Socioeconomic status and occurrence of chronic pain. A meta-analysis

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Word count: 3222 words, excluding tables, figures and supplemental files.

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ABSTRACT

Objective: To examine the association between socioeconomic status (SES) and the occurrence of chronic pain, defined as pain that persists or recurs for more than 3 months.

Methods: We performed a structured search in Medline, Embase, WHO Global Index Medicus and Conference Proceedings Citation Index-Science databases to identify cohort and case-control studies on chronic pain and SES and its subgroups (SES combined index, educational level, income and occupational status).

We extracted study characteristics, outcome measures and measures of association and their 95% confidence intervals (CI). Literature search, data extraction, and risk of bias assessment were conducted by two independent researchers. We performed main and subgroup meta-analyses using random-effects model, and formally assessed heterogeneity and publication bias.

Results: A total of 45 studies, covering a population of approximately 175,000 individuals, were meta-analysed, yielding a pooled Odds Ratio (OR) of 1.32 (95%CI: 1.21-1.44) and 1.16 (95%CI: 1.09-1.23) for low and medium SES levels respectively, compared to high level. We obtained similar results in all the subgroup analyses. Heterogeneity was generally moderate to high across strata, and some evidence of publication bias for low socioeconomic status was found.

Conclusion: Our results support a moderate increase in the risk of chronic pain for low and medium SES when compared to high SES, a feature that remained constant in all measures of exposure or outcome used. Further prospective research on populations from developing countries are needed to confirm our findings as the studies available for this meta-analysis were carried out exclusively in developed countries.

Key words: chronic pain, socioeconomic status, sociological factors, meta-analysis

Key messages

- Low socioeconomic level is associated with higher risk of chronic pain.

- This association is observed in all chronic pain syndromes and all socioeconomic concepts

INTRODUCTION

Chronic pain (CP), a frequent component of rheumatologic diseases, usually defined as the resulting symptom of an injury or a specific health condition, was recently classified by the World Health Organization as an independent condition in the International Classification of Diseases (ICD) 11, in an attempt to emphasize its relevance and the need of its correct management.[1] The definition of CP shifted towards that of "pain that persists or recurs for more than 3 months". In the Global Burden of Disease 2017, the leading causes of the burden of years lived with disability for both genders were the most prevalent CP syndromes: low back pain and headache disorders. In addition, other important causes of disability, diabetes in men and depression in women, are closely related to CP.[2] From an economic perspective, the total costs of the CP syndrome in the USA had been estimated between 560 and 635 billion USD annually, higher than the combined costs of heart diseases, cancer and diabetes together.[3] Finally, in Europe the overall prevalence of the syndrome sways between 19% and 30%,[4] and the incidence is estimated at 8% per year.[5]

Socioeconomic status (SES) was identified as an important determinant of the occurrence and severity of CP, as well as a predictor of its associated complications such as disability and mental health problems.[6] Recent reviews have shown that the prevalence of CP of any origin, as well as that of CP-associated disability, was twice as high in low and middle-income countries as in high-income countries.[7,8] Furthermore, SES was related to the occurrence of rheumatic diseases as well as to that of their comorbidities. Specifically, several studies showed a relation between low SES and the occurrence of rheumatoid arthritis and systemic lupus erythematosus.[9] SES was also associated with other comorbidities including obesity, depression and suicide

ideation in patients with rheumatoid arthritis.[10]. Lower SES was also associated with the development of fibromyalgia in patients with rheumatoid arthritis in a large follow-up,[11] while another international study, QUEST RA, detected a strong negative association between DAS28 score, an index that assesses disease activity in 28 joints, and the country economic welfare.[12]

Commonly, SES is measured using a combination of educational, occupational and economic criteria. In addition, other indicators such as housing, social assistance, and social support are also used.[13] This multiplicity of definitions led to considerable differences in the assessment of the association between SES and CP and to diverging results.

We conducted a systematic review and meta-analysis on the relationship between SES and CP, considered as a health condition independent of the underlying disease to which it is related. We used combined SES index, educational level, employment status, and income status as indicators of the socioeconomic status.

MATERIAL AND METHODS

Search strategy

A systematic literature search was carried out by two epidemiologists (ZK and JP) to identify potentially eligible studies. The following databases were searched: Medline, Embase, Conference Proceedings Citation Index-Science (CPCI-S), and WHO Global Index Medicus since their inception until April 1st, 2020. We used the following syntax in Medline: (pain AND (socioeconomic)) OR (social class)) OR (socioeconomic status)) NOT (cross-sectional), both in plain text and MeSH terms. A similar strategy was used in the other bibliographic databases. We also reviewed the references of the

selected studies and that of recent systematic reviews.[5,6,8,13–16] Subsequently, the search results were merged, and inconsistencies were resolved by consensus. The review protocol of this meta-analysis was registered in the international prospective register of systematic reviews PROSPERO (ID 173446).

Studies inclusion criteria

Relevant studies that met the following criteria were included in this meta-analysis: (1) study design: case-control studies and cohort studies; (2) exposure: any indicator of SES specifically defined as such by the authors; (3) outcome: occurrence of chronic pain; (4) effect measures: Odds Ratios, Relative Risk estimates or sufficient data to calculate them. When the reported data were not sufficient for the calculation of the effect measures, we requested additional information from the authors of the studies before excluding them from the meta-analysis.[17-21] No study was excluded based on the language of publication. When studies were repeated in the same population, the most updated publication was included.

We excluded studies carried out in children and those reporting on acute pain. We focused on reports of the first development of the syndrome and excluded those concerned with recurrence of a previously existing pain syndrome. Due to their impossibility to infer causation, we excluded cross-sectional studies.

Data extraction

Using a structured extraction sheet, the following data were retrieved from the eligible studies: publication date, first author, country, study design, outcome, type of sample, source of controls, exposure assessment, outcome ascertainment, effect measures with 95% CI and adjustment variables. When a study reported different estimates, the one adjusted for the largest number of confounding variables was considered. When authors

reported more than one exposure-outcome association (e.g. education and employment status), a pooled estimate of these measures was used in the main analysis.

Risk of bias assessment

We assessed the risk of bias of the studies included in our meta-analysis according to a 5-point scale extracted from the Newcastle-Ottawa scale.[22] Each fulfilled criterion was rated 1 point, and 0 point if it was not met or not reported.

The risk of bias assessment comprised the following criteria: a) For all studies: confounding assessment: results adjusted for gender, age, and mental health status (1 point); accurate measurement of the duration of exposure (1 point); participation rate ≥ 80% (1 point). The methodological issues that were different between cohort- and case-control studies, were assessed as follows. b) For cohort studies: drop-out rate or losses to follow up ≤ 20% (1 point), and accurate measurement of the changes in SES during follow-up (1 point). c) For case-control studies: recruitment of incident cases (1 point), and controls selected from the population (1 point).

We considered as of low risk of bias those studies that scored 3 points or more, and of high risk the rest of the studies.

Statistical analysis

We extracted adjusted odds ratios (OR) and their 95% confidence intervals (CI) from the eligible studies for the "low" and "medium" categories of SES, using the "high level" category as reference. To obtain the effect measures estimates of the "medium" category, we pooled all the intermediate estimates if more than one intermediate category was reported. If the OR provided used "low" category as reference, we recalculated the estimates by using the inverse of the given OR for the "high" category

as well as their 95%CI. In that situation, the estimates of the "medium" category were not calculated.

When adjusted estimates were not reported, crude ORs were extracted or computed from the available data. For one study,[23] the estimates included in the meta-analysis were calculated from the raw data on education and occupation, provided by the authors upon request.

In two studies carried out in the USA and Canada, the OR estimates of educational level were provided for exposures measured on a continuous scale corresponding to an increase of one year of education.[24,25] We calculated the OR and their 95%CI corresponding to compulsory education (12 years), secondary education (15 years) and high education (17 years). A third study presented its results in a similar fashion, with OR estimates corresponding to an increase of one category of income (7 categories), social class (6 categories) and parental education (5 categories).[26]

We computed pooled ORs and their 95% CIs by weighting the log ORs in case-control studies and log RRs in cohort studies by the inverse of their variance. We calculated pooled ORs for the following subgroups, defined a priori: sex, study design, risk of bias (high/low), SES indicator (SES combined index, educational level, income or occupational status), outcome assessment (self-reported pain/Numerical Rating Scale "NRS", medical diagnosis, register data or validated CP questionnaire), and type of pain syndrome. We classified the studies in 2 main groups: Chronic Widespread Pain (CWP), based on the definition of the American College of Rheumatologists or equivalent, and miscellaneous non-widespread syndromes. The miscellaneous group is composed by all studies that did not belong to the CWP category. It included regional and non-specific pain syndromes and comprised the subgroups Whiplash Acute

Disorders, knee osteoarthritis and low back pain defined as such by the authors of the studies.

