Prevalence of chronic pain after spinal cord injury: a systematic review and meta-analysis

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ABSTRACT

Background The reported prevalence of chronic pain after spinal cord iniury (SCI) varies widely due, in part, to differences in the taxonomy of chronic pain. A widely used classification system is available to describe subcategories of chronic pain in SCI, but the prevalence of chronic pain in SCI based on this system is unknown. **Objective** The primary objective of this systematic review and meta-analysis is to determine the prevalence of chronic pain after SCI based on the International Spinal Cord Injury Pain (ISCIP) classification system. Evidence review A comprehensive search of databases from January 1980 to August 2019 was conducted. The risk of bias was assessed using a modified tool developed for uncontrolled studies. The Grading of Recommendations, Assessment, Development and Evaluation approach was used to assess certainty in prevalence estimates.

Findings A total of 1305 records were screened, and 37 studies met inclusion criteria. The pooled prevalence of overall chronic pain was 68% (95% CI 63% to 73%). The pooled prevalence of neuropathic pain in 13 studies was 58% (95% CI 49% to 68%); the pooled prevalence of musculoskeletal pain in 11 studies was 56% (95% CI 41% to 70%); the pooled prevalence of visceral pain in 8 studies was 20% (95% CI 11% to 29%) and the pooled prevalence of nociceptive pain in 2 studies was 45% (95% CI 13% to 78%). Meta-regression of risk of bias (p=0.20), traumatic versus non-traumatic etiology of injury (p=0.59), and studies where pain was a primary outcome (p=0.32) demonstrated that these factors were not significant moderators of heterogeneity. Certainty in prevalence estimates was judged to be low due to unexplained heterogeneity.

Conclusion This systematic review and meta-analysis extends the findings of previous studies by reporting the prevalence of chronic pain after SCI based on the ISCIP classification system, thereby reducing clinical heterogeneity in the reporting of pain prevalence related to SCI.

Chronic pain after spinal cord injury (SCI) dimin-

The reported prevalence of chronic pain after SCI

varies considerably due, in part, to differences in

the taxonomy of chronic pain.^{3 4} The International

Spinal Cord Injury Pain (ISCIP) classification system

is widely recognized and the first universal classifi-

cation tool in SCI-related chronic pain, combining

the International Association for the Study of Pain

ishes physical and psychosocial functioning.¹

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INTRODUCTION

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related pain conditions.⁵⁻⁷ The ISCIP classification system is used internationally in research and clinical settings to categorize the complex symptom burden commonly presenting in patients with SCI,⁸⁻¹² mitigating the considerable clinical heterogeneity that often complicates accurate and complete diagnosis and treatment of chronic pain in SCI. The ISCIP classification system organizes chronic pain hierarchically into three tiers. The first tier is comprised of four broad categories of chronic pain (neuropathic, nociceptive, other pain and unknown pain), the second tier is comprised of subcategories of neuropathic and nociceptive pain, and the third tier specifies the anatomical source of pain. The neuropathic pain second tier subcategories include at-level pain, below-level pain (occurring at least three levels below the level of injury) and other neuropathic pain diagnoses. Second tier subcategories of nociceptive pain include musculoskeletal, visceral and other nociceptive pain diagnoses. The 'other' pain and 'unknown' pain first tier categories do not have second tier subcategories. Examples of third tier sources of neuropathic pain include spinal cord or nerve root injury and syringomyelia. Tendinopathy, abdominal or genitourinary dysfunction, and pressure ulcerations are examples of nociceptive pain. Examples of third tier sources of other pain include complex regional pain syndrome and fibromyalgia, and no third tier sources of pain are identifiable for the unknown pain category.⁵

and Bryce-Ragnarsson taxonomies specific to SCI-

The prevalence of chronic pain after SCI based on the ISCIP classification system has not been previously reported. This is important because although the ISCIP classification system is widely used in research and data collection with respect to SCIrelated pain, the prevalence of the subcategories of pain according to the ISCIP classification system is unknown. Detailed knowledge about the prevalence of SCI-related chronic pain could help investigators design appropriately powered clinical trials and enhance the accurate deployment of pain therapies based on the rate of anticipated need.^{13 14} Thus, the primary objective of this systematic review and meta-analysis is to determine the overall prevalence of chronic pain after SCI based on the ISCIP pain classification system.

METHODS Study protocol

Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed,¹⁵ and an a priori protocol was followed. The review was registered in the PROSPERO database (CRD42020147090). The investigative process began after the protocol was submitted, but prior to completion of registration.

