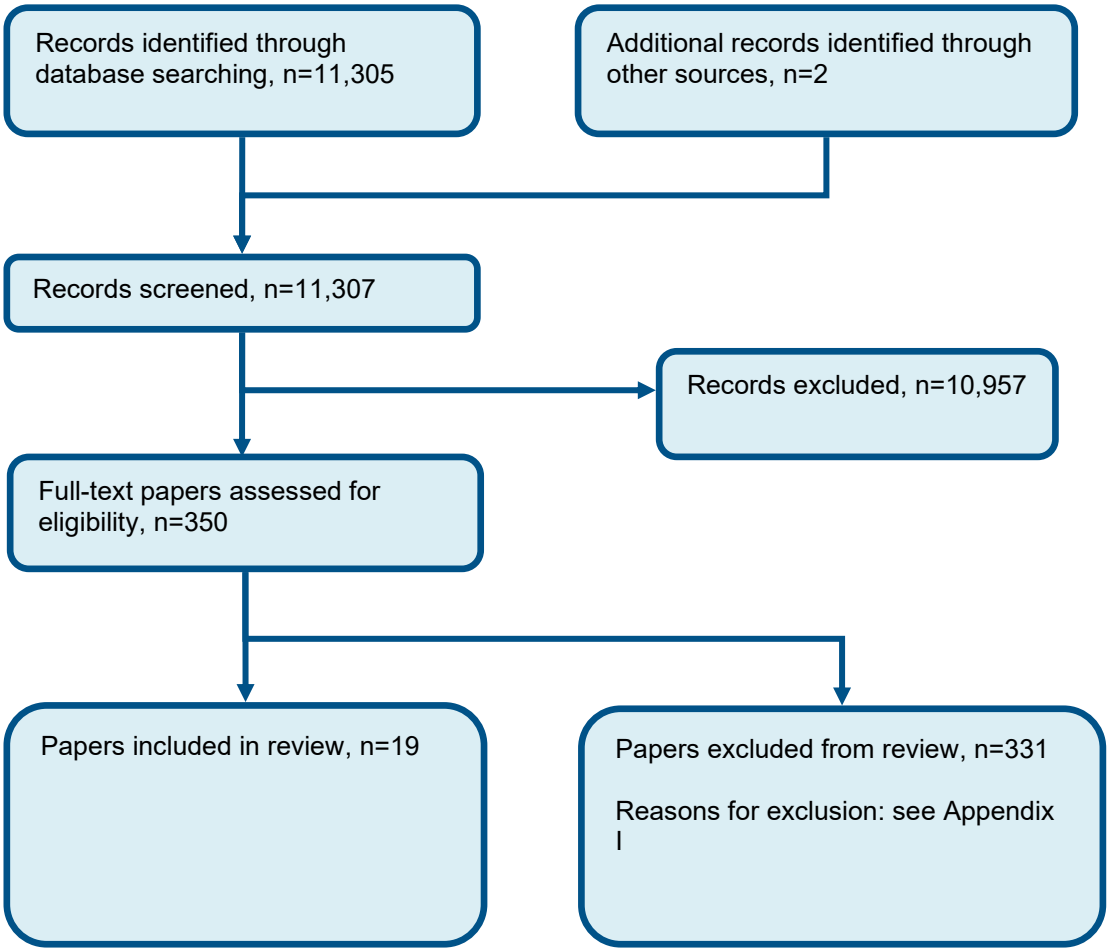
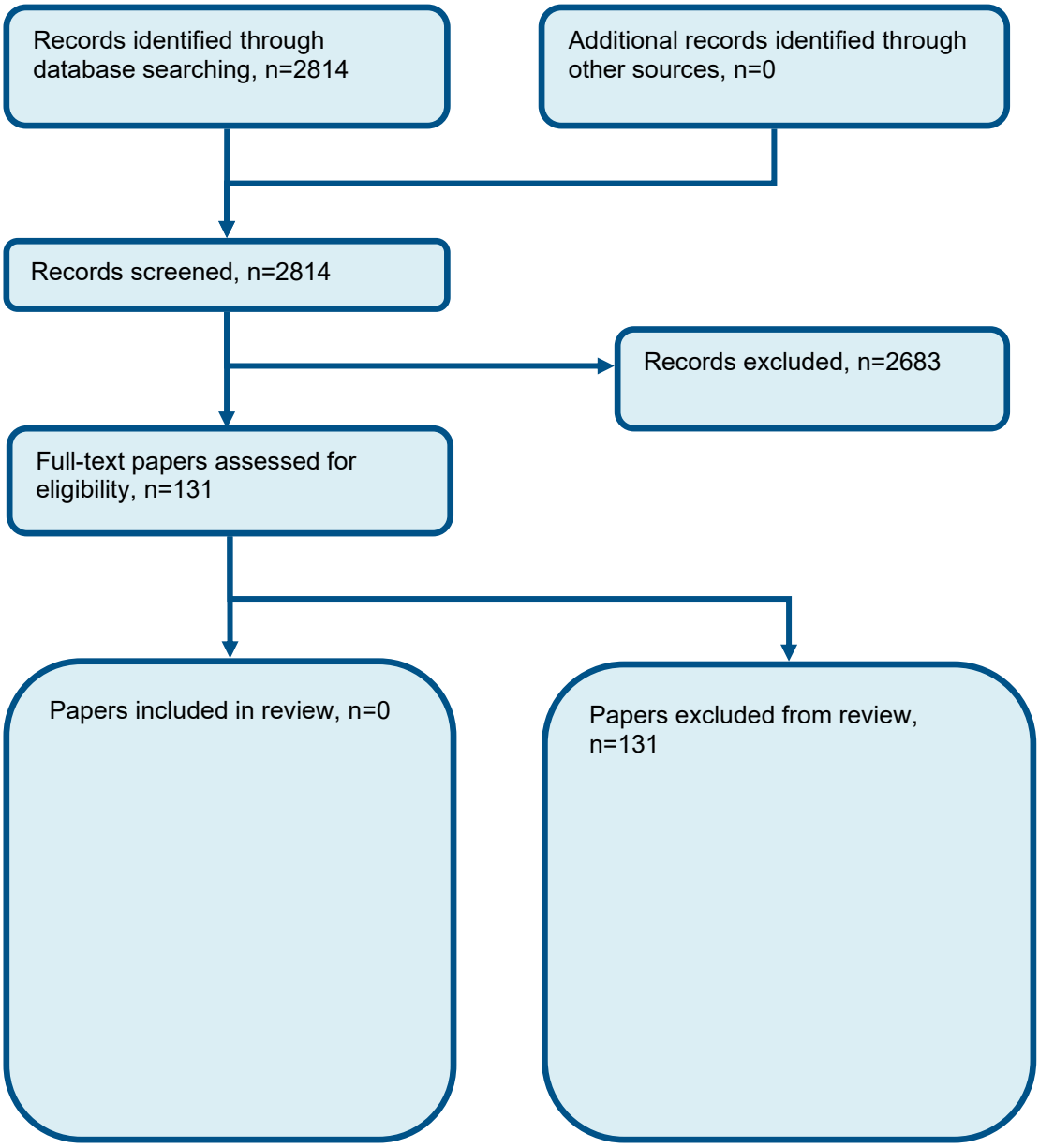


Figure 3: Flow chart of clinical study selection for the review of social factors



Appendix D: Clinical evidence tables

D.1 Biological risk factors

Reference	Chester 2018 [94]
Study type and analysis	Prospective cohort (physiotherapy). Multivariable linear regression: variables with statistically significant relationship with the outcome at the 10% level in simple linear regression models were entered in to multivariable model
Number of participants and characteristics	N=804 people with musculoskeletal shoulder pain (n followed up out of total 1030) Inclusion: aged 18 years or older; shoulder or arm pain aggravated by shoulder movements Exclusion: significant reproduction of shoulder pain on spinal movement, or greater reproduction on spinal movement compared to shoulder movement; radiculopathy, post-surgery, post fracture, posttraumatic dislocation or systemic source aetiologies for shoulder pain Age (mean, SD): 57 (15) years Duration of pain (mean, SD): 14 (28) months Participants were referred to physiotherapy. Prior to the first physiotherapy appointment, participants completed a bespoke questionnaire.
Prognostic variable(s)	Number of additional health problems (None, one, two or more) Most strenuous exercise (none, mild, moderate, strenuous)
Confounders OR Stratification strategy	Confounders adjusted for (in multivariable analysis): • Patient expectation of change • Coping style (pain self-efficacy questionnaire) • Number of additional health problems • Comorbid psychiatric disorder (anxiety or depression in the last 7 days, unclear how measured) • Frequency of pain medication • Most strenuous exercise • Change during scapular facilitation

Reference	Chester 2018 [94]
	• Reported pain intensity (severity of shoulder pain at rest, 0-10 numeric rating scale) • Duration of symptoms • Paraesthesia in the arm • Employment status Other factors considered in initial analysis, but not significant: A total of 71 factors were entered into simple linear regression models
Outcomes and effect sizes	Outcome: Shoulder pain and disability index at 6 months Number of additional health problems (one, two or more, compared to none) One: ß coefficient 3.52, 95% CI 0.3 to 6.75) Two: ß coefficient 6.62, 95% CI 1.48 to 9.75) Most strenuous exercise (none, mild, moderate, strenuous) Mild: ß coefficient −5.53, 95% CI −10.32 to −0.74) Moderate: ß coefficient -8.98, 95% CI −13.86 to −4.11) Strenuous: ß coefficient −6.82, 95% CI −12.17 to −1.47)
Comments	Number of additional health problems (one, two or more, compared to none): high risk of bias (study attrition, study confounding) Most strenuous exercise (none, mild, moderate, strenuous): high risk of bias (study attrition, study confounding, prognostic factor measurement) Outcome indirectness: SPADI includes disability elements

Reference	Forssell 2017 [171]
Study type and analysis	Prospective cohort. Multivariable logistic regression analysis: all variables with p<0.1 in univariable models entered in to multivariable model
Number of participants and characteristics	N=263 temporomandibular disorder pain in the previous month (n followed up out of total 399 enrolled)

Reference	Forssell 2017 [171]
	Inclusion: 18-70 years of age; contacting the oral healthcare unit because of oral or facial pain and confirmed temporomandibular disorder diagnosis Exclusion: temporomandibular disorder pain conditions related to acute trauma or rheumatoid or other inflammatory arthritis and any physical or mental condition that would interfere with the ability to complete the study questionnaire Age (median, quartile range): 41 (30-50) years Duration of pain (median, quartile range): time since onset 3 (1-10) years Patients were screened for possible TMD pain and then one dentist examined those who had screened positive to confirm diagnosis according to research diagnostic criteria for TMD methods. During the initial visit, participants completed a comprehensive multidimensional pain questionnaire assessing TMD pain related and general health factors, and psychological prognostic factors using validated self-report scales.
Prognostic variable(s)	Number of other pain conditions (1-7: back, neck, fibromyalgia, joint, abdominal, chest pain or headache)
Confounders OR Stratification strategy	Confounders adjusted for (in multivariable analysis): • Time since onset • Characteristic pain intensity measured by the Research Diagnostic Criteria for Temporomandibular Disorders questionnaire • Pain-related disability • Number of disability days • Functional jaw limitations (RDC/TMD questionnaire) • SCL-90 depression • SCL-90 somatization • SCL-90 somatization, no pain • SCL-90 sleep disturbance • Pain-related worry (0-10) • Anxiety (0-10) • Tension and stress (0-10) • Catastrophizing (ruminative thoughts from Pain Catastrophising Scale) • Ability to control pain (Coping Strategies Questionnaire) • Ability to decrease pain (Coping Strategies Questionnaire) • Perceived risk of chronicity (0-10)

Reference	Forssell 2017 [171]
	• Number of healthcare visits • Number of other pain conditions • Pain intensity/dysfunction of other pains • General health (5 point scale) • RAND-36 physical function Other factors considered in univariable analysis, but not significant: • Gender • Education • Age • Parafunctions
Outcomes and effect sizes	Outcome: Clinically significant pain (Graded Chronic Pain Scale grade 1, 2 3 and 4) at 1 year Number of other pain conditions (1-7: back, neck, fibromyalgia, joint, abdominal, chest pain or headache) OR 1.3, 95% CI 0.86 to 1.96)
Comments	Number of other pain conditions at baseline: high risk of bias (study attrition; study confounding)

Reference	Helminen 2016 [226]
Study type and analysis	Secondary analysis of an RCT (CBT intervention vs control). Multivariate linear mixed model
Number of participants and characteristics	N=111 patients with radiologically diagnosed knee osteoarthritis and associated pain symptoms Inclusion: radiologically (Kellgren-Lawrence 2–4) diagnosed knee osteoarthritis and associated pain symptoms Exclusion: not reported Age (mean, SD): 63.6 (7.2) years Duration of pain (mean, SD): 7.8 (7) years Those who participated in a randomized controlled trial with a group-based cognitive-behavioural intervention to treat pain were followed up for one year. The outcome measures were recorded at 0-, 3-, and 12-month follow-up points using postal questionnaires.

Reference	Helminen 2016 [226]
	The questionnaires included questions about knee pain and physical function, demographic, socioeconomic and disease-related variables and psychological variables.
Prognostic variable(s)	Exercise (2 or more/week or 1 or less/week)
Confounders OR Stratification strategy	Confounders adjusted for (in multivariate analysis): • Age • Gender • Education • Body mass index • Marital status • Duration of pain • Exercise • Group randomisation • Time • Life satisfaction score • Sense of coherence • Pain self-efficacy questionnaire • Tampa scale of kinesiophobia • Pain catastrophizing scale • Beck depression inventory
Outcomes and effect sizes	Outcome: Pain subscale (0-100mm) of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) at 12 months Exercise (2 or more/week or 1 or less/week): ß coefficient 0.32 (95% CIs: -6.29 to 6.92) Outcome: SF36 Finnish version physical component summary scores at 12 months Exercise (2 or more/week or 1 or less/week) ß coefficient 2.07 (95% CIs: -1.38 to 5.51) Outcome: SF36 Finnish version mental component summary scores at 12 months Exercise (2 or more/week or 1 or less/week) ß coefficient 2.42 (95% CIs: -1.15 to 6)
Comments	Exercise (2 or more/week or 1 or less/week)

Reference	Helminen 2016 [226]
	Pain subscale on the WOMAC at 12 months: high risk of bias due to study confounding, statistical analysis SF-36 physical component summary score at 12 months: high risk of bias due to study confounding, statistical analysis

Reference	McIntosh 2011 [355]
Study type and analysis	Prospective cohort (rehabilitation programme); multivariable logistic regression analysis (Logistic regression analysis was used to model the relationship between the binary response variable (comorbidity present yes/no) and the individual outcome measures for the two groups. Univariate logistic regression analysis was used to identify any significant associations between each independent variable and the dichotomous outcome. Multivariable analysis was used to adjust for covariates. An alpha level of 0.05 (two sided) was used as the criterion for statistical significance)
Number of participants and characteristics	N=2777 chronic low back pain patients Mean age 42.3(10.7) years Duration of pain (mean): 5.8 months Inclusion criteria: pain for at least 90 days. Participants were recruited from a non-operative rehabilitation programme between 2005 and 2006. The population had no identifiable red flags (tumours, infections, fracture) that could cause the pain. Those both working and unemployed were included in the cohort. Minors and surgical candidates were excluded.
Prognostic variable(s)	Presence or absence of comorbid physical condition (comorbidity; including CAD, hypertension, RA, diabetes, COPD, or other conditions)
Confounders OR Stratification strategy	Confounders included in the review protocol • Age • Gender
Outcomes and effect sizes	2 point change in VAS 0-10 pain intensity Presence or absence of comorbid physical condition(s): OR 1.013 (95% CIs 0.963 to 1.065)
Comments	Presence or absence of comorbid physical condition predicting 2 point change in VAS 0-10: high risk of bias (confounding, prognostic factor)

Reference	Tseli 2020 [521]
Study type and analysis	Prospective cohort (interdisciplinary multimodal pain rehabilitation programmes). Multivariable logistic regression analysis: all variables with p≤0.2 in univariable models entered in to multivariable model, stepwise backward elimination used to eliminate variables based on highest p value until only variables significant at p≤0.2 remained, variables eliminated in univariate analysis then included one by one and retained if significant at p<0.05.
Number of participants and characteristics	N=2876 people with persistent back pain (n followed up out of total 6449 participating in a programme) Inclusion: aged 18-67 years; chronic (>3 months) non-malignant musculoskeletal pain; participating in an IMPR programme and 12 month follow up; with consent Exclusion: missing outcome data Age (mean, SD): 43.5 (10.7) years Duration of pain (mean, SD): 106.2 (107.7) months Participants referred to specialist interdisciplinary multimodal pain rehabilitation clinics for assessment and rehabilitation completed baseline assessments.
Prognostic variable(s)	Pain diagnosis (chronic widespread pain)
Confounders OR Stratification strategy	Confounders adjusted for (in multivariable analysis): • Sex • Age category • Education level • Country of origin • Employment status • Beliefs of restored health • Number of pain regions • Pain intensity • Multidimensional pain inventory – pain interference • Multidimensional pain inventory – life control • Multidimensional pain inventory – overall activity • Hospital anxiety and depression scale – anxiety • SF36 mental component • SF36 physical component

Reference	Tseli 2020 [521]
	Other factors considered in initial analysis, but not significant: • Pain duration • Multidimensional pain inventory – social support • Hospital anxiety and depression scale – depression • EQ5D
Outcomes and effect sizes	Outcome: Quality of life physical (difference of ≥3 on SF36 physical component) at 12 months after completion of the 10 week programme Pain diagnosis (chronic widespread pain compared to 0-2 regions): OR 0.69 (95% CI 0.45-1.06)
Comments	Pain diagnosis (chronic widespread pain compared to 0-2 regions): very high risk of bias (study attrition, outcome measurement, study confounding) Outcome indirectness: Results only reported for physical component, not mental component

Reference	Velly 2011 [552]
Study type and analysis	Prospective cohort. Multivariable linear regression analysis
Number of participants and characteristics	N=480 people with a diagnosis of any temporomandibular joint disorder pain (n followed up out of total 570 enrolled). Inclusion: diagnosis of any TMJD pain with a frequency of at least once per week and duration of at least 3 months Exclusion: systemic rheumatic disease; dental, sinus, or other infection that could cause swelling or tenderness in the area; taking prescribed steroids or narcotics for a chronic condition; taking antidepressants and not on a stable dose for at least the last 2 months; primary psychiatric disease (uncontrolled schizophrenia, psychoses, or other serious disorders that interfere with ability to consent and participate); prior TMJ surgery; unable to provide informed consent; >65 or <18 years of age; scheduling problems that would interfere with follow-up; >3 alcoholic drinks per day; pregnant Age (mean, SD): 35.85 (12.48) years Duration of pain: not reported

Reference	Velly 2011 [552]
	Participants recruited through media advertisements and notices distributed to local dentists. Predictor variables measured at baseline.
Prognostic variable(s)	Pain diagnosis (widespread pain yes/no)
Confounders OR Stratification strategy	Confounders adjusted for (in multivariable analysis): • Depression (Beck Depression Inventory) • Widespread pain • Pain intensity (0-100 numeric rating scale) • Catastrophizing (Coping strategies questionnaire) • Gender • Age
Outcomes and effect sizes	Outcome: Pain intensity (0-100 numeric rating scale) at 18 months Pain diagnosis (widespread pain yes/no): ß coefficient 2.88 (95% CIs -0.83 to 6.58)
Comments	Pain diagnosis (widespread pain yes/no): high risk of bias (study participation; study confounding; statistical analysis and presentation)

Reference	Verkerk 2015 [559]
Study type and analysis	Prospective cohort (2 month multidisciplinary treatment). Multivariable logistic regression analysis
Number of participants and characteristics	N=1564 for 5 month outcomes, n=960 for 12 month outcomes chronic non-specific low back pain patients not recovering after primary/secondary care (n followed up out of total 1760 enrolled) Inclusion: men and women aged ≥18 years; chronic non-specific low back pain (duration ≥3 months); previous and insufficient treatment in primary/secondary care; signed informed consent Exclusion: insufficient knowledge of the Dutch language; signs indicating radiculopathy; asymmetric Achilles tendon reflex and/or passive straight led raise test restricted by pain in the lower leg; positive MRI findings for disc herniation; recent (<6 months) fracture, neoplasm or recent previous surgery of the lumbar spine, pelvic girdle, hip joint or femur; specific causes; pregnancy or ≤6 months post-partum Age (mean, SD): 40.1 (10.6) years Duration of pain (mean, SD): 7.7 (8.8) years