We computed fixed effects and random effects models. However, only the random effects model is presented when heterogeneity was present.

Heterogeneity was assessed using DerSimonian and Laird's Q test, and then quantified by calculating the proportion of the total variance due to between study variance (Ri).[27]

Publication bias was assessed, first visually using funnel plots, and then using Egger´s regression test for a more quantitative approach.[28] Also, the effect of any potential publication bias was tested by applying the trim-and-fill method described by Duval and Tweedie.[29] All analyses were performed using HEpiMA version 2.1.3[30] and Stata version 15.1 (StataCorp LP, College Station, TX).

RESULTS

The literature search yielded 2670 publications, of which 110 were selected based on title and abstract. After a detailed review, 46 studies finally met the inclusion criteria of our meta-analysis.[23-26, 31-72] These studies were carried out in 12 countries between 1991 and 2019. The complete flow diagram of the extraction process is shown on figure 1. Detailed information about the risk of bias scoring and adjustment factors of each study is provided in supplemental files S1 and S2, respectively.

Table 1. Characteristics of the studies of the meta-analysis on socio-economic status and chronic pain

Year	Author	Country	Study Design	Health Condition	Sample Type	Population / Controls	Exposure Assessment	Outcome Assessment /Case Ascertaining	Effect Measure	Low SES OR (95%CI)	Medium SES OR (95%CI)	Full Adjustment	Risk of Bias
1991	Viikari-Juntura	Finland	Cohort	Neck-shoulder and LBP in women	General population	154	Educational level, economic status	Self-reported pain/NRS	OR	2.33 (0.35, 15.42)	5.86 (0.28, 21.19)	No	Low
2002	Bergman	Sweden	Cohort	CWP	General population	2425	Educational level, SES index	CP validated questionnaire	OR	0.97 (0.59, 1.58)	1.08 (0.63, 1.88)	No	High
2003	Sterner	Sweden	Cohort	Disability after WAD	General population	296	Educational level	Self-reported pain/NRS	OR	2.08 (1.09, 3.98)	No data	No	Low
2005	Hendriks	Netherlands	Cohort	Neck pain after WAD	General population	125	Educational level	Self-reported pain/NRS	OR	3.51 (1.05, 11.70)	No data	Yes	Low
2005	Kopec	Canada	Cohort	CBP	General population	9552	Educational level, economic status, employment status	Medical diagnosis	RR	1.36 (1.09, 1.72)	No data	Yes	Low
2005	Östergren	Sweden	Cohort	Shoulder and neck pain	General population	4919	Educational level, SES index	CP validated questionnaire	OR	1.70 (1.46, 1.99)	1.10 (0.97, 1.26)	No	High
2006	Ang	USA	Cohort	CWP	Army veterans	370	Education, Income	Self-reported pain	OR	0.92 (0.76, 1.12)	0.90 (0.50, 1.60)	No	High
2006	Berglund	Sweden	Cohort	Neck pain after whiplash injury	General population	2280	Educational level, economic status	Self-reported pain/NRS	OR (for increased pain at follow-up)	1.8 (1.3, 2.4)	1.6 (1.2, 2.1)	No	High
2006	Hawker	Canada	Cohort	TJA after knee/hip complaints	General population	2411	Educational level, economic status, employment status	Register data	HR	0.85 (0.64, 1.12)	No data	No	Low
2006	Jones	United Kingdom	Cohort	Persistent LBP	General population	974	SES index, employment status	Self-reported pain/NRS, CP validated questionnaire	RR	1.50 (1.30, 1.73)	1.30 (1.03, 1.60)	Yes	Low

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2007	Agabiti	Italy	Retrospective cohort	THR	General population	6140	SES index	Register data	RR	0.87 (0.81, 0.95)	1.01 (0.97, 1.06)	No	Low
2007	Andersen	Denmark	Cohort	Severe MSC pain	Workers of Industrial and service companies	3276	Educational level	Self-reported pain/NRS	HR	1.66 (1.08, 2.56)	1.36 (0.96, 1.92)	Yes	Low
2008	Hestbaek	Denmark	Cohort	LBP	Twins	3245	Educational level, economic status, SES Index	CP validated questionnaire	OR	0.98 (0.91, 1.06)	0.94 (0.84, 1.04)	No	High
2008	Kasch	Denmark	Nested cohort in RCT	Neck pain after WAD	General population	688	Educational level	Self-reported pain/NRS	HR	2.40 (1.44, 4.00)	1.78 (1.35, 2.35)	No	High
2009	Carstensen	Denmark	Cohort	Neck pain12 months after WAD	General population	740	Educational level, employment status	Self-reported pain/NRS	OR	3.03 (1.23, 7.14)	No data	Yes	Low
2009	Davies	United Kingdom	Cohort	CWP	General Population	3489	SES index	CP validated questionnaire	OR	1.06 (0.78, 1.45)	1.21 (0,88, 1.67)	Yes	Low
2009	Friedrich	Austria	Case/control	LBP and WMP	General population and hospital patients	97/97	Economic status	Medical diagnosis	OR	5.41 (0.94, 31.08)	No data	Yes	Low
2009	Mcfarlane	United Kingdom	Cohort	CWP/MNW	General population	9377	SES index (only at childhood for CWP)	Self-reported pain/NRS; Medical diagnosis	RR	1.25 (1.12, 1.40)	1.18 (1.12, 1.23)	Yes	Low
2009	Williamson	Australia	Cohort	Pain after orthopedic injury	General population	1290	Educational level	Self-reported pain/NRS	OR	1.50 (1.10, 1.90)	No data	Yes	Low

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Year	Author	Country	Study Design	Health Condition	Sample Type	Population / Controls	Exposure Assessment	Outcome Assessment /Case Ascertaining	Effect Measure	Low SES OR (95%CI)	Medium SES OR (95%CI)	Full Adjustment	Risk of Bias
2010	Clay	Australia	Cohort	Troublesome CP after orthopedic trauma	General population	150	Educational level	CP validated questionnaire	OR	3.80 (1.25, 11.76)	No data	Yes	Low
2010	Holmes	Australia	Cohort	CP after serious injury	General population	238	Employment status	Self-reported pain/NRS and medical diagnosis	OR	4.23 (1.56, 11.53)	No data	Yes	Low
2010	Weijenborg	Netherlands	Cohort	Chronic abdominal pain	Women with acute abdominal pain	115	Educational level, employment status	Self-reported pain/NRS	OR	2.55 (1.30, 5.01)	No data	No	High
2011	Oostrom	Netherlands	Cohort	Persistent LBP	General population	4007	Educational level, employment status	Self-reported pain/NRS	OR	1.09 (0.94, 1.28)	0.94 (0.77, 1.15)	No	High
2011	Rahman	Canada	Cohort	Knee/Hip osteoarthritis	General population	34420	SES Index	Register data	HR	0.75 (0.7, 0.8)	No data	No	Low
2012	Gale	United Kingdom	Cohort	CWP	General population	6902	Educational level, SES index	Self-reported pain/NRS	RR	1.51 (1.17, 1.96)	1.29 (1.13, 1.46)	Yes	Low
2012	Gonzalez	Canada	Cohort	CBP and Migraines	General population	1475	Educational level, economic status	Medical diagnosis	OR	0.99 (0.94, 1.05)	0.88 (0.52, 1.49)	No	High
2012	Jordan	United Kingdom	Cohort	CWP	General population	4756	Educational level, economic status	Medical diagnosis	OR	1.56 (1.13, 2.16)	1.16 (0.67, 2.02)	Yes	High
2012	Pamlöf	Sweden	Cohort	Troublesome neck pain	General population	18871	Economic status	Self-reported pain/NRS	OR	1.46 (1.26, 1.7)	1.16 (1.04, 1.31)	Yes	High