Search strategy

A comprehensive search of several databases from January 1, 1980 to August 20, 2019 was conducted. The databases included Ovid MEDLINE, MEDLINE Epub Ahead of Print, MEDLINE In-Process and Other Non-Indexed Citations, Daily, Ovid EMBASE, Ovid Cochrane Central Register of Controlled Trials, Ovid Cochrane Database of Systematic Reviews and Scopus. The search strategy was designed and conducted by an experienced librarian with input from the principle investigator. Language was restricted to English, and controlled vocabulary supplemented with keywords was used to search for studies of the prevalence of chronic pain in individuals with SCI. The actual strategy listing all search terms used and how they are combined is available in online supplemental appendix A.

Eligibility criteria

Study inclusion criteria included (1) randomized-designed, crossover-designed and parallel-designed clinical trials; (2) prospective and retrospective longitudinal studies; (3) crosssectional studies; (4) age 18 years or older; and (5) publication years 1980 to present. Exclusion criteria included (1) studies that involved adults with SCI without chronic pain; (2) studies that involved adults with SCI with pain of less than 3 months' duration and (3) non-English-language studies.

The primary objective of the literature search was to determine the prevalence at time of injury, 1 year and lifetime prevalence of chronic pain in adults with SCI. The secondary objective was to determine the prevalence at time of injury, 1 year and lifetime prevalence of diagnostic subgroups of chronic pain in adults with SCI based on the ISCIP classification system.

Study selection process

Two independent pairs of reviewers screened all titles and abstracts included in the search results. These reviewers then screened full-text articles for inclusion and exclusion criteria, and the reason for exclusion of each full text was recorded.

Data extraction

Four reviewers abstracted data from the full-text articles using a templated computer database. Based on the a priori protocol, abstracted data included study design, sample size, cohort demographics (eg, mean age, sex), traumatic versus non-traumatic cause of SCI, level of injury, completeness of injury and years since SCI. The ISCIP criteria for chronic neuropathic, nociceptive, other pain and unknown pain were applied to studies that reported sufficient details about specific types of chronic pain.

Risk of bias assessment

The risk of bias was assessed using a tool specifically designed for assessing bias in uncontrolled studies.¹⁶ This tool consisted of four questions: (1) Do(es) the patient(s) represent the whole experience of the investigator (center) or is the selection method unclear to the extent that other patients with similar presentation may not have been reported? (2) Was the exposure adequately ascertained? (3) Was the outcome adequately ascertained? (4) Is the case(s) described with sufficient details to allow other investigators to replicate the research or to allow practitioners make inferences related to their own practice? The risk of bias was reported for each of four questions relating to selection,

Evidence synthesis

When reported, the overall prevalence of chronic pain and prevalence of chronic pain based on the ISCIP classification system were reported for each study. Results were pooled with randomeffects models using the DerSimonian and Laird method and were reported with 95% CIs. Meta-regression with a mixedeffects model was selected to investigate potential moderators of heterogeneity. Statistical analyses were performed using R V.3.5.0 (R Core Team, 2018).

We investigated several potential moderators of heterogeneity including etiology of injury (traumatic or non-traumatic), risk of bias and pain as the primary outcome by performing meta-regression with subgroup analysis. The third characteristic was based on van Gorp *et al*'s findings in a previously published systematic review.⁴

Certainty in prevalence estimates

The GRADE approach (Grading of Recommendations, Assessment, Development and Evaluation)¹⁷ is a comprehensive and transparent process of evaluating the certainty of evidence (previously called quality of evidence) in interventional and diagnostic systematic reviews. The approach has been extended to prevalence studies. We applied GRADE domains of risk of bias, inconsistency or heterogeneity, indirectness, publication bias and imprecision.¹⁸ We considered studies with a small sample size (under 1000) to provide imprecise prevalence estimates and wide CIs.

RESULTS

Characteristics of included studies

The PRISMA flow diagram of the study selection process is depicted in figure 1. Thirty-seven studies met inclusion and exclusion criteria (table 1).¹⁹⁻⁵⁵ The survey conducted by Warms et al⁵³ included two separate cohorts, and the results are presented separately as v1 and v2. When studies included multiple follow-up time points, the results reported for the longest follow-up time point were recorded. Despite our stated outcome of reporting pain prevalence at 1 year following injury, due to inconsistency in reporting of time points of pain following initial injury, we were unable to reliably aggregate 1-year pain prevalence across studies. Thirty-four studies used a cross-sectional design¹⁹⁻²¹ ²³⁻²⁹ ³¹ ³³⁻⁵⁵ and four studies used a prospective cohort design.^{22 30 32 54} Mixed cohorts of traumatic and non-traumatic causes of SCI were used in 25 studies^{19 20 22-24 26-29 31 33-36 40 41 43-46 49 51-53 55} and traumatic only cohorts were used in 12 studies.^{21 25 30 32 37–39 42 47 48 50 54} Although most studies reported the proportion of their population who had sustained a traumatic injury, those with a mixed cohort did not separately report the prevalence of pain in subjects who had sustained traumatic versus non-traumatic injuries. Among the 34 studies reporting level of injury,^{19-40 42 43 45-47 49-55} 3589 patients were tetraplegic and 7048 were paraplegic. Table 2 summarizes the number of patients with each subcategory of pain according to ISCIP criteria.