Reference	Verkerk 2015 [559]
	Participants recruited from a multidisciplinary outpatient rehabilitation clinic and evaluated by physical evaluation and/or questionnaires at baseline.
Prognostic variable(s)	Presence or absence of comorbid physical condition (comorbidity)
Confounders OR Stratification strategy	Confounders adjusted for (in multivariable analysis) - 30% improvement in pain intensity at 5 months: • Age • Gender • Pain intensity (visual analogue scale 0-100) • SF36 physical component summary • SF36 mental component summary • Body mass index • Previous rehabilitation • Work participation Confounders adjusted for (in multivariable analysis) - 30% improvement in pain intensity at 12 months • Age • Gender • Pain intensity (visual analogue scale 0-100) • SF36 physical component summary • Education • Comorbidity • Marital status • B200 Isostation extension • Tampa scale for kinesiophobia Other factors considered but excluded from model as not significant: • Duration of pain • Fatigue • Quebec back pain disability scale • Cause of back pain

Reference	Verkerk 2015 [559]
	• Pain in previous 3 months (stable, increased, decreased) • Duration of walking, sitting, standing
Outcomes and effect sizes	Outcome: 30% improvement in pain intensity at 12 months Presence or absence of comorbid physical condition (co-morbidity yes/no): OR 0.76 (95% CIs 0.52-1.11)
Comments	Outcome: 30% improvement in pain intensity at 5 months Comorbid physical condition: high risk of bias (study attrition, prognostic factor; study confounding)

D.2 Psychological risk factors

Reference	Adnan 2017 [2]
Study type and analysis	Retrospective cohort. Logistic regression: all factors tested one at a time in a univariable logistic regression, multiple model included all statistically significant (p <0.25) variables.
Number of participants and characteristics	Total n=412 chronic low back pain patients (from a total sample of 565 with acute and chronic pain) Inclusion: patients referred to a rehabilitation programme by a physician after adequate medical examination and diagnosis had been established Exclusion criteria: patients with other comorbidities and/or under consideration for surgery Age (mean, SD): favourable outcome 38.8 (10.3) years, unfavourable outcome 42.7 (10.7) years Duration of pain: not stated (other than >14 weeks) Participants were recruited from an exercise-based rehabilitation program (36 treatment sessions, 2 hours, 2-3 times/week). Demographic, psychological and functional self-reported parameters were derived from questionnaires and medical reports.
Prognostic variable(s)	Reported pain intensity (0-10 numeric pain rating scale for back pain) at baseline Comorbid psychiatric disorder (Beck depression index 0-63) at baseline
Confounders OR Stratification strategy	Confounders adjusted for (in multivariate analysis): • Age • Reported pain intensity (NPRS back pain) • Comorbid psychiatric disorder (Beck depression index) • Disability (Oswestry disability index) Other factors considered in univariate analysis, but not significant: • Sex • Body mass index • Fat percentage • Reported pain intensity (NPRS leg pain) • Coping styles (Tampa scale for kinesiophobia)
Outcomes and effect sizes	Outcome: Favourable outcome (30% reduction from baseline in both the Numeric Pain Rating Scale and the Oswestry Disability Index; follow up time not reported)

Reference	Adnan 2017 [2]
	Reported pain intensity (0-10 numeric pain rating scale for back pain, high is poor outcome) at baseline: OR 1.191 (95% CI 1.063-1.333) for high NPRS versus low NPRS (cut-off not reported) Comorbid psychiatric disorder (Beck depression index 0-63, high is poor outcome) at baseline: OR 0.96 (95% CI 0.897-0.971) for every increase in BDI score
Comments	Reported pain intensity (0-10 numeric pain rating scale for back pain) at baseline: very high risk of bias (prognostic factor measurement; study confounding) Comorbid psychiatric disorder (Beck depression index 0-63) at baseline: high risk of bias (study confounding) Outcome indirectness: included disability

Reference	Allaire 2018 [13]
Study type and analysis	Prospective cohort (interdisciplinary interventions). Logistic regression: ordinal logistic regression used to identify factors significantly associated with the outcome ($p<0.05$), significant factors entered in to the multivariable ordinal logistic regression model
Number of participants and characteristics	N=284 women referred to a centre for pelvic pain and endometriosis (n followed up out of the total sample of 525) Inclusion: new or re-referrals to a women's centre for pelvic pain and endometriosis during 1 year Exclusion: menopausal or age >50 years; no follow up visits at the centre Age (mean, SD): 35 (7.8) years Duration of pain (median, interquartile range): 13 (5.2-21) years Participants recruited from a women's centre for pelvic pain and endometriosis, interventions were minimally invasive surgery, medical management and/or a pain programme (education, physiotherapy, counselling). Prior to initial consultation, participants completed online questionnaires to measure pain intensity, quality of life, demographic data and history, supplemented by physical exam findings and review of medical records.
Prognostic variable(s)	Reported pain intensity (chronic pelvic pain severity 0-10 numeric rating scale) at baseline Coping style (pain catastrophizing scale) at baseline

Reference	Allaire 2018 [13]
Confounders OR Stratification strategy	Confounders adjusted for (in multivariable analysis): • Coping style (Pain catastrophizing scale) • Abdominal wall pain • Reported pain intensity (NRS) • Age • Re-referral • History of sexual assault • Surgery at centre Other factors considered in initial analysis, but not significant: • Body mass index • Family history of chronic pain • Smoking • Geography, outside metropolitan Vancouver • Parous • Duration of pain • Previous hysterectomy • Education • Income • Marital status • Endometriosis • Pelvic floor myalgia • Irritable bowel syndrome • Painful bladder syndrome • Depression (patient health questionnaire-9) • Anxiety (generalised anxiety disorder-7) • Re-referral • Total no. of comorbidities
Outcomes and effect sizes	Outcome: Increase in chronic pelvic pain severity (0-10) categorised as none-mild 0-3, moderate 4-6 and severe 7-10 at 1 year

Reference	Allaire 2018 [13]
	Reported pain intensity (chronic pelvic pain severity 0-10 numeric rating scale) at baseline: OR 1.19 (95% CI 1.09-1.31) unclear what increments were used Coping style (pain catastrophizing scale) at baseline: OR 1.1 (95% CI 1-1.21) for every 5-point increment
Comments	Reported pain intensity (chronic pelvic pain severity 0-10 numeric rating scale) at baseline: very high risk of bias (study attrition, prognostic factor measurement; study confounding) Coping style (pain catastrophizing scale) at baseline: very high risk of bias (study attrition, study confounding)

Reference	Boonstra 2015 [52]
Study type and analysis	Prospective cohort (CBT). Multiple linear regression analysis: variables with p<0.2 in univariate analyses identified as potential predictors and clustered in to blocks, variables with p values <0.2 in block analysis entered in to next model, variables with p values <0.05 entered in to final model
Number of participants and characteristics	N=230 chronic musculoskeletal pain patients Inclusion: chronic musculoskeletal pain referred to a rehabilitation centre and given inpatient or outpatient CBT; aged above 18 years; pain lasting over 3 months; involvement of a psychologist in treatment, by way of operationalisation of having moderate to severe psychosocial problems (psychological distress, pain-related fear, mild/moderate depression, compulsive behaviour, personality disorder, etc.) Exclusion: insufficient command of Dutch; comorbidity with severe negative consequences for physical functioning; current major psychiatric disorder Age (mean, SD): outpatient 43 (10), inpatient 43 (13) years Duration of pain (mean, SD): outpatient 4.9 (5.3), inpatient 5.9 (5.8) years Participants recruited from a rehabilitation centre; referred for inpatient or outpatient treatment by rehabilitation physicians depending on location. Series of demographic and psychological questionnaires administered in the first or second week of the programme as part of regular clinical procedures.
Prognostic variable(s)	Reported pain intensity (pain subscale of the SF36) at baseline

Reference	Boonstra 2015 [52]
Confounders OR Stratification strategy	Confounders adjusted for (in multiple linear regression analysis): • Work status Other factors considered in initial analysis, but not significant: • Age • Gender • Marital status • Educational level • Age of youngest child • Ongoing procedure • Duration of complaints • Employed • Work status • Benefit • SF36 sub scales • Personality • Coping sub scales (measured by Coping with pain questionnaire) • Coping composite scores (measured by Coping with pain questionnaire) • Tampa scale for kinesiophobia • Psychological distress (measured by Symptom checklist-90 revised) • Type of treatment
Outcomes and effect sizes	Outcome: Pain subscale of the SF36 (score at discharge minus score at admission) Reported pain intensity (pain subscale of the SF36) at baseline: unstandardized ß coefficient -1.36 (SE 0.07, p<0.001)
Comments	Study reports two other sub scales of SF36 as outcomes – not valid measures of quality of life Reported pain intensity (pain subscale of the SF36) at baseline: very high risk of bias (study attrition, prognostic factor, outcome measurement, study confounding)

Reference	Chester 2018 [94]
Study type and analysis	Prospective cohort (physiotherapy). Multivariable linear regression: variables with statistically significant relationship with the outcome at the 10% level in simple linear regression models were entered in to multivariable model
Number of participants and characteristics	N=804 people with musculoskeletal shoulder pain (n followed up out of total 1030) Inclusion: aged 18 years or older; shoulder or arm pain aggravated by shoulder movements Exclusion: significant reproduction of shoulder pain on spinal movement, or greater reproduction on spinal movement compared to shoulder movement; radiculopathy, post-surgery, post fracture, posttraumatic dislocation or systemic source aetiologies for shoulder pain Age (mean, SD): 57 (15) years Duration of pain (mean, SD): 14 (28) months Participants were referred to physiotherapy. Prior to the first physiotherapy appointment, participants completed a bespoke questionnaire.
Prognostic variable(s)	Reported pan intensity (severity of shoulder pain at rest, 0-10 numeric rating scale) at baseline Comorbid psychiatric disorder (anxiety and depression in the last 7 days, unclear how measured) at baseline Coping style (Pain self-efficacy questionnaire) at baseline
Confounders OR Stratification strategy	Confounders adjusted for (in multivariable analysis): • Patient expectation of change • Coping style (Pain self-efficacy questionnaire) • Number of additional health problems • Comorbid psychiatric disorder (anxiety or depression in the last 7 days, unclear how measured) • Frequency of pain medication • Most strenuous exercise • Change during scapular facilitation • Reported pain intensity (severity of shoulder pain at rest, 0-10 numeric rating scale) • Duration of symptoms • Paraesthesia in the arm • Employment status Other factors considered in initial analysis, but not significant: A total of 71 factors were entered into simple linear regression models

Reference	Chester 2018 [94]
Outcomes and effect sizes	Outcome: Shoulder pain and disability index at 6 months Reported pain intensity (severity of shoulder pain at rest, 0-10 numeric rating scale) at baseline: β coefficient 1.89 (95% CI 1.26-2.51) Comorbid psychiatric disorder (moderate anxiety or depression in the last 7 days, unclear how measured) at baseline: β coefficient 2.19 (95% CI -0.99-5.37) Comorbid psychiatric disorder (extreme anxiety or depression in the last 7 days, unclear how measured) at baseline: β coefficient 12.02 (95% CI 1.49-22.56) Coping style (Pain self-efficacy questionnaire) at baseline: β coefficient -0.36 (95% CI -0.5- -0.22)
Comments	Reported pain intensity (severity of shoulder pain at rest, 0-10 numeric rating scale) at baseline: very high risk of bias (study attrition, study confounding) Comorbid psychiatric disorder (moderate anxiety or depression in the last 7 days, unclear how measured) at baseline: very high risk of bias (study attrition, prognostic factor, study confounding) Comorbid psychiatric disorder (extreme anxiety or depression in the last 7 days, unclear how measured) at baseline: very high risk of bias (study attrition, prognostic factor, study confounding) Coping style (Pain self-efficacy questionnaire) at baseline: very high risk of bias (study attrition, study confounding) Outcome indirectness: SPADI includes disability elements

Reference	De Rooij 2013 [118]
Study type and analysis	Prospective cohort (multidisciplinary intervention). Multiple linear regression: explorative univariate regression analysis identified potential predictors for the multivariate analysis (p<0.2)
Number of participants and characteristics	N=120 with chronic widespread pain (n followed up out of a total of 138 who entered the study) Inclusion: a diagnosis of chronic widespread pain according to the American College of Rheumatology criteria (ACR); eligible for multidisciplinary treatment according to the criteria the Dutch Consensus Report of Pain Rehabilitation, as assessed by both a

Reference	De Rooij 2013 [118]
	rehabilitation physician and a psychologist; these criteria require patients to experience restrictions in daily living (e.g. sport, work) and/or psychosocial functioning; age between 18 and 75 years. Exclusion: pain resulting from known specific pathology; not eligible for multidisciplinary pain treatment because of a somatic disorder, social problem and/or psychiatric disorder (e.g. major depression), or because the patient was currently involved in a legal procedure of conflicting interest, was currently receiving pain treatment elsewhere, or was judged by the rehabilitation physician and/or psychologist not to be motivated for behavioural change; insufficient control of the Dutch language to complete questionnaires; refusal to give informed consent. Age (mean, SD): 45 (10.3) years Duration of pain: not reported Patients with CWP were referred by rheumatologists and general practitioners to the pain management team of a single centre. Baseline measurements took place before start of treatment.
Prognostic variable(s)	Reported pain intensity (numeric rating scale 0-10) at baseline
Confounders OR Stratification strategy	Confounders adjusted for (in multivariate analysis): • Gender Other factors considered in univariate analysis, but not significant: • Multidimensional Pain Inventory interference scale • Depression (Beck depression inventory) • Psychological functioning (symptom checklist 90) • Anxiety (Hospital anxiety and depression scale) • Emotional representation questionnaire (Illness Perception Questionnaire) • Coherence (Illness Perception Questionnaire) • Consequences (Illness Perception Questionnaire) • Personal control (Illness Perception Questionnaire) • Treatment control (Illness Perception Questionnaire) • Timeline cyclical (Illness Perception Questionnaire) • Timeline (Illness Perception Questionnaire) • General self-efficacy scale • Tampa scale for kinesiophobia

Reference	De Rooij 2013 [118]
	• Avoidance behaviour (measured by Pain coping inventory) • Catastrophizing (measured by Coping scale questionnaire) • Impact (Fibromyalgia impact questionnaire) • Fatigue (Fibromyalgia impact questionnaire) • Activity level • Age • Partnership • Ethnicity • Education
Outcomes and effect sizes	Outcome: Pain intensity (numeric rating scale 0-10) at 6 months Reported pain intensity (numeric rating scale 0-10) at baseline: B (unstandardized regression coefficient) -0.53 (95% CI -0.67- -0.39)
Comments	Reported pain intensity (numeric rating scale 0-10) at baseline: high risk of bias (study confounding)

Reference	Demarchi 2019 [123]
Study type and analysis	Prospective cohort. Multivariate linear regression: univariate regression analysis identified potential predictors for the multivariate analysis ($p<0.25$)
Number of participants and characteristics	N=92 with chronic non-specific low back pain (n followed up out of total 102 enrolled) Inclusion: low back pain without any attributable cause lasting for at least 3 months; aged between 18 and 60 years; scored at least moderate in questions 6 and 7 of the SF36 Exclusion: at least 2 signs that indicate neural compression; previous surgical procedure in the spine; serious cardiovascular or neurological pathologies; any red flag confirmed by a checklist Age (mean): 40.4 (11.6) years Duration of pain (median, interquartile rage): 24 (6-60) months Recruited in 2 outpatient university physiotherapy clinics through advertising and social media in the community.

Reference	Demarchi 2019 [123]
	Baseline questionnaire contained sociodemographic, anthropometric data, duration of symptoms, pain intensity, disability, fear of movement, depression, physical activity level and perceived physical overload. Participants were offered a 2 month course of usual physiotherapy program.
Prognostic variable(s)	Reported pain intensity (0-10 numeric rating scale) at baseline Comorbid psychiatric disorder (Beck depression inventory) at baseline
Confounders OR Stratification strategy	Confounders adjusted for (in multivariate analysis): • Age • Pain (NRS) at baseline • Disability (Roland Morris disability questionnaire) at baseline • Depression (BDI) Other factors considered in univariate analysis, but not significant: • Sex • BMI • Perceived physical overload • Fear of movement (TSK)
Outcomes and effect sizes	Outcome: Pain intensity (NRS 0-10) at 6 months Reported pain intensity (NRS 0-10) at baseline: ß coefficient 0.14 (95% CI -0.2-0.49) Comorbid psychiatric disorder (BDI) at baseline: ß coefficient 0.09 (95% CI 0.02-0.16)
Comments	Reported pain intensity (NRS 0-10) at baseline: high risk of bias (study confounding) Comorbid psychiatric disorder (BDI) at baseline: high risk of bias (study confounding)

Reference	Dunn 2011 [144]
Study type and analysis	Prospective cohort. Cox regression: factors that had a statistically significant association with outcome were then adjusted for potential confounders

Reference	Dunn 2011 [144]
Number of participants and characteristics	N=389 with low back pain (n followed up out of total 776 consenting to follow up) Inclusion: aged 30–59 years consulting their General Practitioner (GP) with LBP Exclusion: not reported Age (mean): 46.7 years Duration of pain: 2/5 had pain for ≥3 years, among those with <3 years 1/3 reported that pain had started in the previous 3 months Consecutive patients recruited from 5 GP practices and included in the Backpain Research in North Staffordshire (BaRNS) Study, a prospective cohort of primary care low back pain patients. Baseline questionnaire contained demographic items plus questions relating to LBP intensity, disability and psychological status.
Prognostic variable(s)	Reported pain intensity (mean of 3 0-10 numeric rating scales for least, usual and current low back pain intensity; scores of ≥5 defined as high) at baseline Comorbid psychiatric disorder (probable cases of anxiety defined as scores of ≥11 on the Hospital anxiety and depression scale) at baseline Comorbid psychiatric disorder (probable cases of depression defined as scores of ≥11 on the Hospital anxiety and depression scale) at baseline Coping style (catastrophising measured by the Coping strategies questionnaire) at baseline Coping style (fear- avoidance beliefs measured by Tampa scale for kinesiophobia) at baseline
Confounders OR Stratification strategy	Confounders adjusted for (in multivariate analysis): • Education • Employment • Dissatisfaction with work status • Work absence • Long duration • High functional disability (Roland Morris Disability questionnaire) • High pain intensity (mean of 3 0-10 numeric rating scales for least, usual and current low back pain intensity; scores of ≥5 defined as high) • Leg pain • Distal leg pain • Upper body pain

Reference	Dunn 2011 [144]
	• Bothersomeness • Anxiety (probable cases of anxiety defined as scores of ≥11 on the Hospital anxiety and depression scale) • Depression (probable cases of depression defined as scores of ≥11 on the Hospital anxiety and depression scale) • Fear-avoidance (Tampa scale for kinesiophobia) • Catastrophising (Coping strategies questionnaire) • Poor self-rated health (SF36 general health sub scale) • Low vitality (SF36 vitality sub scale) Other factors considered in univariate analysis, but not significant: • Older age (dichotomised at the mid-point of the study sample, with older age being 45–59 years) • Gender • Previous history
Outcomes and effect sizes	Outcome: Chronic pain grade IV (highly disabling and severely limiting low back pain) at 12 months Reported pain intensity (mean of 3 0-10 numeric rating scales for least, usual and current low back pain intensity; scores of ≥5 defined as high) at baseline: RR 4.13 (95% CI 1.73-9.88) Comorbid psychiatric disorder (probable cases of anxiety defined as scores of ≥11 on the Hospital anxiety and depression scale) at baseline: RR 1.84 (95% CI 1.05-3.25) Comorbid psychiatric disorder (probable cases of depression defined as scores of ≥11 on the Hospital anxiety and depression scale) at baseline: RR 1.53 (95% CI 0.9-2.61) Coping style (catastrophising measured by the Coping strategies questionnaire) at baseline: RR 1.46 (95% CI 0.83-2.54) Coping style (fear- avoidance beliefs measured by Tampa scale for kinesiophobia) at baseline: RR 1.08 (95% CI 0.66-1.78)
Comments	Reported pain intensity (mean of 3 0-10 numeric rating scales for least, usual and current low back pain intensity; scores of ≥5 defined as high) at baseline: very high risk of bias (study attrition; study confounding) Comorbid psychiatric disorder (probable cases of anxiety defined as scores of ≥11 on the Hospital anxiety and depression scale) at baseline: very high risk of bias (study attrition; study confounding)

Reference	Dunn 2011 [144]
	Comorbid psychiatric disorder (probable cases of depression defined as scores of ≥11 on the Hospital anxiety and depression scale) at baseline: very high risk of bias (study attrition; study confounding) Coping style (catastrophising measured by the Coping strategies questionnaire) at baseline: very high risk of bias (study attrition; study confounding) Coping style (fear- avoidance beliefs measured by Tampa scale for kinesiophobia) at baseline: very high risk of bias (study attrition; study confounding)