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Year	Author	Country	Study Design	Health Condition	Sample Type	Population / Controls	Exposure Assessment	Outcome Assessment /Case Ascertaining	Effect Measure	Low SES OR (95%CI)	Medium SES OR (95%CI)	Full Adjustment	Risk of Bias
2012	Thomten	Sweden	Cohort	Pain at least 1 month during the last 3 months	General population (women)	2300 women	Educational level, employment status, economic status	Self-reported pain/NRS and CP validated questionnaire	OR	0.97 (0.86, 1.09)	No data	Yes	High
2013	Holmes	Australia	Cohort	CP after moderate or serious injury	General population	290	Educational level, economic status	Self-reported pain/NRS	OR	4.4 (1.4, 14)	No data	Yes	Low
2013	Hu	Taiwan	Retrospective Cohort	LBP	General population	12862	Educational level, employment status, SES Index	Register data	HR	1.1 (1.04, 1.17)	No data	No	Low
2013	Jørgensen	Denmark	Cohort	LBP	Health care workers	3161	SES Index	Self-reported pain/NRS	OR	0.98 (0.57, 1.68)	0.99 (0.72, 1.36)	No	High
2013	Slade	USA	Cohort	TMD	General population	2737	Educational level, economic status	CP validated questionnaire	HR	1.34 (1.07, 1.68)	1.10 (0.94, 1.29)	Yes	Low
2014	Daugbjerg	Denmark	Cohort	Pain after hysterectomy	General population	10093	Educational level, employment status, economic status	Register data	OR	1.47 (1.35, 1.61)	1.24 (1.12, 1.37)	Yes	Low
2014	Joseph	USA	Cohort	CP	African-American population affected by Hurricane Katrina	215	Educational level, SES index	Self-reported pain/NRS	OR	1.05 (0.92, 1.2)	0.51 (0.13, 2.01)	Yes	Low
2014	Jöud	Sweden	Case/ control	CP	General population	3730/7460	Educational level, employment status, economic status	Medical diagnosis	OR	1.53 (1.41, 1.66)	1.34 (1.25, 1.44)	No	Low
2014	Kastelein	Netherlands	Cohort	Non-traumatic knee symptoms /Patellofemoral pain syndrome	Adolescents and young adults (12-35 y)	172	Educational level	Self-reported pain/NRS	OR	5.31 (2.3, 12.31)	No data	No	High

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Year	Author	Country	Study Design	Health Condition	Sample Type	Population / Controls	Exposure Assessment	Outcome Assessment /Case Ascertaining	Effect Measure	Low SES OR (95%CI)	Medium SES OR (95%CI)	Full Adjustment	Risk of Bias
2014	McBeth	United Kingdom	Cohort	CWP	General population	4326	Educational level, economic status, SES Index	Medical diagnosis	OR	1.01 (0.86, 1.19)	1.20 (0.90, 1.50)	Yes	Low
2015	Carstensen	Denmark	Cohort	Neck pain after whiplash injury	General population	719	Educational level, employment status, economic status	Self-reported pain/NRS	OR	0.92 (0.59, 1.44)	0.93 (0.54, 1.62)	No	High
2015	Momi	United Kingdom	Cohort	CWP	Twins	4234	SES Index	CP validated questionnaire	OR	2.00 (1.32, 3.03)	No data	Yes	High
2015	Wesseling	Netherlands	Cohort	Symptomatic knee OA	General population	705	Educational level	Self-reported pain/NRS	OR	2.10 (1.49, 2.94)	No data	No	High
2017	Andorsen	Norway	Cohort	MSC complaints (pain and/or stiffness)	General population	4496	Educational level	Self-reported pain/NRS	OR	1.73 (1.46, 2.05)	1.33 (1.17, 1.51)	Yes	High
2017	Parry	United Kingdom	Cohort	Knee pain	General population	719	Employment status	Self-reported pain/NRS	OR	0.76 (0.57, 1.03)	0.92 (0.64, 1.33)	No	High
2018	Giummarra	Australia	Cohort	Persistent pain	Car injured population	74217	SES Index	Register data	HR	1.20 (1.10, 1.32)	No data	No	Low
2019	Herrera-Escobar	USA	Cohort	CP after car injury	Car injured population	1537	Educational level, economic status	CP validated questionnaire	OR	1.65 (1.33, 2.04)	No data	Yes	Low
2019	Jay	United Kingdom	Cohort	CWP and MNW	General population	2378	SES Index	Self-reported pain/NRS and medical diagnosis	RR	1.05 (0.98, 1.13)	1.06 (0.97, 1.17)	Yes	Low

LBP: Low back pain; CBP: Chronic Back Pain; CWP: Chronic Widespread Pain; CP: Chronic Pain; MNW: Miscellaneous non-widespread pain; MSC: Musculoskeletal; WMP: Widespread Musculoskeletal Pain; TMD: Temporomandibular disorder; WAD: Whiplash Acute Disorder ; OA: Osteoarthritis ; TJA: Total Joint Arthroplasty ; THR: Total Hip Replacement.

Generally, the analyses yielded moderate to high heterogeneity. Only 3 of the subgroup analyses for medium SES showed low heterogeneity. Consequently, in our results, we report random-effects estimates only, as recommended by experts.

The forest plots of the main analysis for low and medium SES categories are shown on figures 2 and 3, respectively. In the main analysis, compared with high SES, an OR of 1.31 (95% CI: 1.20-1.43) was found for the association between low SES and CP, while for medium SES the pooled OR was 1.16 (95% CI: 1.09-1. 23).

When we stratified our analysis by sex (tables 2 and 3), we observed that women of low and medium SES categories presented a moderate risk increase of CP, when compared to those of high SES levels [(OR=1.28, 95%CI: 1.05-1.56) and OR=1.20 (95%CI: 1.02-1.41 respectively)]. Similar results were obtained for males.

The stratified analysis by design included only 2 case-control studies in the low SES group with a pooled OR of 2.10 (95% CI: 0.72-6.15). For cohort studies, the results were similar to those of the global analysis.

No substantial differences in the risk estimates of CP were observed in both low and medium SES categories when the studies were stratified according to the risk of bias.

All SES measures, except employment status, showed an association with CP: combined SES index ORlow: 1.15 (95% CI: 1.00-1.33); ORmedium: 1.11 (95% CI: 1.01- 1.23)], educational level [ORlow: 1.44 (95% CI: 1.28-1.61); ORmedium: 1.26 (95% CI: 1.15-1.39)], income status [ORlow: 1.25 (95% CI: 1.12-1.38); ORmedium: 1.15 (95% CI: 1.06-1.23)].

Table 2: Pooled Odds Ratios (ORs) and 95% Confidence Intervals (CIs) of Chronic Pain in Low SES.

	Number of studies	Random effect OR 95% CI	Ri	Q-test p-value
All studies	46	1.31 (1.20 - 1.43)	0.92	0.001
Sex				
Male	6	1.26 (0.89 - 1.79)	0.96	0.0001
Female	9	1.28 (1.05 - 1.56)	0.93	0.001
Design				
Case-control studies	2	2.10 (0.72 - 6.15)	0.99	0.16
Cohort studies	44	1.29 (1.19 - 1.41)	0.91	0.001
Risk of bias				
Low	27	1.30 (1.15 - 1.46)	0.93	0.001
High	19	1.33 (1.16 - 1.52)	0.91	0.000
SES measure				
Combined SES Index	17	1.15 (1.00 - 1.33)	0.91	0.001
Educational level	37	1.44 (1.28 - 1.61)	0.87	0.001
Employment status	18	1.14 (0.98 - 1.33)	0.83	0.001
Income status	22	1.25 (1.12 - 1.38)	0.73	0.001
Outcome measure				
Self-reported pain/NRS	21	1.52 (1.31 - 1.78)	0.84	0.001
Medical diagnosis	10	1.29 (1.10 - 1.52)	0.93	0.001
Register data	6	1.02 (0.82 - 1.26)	0.97	0.001
CP Questionnaire	10	1.33 (1.11 - 1.61)	0.91	0.001
CP syndrome				
Chronic Widespread Pain	8	1.19 (1.05 - 1.35)	0.70	0.001
Miscellaneous non-widespread pain	38	1.33 (1.21 - 1.47)	0.93	0.001
Low Back Pain	7	1.17 (1.02 - 1.34)	0.86	0.001
Whiplash Acute Disorders	6	1.88 (1.31 - 2.70)	0.64	0.03
Knee Osteoarthritis	4	1.36 (0.75 - 2.45)	0.99	0.001

SES: Socioeconomic Status. NRS: Numerical Rating Scale.

Table 3: Pooled Odds Ratios (ORs) and 95% Confidence Intervals (CIs) of Chronic Pain in Medium SES.