Table 3 summarizes the results including quality assessment according to GRADE criteria, pooled prevalence estimates and certainty in the estimates based on GRADE analysis. Certainty across all pain categories and subtypes is rated as low to very low due to inconsistency resulting from unexplained statistical heterogeneity.



Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses diagram of study selection process. Adapted from: Moher et al.¹⁵

Risk of bias assessment

The risk of bias summary and the entire risk assessment is contained in online supplemental appendix B. Common sources of bias included selection bias in 27% (N=10) of studies, ascertainment of outcome in 19% (N=7) of studies and ascertainment of exposure in 16% (N=6) of studies. To investigate risk of bias as a source of heterogeneity, we performed subgroup analysis based on whether risk of bias was judged to be high (based on a cut-off of 'no' to two of our questions) (online supplemental appendix C). Seven studies were deemed to have a high risk of bias.²³ 26 $^{28-31}$ 40 The prevalence of pain in these seven studies ranged from 44% to 77%. The pooled prevalence of pain among studies with high risk of bias was 62% (95% CI 51% to 73%) with high heterogeneity (I²=94%). The pooled prevalence of pain among studies with low risk of bias was 69% (95% CI 64% to 74%) with high heterogeneity (I²=97%). Risk of bias was not found to be a significant moderator of heterogeneity.

Prevalence of all chronic pain types

All 37 studies (n=11351) reported chronic pain prevalence and the prevalence of all chronic pain types ranged from 33% to 100% (figure 2). The pooled prevalence of all chronic pain types was 68% (95% CI 63% to 73%) with high heterogeneity (I^2 =97%).

Meta-regression performed with individual covariates including risk of bias (p=0.20), traumatic versus non-traumatic amputation (p=0.59), and studies where SCI pain was a primary outcome (p=0.32) demonstrated that these individual factors were not significant moderators of heterogeneity. Metaregression with these three factors combined as a single covariate resulted in significant residual heterogeneity signifying that this combined factor was not a significant moderator of heterogeneity (p=0.44). The results of this meta-regression can be viewed in online supplemental appendix C.

Prevalence of chronic pain based on subgroup analyses of ISCIP categories

Twenty of 37 studies reported chronic pain that could be classified using the ISCIP classification system. The prevalence of chronic neuropathic pain in 13 studies (n=3512) ranged from 34% to 83% (figure 3). The pooled prevalence of neuropathic pain was 58% (95% CI 49% to 68%) with high heterogeneity (I^2 =97%). Inadequate data were available to further subclassify neuropathic pain as at-level or below-level, and other neuropathic pain diagnoses were not reported.

The prevalence of chronic nociceptive musculoskeletal pain in 11 studies (n=2427) ranged from 26% to 87% (figure 3). The pooled prevalence of musculoskeletal pain was 56% (95% CI 41% to 70%) with high heterogeneity (I^2 =98%).

The prevalence of chronic visceral pain in eight studies ranged from 2% to 34% (figure 3). The pooled prevalence of chronic visceral pain was 20% (95% CI 11% to 29%) with high heterogeneity ($I^2=95\%$).

The prevalence of other chronic nociceptive pain in two studies ranged from 29% to 62% (figure 3). The pooled prevalence of