Reference	Dybowski 2018 [145]
Study type and analysis	Prospective cohort. Ordinary least squares linear regression
Number of participants and characteristics	N=109 people with chronic pelvic pain syndrome (n followed out of total 211 enrolled) Inclusion: valid diagnosis of chronic pelvic pain syndrome; age ≥18 years; sufficient knowledge of German language; written informed consent Exclusion: severe medical conditions; suicidality; pain duration <6 months Age (mean, SD): 49.3 (16.7) years Duration of pain (mean, SD): 5.7 (6.9) years Patients referred by primary or secondary care physicians to an interdisciplinary, specialised outpatient clinic for chronic pelvic pain. Baseline data collected before and during patients first visit using questionnaires comprising sociodemographic items and chronic pelvic pain syndrome specific and psychometric instruments.
Prognostic variable(s)	Reported pain intensity (National institutes of health chronic prostatitis symptom index pain scale) at baseline Comorbid psychiatric disorder (Patient health questionnaire anxiety and depression scale) at baseline Coping style (pain catastrophizing scale) at baseline
Confounders OR Stratification strategy	Confounders adjusted for (in multivariate analysis): • Age • Sex

Reference	Dybowski 2018 [145]
	• Pain duration • National institutes of health chronic prostatitis symptom index pain scale • National institutes of health chronic prostatitis symptom index urinary scale • National institutes of health chronic prostatitis symptom index quality of life scale • Patient health questionnaire anxiety and depression scale • Pain catastrophizing scale • Whiteley Index 7, health anxiety • FsozU, social support
Outcomes and effect sizes	Outcome: Pain symptoms measured by National institutes of health chronic prostatitis symptom index (modified version with female homologs) at 11 months Reported pain intensity (National institutes of health chronic prostatitis symptom index pain scale) at baseline: unstandardized regression coefficient B 0.38 (SE 0.13) Comorbid psychiatric disorder (Patient health questionnaire anxiety and depression scale) at baseline: unstandardized regression coefficient B 0.14 (SE 0.05) Coping style (pain catastrophizing scale) at baseline: unstandardized regression coefficient B 0.02 (SE 0.04) Outcome: Quality of life measured by National institutes of health chronic prostatitis symptom index (modified version with female homologs) at 11 months Reported pain intensity (National institutes of health chronic prostatitis symptom index pain scale) at baseline: unstandardized regression coefficient B -0.11 (SE 0.09) Comorbid psychiatric disorder (Patient health questionnaire anxiety and depression scale) at baseline: unstandardized regression coefficient B 0.09 (SE 0.04) Coping style (pain catastrophizing scale) at baseline: unstandardized regression coefficient B 0.05 (SE 0.03)
Comments	Outcome: Pain symptoms measured by National institutes of health chronic prostatitis symptom index (modified version with female homologs) at 11 months

Reference	Dybowski 2018 [145]
	Reported pain intensity (National institutes of health chronic prostatitis symptom index pain scale) at baseline: very high risk of bias (study attrition; study confounding) Comorbid psychiatric disorder (Patient health questionnaire anxiety and depression scale) at baseline: very high risk of bias (study attrition; study confounding) Coping style (pain catastrophizing scale) at baseline: very high risk of bias (study attrition; study confounding) Outcome: Quality of life measured by National institutes of health chronic prostatitis symptom index (modified version with female homologs) at 11 months Reported pain intensity (National institutes of health chronic prostatitis symptom index pain scale) at baseline: very high risk of bias (study attrition; study confounding) Comorbid psychiatric disorder (Patient health questionnaire anxiety and depression scale) at baseline: very high risk of bias (study attrition; study confounding) Coping style (pain catastrophizing scale) at baseline: very high risk of bias (study attrition; study confounding)

Reference	Forssell 2017 [171]
Study type and analysis	Prospective cohort. Multivariable logistic regression analysis: all variables with p<0.1 in univariable models entered in to multivariable model
Number of participants and characteristics	N=263 temporomandibular disorder pain in the previous month (n followed up out of total 399 enrolled) Inclusion: 18-70 years of age; contacting the oral healthcare unit because of oral or facial pain and confirmed temporomandibular disorder diagnosis Exclusion: temporomandibular disorder pain conditions related to acute trauma or rheumatoid or other inflammatory arthritis and any physical or mental condition that would interfere with the ability to complete the study questionnaire Age (median, quartile range): 41 (30-50) years Duration of pain (median, quartile range): time since onset 3 (1-10) years

Reference	Forssell 2017 [171]
	Patients were screened for possible TMD pain and then one dentist examined those who had screened positive to confirm diagnosis according to research diagnostic criteria for TMD methods. During the initial visit, participants completed a comprehensive multidimensional pain questionnaire assessing TMD pain related and general health factors, and psychological prognostic factors using validated self-report scales.
Prognostic variable(s)	Reported pain intensity (characteristic pain intensity measured by the Research Diagnostic Criteria for Temporomandibular Disorders questionnaire) at baseline Comorbid psychiatric disorder (depression measured by the Symptom Checklist-90 Revised) at baseline Comorbid psychiatric disorder (somatization with pain items measured by the Symptom Checklist-90 Revised) at baseline Coping style (catastrophizing measured by ruminative thoughts from Pain Catastrophising Scale) at baseline Coping style (confidence in ability to control pain measured by the Coping Strategies Questionnaire) at baseline Coping style (confidence in ability to decrease pain measured by the Coping Strategies Questionnaire) at baseline
Confounders OR Stratification strategy	Confounders adjusted for (in multivariable analysis): • Time since onset • Characteristic pain intensity measured by the Research Diagnostic Criteria for Temporomandibular Disorders questionnaire • Pain-related disability • Number of disability days • Functional jaw limitations (RDC/TMD questionnaire) • SCL-90 depression • SCL-90 somatization • SCL-90 somatization, no pain • SCL-90 sleep disturbance • Pain-related worry (0-10) • Anxiety (0-10) • Tension and stress (0-10) • Catastrophizing (ruminative thoughts from Pain Catastrophising Scale) • Ability to control pain (Coping Strategies Questionnaire) • Ability to decrease pain (Coping Strategies Questionnaire) • Perceived risk of chronicity (0-10) • Number of healthcare visits • Number of other pain conditions • Pain intensity/dysfunction of other pains

Reference	Forssell 2017 [171]
	• General health (5 point scale) • RAND-36 physical function Other factors considered in univariable analysis, but not significant: • Gender • Education • Age • Parafunctions
Outcomes and effect sizes	Outcome: Clinically significant pain (Graded Chronic Pain Scale grade 1, 2 3 and 4) at 1 year Reported pain intensity (characteristic pain intensity measured by the Research Diagnostic Criteria for Temporomandibular Disorders questionnaire) at baseline: OR 1.1 (95% CI 0.84-1.43) for each unit change Comorbid psychiatric disorder (depression measured by the Symptom Checklist-90 Revised) at baseline: OR 0.36 (95% CI 0.11-1.17) for each unit change Comorbid psychiatric disorder (somatization with pain items measured by the Symptom Checklist-90 Revised) at baseline: OR 0.21 (95% CI 0.02-1.76) for each unit change Coping style (catastrophizing measured by ruminative thoughts from Pain Catastrophising Scale) at baseline: OR 1.06 (95% CI 0.94-1.19) for each unit change Coping style (confidence in ability to control pain measured by the Coping Strategies Questionnaire) at baseline: OR 0.73 (95% CI 0.52-1.04) for each unit change Coping style (confidence in ability to decrease pain measured by the Coping Strategies Questionnaire) at baseline: OR 0.95 (95% CI 0.66-1.37) for each unit change
Comments	Reported pain intensity (characteristic pain intensity measured by the Research Diagnostic Criteria for Temporomandibular Disorders questionnaire) at baseline: very high risk of bias (study attrition; study confounding) Comorbid psychiatric disorder (depression measured by the Symptom Checklist-90 Revised) at baseline: very high risk of bias (study attrition; study confounding)

Reference	Forssell 2017 [171]
	Comorbid psychiatric disorder (somatization with pain items measured by the Symptom Checklist-90 Revised) at baseline: very high risk of bias (study attrition; study confounding) Coping style (catastrophizing measured by ruminative thoughts from Pain Catastrophising Scale) at baseline: very high risk of bias (study attrition; prognostic factor; study confounding) Coping style (confidence in ability to control pain measured by the Coping Strategies Questionnaire) at baseline: very high risk of bias (study attrition; study confounding) Coping style (confidence in ability to decrease pain measured by the Coping Strategies Questionnaire) at baseline: very high risk of bias (study attrition; study confounding)

Reference	Michaelson 2004 [364]
Study type and analysis	Prospective cohort (multimodal programme). Logistic regression: models built by adding one variable at a time with the criteria of keeping/removing variable as a result of the corresponding p value
Number of participants and characteristics	N=235 patients with chronic low back (n=149) and neck (n=106) pain (n followed up out of total 315 enrolled) Inclusion: 18-65 years of age; primary pain region neck or lower back; pain intensity ≥25mm on a 100mm visual analogue scale Exclusion: neurologic disease; signs of brain damage; rheumatic and psychiatric diagnoses; pain in the primary region for more than 6 consecutive months Age (mean): 43 years Duration of pain (mean, SD): 106 (91) months
Prognostic variable(s)	Reported pain intensity (average pain intensity over the last 7 days 0-100mm visual analogue scale) at baseline Coping style (Optimism index) at baseline Comorbid psychiatric disorder (somatic and psychosomatic complaints measured by a 29-item questionnaire on general health) at baseline
Confounders OR Stratification strategy	Confounders adjusted for (in multivariate analysis): • Multidimensional pain inventory pain severity • Multidimensional pain inventory affective distress

Reference	Michaelson 2004 [364]
	• Optimism index • Sociability index • Endurance index • Other symptoms index (somatic and psychosomatic complaints measured by a 29-item questionnaire on general health) • Age • Average pain intensity (100mm visual analogue scale) Other factors considered but excluded from model as not significant: • Sex • Work/sick leave status • Number of days on sick leave • Pain related to an accident • Pain duration • Beck depression inventory • Multidimensional pain inventory interference • Multidimensional pain inventory support • Multidimensional pain inventory life control
Outcomes and effect sizes	Outcome: Reduced low back pain (reduction in pain intensity ≥25mm on a 0-100mm visual analogue scale from baseline) at 12 months Reported pain intensity (average pain intensity over the last 7 days 0-100mm visual analogue scale) at baseline: OR 1.06 (95% CI 1.03-1.09) (cut-off/increments not reported) Outcome: Reduced neck pain (reduction in pain intensity ≥25mm on a 0-100mm visual analogue scale from baseline) at 12 months Reported pain intensity (average pain intensity over the last 7 days 0-100mm visual analogue scale) at baseline: OR 1.05 (95% CI 1.01-1.09) (cut-off/increments not reported) Coping style (Optimism index) at baseline: OR 2.95 (95% CI 1.26-6.88) for high vs. low score (cut-off not reported) Comorbid psychiatric disorder (somatic and psychosomatic complaints measured by a 29-item questionnaire on general health) for few other symptoms at baseline: OR 0.92 (95% CI 0.87-0.96) for more vs. fewer symptoms (cut-off not reported)

Reference	Michaelson 2004 [364]
Comments	Outcome: Reduced low back pain (reduction in pain intensity ≥25mm on a 0-100mm visual analogue scale from baseline) at 12 months Reported pain intensity (average pain intensity over the last 7 days 0-100mm visual analogue scale) at baseline: very high risk of bias (study participation; study attrition; prognostic factor; study confounding) Outcome: Reduced neck pain (reduction in pain intensity ≥25mm on a 0-100mm visual analogue scale from baseline) at 12 months Reported pain intensity (average pain intensity over the last 7 days 0-100mm visual analogue scale) at baseline: very high risk of bias (study participation; study attrition; prognostic factor; study confounding) Coping style (Optimism index) at baseline: very high risk of bias (study participation; study attrition; prognostic factor; study confounding) Comorbid psychiatric disorder (somatic and psychosomatic complaints measured by a 29-item questionnaire on general health) for few other symptoms at baseline: very high risk of bias (study participation; study attrition; prognostic factor; study confounding)

Reference	Naliboff 2017 [380]
Study type and analysis	Prospective cohort. Exploratory multivariable stepwise ordinal logistic regression
Number of participants and characteristics	N=397 interstitial cystitis/bladder pain syndrome or chronic prostatitis/chronic pelvic pain syndrome Inclusion: clinical diagnosis of IC/BPS or CP/CPPS; pain severity of at least 1 on a 0–10 Likert pain scale; over age 18; urinary symptoms present the majority of the time during 3 of the previous 6 months Exclusion: not reported Age (mean, SD): males 47.7 (15.5), females 40.6 (14.3) years Duration of pain (mean, SD): males 8.1 (10.9), females 9.1 (10.3) years Males and females with urologic chronic pelvic pain syndrome enrolled at six US discovery sites were followed to describe a prospectively studied, usual care cohort. Participants filled out all the study assessments via computer during a single baseline visit. They were subsequently contacted every two weeks for the next 52 weeks for online ratings of current symptoms on the urinary and pain severity outcomes.

Reference	Naliboff 2017 [380]
Prognostic variable(s)	Reported pain intensity (pain severity) at baseline
Confounders OR Stratification strategy	Confounders adjusted for (in multivariable analysis): • Age • SF12 physical component summary Other factors considered but excluded from model as not significant: • Sex • Race • Income • Duration of symptoms • Urinary severity • Complex Multi-Symptom Inventory non-uro symptoms • Body map sites non-pelvic • Body map: head • SF12 mental component summary • Fatigue (NIH Patient Reported Outcomes Measurement Information System (PROMIS) questionnaires) • Sleep disturbance (NIH Patient Reported Outcomes Measurement Information System (PROMIS) questionnaires) • Hospital anxiety and depression scale: depression • Hospital anxiety and depression scale: anxiety • Coping strategies questionnaire: catastrophizing score • Perceived Stress Scale • Relationship satisfaction with the Self-Esteem and Relationship questionnaire • Number of medication changes
Outcomes and effect sizes	Outcome: Improvement in pain severity (functional clustering procedure applied to biweekly severity scores to classify overall symptom trajectory as worsening, stable or improving) Reported pain intensity (pain severity) at baseline: OR 1.184 (95% CI 1.117-1.254) (cut-off/increments not reported)
Comments	Reported pain intensity (pain severity) at baseline: very high risk of bias (prognostic factor; study confounding)

Reference	Rabey 2017 [425]
Study type and analysis	Prospective cohort. Multivariable regression models: variables with univariable associations ($p<0.1$) were considered candidate variables and selected for final multivariable regression models using a backwards stepwise method combined with purposeful selection of covariates, variables significant at $p<0.05$ were included in the final multivariable models
Number of participants and characteristics	N=266 people with axial chronic low back pain (n followed up out of total 294 enrolled) Inclusion: 18-70 years old; low back pain >3 month duration; ≥2 points on 11-point numeric rating scale for pain intensity; ≥5 points on the Roland Morris Disability Questionnaire; ≥60% low back pain on the question 'which situation best describes your pain over the past 4 weeks?' (% backs vs. % legs) Exclusion: previous extensive spinal surgery; spinal surgery in the past 6 months; serious spinal pathology; diagnosed neurological disease; bilateral dorsal wrist/hand pain; pregnancy; inability to understand English Age (median, interquartile range): 51 (39-60) years Duration of pain (median, interquartile range): 120 (42-240) months Participants recruited through multimedia advertisements, private physiotherapy clinics, public hospitals and private pain management and general practice clinics. Potential prognostic factors were measured at baseline.
Prognostic variable(s)	Reported pain intensity (11-point numeric rating scale) at baseline
Confounders OR Stratification strategy	Factors considered in univariable analyses but not significant (summarised list): • Age • Gender • Disability (Roland Morris Disability questionnaire) • Duration of chronic low back pain • 100% of pain in low back region • Aggravated by activity • Aggravated by position • Bothersomeness • Intervention • Pain sensitivity • Movement dimension • Psychological cluster

Reference	Rabey 2017 [425]
	• Depression anxiety stress scale • Fear avoidance beliefs questionnaire • Pain Catastrophising scale • Pain self-efficacy questionnaire • Avoidance endurance questionnaire • Chronic pain acceptance questionnaire • Mindful attention awareness scale • Perceived risk of persistent pain • Fremantle back awareness questionnaire • Comorbidities • Pittsburgh sleep quality index • Smoking status • Physical activity • Education • Compensation claims • Work status • Occupation • Job satisfaction • Life events • Multidimensional pain inventory
Outcomes and effect sizes	Outcome: Pain intensity (numeric rating scale 0-10) at 1 year Reported pain intensity (11-point numeric rating scale) at baseline: unstandardized coefficient 0.32 (95% CI 0.19-0.45)
Comments	Reported pain intensity (11-point numeric rating scale) at baseline: high risk of bias (study confounding)

Reference	Rollman 2013 [451]
Study type and analysis	Prospective cohort. Multiple logistic regression analysis: predictors with at least moderate association with improvement (p≤0.1) in univariate analysis were entered in to multiple regression analysis, then the variable with the weakest association was removed until all variables showed a p≤0.05

Reference	Rollman 2013 [451]
Number of participants and characteristics	N=100 patients with temporomandibular disorder pain (n followed up out of total 129 enrolled) Inclusion: referral for a TMD-pain complaint to one of seven participating centres; self-report of orofacial pain within the last month; good understanding of the Dutch language Exclusion: any report of toothache, burning sensations in the orofacial region, shooting pain that is provoked by touch, diagnosis of a systemic disease, or cancer Age (mean, SD): improved 47.1 (13.3) years, not improved 44.8 (14.2) years Duration of pain: 0-3 months 9%, 3-6 months 20%, 6-12 months 14%, 1-3 years 25%, 3-10 years 15%, >10 years 17% Participants meeting the inclusion criteria completed a baseline questionnaire measuring a variety of variables that could predict likely improvement in pain.
Prognostic variable(s)	Coping style (pain coping measured by the Pain coping and cognition list; 1-6 higher scores denote the use of more different strategies to cope with pain) at baseline
Confounders OR Stratification strategy	Confounders adjusted for (in multiple regression analysis): • Pain duration • Number of care practitioners • Hindrance on function (measured by Patient specific approach) • Pain-related disability (disability score measured by Chronic pain scale) Other factors considered in univariate analysis but not significant: • Pain intensity (Characteristic pain intensity, part of the Graded chronic pain scale) • Widespread pain (McGill pain questionnaire) • Use of pain killers • Tampa scale of kinesiophobia • Psychological distress (Symptom checklist 90) • Dental anxiety • Education • Employment • Household situation (living alone)

Reference	Rollman 2013 [451]
Outcomes and effect sizes	Outcome: Improvement (based on the question: 'did the pain in your face that you reported half a year ago…': 'completely disappear', 'largely decrease', 'slightly decrease', 'remain the same', 'increase slightly' or 'increase a lot?' Those reporting 'completely disappear' or 'largely decrease' were classified as improved) at 6 months Coping style (pain coping measured by the Pain coping and cognition list) at baseline: OR 1.28 (95% CI 0.76-2.15) (increment/cut-off not reported)
Comments	Coping style (pain coping measured by the Pain coping and cognition list) at baseline: very high risk of bias (prognostic factor; confounding)

Reference	Trinderup 2018
Study type and analysis	Secondary analysis of an RCT (12 week work-orientated multidisciplinary intervention vs. usual multidisciplinary care). Multiple logistic regression analyses: univariate regression analysis identified potential predictors for the multivariate analysis (p<0.2)
Number of participants and characteristics	N=284 chronic low back pain (n followed up out of 559 enrolled) Inclusion: working age adults (18–65 years) with LBP for at least 3 months, on sick leave or at risk for eminent sick leave Exclusion: pending application for early retirement pension, pregnancy, comorbidity (i.e. severe consequences of cancer, cardiopulmonary diseases, mental or psychological diseases) or difficulties in reading and writing Danish Age (mean, SD): 38.90 (10.42) years Duration of pain <12 months, n (%): 273 (51.41) Participants were referred from general practitioner, rheumatologist or municipal sickness benefit office for treatment of persistent LBP. Participants in both trial arms were included in the analysis.
Prognostic variable(s)	Reported pain intensity (Back pain questionnaire included 3 separate 11-point numeric rating scales comprising pain at the moment, worst pain within the last 2 weeks and average pain within the last 2 weeks: high/low 0-30) at baseline Coping style (High fear-avoidance beliefs about work measured by Fear Avoidance Beliefs Questionnaire: low, 0–29; high, 30–42) at baseline
Confounders OR Stratification strategy	Confounders adjusted for (in multivariate analysis): • Fear avoidance beliefs about work • Smoking • Pain intensity

Reference	Trinderup 2018
	• Disability (Roland Morris Disability Questionnaire) • Duration of pain ≥12 months and little physical job demands • Male and little physical job demands Other factors considered in univariate analysis but not significant: • Sex • Age • BMI • Education • Alcohol consumption • Physical activity level • Sick leave • Duration of sick leave • Employment • Compensation case • Physical job demands • Physical health • Mental health • Depression • Anxiety • Age at first episode of pain • Family history of low back pain • Fear avoidance beliefs physical activity • Group intervention
Outcomes and effect sizes	Outcome: Unsuccessful outcome (reduction of less than 6 points on the Numeric Pain Rating Scale) at 12 months Reported pain intensity (Low score on Back pain questionnaire 0-30 included 3 separate 11-point numeric rating scales comprising pain at the moment, worst pain within the last 2 weeks and average pain within the last 2 weeks) at baseline: OR 1.14 (95% CI 1.08-1.2)