	Number of studies	Random effect OR 95% CI	Ri	Q-test p-value
All studies	27	1.16 (1.09 - 1.23)	0.78	0.001
Sex				
Male	5	1.22 (1.00 - 1.49)	0.91	0.001
Female	6	1.20 (1.02 - 1.41)	0.93	0.0001
Design				
Case-control studies	1	1.34 (1.25 - 1.44)	-	-
Cohort studies	26	1.15 (1.08 - 1.22)	0.73	0.0001
Risk of bias				
Low	13	1.18 (1.10 - 1.28)	0.83	0.001
High	13	1.13 (1.01 - 1.28)	0.73	0.001
SES measure				
Combined SES Index	12	1.11 (1.01 - 1.23)	0.86	0.001
Educational level	18	1.26 (1.15 - 1.39)	0.55	0.01
Employment status	10	1.06 (0.96 - 1.17)	0.00	0.61
Income status	9	1.15 (1.06 - 1.23)	0.31	0.18
Outcome measure				
Self-reported pain/NRS	12	1.19 (1.08 - 1.32)	0.72	0.001
Medical diagnosis	7	1.20 (1.08 - 1.33)	0.69	0.01
Register data	2	1.11 (0.91 - 1.36)	0.95	0.001
CP Questionnaire	6	1.09 (0.98 - 1.21)	0.55	0.001
CP syndrome				
Chronic Widespread Pain	7	1.19 (1.14 - 1.23)	0.00	0.87
Miscellaneous non-widespread pain	21	1.13 (1.05 - 1.23)	0.86	0.001
Low Back Pain	5	1.03 (0.88 - 1.21)	0.65	0.06
Whiplash Acute Disorders	3	1.51 (1.13 - 2.01)	0.56	0.12
Knee Osteoarthritis	1	0.92 (0.64 – 1.33)	--	--

SES: Socioeconomic Status. NRS: Numerical Rating Scale.

Studies that used self-reported measurement of pain or NRS [ORlow 1.52 (95% CI: 1.31-1.78); ORmedium 1.19 (95% CI: 1.08-1.32)] and medical diagnosis [ORlow 1.29 (95% CI: 1.10-1.52);

ORmedium 1.20 (95% CI: 1.08-1.33)] yielded pooled odds ratios that were more consistent through SES categories than those corresponding to data extracted from registers or questionnaires.

Finally, stratified analysis by CP syndrome showed moderate associations for all syndromes with low and medium SES, except for low back pain in medium SES and knee osteoarthritis: Chronic Widespread Pain [ORlow: 1.19 (95% CI: 1.05-1.35); ORmedium: 1.19 (95% CI: 1.14-1.23)]; miscellaneous non-widespread pain [ORlow: 1.33 (95% CI: 1.21-1.47); ORmedium: 1.13 (95% CI: 1.05-1.23)]; low back pain [ORlow: 1.17 (95% CI: 1.02-1.34); ORmedium: 1.03 (95% CI: 0.88-1.21)] and Whiplash Acute Disorder [ORlow: 1.88 (95% CI: 1.31-2.70); ORmedium: 1.51 (95% CI: 1.13-2.01)].

Publication bias

The visual assessment of the funnel plot of low SES studies (figure 2) showed an asymmetry towards the right, that is, towards the increased risk side, while the funnel plot corresponding to the medium SES studies (figure 4) did not provide any evidence of asymmetry. The quantitative assessment of publication bias using Egger's test yielded evidence of publication bias for low SES ($p = 0.001$), but not for medium SES studies ($p = 0.69$). Furthermore, the trim-and-fill random effects method imputed 10 studies for low SES, yielding a corrected pooled estimate OR of 1.23 (95% CI 1.13-1.34), while for medium SES no study was imputed.

DISCUSSION

To our knowledge, this is the first meta-analysis examining the association between SES and CP. Our results support the existence of an increased risk of CP associated to low and medium SES when compared to high levels of SES. A remarkable feature of our results is that, both in the global analysis and in the subgroup analyses, the pooled estimates are constantly higher in the lower SES categories than those in the medium SES category.

The results of our study underscore the relevance of the psychosocial and environmental aspects of CP, a feature often neglected in the clinical management in rheumatology, usually more focused on proximal causes of pain (injury, inflammation). The need for a multidisciplinary approach to the rheumatic pain management and pain-focused research was strongly encouraged in a 2010 report of the American College of Rheumatologists, which also reported the results of a clinical survey showing that the majority of patients evaluated by rheumatologists have non-inflammatory diseases, such as osteoarthritis, low back pain or fibromyalgia.[73]

The association between low SES, poor health-related quality of life and the occurrence of chronic conditions, including CP, has been previously reported in the literature.[74,75] Low SES populations tend to report both higher CP prevalence and CP severity.[16] Furthermore, low SES is included among the main risk factors for developing CP.[13] In patients suffering from rheumatoid arthritis, low SES was associated to the development of fibromyalgia, the main feature of which is Chronic Widespread Pain.[13]

However, the results of observational studies have been sometimes conflicting, showing divergent associations.[44,47,64] This could be in part related to the broad scope of the definition of SES, which encompasses several heterogeneous proxy measures, such as education, income, employment status or social benefits. Although closely related to the definition of SES, each of these indicators is associated with different potential causal mechanisms in its relation with CP.

Multiple and, presumably, synergistic or additive mechanisms mediate the association between lower SES and CP. First, lower SES is closely related to manual jobs, which often involve heavy physical workload and/or high strain work environments, features that are associated to musculoskeletal job injuries and job stress.[76] Second, lower education is associated with ineffective pain coping strategies such as catastrophizing, and prayer and hoping strategies.[77,78] Third, unhealthy lifestyle factors such as tobacco, alcohol or low physical activity, in addition to other social and individual

factors such as lack of social support or child abuse, are more prevalent in low SES populations.[79,80] All of these mediators of the SES-CP relationship are concurrently related to chronic stress and psychological distress which, both in animal and human neuroimaging studies, were related to dysregulation in the Hypothalamus-Pituitary-Amygdala (HPA) axis and to a neuroinflammatory state linked to CP syndromes including Chronic Widespread Pain and chronic back pain.[81] Finally, the economic impact of the CP consequences closes the cycle of this complex SES-CP relationship, exacerbating and perpetuating this situation.[14]

The large number of studies, the majority of them cohort studies which covered 12 countries and a population of near 175.000 individuals, the low risk of bias of the majority of the sample, and the comprehensive list of CP syndromes and SES measures included are among the major strengths of our study. However, some limitations can affect our results and should be considered.

A possible limitation of this meta-analysis is the presence of publication bias in the low SES studies. This kind of bias can lead to an overestimation of the effect of studies reporting positive results, as a consequence of not including small studies that report null or negative effect, which tend to be rejected for publication.[82] In general, case-control studies are more likely to be rejected than sound cohort studies. Only 2 studies included in our meta-analysis used a case-control design. To assess the magnitude of the publication bias, we recalculated the pooled OR under the following extreme assumptions: 1) the case–control studies retrieved in our search represent only half of the case-control studies ever conducted on the topic, 2) the rejected studies found a null association (OR=1) and, 3) the rejected studies included the same number of cases and controls as the average of the published case-control studies. We re-calculated the pooled OR under these extreme assumptions and found an OR of 1.28 (95% CI: 1.18–1.39), close to the original results. In our study we conducted a broad search, without language limitations. Furthermore, we included grey literature and contacted all authors of the studies with potentially useful data. In addition, the quantitative assessment of publication bias by the trim-and-fill method imputed 10 articles, which only slightly reduced the magnitude of the OR from

1.31 to 1.23, but kept its statistical significance, thus showing a very limited effect of this bias on the results.

A second important limitation is the presence of high between-study heterogeneity, which, to a certain point, was expected, due to the wide range of SES measures, CP syndromes and pain assessment methods used in the different studies. This heterogeneity did not subside upon stratification by subgroups of studies. We therefore based our interpretation on the random effects estimates as recommended.[83, 84] Meta-analysis experts emphasize that no degree of heterogeneity can be deemed unacceptable, provided the eligibility criteria are clear and the data are correct,[83] and that heterogeneity in meta-analysis, due to the differences in methods and populations, should be viewed as the "expectation, rather than the exception".[85]

Three studies included in the meta-analysis reported register data of surgical consultations or total joint arthroplasty in knee and hip osteoarthritis.[31,45,64] This was considered to be a proxy of CP, as osteoarthritis is among the leading causes of CP, while the main cause of surgical consultation and total joint arthroplasty is disabling pain.[64] This could have led to reverse causality, as subjects with lower SES may tend to delay consultation or surgery compared to high SES individuals. In order to account for this possibility, we performed a sensitivity analysis by excluding those studies from the main analyses. This yielded a random-effects OR of 1.36 (95% CI 1.26, 1.48) for low SES and of 1.17 (95% CI 1.11, 1.25) for medium SES, very similar to the initial results.

Last, we found an overrepresentation of studies from developed countries. Low and middle-income countries have reported higher prevalence of CP and CP disability than developed ones,[7] and some social features directly involved in the SES measurement, like housing conditions, social benefits or healthcare system, are very different from those of developed countries.[86] This affects the generalizability and extrapolation of the results and evidences the need of studies carried out in

developing countries, in order to assess, compare and balance the magnitude of the SES-CP association.

CONCLUSION

This study provides evidence of a moderate, albeit relevant association of SES and CP occurrence. This should be considered when implementing and allocating resources to health policies, given the magnitude and relevance of CP as a public health issue. Further prospective research and intervention studies on populations from developing countries are needed to measure the incidence in low SES communities.

DECLARATIONS

Ethical approval: Not applicable.

Consent for publication: Not applicable.

Availability of data and materials: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors have no conflicts of interest to declare.

Acknowledgements: Not applicable.

Funding: No specific funding for this work. Dr Takkouche's work is funded by a grant from the Regional Ministry of Education, Universities and Vocational Training, Santiago de Compostela, Spain, ED431C 2018/20.

Author contributions: J. Prego and Z. Khazaeipour independently conducted the systematical review, extraction and risk of bias scoring. J. Prego and N. Mallah elaborated the first version of the

manuscript. All authors reviewed critically and approved the final version of the manuscript. J. Prego and B. Takkouche designed the statistical analyses.

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Tables and figures:

Table 1. Characteristics of the studies of the meta-analysis on socio-economic status and chronic pain.

Table 2: Pooled Odds Ratios (ORs) and 95% Confidence Intervals (CIs) of chronic pain in low SES.

Table 3: Pooled Odds Ratios (ORs) and 95% Confidence Intervals (CIs) of chronic pain in medium SES.

Figure 1: Flow diagram of the study selection.

Figure 2: Forest plot of studies on low socioeconomic status and chronic pain.

Figure 3: Forest plot of studies on medium socioeconomic status and chronic pain.

Figure 4: Funnel plots of studies on low and medium socioeconomic status and chronic pain.

Figure 1. PRISMA flow diagram of the meta-analysis on socioeconomic status and chronic pain.

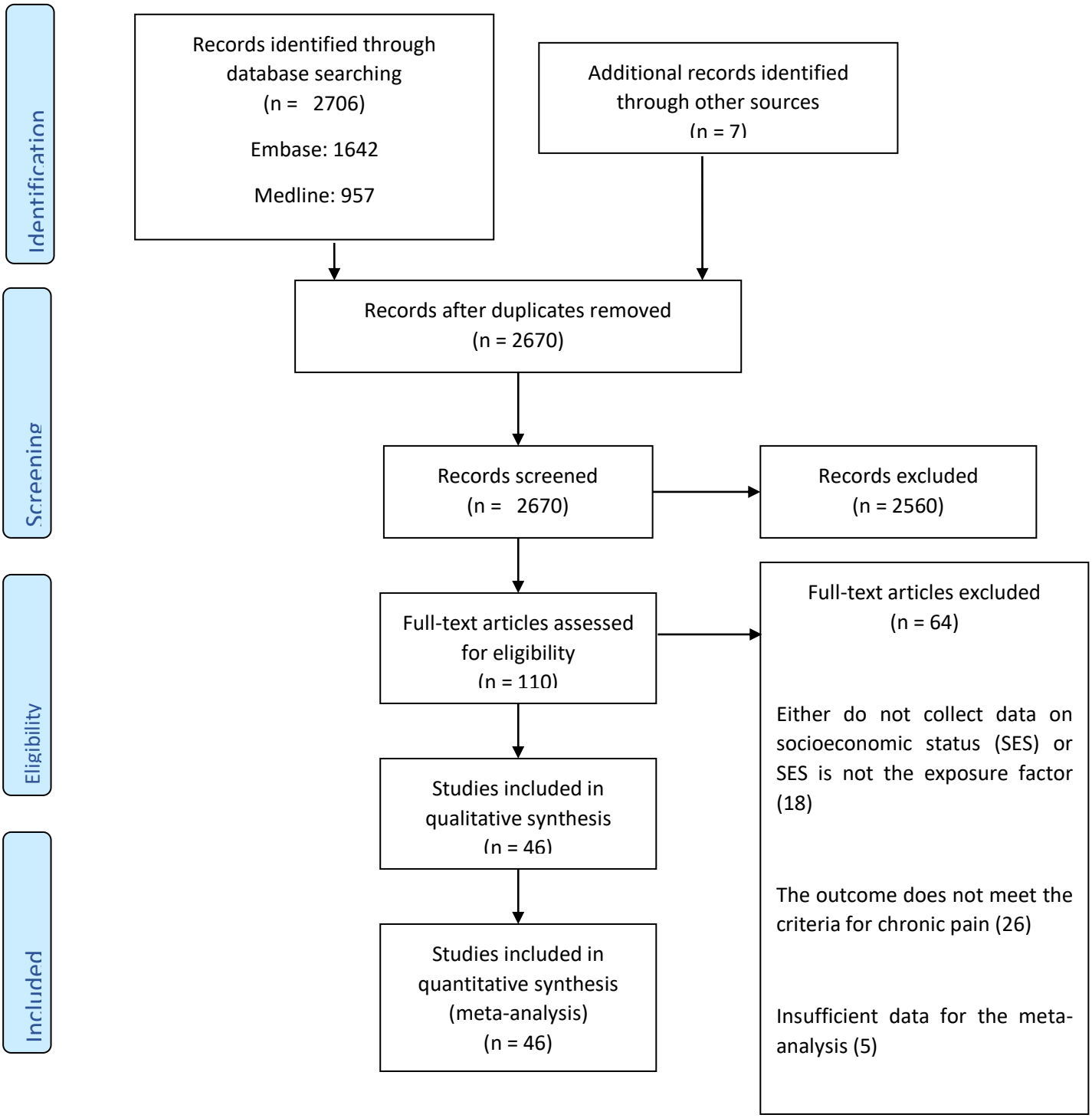


Figure 2. Forest plot of studies of the meta-analysis on low socioeconomic status and chronic pain