Reference	Trinderup 2018
	Coping style (Fear-avoidance beliefs about work measured by Fear Avoidance Beliefs Questionnaire: low, 0–29; high, 30–42) at baseline: OR 1.04 (95% CI 1.01-1.08)
Comments	Outcome: Unsuccessful outcome (reduction of less than 6 points on the Numeric Pain Rating Scale) at 12 months Reported pain intensity (Low score on Back pain questionnaire 0-30 included 3 separate 11-point numeric rating scales comprising pain at the moment, worst pain within the last 2 weeks and average pain within the last 2 weeks) at baseline: very high risk of bias (study attrition, prognostic factor, confounding) Coping style (High fear-avoidance beliefs about work measured by Fear Avoidance Beliefs Questionnaire: low, 0–29; high, 30–42) at baseline: very high risk of bias (study attrition, confounding)

Reference	van der Hulst 2008 [538]
Study type and analysis	Secondary analysis of an RCT (7 week back rehabilitation programme vs. waiting list). Multivariate linear regression analysis
Number of participants and characteristics	N=163 nonspecific chronic low back pain Inclusion: duration of pain >3 months; age between 18 and 60 years; no surgery of the spine in the past 3 months Exclusion: structural pathology like active radiculopathy, tumour of the spine, or severe deformities and patients with a medical contraindication for physical training Age (mean, SD): rehabilitation programme 38 (10), usual care 40 (10) years Duration of pain (median, range): rehab programme 72 (380), waiting list 48 (559) months Participants in both trial arms were included in the analysis. Baseline measurements were performed before randomisation.
Prognostic variable(s)	Reported pain intensity (visual analogue scale 0-10) at baseline Comorbid psychiatric disorder (Symptom checklist questionnaire-90 depression subscale) at baseline Coping style (Tampa scale of kinesiophobia) at baseline Coping style (Multidimensional pain inventory classification adaptive coper/average/anomalous or dysfunction/distressed) at baseline
Confounders OR Stratification strategy	Confounders adjusted for (in multivariate analysis): • Intercept • Treatment

Reference	van der Hulst 2008 [538]
	• Pain (visual analogue scale 0-10) • Work status • Multidimensional pain inventory- Dutch version • Baseline value • Sick leave • Symptom checklist questionnaire-90 depression • Tampa scale of kinesiophobia
Outcomes and effect sizes	Outcome: Difference in SF36 physical component scale scores from baseline to 4 weeks after treatment Reported pain intensity (visual analogue scale 0-10) at baseline: unstandardized ß coefficient 0.2 (SE 0.37) favourable change per unit Comorbid psychiatric disorder (Symptom checklist questionnaire-90 depression subscale) at baseline: unstandardized ß coefficient -0.03 (SE 0.1) favourable change per unit Coping style (Tampa scale of kinesiophobia) at baseline: unstandardized ß coefficient -0.05 (SE 0.11) unfavourable change per unit Coping style (Multidimensional pain inventory classification adaptive coper/average/anomalous or dysfunction/distressed) at baseline: unstandardized ß coefficient 1.54 (SE 1.51) favourable change per unit Outcome: Difference in SF36 mental component scale scores from baseline to 4 weeks after treatment Reported pain intensity (visual analogue scale 0-10) at baseline: unstandardized ß coefficient -0.13 (SE 0.36) unfavourable change per unit Comorbid psychiatric disorder (Symptom checklist questionnaire-90 depression subscale) at baseline: unstandardized ß coefficient -0.35 (SE 0.13) favourable change per unit Coping style (Tampa scale of kinesiophobia) at baseline: unstandardized ß coefficient 0.1 (SE 0.12) favourable change per unit Coping style (Multidimensional pain inventory classification adaptive coper/average/anomalous or dysfunction/distressed) at baseline: unstandardized ß coefficient -0.78 (SE 1.69) unfavourable change per unit
Comments	Outcome: Difference in SF36 physical component scale scores from baseline to 4 weeks after treatment

Reference	van der Hulst 2008 [538]
	Reported pain intensity (visual analogue scale 0-10) at baseline: high risk of bias (study confounding) Comorbid psychiatric disorder (Symptom checklist questionnaire-90 depression subscale) at baseline: high risk of bias (study confounding) Coping style (Tampa scale of kinesiophobia) at baseline: high risk of bias (study confounding) Coping style (Multidimensional pain inventory classification adaptive coper/average/anomalous or dysfunction/distressed) at baseline: high risk of bias (study confounding) Outcome: Difference in SF36 mental component scale scores from baseline to 4 weeks after treatment Reported pain intensity (visual analogue scale 0-10) at baseline: high risk of bias (study confounding) Comorbid psychiatric disorder (Symptom checklist questionnaire-90 depression subscale) at baseline: high risk of bias (study confounding) Coping style (Tampa scale of kinesiophobia) at baseline: high risk of bias (study confounding) Coping style (Multidimensional pain inventory classification adaptive coper/average/anomalous or dysfunction/distressed) at baseline: high risk of bias (study confounding)

Reference	Velly 2011 [552]
Study type and analysis	Prospective cohort. Multivariable linear regression analysis
Number of participants and characteristics	N=480 people with a diagnosis of any temporomandibular joint disorder pain (n followed up out of total 570 enrolled). Inclusion: diagnosis of any TMJD pain with a frequency of at least once per week and duration of at least 3 months Exclusion: systemic rheumatic disease; dental, sinus, or other infection that could cause swelling or tenderness in the area; taking prescribed steroids or narcotics for a chronic condition; taking antidepressants and not on a stable dose for at least the last 2 months; primary psychiatric disease (uncontrolled schizophrenia, psychoses, or other serious disorders that interfere with ability to consent and

Reference	Velly 2011 [552]
	participate); prior TMJ surgery; unable to provide informed consent; >65 or <18 years of age; scheduling problems that would interfere with follow-up; >3 alcoholic drinks per day; pregnant Age (mean, SD): 35.85 (12.48) years Duration of pain: not reported Participants recruited through media advertisements and notices distributed to local dentists. Predictor variables measured at baseline.
Prognostic variable(s)	Reported pain intensity (0-100 numeric rating scale) at baseline Comorbid psychiatric disorder (Beck Depression Inventory) at baseline Coping style (catastrophizing measured by the Coping strategies questionnaire) at baseline
Confounders OR Stratification strategy	Confounders adjusted for (in multivariable analysis): • Depression (Beck Depression Inventory) • Widespread pain • Pain intensity (0-100 numeric rating scale) • Catastrophizing (Coping strategies questionnaire) • Gender • Age
Outcomes and effect sizes	Outcome: Pain intensity (0-100 numeric rating scale) at 18 months Reported pain intensity (0-100 numeric rating scale) at baseline: ß coefficient 0.39 (95% CI 0.31-0.46) Comorbid psychiatric disorder (Beck Depression Inventory) at baseline: ß coefficient 1.1 (95% CI -0.81- -3) Coping style (catastrophizing measured by the Coping strategies questionnaire) at baseline: ß coefficient 3.79 (95% CI 2.09-5.49)
Comments	Reported pain intensity (0-100 numeric rating scale) at baseline: very high risk of bias (study participation; study confounding; statistical analysis and presentation) Comorbid psychiatric disorder (Beck Depression Inventory) at baseline: very high risk of bias (study participation; study confounding; statistical analysis and presentation)

Reference	Velly 2011 [552]
	Coping style (catastrophizing measured by the Coping strategies questionnaire) at baseline: very high risk of bias (study participation; study confounding; statistical analysis and presentation)

Reference	Verkerk 2015 [559]
Study type and analysis	Prospective cohort (2 month multidisciplinary treatment). Multivariable logistic regression analysis
Number of participants and characteristics	N=1564 for 5 month outcomes, n=960 for 12 month outcomes chronic non-specific low back pain patients not recovering after primary/secondary care (n followed up out of total 1760 enrolled) Inclusion: men and women aged ≥18 years; chronic non-specific low back pain (duration ≥3 months); previous and insufficient treatment in primary/secondary care; signed informed consent Exclusion: insufficient knowledge of the Dutch language; signs indicating radiculopathy; asymmetric Achilles tendon reflex and/or passive straight led raise test restricted by pain in the lower leg; positive MRI findings for disc herniation; recent (<6 months) fracture, neoplasm or recent previous surgery of the lumbar spine, pelvic girdle, hip joint or femur; specific causes; pregnancy or ≤6 months post-partum Age (mean, SD): 40.1 (10.6) years Duration of pain (mean, SD): 7.7 (8.8) years Participants recruited from a multidisciplinary outpatient rehabilitation clinic and evaluated by physical evaluation and/or questionnaires at baseline.
Prognostic variable(s)	Reported pain intensity (visual analogue scale 0-100) at baseline Comorbid psychiatric disorder (Symptom Checklist-90 item 9 – psychoneurosis) at baseline Coping style (Tampa scale for kinesiophobia) at baseline
Confounders OR Stratification strategy	Confounders adjusted for (in multivariable analysis) - 30% improvement in pain intensity at 5 months: • Age • Gender • Pain intensity (visual analogue scale 0-100) • SF36 physical component summary • SF36 mental component summary • Body mass index

Reference	Verkerk 2015 [559]
	• Previous rehabilitation • Work participation Confounders adjusted for (in multivariable analysis) - 30% improvement in pain intensity at 12 months • Age • Gender • Pain intensity (visual analogue scale 0-100) • SF36 physical component summary • Education • Comorbidity • Marital status • B200 Isostation extension • Tampa scale for kinesiophobia Other factors considered but excluded from model as not significant: • Duration of pain • Fatigue • Quebec back pain disability scale • Cause of back pain • Pain in previous 3 months (stable, increased, decreased) • Duration of walking, sitting, standing
Outcomes and effect sizes	Outcome: 30% improvement in pain intensity at 5 months Comorbid psychiatric disorder (Symptom Checklist-90 item 9 – psychoneurosis) at baseline: OR 0.99 (95% CI 0.99-0.99) (increment/cut-off not reported) Outcome: 30% improvement in pain intensity at 12 months Reported pain intensity (visual analogue scale 0-100) at baseline: OR 1.01 (95% CI 1.01-1.02) (increment/cut-off not reported) Coping style (Tampa scale for kinesiophobia) at baseline: OR 0.97 (95% CI 0.95-0.99) (increment/cut-off not reported)

Reference	Verkerk 2015 [559]
Comments	Outcome: 30% improvement in pain intensity at 5 months Comorbid psychiatric disorder (Symptom Checklist-90 item 9 – psychoneurosis) at baseline: very high risk of bias (prognostic factor; study confounding) Outcome: 30% improvement in pain intensity at 12 months Reported pain intensity (visual analogue scale 0-100) at baseline: very high risk of bias (study attrition; prognostic factor; study confounding) Coping style (Tampa scale for kinesiophobia) at baseline: very high risk of bias (study attrition; prognostic factor; study confounding)

Reference	Weiner 2013 [568]
Study type and analysis	Secondary analysis of an RCT (periosteal stimulation therapy vs. control; all arms included in analysis). Linear mixed models and generalised estimating equations
Number of participants and characteristics	N=190 people with knee osteoarthritis Inclusion: knee pain for at least 3 months with pain of at least moderate intensity (measured with a verbal descriptor scale) every day or almost every day; knee pain severity greater than pain severity in other parts of body; ambulatory with or without a cane; Folstein Mini-Mental State Examination score Z24; adequate vision and hearing (with or without correction) to hear over the telephone and read the newspaper; KL grade 3 or 4 Exclusion: non-OA causes of knee pain (e.g. rheumatoid arthritis and gout); large knee effusion; recent diagnosis of cancer; knee injections (corticosteroid or hyaluronic acid) within the previous 3 months; acute or terminal illness; anticoagulation; corticosteroids or other immune suppressants; HIV/AIDS; pacemaker; previous exposure to PST Age (mean, SD): PST + PST 67.1 (8.9), PST + control 65.8 (8.7), control 66.8 (10.4) years Duration of pain (mean, SD): PST + PST 5.7 (6.4), PST + control 6.2 (6.8), control 7.2 (8.3) years Participants were recruited through query of the Veterans Administration Pittsburgh Healthcare System data warehouse to identify potential participants with upcoming primary care appointments, study brochures placed in Veterans Administration Pittsburgh Healthcare System clinic waiting rooms, advertisements in local newspapers and a targeted mailing of brochures to residents. Potential prognostic factors were measured at baseline.

Reference	Weiner 2013 [568]
Prognostic variable(s)	Reported pain intensity (Western Ontario and McMaster Universities Osteoarthritis Index pain scale) at baseline Comorbid psychiatric disorder (Centre for Epidemiological studies- depression) at baseline Coping style (catastrophizing measured by coping strategies questionnaire) at baseline Coping style (pain self-efficacy measured by Arthritis self-efficacy scale) at baseline
Confounders OR Stratification strategy	Confounders adjusted for (in multivariable analysis): • Age • Sex • Race • Body mass index • Depression (Centre for Epidemiological studies) • Catastrophizing (Coping strategies questionnaire) • Self-efficacy function (Arthritis self-efficacy scale) • Self-efficacy other symptoms (Arthritis self-efficacy scale) • Self-efficacy pain (Arthritis self-efficacy scale) • WOMAC pain • WOMAC difficulty performing daily activities • WOMAC stiffness • Short physical performance battery • Duration of knee pain • Kellgren-Lawrence score
Outcomes and effect sizes	Outcome: Western Ontario and McMaster Universities Osteoarthritis Index at 9 months (6 months after end of treatment) Reported pain intensity (Western Ontario and McMaster Universities Osteoarthritis Index pain scale) at baseline: ß coefficient -0.6798 (SE 0.067) Comorbid psychiatric disorder (Centre for Epidemiological studies- depression) at baseline: ß coefficient 0.017 (SE 0.03) Coping style (catastrophizing measured by coping strategies questionnaire) at baseline: ß coefficient -0.013 (SE 0.035) Coping style (pain self-efficacy measured by Arthritis self-efficacy scale) at baseline: ß coefficient 0.015 (SE 0.014)

Reference	Weiner 2013 [568]
Comments	Reported pain intensity (Western Ontario and McMaster Universities Osteoarthritis Index pain scale) at baseline: very high risk of bias (study confounding; statistical analysis and presentation) Comorbid psychiatric disorder (Centre for Epidemiological studies- depression) at baseline: very high risk of bias (study confounding; statistical analysis and presentation) Coping style (catastrophizing measured by coping strategies questionnaire) at baseline: very high risk of bias (study confounding; statistical analysis and presentation) Coping style (pain self-efficacy measured by Arthritis self-efficacy scale) at baseline: very high risk of bias (study confounding; statistical analysis and presentation)

Reference	Wong 2015 [585]
Study type and analysis	Prospective cohort. Multivariate linear mixed effects model
Number of participants and characteristics	N=184 at 3 months and 178 at 6 months chronic non-malignant musculoskeletal pain (n followed up out of total 226 enrolled) Inclusion: ≥18 years of age; native Chinese speakers; chronic non-malignant pain for at least 3 months Exclusion: communication, neurological or physical conditions preventing the completion of the study Age (mean, SD): 44.89 (9.24) years Duration of pain (mean, SD): 7.19 (6.15) years Consecutive patients attending 2 multidisciplinary pain clinics were invited to participate. Participants were interviewed within clinics by research assistants using a structured questionnaire at baseline.
Prognostic variable(s)	Reported pain intensity (measured by Chronic pain grade questionnaire pain intensity scale) at baseline Comorbid psychiatric disorder (Hospital anxiety and depression scale depression sub scale) at baseline Coping style (rumination, magnification and helplessness measured by the Pain catastrophizing scale at baseline Coping style (Tampa scale for Kinesiophobia) at baseline

Reference	Wong 2015 [585]
Confounders OR Stratification strategy	Confounders adjusted for (in multivariable analysis): • Time • Age • Sex • Marital status • Education • Occupation • Religion • Family income • Number of pain sites • Pain duration • Pain intensity (Chronic pain grade questionnaire pain intensity scale) • Depression (Hospital anxiety and depression scale depression sub scale) • Pain-related fear (Tampa scale for Kinesiophobia) • Rumination (Pain catastrophizing scale) • Magnification (Pain catastrophizing scale) • Helplessness (Pain catastrophizing scale) • Medical adherence • Pain treatment satisfaction
Outcomes and effect sizes	Outcome: Medical Outcomes study 12-item short form health survey (QoL-physical component score) at 6 months Reported pain intensity (measured by Chronic pain grade questionnaire pain intensity scale) at baseline: standardised ß coefficient 0.03 (95% CI -0.07-0.13) Comorbid psychiatric disorder (Hospital anxiety and depression scale depression sub scale) at baseline: standardised ß coefficient -0.11 (95% CI -0.24-0.02) Coping style (rumination, measured by the Pain catastrophizing scale) at baseline: standardised ß coefficient 0.03 (95% CI -0.08-0.14) Coping style (magnification, measured by the Pain catastrophizing scale) at baseline: standardised ß coefficient 0.00 (95% CI -0.13-0.12)

Reference	Wong 2015 [585]
	Coping style (helplessness, measured by the Pain catastrophizing scale) at baseline: standardised ß coefficient 0.09 (95% CI -0.03-0.22) Coping style (Tampa scale for Kinesiophobia) at baseline: standardised ß coefficient -0.18 (95% CI -0.29- -0.07) Outcome: Medical Outcomes study 12-item short form health survey (QoL-mental component score) at 6 months Reported pain intensity (measured by Chronic pain grade questionnaire pain intensity scale) at baseline: standardised ß coefficient 0.12 (95% CI 0.02-0.23) Comorbid psychiatric disorder (Hospital anxiety and depression scale depression sub scale) at baseline: standardised ß coefficient -0.14 (95% CI -0.27-0.00) Coping style (rumination, measured by the Pain catastrophizing scale) at baseline: standardised ß coefficient -0.03 (95% CI -0.27-0.00) Coping style (magnification, measured by the Pain catastrophizing scale) at baseline: standardised ß coefficient standardised ß coefficient 0.00 (95% CI -0.15-0.09) Coping style (helplessness, measured by the Pain catastrophizing scale) at baseline: standardised ß coefficient standardised ß coefficient -0.01 (95% CI -0.13-0.14) Coping style (Tampa scale for Kinesiophobia) at baseline: standardised ß coefficient 0.1 (95% CI -0.02-0.21)
Comments	Outcome: Medical Outcomes study 12-item short form health survey (QoL-physical component score) at 6 months Reported pain intensity (measured by Chronic pain grade questionnaire pain intensity scale) at baseline: high risk of bias (study confounding) Comorbid psychiatric disorder (Hospital anxiety and depression scale depression sub scale) at baseline: high risk of bias (study confounding) Coping style (rumination, measured by the Pain catastrophizing scale) at baseline: high risk of bias (study confounding)

Reference	Wong 2015 [585]
	Coping style (magnification, measured by the Pain catastrophizing scale) at baseline: high risk of bias (study confounding) Coping style (helplessness, measured by the Pain catastrophizing scale) at baseline: high risk of bias (study confounding) Coping style (Tampa scale for Kinesiophobia) at baseline: high risk of bias (study confounding) Outcome: Medical Outcomes study 12-item short form health survey (QoL-mental component score) at 6 months Reported pain intensity (measured by Chronic pain grade questionnaire pain intensity scale) at baseline: high risk of bias (study confounding) Comorbid psychiatric disorder (Hospital anxiety and depression scale depression sub scale) at baseline: high risk of bias (study confounding) Coping style (rumination, measured by the Pain catastrophizing scale) at baseline: high risk of bias (study confounding) Coping style (magnification, measured by the Pain catastrophizing scale) at baseline: high risk of bias (study confounding) Coping style (helplessness, measured by the Pain catastrophizing scale) at baseline: high risk of bias (study confounding) Coping style (Tampa scale for Kinesiophobia) at baseline: high risk of bias (study confounding)

D.3 Social risk factors

None

Appendix E: Forest plots

E.1 Biological risk factors

E.1.1 Presence or absence of a comorbid physical conditions

Figure 4: Presence or absence of a comorbid physical condition for predicting pain reduction (2 point change on the VAS, 0-10, high is poor outcome, follow up time not stated)

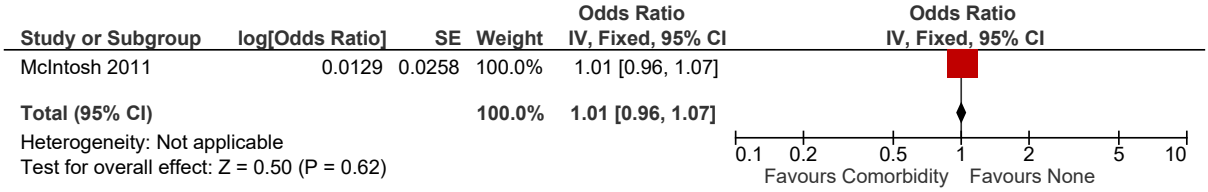


Figure 5: Presence or absence of a comorbid physical condition for predicting pain reduction (30% improvement in pain intensity) at 12 months

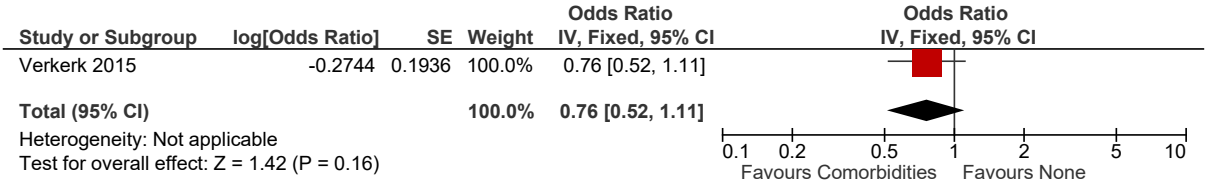
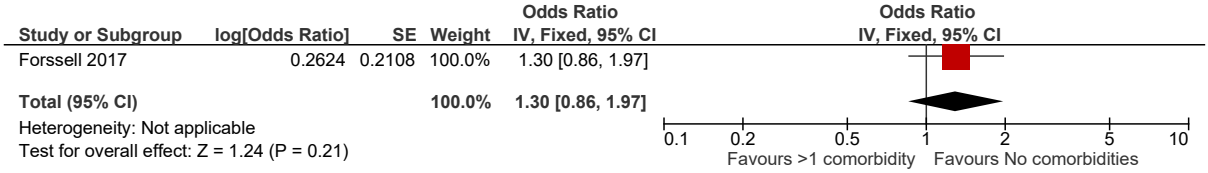
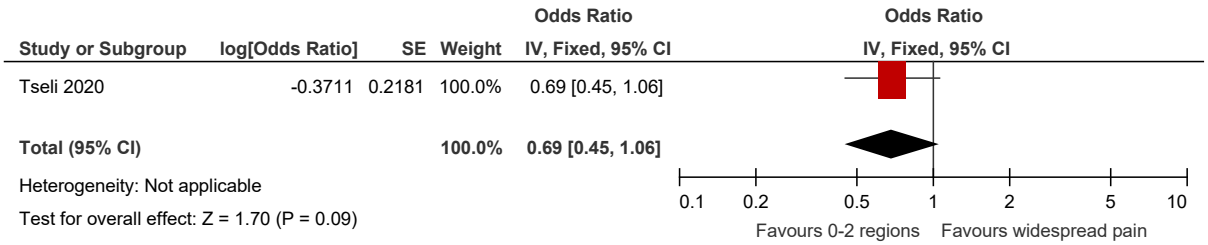


Figure 6: Number of other pain conditions (none versus >1) for predicting pain (GCPS Grade 1-4) at 12 months



E.1.2 Pain diagnosis (widespread pain)

Figure 7: Pain diagnosis (widespread pain compared to 0-2 regions) for predicting quality of life (difference of ≥3 on SF36 physical component)



E.2 Psychological risk factors

E.2.1 Reported pain intensity

Figure 8: 30% reduction from baseline in NRS and ODI

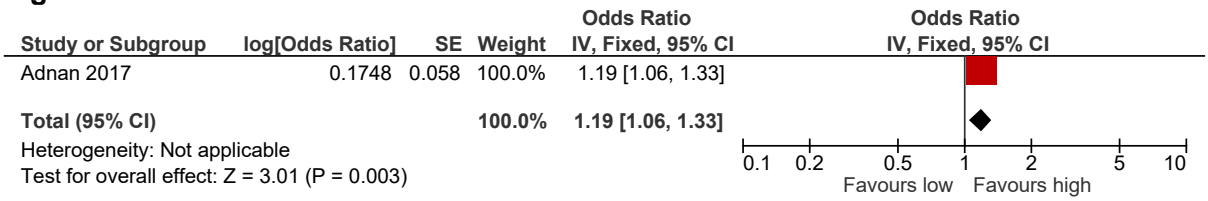


Figure 9: Increase in CPP severity

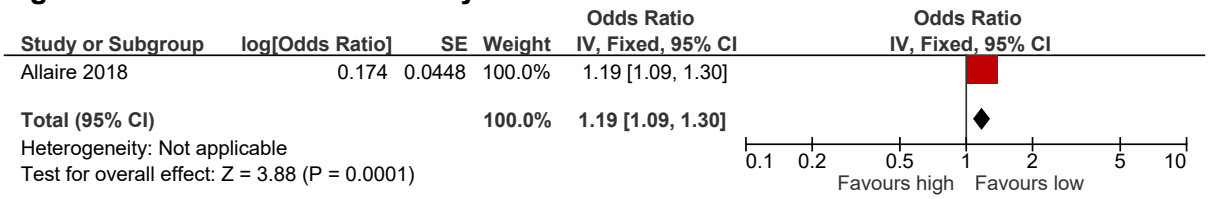


Figure 10: Chronic pain grade IV

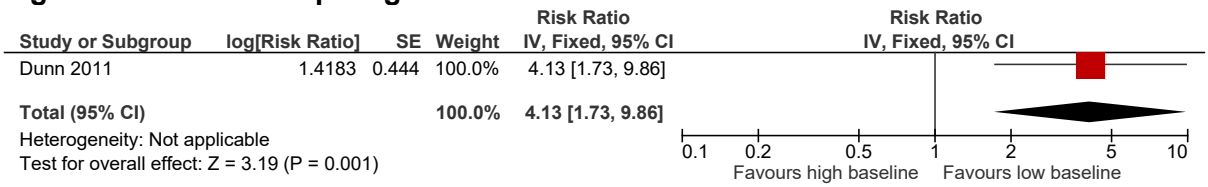


Figure 11: Clinically significant pain (Graded chronic pain scale 1,2,3,4)

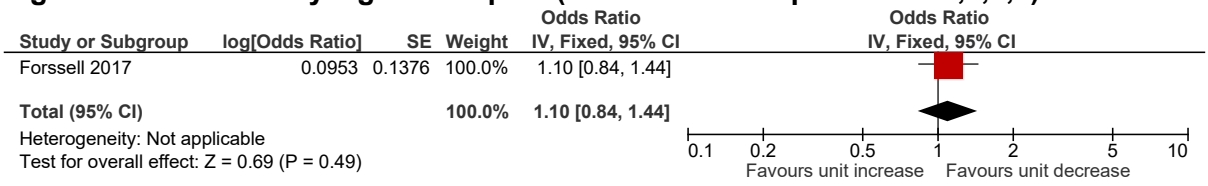


Figure 12: ≥25mm reduction on 0-100mm VAS from baseline

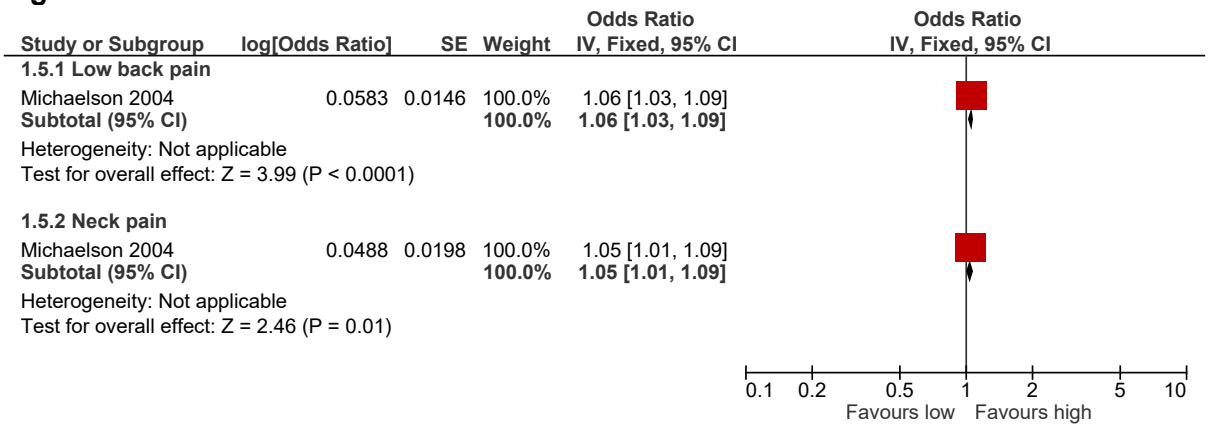


Figure 13: Improvement in pain severity

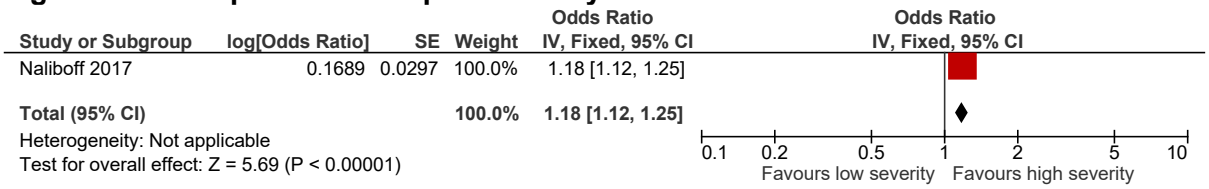


Figure 14: Unsuccessful outcome (<6 point reduction in pain severity)

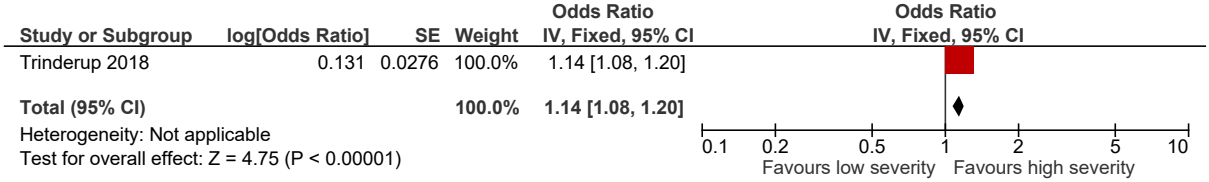
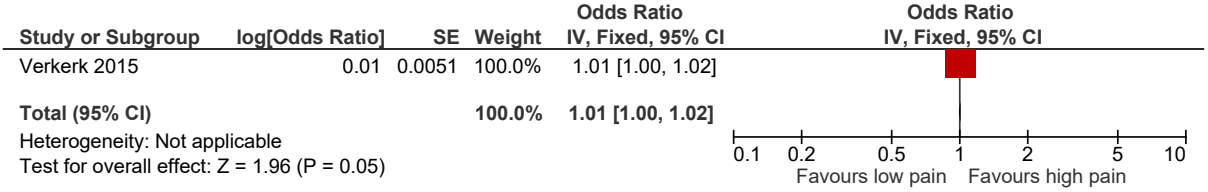


Figure 15: 30% improvement in pain intensity from baseline



E.2.2 Comorbid psychiatric disorder

Figure 16: 30% reduction from baseline in NRS and ODI

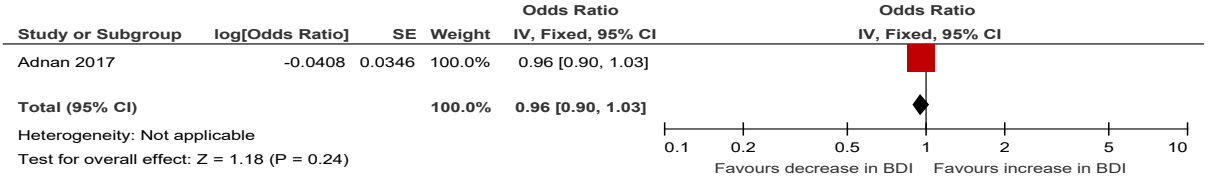


Figure 17: Chronic pain grade IV

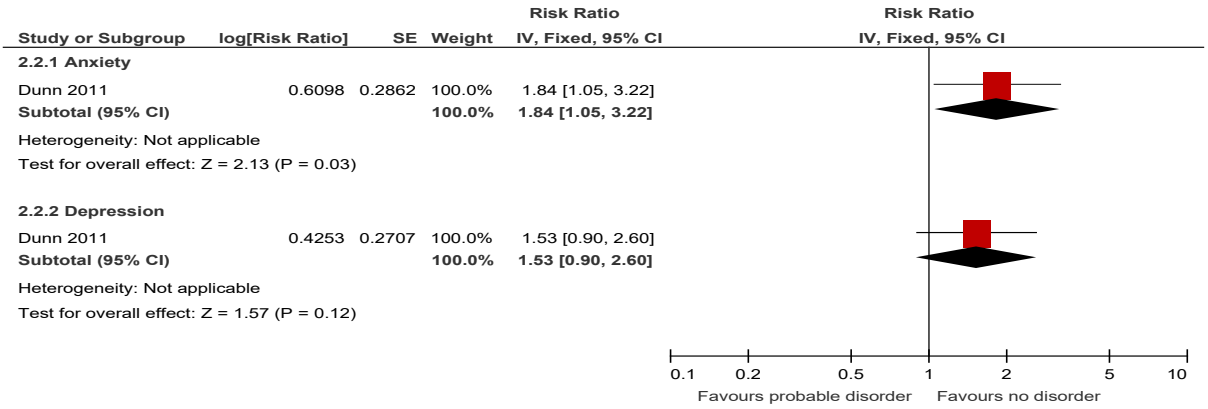


Figure 18: Clinically significant pain (Graded chronic pain scale 1,2,3,4)

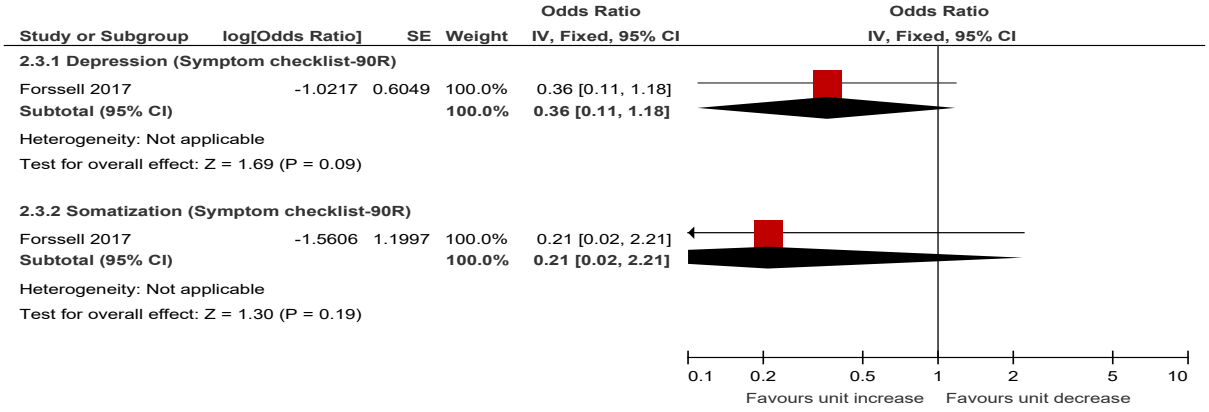


Figure 19: ≥25mm reduction on 0-100mm VAS from baseline

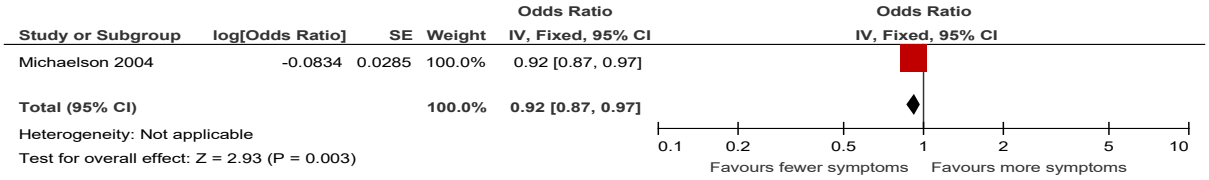
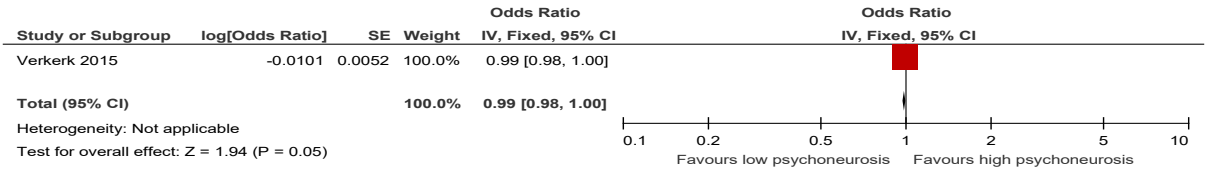


Figure 20: 30% improvement in pain intensity from baseline



E.2.3 Coping style

Figure 21: Increase in CPP severity

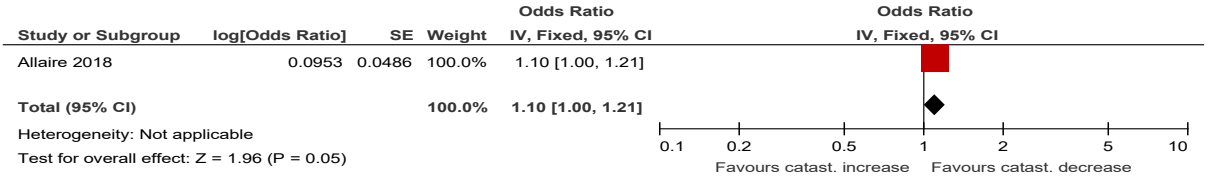


Figure 22: Chronic pain grade IV

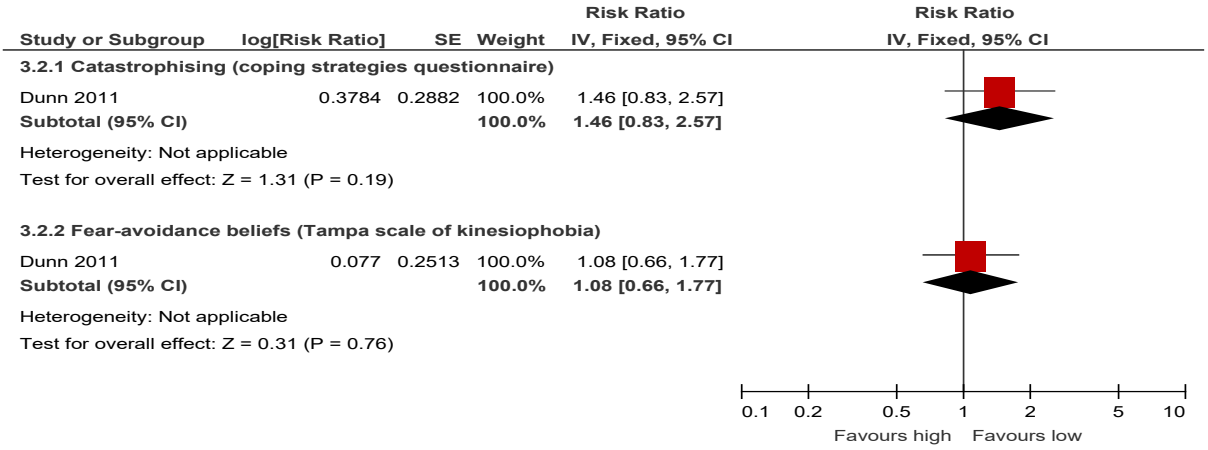


Figure 23: Clinically significant pain (Graded chronic pain scale 1,2,3,4)