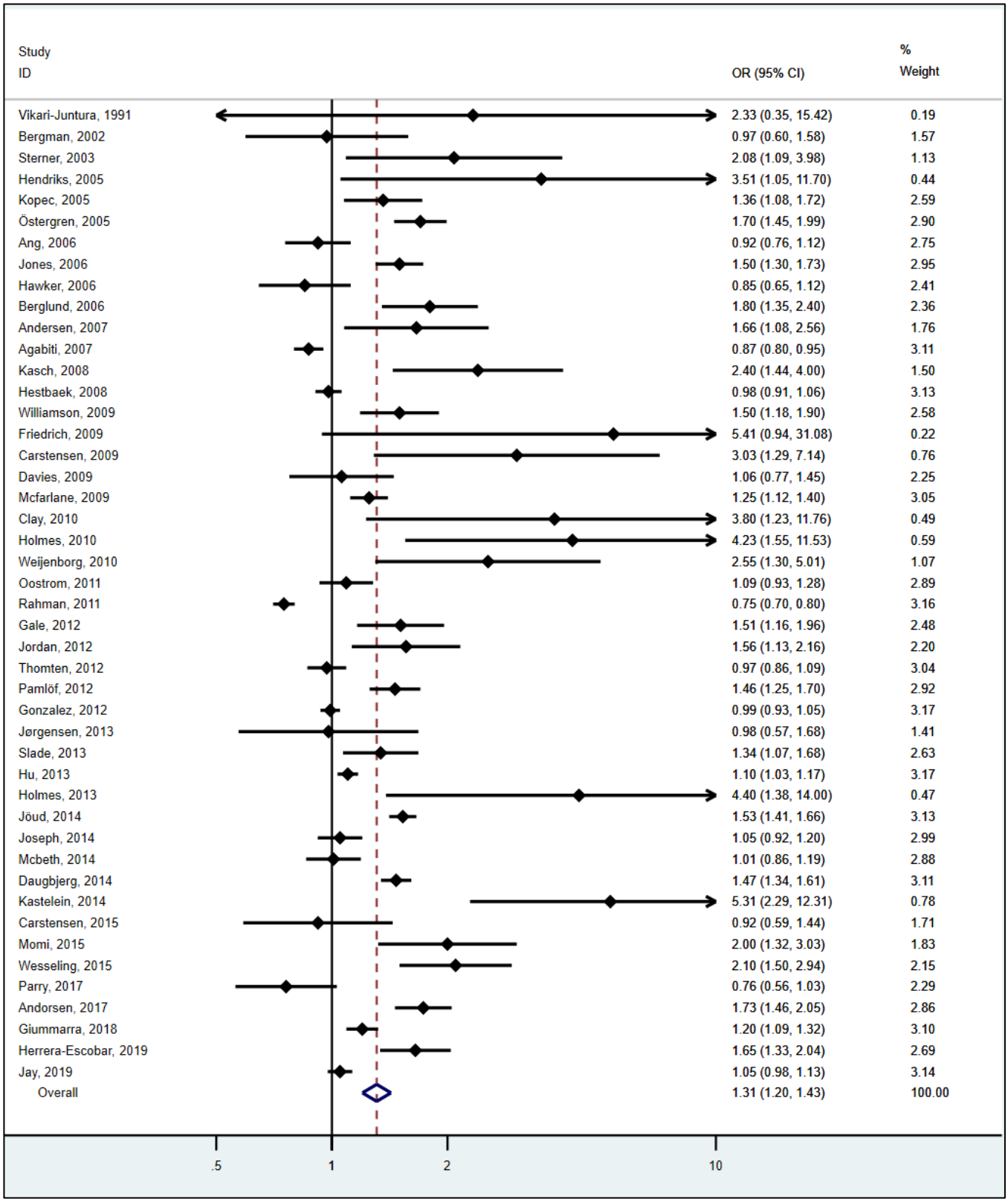


Figure 3. Forest plot of studies of the meta-analysis on medium socioeconomic status and chronic pain.

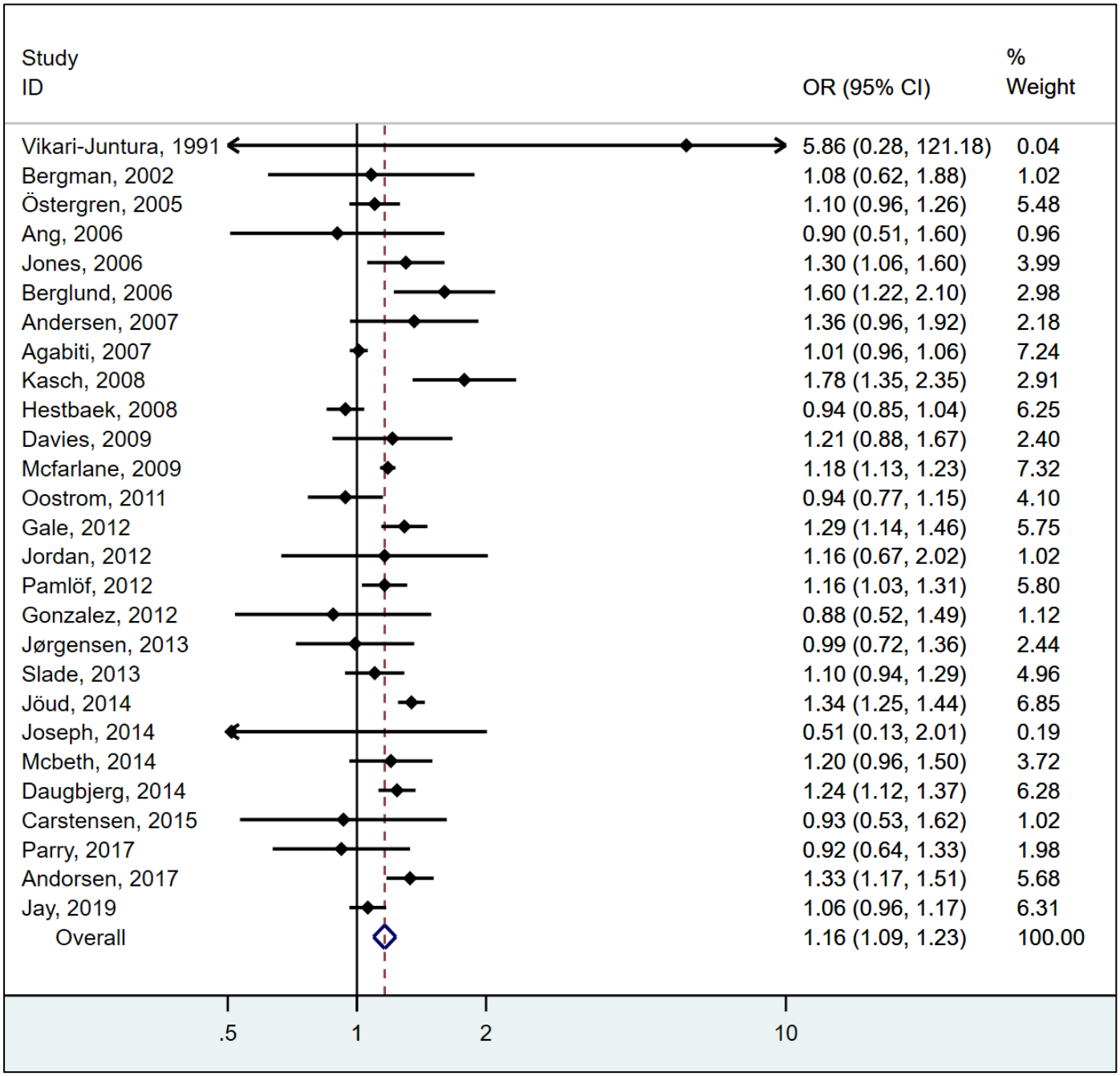
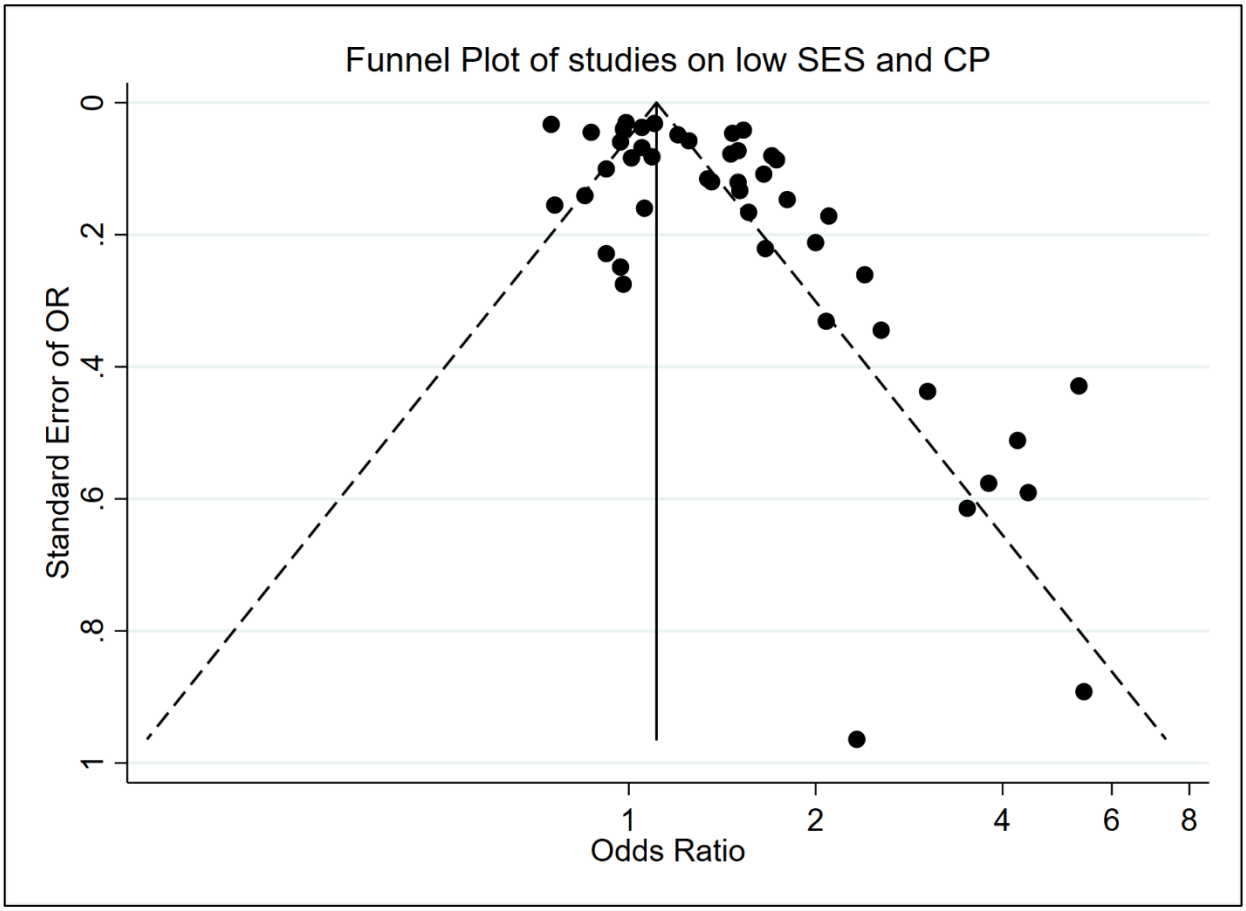
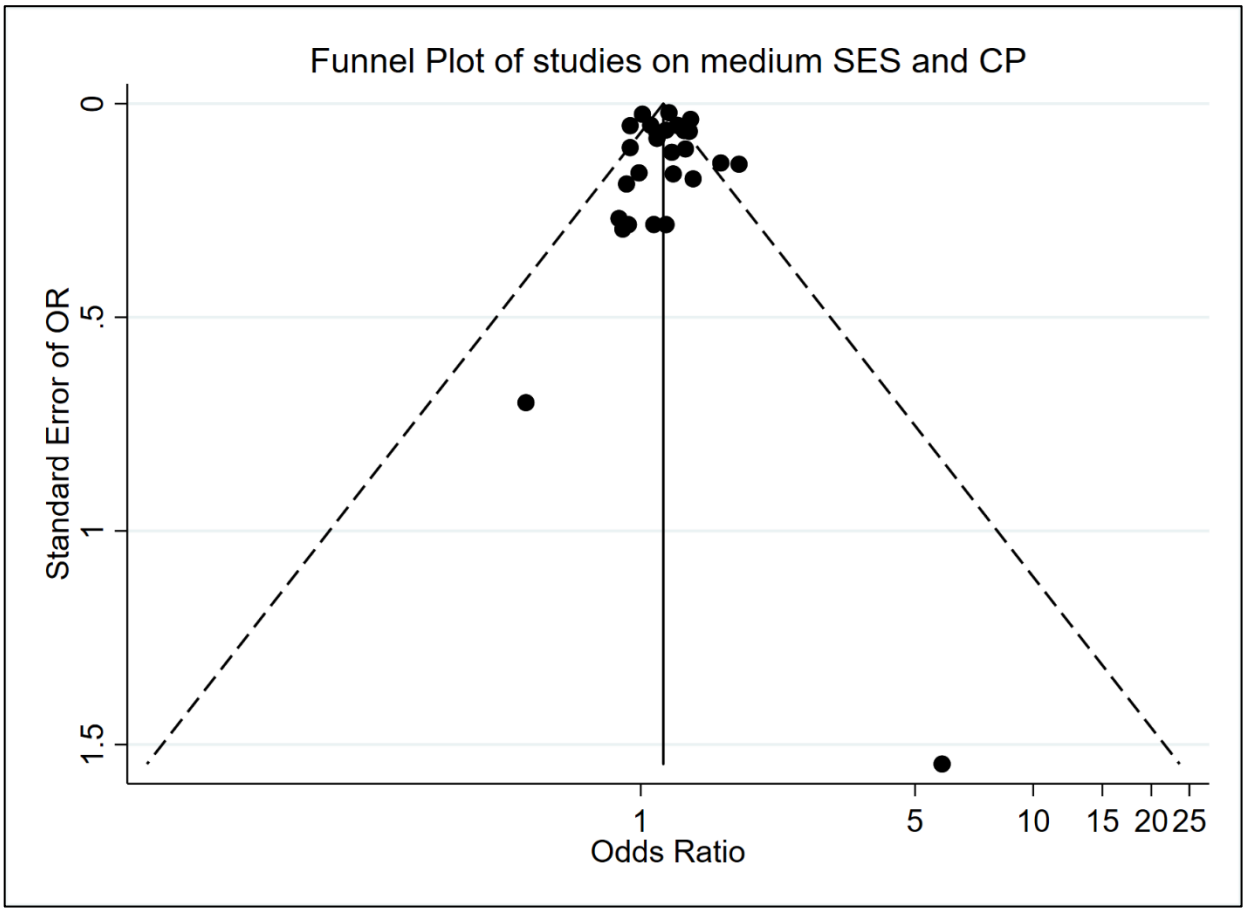