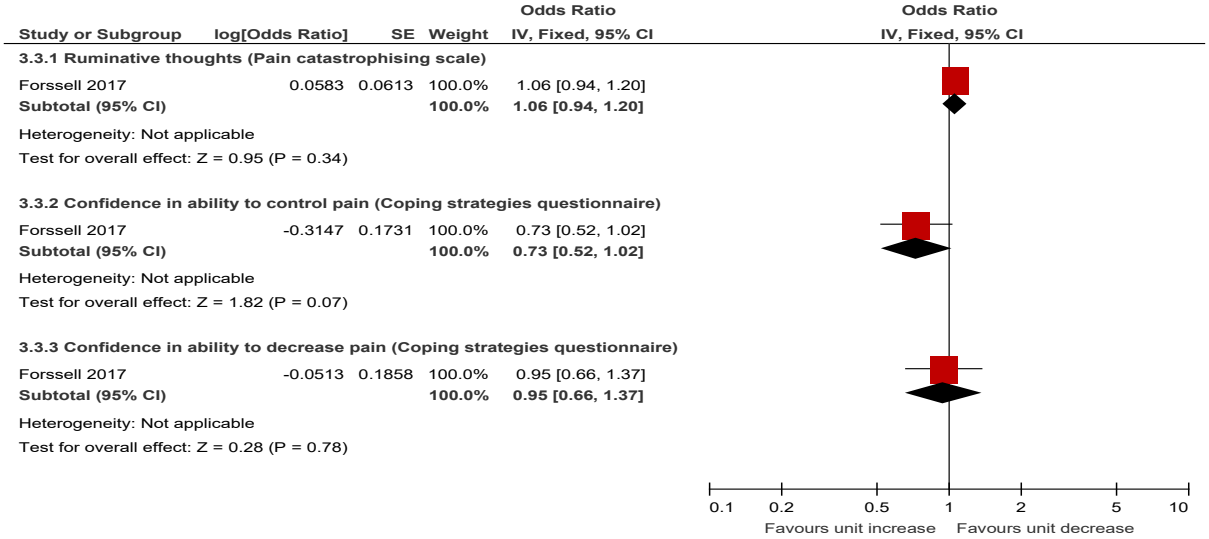


Figure 24: ≥25mm reduction on 0-100mm VAS from baseline

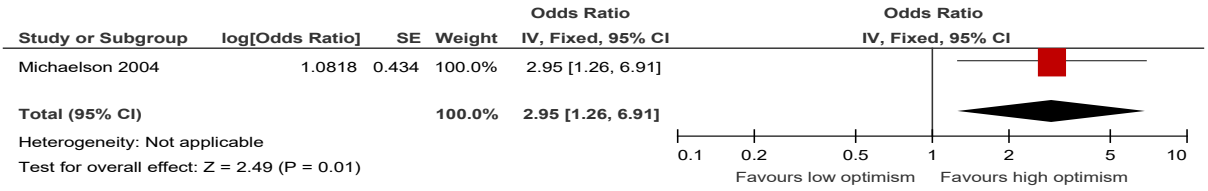


Figure 25: Improvement

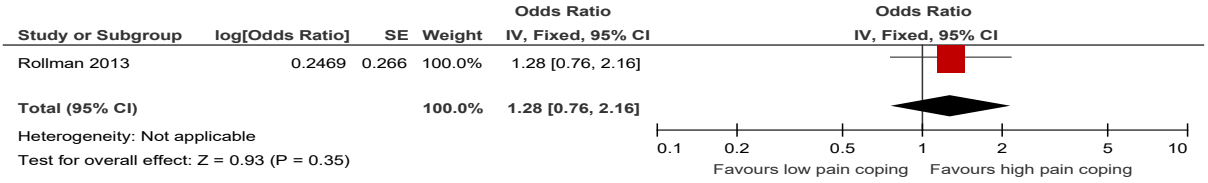


Figure 26: Unsuccessful outcome (<6 point reduction in pain severity)

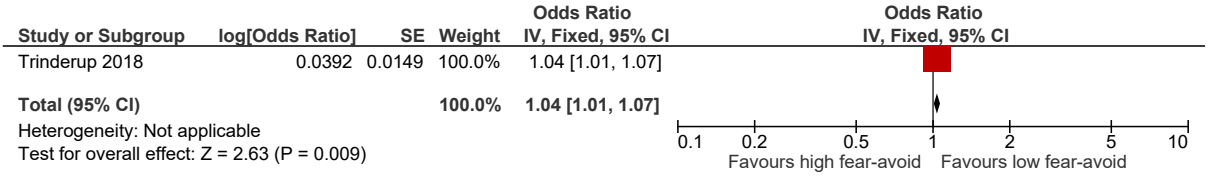
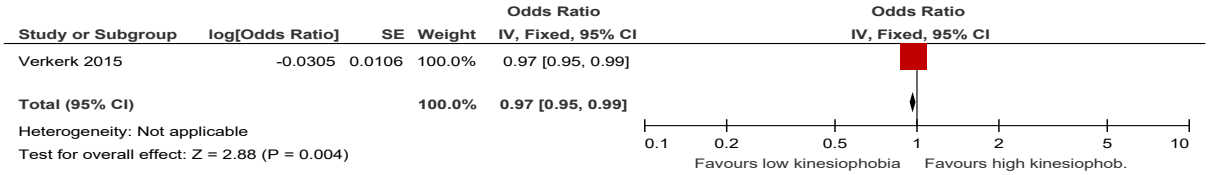


Figure 27: 30% improvement in pain intensity from baseline



E.3 Social risk factors

None

Appendix F: GRADE tables

F.1 Biological risk factors

Table 13: Clinical evidence profile: physical activity at baseline

Quality assessment							Effect	Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Most strenuous exercise (mild versus none) for predicting pain reduction (Shoulder pain and disability index at 6 months)									
1	observational studies	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	Coefficient 5.53 lower (10.32 to 0.74 lower)	⊕OOO VERY LOW	CRITICAL
Most strenuous exercise (moderate versus none) for predicting pain reduction (Shoulder pain and disability index at 6 months)									
1	observational studies	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	coefficient 8.98 lower (13.86 to 4.11 lower)	⊕OOO VERY LOW	CRITICAL
Most strenuous exercise (strenuous versus none) for predicting pain reduction (Shoulder pain and disability index at 6 months)									
1	observational studies	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	coefficient 6.82 lower (12.17 to 1.47 lower)	⊕OOO VERY LOW	CRITICAL
Exercise (2 or more/week or 1 or less/week): for predicting pain reduction (Pain subscale (0-100mm) of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) at 12 months)									

1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	coefficient 0.32 higher (6.29 lower to 6.92 higher)	⊕OOO VERY LOW	CRITICAL
Exercise (2 or more/week or 1 or less/week) for predicting quality of life (SF36 Finnish version physical component summary scores at 12 months)									
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	coefficient 2.07 higher (1.38 lower to 5.51 higher)	⊕OOO VERY LOW	CRITICAL
Exercise (2 or more/week or 1 or less/week) for predicting quality of life (SF36 Finnish version mental component summary scores at 12 months)									
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	coefficient 2.42 higher (1.15 lower to 6 higher)	⊕OOO VERY LOW	CRITICAL

1 Downgraded by 1 or 2 increments because the majority of the evidence was at high or very high risk of bias
2 Downgraded for outcome indirectness
3 Downgraded for imprecision because the 95% CIs around the effect crossed the null line

Table 14: Clinical evidence profile: presence or absence of comorbid physical condition

Quality assessment							Effect	Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			
Number of other conditions 0 versus >1) for predicting clinically significant pain (Graded Chronic Pain Scale grade 1, 2 3 and 4) at 12 months									
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	OR 1.3 (0.86 to 1.96)	⊕OOO VERY LOW	CRITICAL
Number of additional health problems (one versus none) for predicting shoulder pain and disability index at 6 months									
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	coefficient 3.52 higher (0.3 to 6.75 higher)	⊕⊕OO LOW	CRITICAL

Number of additional health problems (two versus none) for predicting shoulder pain and disability index at 6 months									
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	coefficient 6.62 higher (1.48 to 9.75 higher)	⊕⊕OO LOW	CRITICAL
Presence or absence of comorbid physical condition(s): for predicting 2 point change in VAS 0-10 pain intensity (Low back pain)									
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	OR 1.013 (0.963 to 1.065)	⊕OOO VERY LOW	CRITICAL
Presence or absence of comorbid physical condition (co-morbidity yes/no) for predicting 30% improvement in pain intensity at 12 months									
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	OR 0.76 (0.52 to 1.11)	⊕OOO VERY LOW	CRITICAL

1 Downgraded by 1 or 2 increments because the majority of the evidence was at high or very high risk of bias
2 Downgraded for imprecision because the 95% CIs around the effect crossed the null line

Table 15: Clinical evidence profile: Pain diagnosis

Quality assessment							Effect	Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			
Pain diagnosis (widespread pain yes/no) for predicting pain intensity (0-100)									
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	coefficient 2.88 higher (0.38 lower to 6.58 higher)	⊕OOO VERY LOW	CRITICAL
Pain diagnosis (widespread pain compared with 0-2 pain regions) for predicting quality of life (difference of ≥3 on SF36 physical component)									

1	observational studies	very serious[1]	no serious inconsistency	serious[3]	serious[2]	none	OR 0.69 (0.45-1.06)	⊕OOO VERY LOW	CRITICAL

1 Downgraded by 1 or 2 increments because the majority of the evidence was at high or very high risk of bias
2 Downgraded for imprecision because the 95% CIs around the effect crossed the null line
3 Downgraded for outcome indirectness

F.2 Psychological risk factors

Table 16: Clinical evidence profile: reported pain intensity

Quality assessment							Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Relative (95% CI)	Absolute		
1	cohort study	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	OR 1.19 (1.06 to 1.33)	-	⊕OOO VERY LOW	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	OR 1.19 (1.09 to 1.3)	-	⊕⊕OO LOW	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	unstandardized ß coefficient 1.36 lower (1.4972 to 1.2228 lower)	⊕⊕OO LOW	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	-	β coefficient 1.89 higher (1.26 to 2.51 higher)	⊕OOO VERY LOW	CRITICAL
1	cohort study	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	B (unstandardized regression coefficient) 0.53 lower (0.67 to 0.39 lower)	⊕⊕⊕O MODERATE	CRITICAL
1	cohort study	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	-	ß coefficient 0.14 higher (0.2 lower to 0.49 higher)	⊕⊕OO LOW	CRITICAL

1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	RR 4.13 (1.73 to 9.86)	-	⊕⊕OO LOW	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	unstandardized regression coefficient B 0.38 higher (0.1252 to 0.6348 higher)	⊕⊕OO LOW	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	-	unstandardized regression coefficient B 0.11 lower (0.2864 lower to 0.0664 higher)	⊕OOO VERY LOW	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	OR 1.1 (0.84 to 1.44)	-	⊕OOO VERY LOW	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	OR 1.06 (1.03 to 1.09)	-	⊕⊕OO LOW	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	OR 1.05 (1.01 to 1.09)	-	⊕⊕OO LOW	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	OR 1.18 (1.12 to 1.25)	-	⊕⊕OO LOW	CRITICAL
1	cohort study	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	unstandardized coefficient 0.32 higher (0.19 to 0.45 higher)	⊕⊕⊕O MODERATE	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	OR 1.14 (1.08 to 1.2)	-	⊕⊕OO LOW	CRITICAL
1	cohort study	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	-	unstandardized ß coefficient 0.2 higher (0.5252 lower to 0.9252 higher)	⊕⊕OO LOW	CRITICAL
1	cohort study	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	-	unstandardized ß coefficient 0.13 lower (2.45 lower to 2.37 higher)	⊕⊕OO LOW	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	ß coefficient 0.39 higher (0.31 to 0.46 higher)	⊕⊕OO LOW	CRITICAL

1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	OR 1.01 (1 to 1.02)	-	⊕⊕OO LOW	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	ß coefficient 0.6798 lower (0.81112 to 0.54848 lower)	⊕⊕OO LOW	CRITICAL
1	cohort study	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	-	standardised ß coefficient 0.03 higher (0.07 lower to 0.13 higher)	⊕⊕OO LOW	CRITICAL
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	standardised ß coefficient 0.12 higher (0.02 to 0.23 higher)	⊕⊕⊕O MODERATE	CRITICAL

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 or 2 increments because the majority of the evidence had indirect outcomes
3 Downgraded by 1 increment if the confidence interval crossed the null line

Table 17: Clinical evidence profile: comorbid psychiatric disorder

Quality assessment							Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Relative (95% CI)**	**Absolute**		
1	cohort study	serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	OR 0.96 (0.897 to 0.971)	-	⊕⊕OO LOW	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	-	β coefficient 2.19 higher (0.99 lower to 5.37 higher)	⊕OOO VERY LOW	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	β coefficient 12.02 higher (1.49 to 22.56 higher)	⊕⊕OO LOW	CRITICAL
1	cohort study	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	ß coefficient 0.09 (0.02 to 0.16 higher)	⊕⊕⊕O MODERATE	CRITICAL

1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	RR 1.84 (1.05 to 3.22)	-	⊕⊕OO LOW	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	no serious[3]	none	RR 1.53 (0.9 to 2.6)	-	⊕OOO VERY LOW	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	unstandardized regression coefficient B 0.14 higher (0.042 to 0.238 higher)	⊕⊕OO LOW	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	unstandardized regression coefficient B 0.09 higher (0.0116 to 0.1684 higher)	⊕⊕OO LOW	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	OR 0.36 (0.11 to 1.18)	-	⊕OOO VERY LOW	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	OR 0.21 (0.02 to 2.21)	-	⊕OOO VERY LOW	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	OR 0.92 (0.87 to 0.97)	-	⊕⊕OO LOW	CRITICAL
1	cohort study	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	-	unstandardized ß coefficient 0.03 higher (0.166 lower to 0.226 higher)	⊕⊕OO LOW	CRITICAL
1	cohort study	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	unstandardized ß coefficient 0.35 higher (0.0952 to 0.6048 higher)	⊕⊕⊕O MODERATE	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	ß coefficient 1.1 higher (0.81 to 3 lower)	⊕⊕OO LOW	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	OR 0.99 (0.99 to 0.99)	-	⊕⊕OO LOW	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	-	ß coefficient 0.017 higher (0.0418 lower to 0.0758 higher)	⊕OOO VERY LOW	CRITICAL

1	cohort study	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	standardised ß coefficient 0.14 higher (0.27 lower to 0 higher)	⊕⊕⊕O MODERATE	CRITICAL
1	cohort study	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	-	standardised ß coefficient 0.11 higher (0.24 lower to 0.02 higher)	⊕⊕OO LOW	CRITICAL

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 or 2 increments because the majority of the evidence had indirect outcomes
3 Downgraded by one increment if the confidence interval crossed the null line

Table 18: Clinical evidence profile: coping style

Quality assessment							Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Relative (95% CI)	Absolute		
1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	OR 1.1 (1 to 1.21)	-	⊕⊕OO LOW	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	-	β coefficient 0.36 lower (0.5 to 0.22 lower)	⊕OOO VERY LOW	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	RR 1.46 (0.83 to 2.57)	-	⊕OOO VERY LOW	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	RR 1.08 (0.66 to 1.77)	-	⊕OOO VERY LOW	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	-	unstandardized regression coefficient 0.02 higher (0.0584 lower to 0.0984 higher)	⊕OOO VERY LOW	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	-	unstandardized regression coefficient	⊕OOO VERY LOW	CRITICAL

								0.05 higher (0.01 lower to 0.11 higher)		
1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	OR 1.06 (0.94 to 1.2)	-	⊕OOO VERY LOW	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	OR 0.73 (0.52 to 1.02)	-	⊕OOO VERY LOW	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	OR 0.95 (0.66 to 1.37)	-	⊕OOO VERY LOW	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	OR 2.95 (1.26 to 6.91)	-	⊕⊕OO LOW	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	OR 1.28 (0.76 to 2.16)	-	⊕OOO VERY LOW	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	OR1.04 (1.01 to 1.08)	-	⊕⊕OO LOW	CRITICAL
1	cohort study	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	-	unstandardized ß coefficient 0.05 lower (0.2656 lower to 0.1656 higher)	⊕⊕OO LOW	CRITICAL
1	cohort study	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	-	unstandardized ß coefficient 1.54 higher (1.4196 lower to 4.5 higher)	⊕⊕OO LOW	CRITICAL
1	cohort study	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	-	unstandardized ß coefficient 0.1 higher (0.1352 lower to 0.3352 higher)	⊕⊕OO LOW	CRITICAL
1	cohort study	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	-	unstandardized ß coefficient 0.78 lower (4.09 lower to 2.53 higher)	⊕⊕OO LOW	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	ß coefficient 3.79 higher (2.09 to 5.49 higher)	⊕⊕OO LOW	CRITICAL

1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	OR 0.97 (0.95 to 0.99)	-	⊕⊕OO LOW	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	-	ß coefficient 0.013 lower (0.08 lower to 0.06 higher)	⊕OOO VERY LOW	CRITICAL
1	cohort study	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	-	ß coefficient 0.015 higher (0.3 lower to 0.29 higher)	⊕OOO VERY LOW	CRITICAL
1	cohort study	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	-	standardised ß coefficient 0.03 higher (0.08 lower to 0.14 higher)	⊕⊕OO LOW	CRITICAL
1	cohort study	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	-	standardised ß coefficient 0 higher (0.13 lower to 0.12 higher)	⊕⊕OO LOW	CRITICAL
1	cohort study	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	-	standardised ß coefficient 0.09 higher (0.03 lower to 0.22 higher)	⊕⊕OO LOW	CRITICAL
1	cohort study	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	standardised ß coefficient 0.18 lower (0.29 to 0.07 lower)	⊕⊕⊕O MODERATE	CRITICAL
1	cohort study	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	standardised ß coefficient 0.03 lower (0.27 lower to 0 higher)	⊕⊕⊕O MODERATE	CRITICAL
1	cohort study	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	-	standardised ß coefficient 0 higher (0.15 lower to 0.09 higher)	⊕⊕OO LOW	CRITICAL
1	cohort study	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	-	standardised ß coefficient 0.1 higher (0.02 lower to 0.21 higher)	⊕⊕OO LOW	CRITICAL
1	cohort study	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	-	standardised ß coefficient 0.01 lower (0.13 lower to 0.14 higher)	⊕⊕OO LOW	CRITICAL

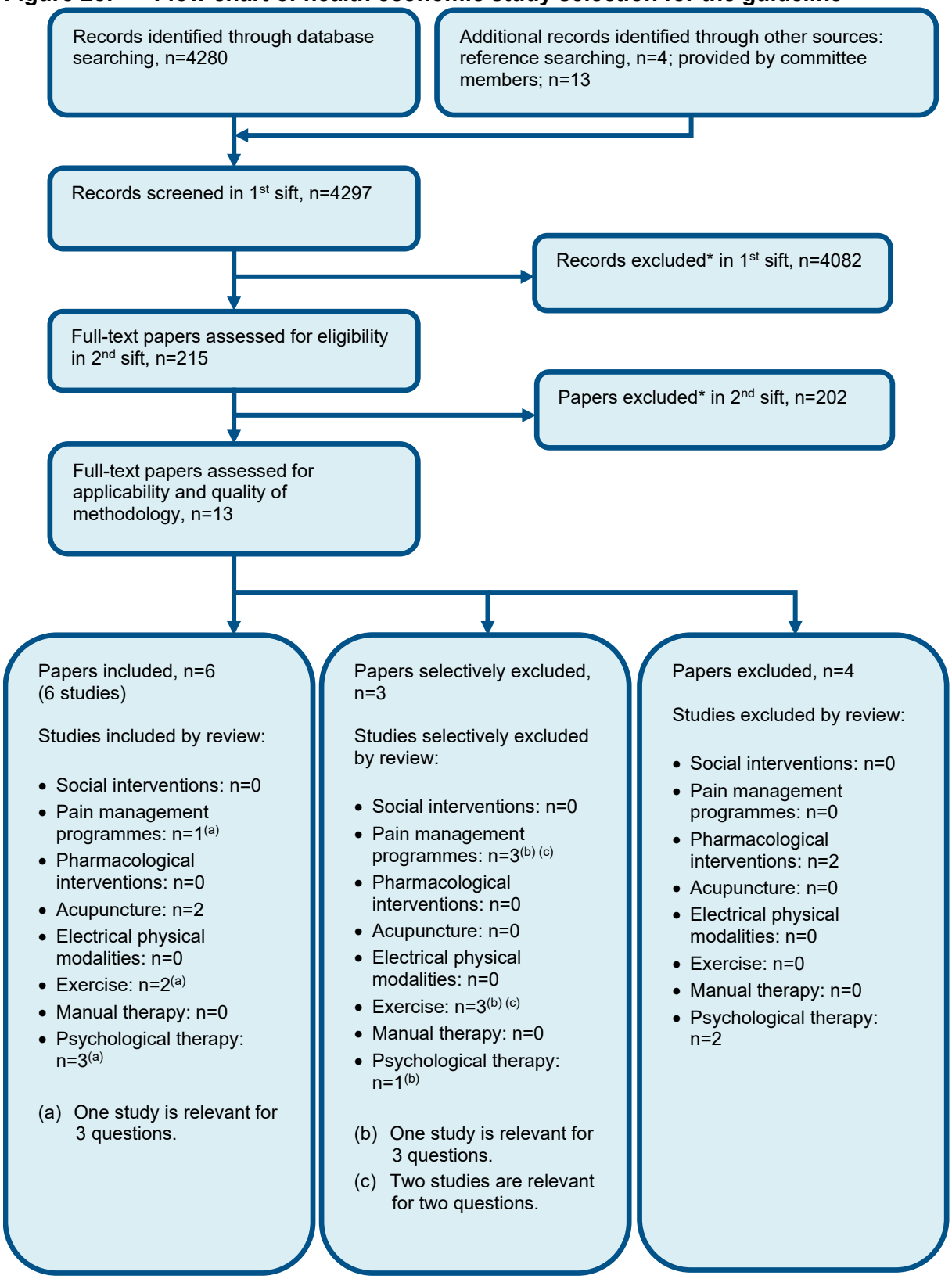
1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 or 2 increments because the majority of the evidence had indirect outcomes
3 Downgraded by 1 increment if the confidence interval crossed the null line

F.3 Social risk factors

None

Appendix G: Health economic evidence selection

Figure 28: Flow chart of health economic study selection for the guideline



* Non-relevant population, intervention, comparison, design or setting; non-English language

Appendix H: Health economic evidence tables

None

Appendix I: Excluded studies

I.1 Excluded clinical studies

I.1.1 Biological risk factors

Table 19: Studies excluded from the clinical review

Reference	Reason for exclusion
Adams, 2018[1]	Insufficient adjustment for confounders
Adnan, 2017[2]	No relevant outcomes
Agius, 2014[4]	Incorrect study design; not prognostic
Alamam 2019 [11]	No relevant outcomes
Al-Kaisy, 2018[10]	Incorrect study design; not prognostic
Allaire, 2018[13]	No relevant outcomes
Anastas, 2018[16]	No relevant outcomes
Andersen, 2012[19]	Incorrect study design; predicting long-term sickness
Andersen, 2012[18]	No useable outcomes (number of pain days)
Atli, 2010[24]	No relevant outcomes
Beneciuk, 2018[33]	Incorrect study design; predicting persistent pain
Bergman, 2004[38]	Incorrect study design (quality of life predicting pain)
Billy, 2017[43]	No useable outcomes
Bjorland 2019 [44]	Unclear population (duration of pain not reported)
Bohman, 2013[48]	Incorrect analysis; insufficient adjustment for confounders
Bohman, 2014[49]	No relevant risk factors
Bonvanie, 2016[51]	No relevant outcomes
Boonstra, 2015[52]	No relevant outcomes
Braden, 2012[53]	Incorrect study design; predicting employment based on pain or mental health conditions
Brady 2019 [55]	Incorrect population
Brain, 2017[56]	Incorrect study design
Brooks, 2013[63]	No relevant risk factors
Buchner, 2007[65]	No relevant outcomes
Burns, 1998[73]	No relevant outcomes
Butchart, 2009[74]	No relevant outcomes
Butler, 2013[75]	Incorrect study design (not multivariate analysis)
Campbell, 2013[77]	Unclear population
Campbell, 2015[76]	Incorrect study design, no relevant analysis
Castien, 2012[84]	No useable outcomes
Cecchi, 2012[87]	No relevant prognostic factors
Cecchi, 2014[88]	No relevant outcomes
Chen, 2017[92]	No relevant prognostic factors
Choma, 2011[96]	Incorrect study design
Costa Lda, 2009[102]	No useable outcomes (time to event data)
Da Luz, 2018[108]	Incorrect study design (cross-sectional)
Demarchi 2019 [123]	No relevant outcomes

Reference	Reason for exclusion
de Rooij, 2013[116]	Systematic review with different PICO
de Rooij, 2015[117]	No relevant outcomes; fatigue
Di Iorio, 2007[128]	Incorrect comparison; healthy participants
DiBenedetto, 2019[129]	No useable outcomes, incorrect study design
Dobscha, 2016[134]	No relevant outcomes
Doualla, 2019[136]	No relevant outcomes
Dragioti, 2018[138]	No relevant outcomes
Dunn, 2006[141]	Incorrect analysis; univariate
Dunn, 2008[142]	No relevant outcomes
Dunn, 2011[144]	Incorrect population
Dunn, 2013[140]	No useable outcomes (baseline characteristics only)
Dybowski, 2018[145]	No relevant outcomes
Egan, 2013[150]	Incorrect study design
Elliott, 2014[154]	No relevant outcomes
Enthoven, 2016[155]	Incorrect population
Epping-Jordan, 1998[156]	Insufficient adjustment for confounders
Etropolski, 2013[160]	Incorrect analysis; not prognostic
Ferrari 2019 [165]	No relevant outcomes (full multivariable analysis not reported)
Fuss, 2014[175]	No relevant outcomes
Generaal, 2017[178]	No relevant outcomes
George, 2015[180]	Incorrect intervention (surgery)
Gerdle, 2016[181]	Insufficient adjustment for confounders
Ginn, 2004[187]	Insufficient adjustment for confounders
Gore, 2012[193]	Incorrect comparison
Grosen, 2017[195]	Insufficient adjustment for confounders
Gustavsson, 2013[205]	Confounders not described
Hankin, 2004[213]	No relevant outcomes
Hartvigsen 2020 [216]	Incorrect population (majority pain duration <2 weeks)
Hegarty, 2012[222]	Incorrect intervention (surgery)
Helminen 2020 [225]	Unclear population (unclear duration of pain); insufficient detail reported on analysis methodology
Henschke, 2012[227]	Insufficient adjustment for confounders
Hermsen, 2011[230]	No useable outcomes
Hill, 2004[233]	No relevant outcomes, incorrect population; predicting persistent neck pain
Hirase, 2018[234]	No relevant outcomes
Holman, 2008[237]	Incorrect study design; lab-based MRI
Hong, 1996[238]	No useable outcomes
Hoving, 2004[243]	Insufficient adjustment for confounders
Huang, 2011[244]	No relevant risk factors
Hysing, 2017[247]	Incorrect study design; patient characteristics only
Jensen, 1994[255]	No relevant outcomes
Jensen, 2016[251]	No useable outcomes (median and IQR)
Jeong, 2017[257]	No useable outcomes
Jones, 2006[259]	No useable outcomes
Kabore 2020 [263]	No relevant outcomes (only significant factors reported)

Reference	Reason for exclusion
Kapos, 2018[264]	Unclear population and no relevant outcomes
Karapetyan, 2015[265]	Incorrect study design (not prognostic)
Karasawa 2019 [266]	No relevant outcomes
Kasch, 2008[270]	Incorrect population; not chronic
Kawi, 2016[272]	No relevant outcomes (biomarkers)
Keating, 2005[274]	No relevant outcomes
Kendell, 2018[279]	Incorrect analysis
Koke, 2015[288]	No relevant outcomes
Kovacs, 2012[293]	Insufficient adjustment for confounders, incorrect population
Kovacs 2019 [292]	Incorrect population (one third had an acute pain episode)
Lame, 2005[298]	Incorrect study design (cross-sectional)
Lan, 2010[300]	Confounders not described
Landmark, 2018[301]	Incorrect population
Lazaridou 2019 [306]	Incorrect study design (daily diary analysis)
Lee, 2014[309]	Univariate analysis
LeResche, 2013[315]	No relevant risk factors
Lillefjell, 2007[320]	No useable outcomes; functional status screening
Liu, 2017[324]	Validation study
Long, 1995[326]	No relevant outcomes
Macedo, 2014[330]	Univariate analysis
Machado, 2016[332]	No relevant outcomes (predicting persistent low back pain)
Majedi 2019 [335]	Incorrect study design (cross-sectional)
Makris, 2015[336]	No relevant outcomes
Mallen, 2007[337]	No relevant outcomes
Manchikanti, 2001[338]	No multivariate analysis
Marin, 2006[340]	No relevant outcomes
Markkula, 2016[341]	Incorrect study design, predicting pain diagnosis
Martinez-Calderon, 2018[348]	Systematic review with different PICO
Mehling, 2012[358]	Incorrect population (acute pain)
Mehta, 2015[359]	Incorrect analysis, not adjusted for confounders
Mekhail, 2019[360]	No useable outcomes
Mendonca, 2018[361]	Systematic review protocol
Michaelson, 2004[364]	No relevant prognostic factors
Mlekusch, 2013[367]	No useable outcomes
Moloney 2018 [368]	Insufficient adjustment for confounders
Moradi, 2010[371]	Incorrect analysis (not prognostic)
Mun 2019 [376]	Incorrect study design (cross-sectional; no relevant outcomes at 3 month follow up)
Myhrvold 2019 [378]	Incorrect population (included non-chronic pain)
Nilsson, 1997[389]	No relevant outcomes
Nolet, 2012[390]	Incorrect analysis baseline characteristics only
Nordeman, 2017[391]	No relevant outcomes
Nordstoga, 2017[392]	Insufficient adjustment for confounders
Ogollah, 2018[397]	Incorrect population
Otto 2019 [404]	No relevant outcomes
Page, 2015[406]	No relevant outcomes

Reference	Reason for exclusion
Pape, 2007[408]	Incorrect population; not chronic
Parreira, 2017[410]	No relevant outcomes; onset and prognosis
Perez, 2015[414]	No relevant outcomes
Perez, 2017[413]	Incorrect study design; cross-sectional
Petersen, 2007[415]	Insufficient adjustment for confounders
Plunkett, 2017[420]	Insufficient adjustment for confounders
Puschmann 2020 [423]	Incorrect population (intermittent low back pain)
Rabey, 2017[425]	No relevant outcomes
Rahman, 2004[427]	No relevant outcomes
Rapo-Pylkko, 2017[431]	No adjustment for confounders
Rasmussen-Barr, 2013[432]	No relevant outcomes; predicting recovery
Reynolds, 1983[438]	No relevant outcomes
Rundell 2019 [456]	No relevant outcomes
Ruscheweyh, 2015[457]	No relevant outcomes
Ryall, 2007[458]	No relevant outcomes; predicting recovery
Sadeghian, 2013[461]	No useable outcomes (presence or absence of pain)
Sanson 2020 [463]	Incorrect study design (cross-sectional)
Santos, 2017[464]	Incorrect population; children
Schaefer, 2016[467]	Incorrect analysis; not prognostic
Scherer, 2016[469]	Incorrect study design; cross-sectional
Siebenhuener, 2017[482]	No relevant outcomes
Sellinger, 2010[477]	Incorrect analysis; not multivariate
Sihawong, 2016[483]	Incorrect study design, predicting onset of low back pain
Skillgate, 2017[485]	Incorrect study design, predicting onset of low back pain
Slack, 2018[486]	Incorrect comparison (acute versus chronic)
Slade, 2013[487]	Incorrect analysis; not multivariate
Slepian 2020 [488]	Incorrect population (not chronic)
Smeets, 2007[491]	No relevant outcomes
Smidt, 2006[492]	Incorrect population
Solodiuk, 2014[497]	Incorrect population (children)
Staudt, 2018[498]	Incorrect analysis; not prognostic
Taylor, 2006[505]	No relevant outcomes
Thomas, 2008[509]	No relevant outcomes
Torma, 2013[512]	No relevant outcomes; physical function
Tripp, 2004[516]	No useable outcomes
Tubach, 2004[523]	No relevant outcomes (persistence or reoccurrence)
Tyack, 2016[529]	Incorrect population (all chronic conditions)
van den Hoogen, 1997[536]	No useable outcomes (time to recovery)
van Oostrom, 2011[545]	No relevant outcomes
van Oostrom, 2012[546]	Incorrect study design, in relevant outcomes (predicting LBP)
van Tulder, 1998[547]	Incorrect analysis; not multivariate
Vavrek, 2015[550]	Insufficient adjustment for confounders
Velly, 2010[553]	Insufficient adjustment for confounders
Verkerk, 2011[558]	Protocol
Verkerk, 2013[556]	No relevant outcomes

Reference	Reason for exclusion
Videla, 2017[561]	Incorrect study design; patient characteristics only
Weijenborg, 2009[567]	Insufficient adjustment for confounders
Werneke, 2001[569]	Incorrect population
Wideman, 2011[574]	Insufficient adjustment for confounders
Wilkens, 2013[576]	No relevant outcomes
Zheng, 2005[595]	Incorrect analysis; univariate

I.1.2 Psychological risk factors

Table 20: Studies excluded from the clinical review

Reference	Reason for exclusion
Ailliet 2016 [5]	Incorrect population
Ailliet 2018 [6]	Incorrect population
Akerblom 2015 [8]	No relevant outcomes
Akerblom 2020 [7]	Insufficient adjustment for confounders
Akerlind 1992 [9]	No relevant outcomes
Alamam 2019 [11]	No relevant outcomes
Alhowimel 2018 [12]	Systematic review with difference PICO
Alyousef 2018 [14]	No relevant outcomes
Anamkath 2018 [15]	No relevant outcomes
Andersen 2014 [20]	No adjustment for confounders
Ang 2010 [21]	No relevant outcomes
Arnstad 2019 [22]	Incorrect population
Arola 2010 [23]	Incorrect population and no relevant outcomes
Ayis 2009 [25]	No relevant outcomes
Badcock 2002 [26]	Incorrect population
Bair 2013 [27]	Insufficient adjustment for confounders
Baltov 2008 [28]	No relevant outcomes
Barnes 1989 [29]	No relevant outcomes
Beerthuizen 2009 [30]	Systematic review with different PICO
BenDebba 1997 [31]	Insufficient adjustment for confounders
Bendix 1998 [32]	Insufficient adjustment for confounders
Bennett 1996 [34]	No adjustment for confounders
Benyon 2013 [35]	Unclear population
Bergenheim 2019 [36]	Insufficient adjustment for confounders
Bertisch 2009 [39]	Insufficient adjustment for confounders
Bhat 2010 [40]	Insufficient adjustment for confounders
Bierman 2018 [41]	Incorrect population
Bigatti 2008 [42]	No usable data
Boersma 2005 [46]	Incorrect study design
Boersma 2006 [47]	Insufficient adjustment for confounders
Bohman 2019 [50]	No relevant outcomes
Braden 2012 [53]	Insufficient adjustment for confounders
Brekke 2011	Insufficient adjustment for confounders

Reference	Reason for exclusion
Brekke 2003 [58]	Insufficient adjustment for confounders
Bremander 2011 [59]	Insufficient adjustment for confounders
Brennan 1986 [61]	Insufficient adjustment for confounders
Broderick 2016 [62]	No relevant outcomes
Brown 1990 [64]	No adjustment for confounders
Buckelew 1996 [66]	Insufficient adjustment for confounders
Buenaver 2012 [67]	Incorrect study design
Burckhardt 1997 [68]	Insufficient adjustment for confounders
Burns 2000 [69]	Insufficient adjustment for confounders
Burns 2017 [70]	Insufficient adjustment for confounders
Burns 2003 [71]	No relevant outcomes
Burns 1998 [72]	No relevant outcomes
Campbell 2013 [77]	Unclear population
Carlesso 2016 [79]	Insufficient adjustment for confounders
Carroll 2007 [82]	Insufficient adjustment for confounders
Castelnuovo 2016 [83]	Systematic review with difference PICO
Castillo 2013 [85]	Incorrect population
Cecchi 2011 [86]	Insufficient adjustment for confounders
Cecchi 2014 [88]	No relevant outcomes
Chen 2018 [93]	Unclear population
Cipher 2007 [97]	Unclear population
Cook 2015 [98]	No relevant outcomes
Coombes 2015 [99]	Unclear population; no relevant outcomes
Cormier 2016 [100]	No relevant outcomes
Coronado 2017 [101]	Unclear population and insufficient adjustment for confounders
Covic 2003 [104]	Insufficient adjustment for confounders
Craner 2016 [105]	No relevant outcomes
Cucciare 2009 [106]	No relevant outcomes
Cyteval 2006 [107]	No adjustment for confounders
Dammen 2006 [109]	Unclear population
Daubs 2011 [110]	Systematic review with different PICO
Davis 2015 [112]	Insufficient adjustment for confounders
Day 2018 [113]	No relevant outcomes
Dear 2016 [121]	No useable outcome data
De Pauw 2015 [115]	Insufficient adjustment for confounders
de Rooij 2013 [116]	Systematic review with different PICO
Demmelmaier 2010 [124]	Insufficient adjustment for confounders
Dersh 2008 [125]	No relevant outcomes
Desbiens 1997 [126]	Incorrect population
Dezutter 2017 [127]	No relevant outcomes
Dickens 2000 [130]	No relevant outcomes
Dobkin 2010 [133]	Insufficient adjustment for confounders
Dobscha 2016 [134]	Insufficient adjustment for confounders
Dobscha 2015 [135]	No relevant outcomes
Dozois 1996 [137]	No relevant outcomes

Reference	Reason for exclusion
Driscoll 2015 [139]	Incorrect study design
Dunn 2008 [142]	No relevant outcomes
Dunn 2006 [143]	Unclear population and no relevant outcomes
Edmond 2010 [147]	Incorrect population
Edwards 2003 [148]	p values only
Edwards 2016 [149]	No relevant outcomes
Ekeberg 2010 [151]	No relevant outcomes
Elander 2013 [152]	Incorrect population
Enthoven 2016 [155]	Incorrect population
Eriksen 2004 [157]	Incorrect population and no relevant outcomes
Estlander 1998 [159]	Incorrect population
Evers 2001 [162]	Insufficient adjustment for confounders
Evers 2003 [161]	Insufficient adjustment for confounders
Feitosa 2016 [164]	Article not in English
Fiegl 2019 [167]	Insufficient adjustment for confounders
Finset 2004 [168]	No relevant outcomes
Fouquet 1997 [172]	No relevant outcomes
France 2020 [173]	Insufficient adjustment for confounders
Fricton 1996 [174]	No relevant outcomes
Fuss 2014 [175]	No useable outcome data
Galli 2010 [176]	No useable outcome data
Generaal 2017 [178]	No relevant outcomes
George 2011 [179]	Incorrect population
Gerdle 2016 [181]	Insufficient adjustment for confounders
Gere 2014 [182]	Insufficient adjustment for confounders
Gessel 1975 [183]	No adjustment for confounders
Ginn 2004 [187]	Insufficient adjustment for confounders
Glattacker 2018 [188]	No useable outcome data
Glattacker 2013 [189]	No useable outcome data
Glattacker 2010 [190]	Insufficient adjustment for confounders
Glombiewski 2010 [191]	No outcome useable data
Goldberg 1994 [192]	No adjustment for confounders and unclear population
Grosen 2017 [195]	Insufficient adjustment for confounders
Grotle 2010 [201]	No relevant outcomes
Grotle 2006 [202]	No useable outcome data
Guck 1999 [203]	No relevant outcomes
Gureje 2001 [204]	Incorrect population
Haas 2002 [206]	Insufficient adjustment for confounders
Hallstam 2017 [208]	No relevant outcomes
Hallstam 2016 [209]	No useable outcome data
Hammond 2006 [211]	No relevant outcomes
Han 2019 [212]	Incorrect study design
Hankin 2004 [213]	No relevant outcomes
Havermark 2006 [217]	No relevant outcomes
Hayashi 2015 [218]	No adjustment for confounders

Reference	Reason for exclusion
Haythornthwaite 2003 [219]	No useable outcome data
Healy 2015 [220]	No relevant outcomes
Hedman-Lagerlof 2019 [221]	Insufficient adjustment for confounders
Heiskanen 2012 [223]	No adjustment for confounders
Helmhout 2010 [224]	No relevant outcomes
Helminen 2016 [226]	Insufficient adjustment for confounders
Helminen 2020 [225]	Unclear population and insufficient detail on analysis
Henschke 2012 [227]	Insufficient adjustment for confounders
Herbert 2019 [228]	No adjustment for confounders
Hermansson 2001 [229]	No adjustment for confounders
Hicks 2012 [231]	Insufficient adjustment for confounders
Hildebrandt 1997 [232]	Insufficient adjustment for confounders
Holm 1998 [236]	No relevant outcomes
Hooten 2011 [240]	Incorrect study design
Hopwood 2007 [241]	No relevant outcomes
Huang 2011 [244]	Insufficient adjustment for confounders
Huffman 2019 [245]	Insufficient adjustment for confounders
Jensen 2005 [252]	Unclear population; no relevant outcomes
Jensen 2010 [256]	Insufficient adjustment for confounders
Jensen 2011 [253]	Systematic review with different PICO
Jensen 2016 [254]	No relevant outcomes
Jia 2016 [258]	Systematic review with different PICO
Julkunen 1988 [261]	No relevant outcomes
Kapos 2018 [264]	Unclear population and no relevant outcomes
Karels 2007 [268]	Incorrect population
Karlsson 2016 [269]	No relevant outcomes
Katyayan 2017 [271]	No adjustment for confounders
Keedy 2014 [275]	Insufficient adjustment for confounders
Keefe 1989 [276]	Insufficient adjustment for confounders
Keeley 2008 [277]	Insufficient adjustment for confounders
Keltner 2012 [278]	Incorrect study design
Kirschneck 2013 [282]	No relevant outcomes
Kleinke 1991 [283]	No useable outcome data
Kleinke 1988 [284]	Insufficient adjustment for confounders
Ko 2011 [285]	No adjustment of confounders
Koenig 2014 [286]	Incorrect study design
Koh 2014 [287]	No adjustment for confounders
Koke 2015 [288]	No relevant outcomes
Kovacs 2012 [293]	Insufficient adjustment for confounders
Kowal 2011 [294]	No useable outcome data
Krantz 2019 [295]	Incorrect study design
Kroenke 2012 [296]	No adjustment for confounders
Lam Chan 2008 [89]	Insufficient adjustment for confounders
Lampl 1998 [299]	No adjustment for confounders
Lankhorst 2016 [303]	Insufficient adjustment for confounders