Figure 4. Funnel plots of studies of the meta-analysis of socioeconomic status (SES) and chronic pain (CP).




Funnel Plot of studies on medium SES and CP
Standard Error of OR
0
.5
1
1.5
1
5
10
15
20
25
Odds Ratio

Supplemental file S1. Risk of bias scoring of the studies of the meta-analysis on socioeconomic status and chronic pain.

Author	Year	Participation rate	Adjustment	Follow-up loss / Incident Cases	Change of exposure assessment / Population Controls	Duration of exposure	**TOTAL**	**Risk of bias**
Viikari-Juntura	1991	1	0	1	1	1	4	Low
Bergman	2002	0	0	0	1	1	2	High
Sterner	2003	1	0	1	1	1	4	Low
Hendriks	2005	1	1	1	1	1	5	Low
Kopec	2005	1	1	1	1	1	5	Low
Östergren	2005	0	0	1	1	1	3	High
Ang	2006	0	0	0	1	1	2	High
Berglund	2006	0	0	0	1	1	2	High
Hawker	2006	1	0	1	1	1	4	Low
Jones	2006	0	1	1	1	1	4	Low
Agabiti	2007	1	0	1	1	1	4	Low
Andersen	2007	0	1	1	1	1	4	Low
Hestbaek	2008	1	0	0	0	1	2	High
Kasch	2008	0	0	1	1	1	3	High
Carstensen	2009	0	1	1	1	1	4	Low
Davies	2009	1	1	0	1	1	4	Low

Score = 1 if: For case-control studies: 1) Participation in both groups> 80%; 2) Incident cases; 3) Population controls; 4) Adjustment for sex, age, and mental health status; 5) Duration of exposure accurately measured. **For cohort studies:** 1) Participation > 80%; 2) Changes of exposure accurately measured; 3) loss to follow-up < 20%; 4) Adjustment for sex, age, and mental health status; 5) Duration of exposure accurately measured. **Score = 0**: Else or not reported. **Risk of bias**: low if total score ≥ 4, high if total score < 4

Supplemental file S1 (cont.). Risk of bias scoring of the studies of the meta-analysis on socioeconomic status and chronic pain.

Friedrich	2009	1	1	1	1	1	5	Low
Macfarlane	2009	1	1	0	1	1	4	Low
Williamson	2009	1	1	0	1	1	4	Low
Clay	2010	1	1	1	1	1	5	Low
Holmes	2010	0	1	1	1	1	4	Low
Weijenborg	2010	0	0	1	1	1	3	High
Oostrom	2011	0	0	0	1	1	2	High
Rahman	2011	1	0	1	1	1	4	Low
Gale	2012	0	1	1	1	1	4	Low
Gonzalez	2012	0	0	0	1	1	2	High
Jordan	2012	0	1	0	1	1	3	High
Pamlöf	2012	0	1	0	1	1	3	High
Thomten	2012	0	1	0	1	1	3	High
Holmes	2013	1	1	0	1	1	4	Low
Hu	2013	1	0	1	1	1	4	Low
Jørgensen	2013	1	0	0	1	1	3	High

Score = 1 if: For case-control studies: 1) Participation in both groups> 80%; 2) Incident cases; 3) Population controls; 4) Adjustment for sex, age, and mental health status; 5) Duration of exposure accurately measured. **For cohort studies:** 1) Participation > 80%; 2) Changes of exposure accurately measured; 3) loss to follow-up < 20%; 4) Adjustment for sex, age, and mental health status; 5) Duration of exposure accurately measured. **Score = 0**: Else or not reported. **Risk of bias**: low if total score ≥ 4, high if total score < 4

Supplemental file S1 (cont.). Risk of bias scoring of the studies of the meta-analysis on socioeconomic status and chronic pain.

Slade	2013	0	1	1	1	1	4	Low
Daugbjerg	2014	1	1	1	1	1	5	Low
Joseph	2014	1	1	1	1	1	5	Low
Jöud	2014	1	0	1	1	1	4	Low
Kastelein	2014	1	0	0	1	1	3	High
McBeth	2014	1	1	1	1	1	5	Low
Carstensen	2015	0	0	0	1	1	2	High
Momi	2015	0	1	0	1	1	3	High
Wesseling	2015	0	0	0	1	1	2	High
Andorsen	2017	0	1	0	1	1	3	High
Giummarra	2017	1	0	1	1	1	4	Low
Parry	2017	1	0	0	1	1	3	High
Herrera-Escobar	2019	0	1	1	1	1	4	Low
Jay	2019	1	1	1	1	1	5	Low

Score = 1 if: For case-control studies: 1) Participation in both groups> 80%; 2) Incident cases; 3) Population controls; 4) Adjustment for sex, age, and mental health status; 5) Duration of exposure accurately measured. **For cohort studies:** 1) Participation > 80%; 2) Changes of exposure accurately measured; 3) loss to follow-up < 20%; 4) Adjustment for sex, age, and mental health status; 5) Duration of exposure accurately measured. **Score = 0**: Else or not reported. **Risk of bias**: low if total score ≥ 4, high if total score < 4

Supplemental file S1 (cont.). Risk of bias scoring of the studies of the meta-analysis on socioeconomic status and chronic pain.

Year	Author	Adjustment variables
1991	Viikari-Juntura	Gender, education, workload factors, health resources.
2002	Bergman	Age, gender, immigrant status, housing area, smoking, alcohol, personal support, family history of chronic pain, regions with pain at baseline.
2003	Sterner	Age, gender, whiplash acute disorder grade, accident type, prior pain.
2005	Hendriks	Treatment effects.
2005	Kopec	Gender, education, income, self-rated health.
2005	Östergren	Age.
2006	Ang	Not adjusted.
2006	Berglund	Initial neck pain, gender, subjective severity, initial headache, helplessness, time of follow-up.
2006	Hawker	Not adjusted.
2006	Jones	Age, gender, socioeconomic status (for employment status).
2007	Agabiti	Standardized for age, gender and city of residence
2007	Andersen	Gender, age, occupational group, intervention group, type of work, Body Mass Index, fear-avoidance, psychosocial work factors, chronic disease.
2008	Hestbaek	Body Mass Index, smoking, alcohol, SES variables.
2008	Kasch	Age.
2009	Carstensen	Age, gender, pre-collision psychological distress, pre-collision health, collision-related index.
2009	Davies	Age, gender, psychological status

Score = 1 if: For case-control studies: 1) Participation in both groups> 80%; 2) Incident cases; 3) Population controls; 4) Adjustment for sex, age, and mental health status; 5) Duration of exposure accurately measured. **For cohort studies:** 1) Participation > 80%; 2) Changes of exposure accurately measured; 3) loss to follow-up < 20%; 4) Adjustment for sex, age, and mental health status; 5) Duration of exposure accurately measured. **Score = 0**: Else or not reported. **Risk of bias**: low if total score ≥ 4, high if total score < 4

Supplemental file S1 (cont.). Risk of bias scoring of the studies of the meta-analysis on socioeconomic status and chronic pain.

2009	Friedrich	Depression, anxiety, fear-avoidance.
2009	Macfarlane	Body Mass Index, smoking, recent life events, General Health Questionnaire -12 score, mental health, regular exercise.
2009	Williamson	Gender, age, pre-injury psychological status, pre-injury pain interference, compensation status, pain at discharge, injury severity score.
2010	Clay	Prior pain, need for surgery.
2010	Holmes	Living status, preinjury HRQoL, social support, pain prior to injury, injury severity, injury site, initial pain severity, pain cognitions, current psychological symptoms, morphine use, pain management.
2010	Weijenborg	Not adjusted.
2011	Oostrom	Age, gender, Body Mass Index, smoking, physical activity.
2011	Rahman	Diabetes, hypertension, ischemic heart disease, and Charlson Comorbidity Index.
2012	Gale	Gender, smoking, Body Mass Index, GHQ-12 score, intelligence quotient at age 11.
2012	Gonzalez	Age, gender, education level, income.
2012	Jordan	Age, gender, obesity, smoking, alcohol, living alone, comorbidity, depression/anxiety, social support.
2012	Pamlöf	Age, gender, alcohol consumption, immigrant status.
2012	Thomten	Age, Body Mass Index, chronic disease, pain at baseline.
2013	Holmes	Initial current pain, injury severity, family history of depression, pain beliefs regarding medication.
2013	Hu	Age, gender, ethnicity, Body Mass Index, smoking, alcohol use, exercise frequency.
2013	Jørgensen	Age, previous low back pain, education, physical workload.

Score = 1 if: For case-control studies: 1) Participation in both groups> 80%; 2) Incident cases; 3) Population controls; 4) Adjustment for sex, age, and mental health status; 5) Duration of exposure accurately measured. **For cohort studies:** 1) Participation > 80%; 2) Changes of exposure accurately measured; 3) loss to follow-up < 20%; 4) Adjustment for sex, age, and mental health status; 5) Duration of exposure accurately measured. **Score = 0**: Else or not reported. **Risk of bias**: low if total score ≥ 4, high if total score < 4

Supplemental file S1 (cont.). Risk of bias scoring of the studies of the meta-analysis on socioeconomic status and chronic pain.

2013	Slade	Age, gender, race/ethnicity, and lifetime U.S. residence, study site.
2014	Daugbjerg	Age, purchase of prescribed analgesics before hysterectomy, Body Mass Index, smoking, comorbidity status, American Society of Anesthesiologists score, uterus weight, indication for surgery, route of hysterectomy, considerable adhesion formation, complications, readmission/reoperation after hysterectomy.
2014	Joseph	Age, gender, marital status, pre-hurricane health, hurricane trauma.
2014	Jöud	Marital status, education, income, geographic area.
2014	Kastelein	Gender, Body Mass Index, comorbidity, physical activity, knee symptoms, poor health.
2014	McBeth	Age, gender, baseline pain, social networks, smoking, alcohol, social participation, depression, SF-12 score, cognitive complaint, Body Mass Index, health condition, health impairments, comorbidities, trouble with sleep.
2015	Carstensen	Age, gender, sickness benefit, pre-collision pain condition, neck pain at inclusion.
2015	Momi	Age, Body Mass Index, smoking, twin-relatedness.
2015	Wesseling	Age, gender, hip pain, Body Mass Index, smoking, alcohol, physical activity, pain coping, comorbidity, radiographic features.
2017	Andorsen	Age, gender, current smoking, self-perceived general health (poor vs good), mental health complaints, Body Mass Index, Physical activity.
2017	Parry	Age, gender, Body Mass Index, WOMAC score, physical function score, radiographic features, HADS score, previous knee injury, time since onset, knee symptoms, physical activity.
2018	Giummarra	Age, gender, region, accident features, injury features, work disability, surgery.
2019	Herrera-Escobar	Age, gender, race, comorbidities, injury features, insurance features, psychiatric illness, comorbidities, mechanical ventilation, hospital stay features.
2019	Jay	Gender, Body Mass Index, smoking, alcohol, physical activity, mental health status, marital status.

Score = 1 if: For case-control studies: 1) Participation in both groups> 80%; 2) Incident cases; 3) Population controls; 4) Adjustment for sex, age, and mental health status; 5) Duration of exposure accurately measured. **For cohort studies:** 1) Participation > 80%; 2) Changes of exposure accurately measured; 3) loss to follow-up < 20%; 4) Adjustment for sex, age, and mental health status; 5) Duration of exposure accurately measured. **Score = 0**: Else or not reported. **Risk of bias**: low if total score ≥ 4, high if total score < 4

Supplemental file S1 (cont.). Risk of bias scoring of the studies of the meta-analysis on socioeconomic status and chronic pain.

Score = 1 if: For case-control studies: 1) Participation in both groups> 80%; 2) Incident cases; 3) Population controls; 4) Adjustment for sex, age, and mental health status; 5) Duration of exposure accurately measured. **For cohort studies:** 1) Participation > 80%; 2) Changes of exposure accurately measured; 3) loss to follow-up < 20%; 4) Adjustment for sex, age, and mental health status; 5) Duration of exposure accurately measured. **Score = 0**: Else or not reported. **Risk of bias**: low if total score ≥ 4, high if total score < 4