Reference	Reason for exclusion
Lattie 2013 [305]	Insufficient adjustment for confounders
Learman 2011 [307]	No relevant outcomes
Leboeuf-Yde 2004 [308]	Insufficient adjustment for confounders
Lee 2008 [311]	Incorrect population and no relevant outcomes
Leeuw 2008 [312]	No relevant outcomes
Leino-Arjas 2018 [314]	Incorrect population
Lerman 2015 [316]	Insufficient adjustment for confounders
Licciardone 2013 [319]	No useable outcome data
Lindholm 2016 [321]	No useable outcome data
Linton 2000 [322]	Systematic review with different PICO
Linton 2011 [323]	Incorrect study design
Lohnberg 2013 [325]	Incorrect study design
Luque-Suarez 2019 [329]	Systematic review with different PICO
Macedo 2014 [330]	No relevant outcomes
Magni 1994 [334]	Incorrect population
Mallen 2007 [337]	No relevant outcomes
Mannion 1999 [339]	No adjustment for confounders
Martin 2014 [342]	Incorrect population
Martin 2011 [343]	Insufficient adjustment for confounders
Martin 2017 [344]	Insufficient adjustment for confounders
Martinez-Calderon 2018 [347]	Systematic review with different PICO
Martinez-Calderon 2018 [348]	Systematic review with different PICO
Martinez-Calderon 2019 [345]	Systematic review with different PICO
Martinez-Calderon 2019 [346]	Systematic review with different PICO
Matsudaira 2014 [350]	Incorrect population
Mayer 2014 [351]	No relevant outcomes
McCreary 1979 [353]	No adjustment for confounders
McGeary 2016 [354]	Insufficient adjustment for confounders
McWilliams 2016 [357]	Insufficient adjustment for confounders
Mercado 2005 [362]	Incorrect population
Merrick 2009 [363]	No relevant outcomes
Mills 2019 [365]	No adjustment for confounders
Miro 2018 [366]	No relevant outcomes
Moloney 2018 [368]	Insufficient adjustment for confounders
Moon 2008 [369]	No useable outcomes
Moradi 2012 [370]	No relevant outcomes
Morasco 2011 [372]	No relevant outcomes
Morasco 2011 [373]	Systematic review with different PICO
Morris 2019 [374]	Incorrect population
Moulin 2015 [375]	No adjustment for confounders
Mutubuki 2019 [377]	No relevant outcomes
Ng 2018 [384]	Incorrect population

Reference	Reason for exclusion
Ng 2017 [385]	Incorrect population and no relevant outcomes
Nicassio 1995 [386]	Insufficient adjustment for confounders
Nicholas 2006 [387]	Incorrect study design
Nickel 2008 [388]	Incorrect study design
Nordstoga 2017 [392]	Insufficient adjustment for confounders
Norman 2004 [393]	No relevant outcomes
Noyman-Veksler 2017 [394]	No adjustment for confounders
Nyiendo 2001 [395]	Insufficient adjustment for confounders
Nyiendo 2000 [396]	No adjustment for confounders
Ogollah 2018 [397]	Incorrect population
Oliveira 2019 [400]	Insufficient adjustment for confounders
Oliveira 2018 [401]	Insufficient adjustment for confounders
Oliveira 2019 [399]	No relevant outcomes
Oosterhof 2008 [402]	Insufficient adjustment for confounders
Orenius 2013 [403]	Insufficient adjustment for confounders
Page 2015 [406]	No relevant outcomes
Panken 2016 [407]	Incorrect population
Paquet 2019 [409]	Insufficient adjustment for confounders
Peng 2015 [411]	No useable outcome data
Penlington 2019 [412]	Insufficient adjustment for confounders
Petersen 2007 [415]	Insufficient adjustment for confounders
Peterson 2012 [416]	Insufficient adjustment for confounders
Peterson 2014 [417]	Insufficient adjustment for confounders
Pfingsten 1997 [418]	No relevant outcomes
Pigg 2013 [419]	No adjustment for confounders
Plunkett 2017 [420]	Insufficient adjustment for confounders
Prins 2013 [422]	No relevant outcomes
Puschmann 2020 [423]	Incorrect population
Racine 2016 [426]	Insufficient adjustment for confounders
Rahman 2008 [428]	Incorrect study design
Rainville 1993 [429]	No relevant outcomes
Rammelsberg 2003 [430]	Insufficient adjustment for confounders
Rapo-Pylkko 2017 [431]	No adjustment for confounders
Rayahin 2014 [434]	Insufficient adjustment for confounders
Rayner 2016 [435]	No relevant outcomes
Reilingh 2008 [436]	No useable outcome data
Reimer 2017 [437]	Insufficient adjustment for confounders
Reynolds 1983 [438]	No useable outcome data
Richards 1980 [439]	Incorrect population
Richardson 1999 [440]	No relevant outcomes
Riegel 2014 [442]	Systematic review with different PICO
Riipinen 2005 [443]	No adjustment for confounders or useable data
Riley 2001 [444]	Insufficient adjustment for confounders
Riley 2020 [445]	No relevant outcomes
Ringe 2003 [446]	Unclear population and insufficient adjustment for confounders

Reference	Reason for exclusion
Roberts 1986 [448]	Insufficient adjustment for confounders
Roditi 2010 [450]	Incorrect study design
Rosso 2008 [453]	Incorrect population
Ruscheweyh 2015 [457]	No relevant outcomes
Saariaho 2016 [459]	Insufficient adjustment for confounders
Saariaho 2017 [460]	No adjustment for confounders
Samwel 2009 [462]	No useable outcome data
Schellingerhout 2008 [468]	Insufficient adjustment for confounders
Schieir 2009 [471]	Insufficient adjustment for confounders
Scholich 2012 [472]	No adjustment for confounders
Schuessler 1993 [473]	No relevant outcomes
Scott 2018 [475]	Systematic review with different PICO
Seery 2010 [476]	No relevant outcomes
Shahar 2018 [478]	No relevant outcomes
Shaygan 2018 [480]	Insufficient adjustment for confounders
Sirois 2017 [484]	No relevant outcomes
Smedbraten 2018 [489]	Insufficient adjustment for confounders
Smeeding 2010 [490]	Insufficient adjustment for confounders
Smidt 2006 [492]	Incorrect population
Smith 1992 [493]	No useable outcome data
Steffens 2014 [499]	Insufficient adjustment for confounders
Sweeney 2018 [503]	Systematic review with different PICO
Thieme 2007 [508]	Insufficient adjustment for confounders
Thompson 2019 [510]	Study protocol
Tota-Faucette 1993 [513]	No relevant outcomes
Trief 1995 [514]	No relevant outcomes
Trompetter 2015 [518]	No relevant outcomes
Trompetter 2016 [519]	No relevant outcomes
Tsuji 2019 [522]	No relevant outcomes
Turk 1998 [525]	No adjustment for confounders
Turk 1998 [524]	No adjustment for confounders
Turner 2004 [526]	Incorrect study design
Turner 2007 [527]	No relevant outcomes
Turner 2000 [528]	Incorrect study design
Ullrich 2005 [530]	Incorrect population
Uysal 2011 [531]	Thesis, not available
Uysal 2017 [532]	Insufficient adjustment for confounders
Van Den Houte 2017 [537]	Insufficient adjustment for confounders
van der Hulst 2005 [539]	Systematic review with different PICO
Van Liew 2013 [541]	No useable outcome data
Van Liew 2013 [542]	No useable outcome data
Van Liew 2019 [543]	Insufficient adjustment for confounders
van Lunteren 2018 [544]	Incorrect study design
van Wijk 2008 [548]	No relevant outcomes
Vase 2015 [549]	No relevant outcomes

Reference	Reason for exclusion
Vavrek 2015 [550]	Insufficient adjustment for confounders
Velazquez 2015 [551]	Insufficient adjustment for confounders
Velly 2010 [553]	Insufficient adjustment for confounders
Vendrig 1999 [555]	No adjustment for confounders
Verkerk 2012 [557]	Systematic review with different PICO
Verwoerd 2013 [560]	Systematic review with different PICO
Von Korff 1993 [563]	Unclear population and insufficient adjustment for confounders
Wasan 2006 [564]	Insufficient adjustment for confounders
Wasan 2015 [565]	No useable outcome data
Weijenborg 2007 [566]	No useable data
Weijenborg 2009 [567]	Insufficient adjustment for confounders
Wertli 2014 [570]	Systematic review with different PICO
Wertli 2014 [571]	Systematic review with different PICO
Wertli 2014 [572]	Systematic review with different PICO
Wertli 2014 [573]	Systematic review with different PICO
Williams 2015 [577]	Thesis, not available
Wilt 2016 [578]	Insufficient adjustment for confounders
Wirth 2019 [580]	Insufficient adjustment for confounders
Witt 2019 [581]	Insufficient adjustment for confounders
Woby 2005 [583]	Incorrect study design
Woby 2007 [582]	Incorrect study design
Wolfensberger 2016 [584]	No relevant outcomes
Wood 2016 [586]	No relevant outcomes
Woods 2019 [587]	Insufficient adjustment for confounders
Workman 2002 [588]	No adjustment for confounders
Yang 1991 [590]	Insufficient adjustment for confounders
Yu 2019 [592]	Insufficient adjustment for confounders
Yue 1978 [593]	No useable outcome data
Zautra 2001 [594]	Insufficient adjustment for confounders
Zhu 2014 [596]	Incorrect population and no relevant outcomes
Zonneveld 2012 [597]	Insufficient adjustment for confounders

I.1.3 Social risk factors

Table 21: Studies excluded from the clinical review

Reference	Reason for exclusion
Agaliotis 2013 [3]	Incorrect study design (work participation outcome not predictor)
Ailliet 2016 [5]	No relevant outcomes
Andersen 2015 [17]	Incorrect outcomes
Baltov 2008 [28]	No relevant outcomes
Bergman 2002 [37]	Incorrect analysis, not adjusted for confounders
Bethge 2017 #3602	Protocol
Blyth 2008 [45]	Incorrect study design (cross-sectional relationship between caregiving and outcomes)

Reference	Reason for exclusion
Braden 2008 [54]	Incorrect study design; predicting employment based on pain or mental health conditions
Brauer 2014 [57]	Incorrect study design
Brendbekken 2018 [60]	Incorrect study design; work participation is an outcome not predictor
Caneiro 2016 [78]	Incorrect study design
Carlesso 2018 [80]	Incorrect analysis, unclear if adjusted for confounders
Carroll 2010 [81]	Incorrect study design (work participation outcome not predictor)
Chandran 2012 [90]	Incorrect study design
Chen 2007 [91]	Incorrect study design; compensation as outcome rather than predictor
Chibnall 2009 [95]	No relevant outcomes
Cougot 2015 [103]	Incorrect study design (predicting return to work)
Davidson 2017 [111]	Incorrect population (end of life population)
Day 2010 [114]	No useable outcomes
de Vries 2012 [120]	Incorrect study design (work participation outcome not predictor)
de Vries 2012 [119]	Incorrect study design; predicting return to work
Delongis 2004 [122]	Incorrect study design
Dionne 2007 [131]	Incorrect study design; predicting return to work
Dixon 1999 [132]	No useable outcomes
Dunn 2011 [144]	Insufficient adjustment for confounders
Dybowski 2018 [145]	Abstract
Dysvik 2004 [146]	Incorrect study design: cross-sectional
Egan 2013 [150]	Incorrect study design
Elkayam 1996 [153]	No useable outcomes
Ernstsen 2014 [158]	Incorrect study design; predicting return to work
Evers 2003 [161]	Insufficient adjustment for confounders
Fancourt 2018 [163]	Incorrect study design; predicting onset of chronic pain
Ferreira 2007 [166]	Incorrect study design: cross-sectional
Fishbain 1997 [169]	Incorrect study design, predicting return to work
Fisher 2007 [170]	Incorrect study design; qualitative
Gatchel 2005 [177]	No useable data
Gesztelyi 2006 [184]	No relevant outcomes
Gheldof 2007 [185]	Incorrect population (>30 days pain)
Gibson 1998 [186]	Literature review no relevant outcomes (return to work)
Greve 2009 [194]	No useable outcomes
Gross 2004 [200]	No relevant outcomes
Gross 2004 [196]	No relevant outcomes
Gross 2005 [197]	No relevant outcomes; functional outcomes only
Gross 2005 [198]	No relevant outcomes; functional outcomes only
Gross 2005 [199]	No relevant outcomes; predicting return to work
Haldorsen 1998 [207]	No relevant outcomes (predicting return to work)
Hamer 2013 [210]	Incorrect study design; predicting return to work
Hanley 2011 [214]	No relevant outcomes; prevalence of chronic pain
Hardman 2019 [215]	No relevant outcomes
Helmhout 2010 [224]	No relevant outcomes; functional outcomes only
Hoffman 2002 [235]	No useable outcomes; correlations only
Hoogendoorn 2001 [239]	Incorrect study design; predictors of onset of pain

Reference	Reason for exclusion
Hopwood 1994 [242]	Outcome not clearly defined
Hung 2017 [246]	No useable outcomes (not validated scale)
Imagama 2020 [248]	No relevant outcomes
Iversen 2015 [249]	Insufficient adjustment for confounders
Jablonska 2006 [250]	Incorrect study design; predictors of onset of pain
Jones 2009 [260]	Incorrect study design; onset of pain
Kaaria 2005 [262]	No relevant outcomes
Karayannis 2019 [267]	No useable outcomes
Kawi 2014 [273]	No relevant factors or outcomes
Kho 2017 [280]	Incorrect study design; predicting return to work
Kindler 2010 [281]	No relevant outcomes (regional pain progressing to widespread pain)
Koleck 2006 [289]	Incorrect study design, incorrect population
Kool 2002 [290]	Incorrect study design; predictors of return to work
Koster 2004 [291]	No relevant outcomes; decline in mobility
Krok 2012 [297]	Abstract
Lanier 2018 [302]	Incorrect population
Larsson 2012 [304]	Systematic review with different PICO
Lee 2016 [310]	No relevant outcomes; depression
Lehmann 1993 [313]	No relevant outcomes
Leroux 2004 [317]	Incorrect population (acute to chronic pain)
Leue 2012 [318]	Incorrect study design
Lillefjell 2007 [320]	No useable outcomes; functional status screening
Loyland 2016 [327]	No relevant outcomes
Luk 2010 [328]	Incorrect study design; predicting return to work
Macfarlane 2009 [331]	Systematic review with different PICO
Mackenbach 2001 [333]	Incorrect population, no useable outcomes (correlations only)
Matos 2017 [349]	No relevant risk factors
Mayer 2008 [352]	Incorrect study design; comparison of those with and without pain
McKillop 2017 [356]	Incorrect study design no useable outcomes (predicting depressive symptoms based on social support)
Mendonca 2018 [361]	Systematic review with different PICO
Nakagawa 2017 [379]	Incorrect study design (cross-sectional)
Natvig 1970 [382]	No relevant outcomes not adjusted for confounders
Newman 2017 [383]	Cross-sectional
Nickel 2008 [388]	Incorrect study design; cross-sectional
Nordeman 2017 [391]	No relevant outcomes
Olaya-Contreras 2013 [398]	Incorrect study design
Owari 2018 [405]	No useable outcomes, incorrect study design
Petersen 2007 [415]	No useable outcomes (not pain reduction or intensity)
Prang 2015 [421]	Incorrect study design (cross-sectional), incorrect population (not all chronic pain)
Raak 2006 [424]	Incorrect study design
Rasmussen 2008 [433]	Incorrect analysis (group comparison)
Reynolds 1983 [438]	No relevant outcomes
Richmond 2018 [441]	Incorrect population (trauma, not all chronic pain)
Riipinen 2005 [443]	No useable data

Reference	Reason for exclusion
Riskowski 2014 [447]	Incorrect study design, predicting pain prevalence
Robinson 2011 [449]	Incorrect study design, predicting return to work
Rosomoff 1995 [452]	No relevant outcomes
Rucker 1995 [454]	Incorrect study design (validation of risk prediction tool)
Ruiz Moral 1997 [455]	No useable outcomes; describing patient characteristics
Sarda 2009 [465]	No relevant outcomes
Sargeant 2009 [466]	No relevant outcomes
Schiaffino 1995 [470]	No relevant outcomes
Schultz 2004 [474]	No relevant outcomes
Shaw 2005 [479]	No relevant outcomes (functional disability, return to work)
Shipp 2009 [481]	Incorrect study design (predicting onset of pain)
Smith 2017 [494]	Conceptual paper
Smith 2018 [495]	Incorrect study design; predicting existence of pain rather than symptom improvement or worsening
Soderlund 2018 [496]	No relevant outcomes (pain acceptance, engagement in activities)
Sterling 2010 [500]	No relevant outcomes
Strating 2007 [501]	No relevant outcomes; disability
Suter 2002 [502]	Incorrect study design; no relevant risk factors or outcomes
Sylwander 2020 [504]	No relevant outcomes
Teasell 2001 [506]	Literature review
Tevaarwerk 2013 [507]	Incorrect population (cancer)
Thomten 2011 [511]	Incorrect population (pain for >1 month), no useable outcomes (dichotomised pain outcome)
Tripp 2004 [516]	No useable outcomes
Tripp 2013 [517]	No useable outcomes
Tseli 2017 [520]	Systematic review with different PICO
Valat 1997 [533]	No relevant outcomes
Valerie 2017 [534]	Literature review
van Abbema 2011 [535]	Systematic review with different PICO
Van Hooff 2014 [540]	Inappropriate dichotomisation of outcome
Vendrig 1999 [554]	Incorrect study design, predicting return to work
Verkerk 2011 [558]	No useable outcomes, baseline characteristics only
Viniol 2012 [562]	Study protocol
Widerstrom-Noga 2003 [575]	No relevant outcomes; predicting use of medications
Wippert 2017 [579]	Incorrect study design; predictor disability and pain at the start of rehabilitation programme
Wormgoor 2008 [589]	Incorrect study design; not prognostic
Yosef 2016 [591]	Incorrect study design (cross-sectional), incorrect analysis (univariate)

I.2 Excluded health economic studies

Table 22: Studies excluded from the health economic review

Reference	Reason for exclusion
None	-

Appendix J: Research recommendations

J.1 Risk factors

Research question: What risk factors enable stratification of treatment for people aged 16 years and over with chronic pain?

Why this is important:

There is a body of clinical knowledge that illustrates the widely varying ways people living with chronic pain feel about and engage with many chronic pain management interventions. Patient-reported health outcomes also vary widely following completion of such interventions. Greater knowledge of the various risk factors that may contribute to this diverse range of reactions and responses should enable better choice and tailoring of pain management interventions to meet individual need. Validation of that greater knowledge in the field would inform future resource planning.

The committee recognised that there is complex interplay between risk factors, some of which are permanent, others transient. Due to the multi-factorial nature of chronic pain, there are also complex feedback loops to contend with. When studying published literature to identify and better understand potential risk factors, the committee found very limited evidence that was of high enough quality to enable conclusions to be drawn. As successful stratification may enable health care professionals to more effectively manage the expectations, treatment and prognosis of people with chronic pain, the committee has made this research recommendation to address the current knowledge gap.

Criteria for selecting high-priority research recommendations:

PICO question	Population: People aged 16 years or over with chronic pain (pain that persists or recurs for more than three months) Exposure(s): Risk factors that may affect management and /or prognosis for people with chronic pain Comparison: N/A Outcome(s): • health related quality of life (including meaningful activity) • pain reduction (any validated scale)
Importance to patients or the population	Greater knowledge of the various risk factors that may contribute to the range of reactions and responses to pain management interventions should enable better choice and tailoring of pain management interventions to meet individual need, accelerating the process of finding a successful management strategy. Understanding the link between risk factors and prognosis in people with chronic pain will assist in prioritising patients with the greatest need.
Relevance to NICE guidance	High quality research in this area would generate new evidence and inform future updates of this guidance to make recommendations on specific modalities of chronic pain management for particular sub-groups of the population.
Relevance to the NHS	High quality research in this area would enable evidence-based stratification of people with chronic pain to occur, allowing patients to be offered those interventions with the greatest chance of success first. This has the potential to improve patient health outcomes and reduce time and resource involved in managing pain.
National priorities	None
Current evidence base	The committee identified very limited, low-quality evidence on biological, social or psychological risk factors for chronic pain management. Evidence identified rarely accounted for potential confounding factors that may explain the association.

Equality	Potentially. There is insufficient evidence at present to say if particular characteristics impact on an individual's ability to engage with and benefit from pain management interventions. High quality research in this area could identify factors leading to inequality or highlight inequality as a prognostic factor. High-quality research should also provide information on how these could be addressed in the future.
Study design	The ideal study design would be a prospective cohort study with multivariate analysis adjusting for relevant potential confounding factors. A long term follow up is required to demonstrate effect.
Feasibility	Chronic pain is a multi-factorial experience, and highly individual. Chronic pain management interventions are commonly multi-factorial as a result. Research with this population is therefore more complex to conduct than, for example, establishing risk factors for a surgical intervention. However, the scale of the population affected by chronic pain, the associated health and social economic impacts, and the lack of high-quality evidence to guide chronic pain interventions means this should be a high priority area for funding. It would be important that any future research in this area is sufficiently large in scale to deliver scientifically convincing conclusions. A network of research centres to generate this evidence may be the most cost-effective and scientifically robust manner in which to ensure the sample size is sufficiently large and heterogeneous.
Other comments	It was the small sample size of published studies, the poor description of interventions and populations and lack of multivariate analysis within studies that restricted the committee from making any clear recommendations about risk factors in this guidance. Future research needs to address these issues in order to be useful to NICE Guidance committees.
Importance	Medium: the research is relevant to the recommendations in the guideline, but the research recommendations are not key to future updates.