						Level of inj	nry			Pain cat	egory			
										Nocicep	tive			
Study	Study design	SCI cohort	Total number	Male sex	Mean age	Cervical	Lumbar-thoracic	Complete injury	All pain	MSK	Visceral	NP Oth	er pain	Years since injury
Adriaansen <i>et al</i> ¹⁹	CS	Mixed	139	88	44	41	80	70	121	121	I	121 –		5.0
Adriaansen <i>et al</i> ²⁰	S	Mixed	282	209	48	116	166	195	179	179	I	- 96		22.0
Andresen <i>et al</i> ²¹	S	Trauma	537	413	55	274	263	193	392	I	I	234 –		18.2
Barrett <i>et al²²</i>	PC	Mixed	88	74	48	53	35		66	38	13	31 -		16.7
Cragg et al ²³	S	Mixed	1493	1003	50	633	859	662	937	I	I	937 –		18.4
Craig <i>et al²⁴</i>	S	Mixed	70	63	47	21	49	32	65	I	I	ı I		17.4
Cruz-Almeida <i>et al²⁵</i>	S	Trauma	123	96	40	65	57	38	75	75	I	I I		8.5
Cudeiro-Blanco <i>et al²⁶</i>	S	Mixed	253	163	I	93	157	134	169	I	I	1		1
Figoni and Chen ²⁷	S	Mixed	178	167	64	59	49	24	85	I	I	I I		12.0
Finnerup <i>et al²⁸</i>	S	Mixed	330	230	43	113	217	158	255	I	75	255 –		9.3
Finnerup <i>et al²⁹</i>	S	Mixed	193	133	47	99	127	I	107	I	99	I I		22.0
Finnerup <i>et al</i> ³⁰	PC	Trauma	81	71	52	45	34	24	61	53	2	40 –		3.5
Gironda <i>et al³¹</i>	S	Mixed	669	657	51	0	669	363	345	188	I	I I		20.3
Grabher <i>et al^{a2}</i>	PC	Trauma	14	13	46	80	9	5	9	I	I	- 9		1.0
Hogholen <i>et al</i> ³³	S	Mixed*	105	99	53	40	57	38	66	I	I	I I		19.0
Jain <i>et al³⁴</i>	S	Mixed*	93	87	54	12	29	I	65	ı	I	ı ı		I
Jensen <i>et al</i> ³⁵	S	Mixed*	147	110	49	74	73	I	117	I	I	I I		16.6
Jorgensen <i>et al³⁶</i>	S	Mixed	123	87	63	22	101	38	105	ı	I	81 76		24.0
Kentar <i>et al³⁷</i>	S	Trauma	451	322	49	0	451	294	365	365	I	I I		20.9
Khazaeipour <i>et al</i> ³⁸	S	Trauma	140	101	29	47	93	60	70	ı	I	ı ı		3.9
Kogos <i>et al</i> ³⁹	S	Trauma	261	196	28	117	144	156	129	I	63	I I		11.0
Lamid <i>et al</i> ⁴⁰	S	Mixed*	64	63	I	31	33	I	28	I	I	ı ı		I
Michailidou <i>et al</i> ⁴¹	S	Mixed	219	136	50	I	1	0	96	96	I	I I		12.0
Modirian <i>et al</i> ⁴²	S	Trauma	1295	1276	36	120	1175	1163	840	I	I	I		13.9
New ⁴³	CS	Mixed	150	100	50	62	88	I	68	I	I	I I		10.0
Nielsen <i>et al</i> ⁴⁴	S	Mixed*	125	94	56	I	I	I	41	I	41	1		30.5
Rintala <i>et al</i> ⁴⁵	S	Mixed*	348	345	55	112	228	1	265	I	I	I I		17.5
Sauri <i>et al⁴⁶</i>	S	Mixed	831	597	50	272	559	400	381	I	I	I I		12.7
Siddall <i>et al</i> ⁴⁷	S	Trauma	73	60	40	36	37	28	59	43	4	55 -		5.0
Singh <i>et al</i> ⁴⁸	S	Trauma	50	36	38	I	I	12	21	I	I	21 –		I
Stormer <i>et al</i> ⁴⁹	S	Mixed	901	667	42	378	523	1	591	I	I	I I		1
Tibbett <i>et al</i> ⁵⁰	S	Trauma	20	17	40	5	15	11	19	I	I	1		I
Turner <i>et al</i> ⁵¹	S	Mixed*	384	283	43	196	188	143	315	I	I	I I		12.2
Vogel <i>et al^{sz}</i>	S	Mixed*	216	150	29	123	93	I	149	I	I	1		I
Warms et al ⁵³ v1	S	Mixed*	388	I	1	154	145	1	308	I	I	I I		1
Warms v2	I	I	215	I	I	85	76	I	163	I	I	ı I		I
Wen et al ⁵⁴	PC	Trauma	23	10	54	c	20	5	23	9	I	19 -		3.5
Wollaars <i>et al</i> ⁵⁵	S	Mixed	279	176	51	113	152	115	215	141	67	155 80	-	11.8
Total	I	I	11 351	8359	47 (mean)	3589	7048	4361	7395	1305	331	2051 156		14 (mean)

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Review

Table 2 Categories of report	ted pain according to ISCIP	classification criteria			
Study	Total reported pain (N)	Neuropathic pain (N)	Musculoskeletal pain (N)	Visceral pain (N)	Other pain (N)
Adriaansen <i>et al</i> ¹⁹	121	121	121		
Adriaansen <i>et al</i> ²⁰	179	96	179		
Andresen <i>et al</i> ²¹	392	234			
Barrett <i>et al</i> ²²	66	31	38	13	
Cragg <i>et al</i> ²³	937	937			
Craig <i>et al</i> ²⁴	65				
Cruz-Almeida <i>et al</i> ²⁵	75		75		
Cudeiro-Blanco et al ²⁶	169				
Figoni and Chen ²⁷	85				
Finnerup <i>et al²⁸</i>	255	255		75	
Finnerup <i>et al</i> ²⁹	107			66	
Finnerup <i>et al</i> ³⁰	61	40	53	2	
Gironda <i>et al</i> ³¹	345		188		
Grabher <i>et al</i> ³²	6	6			
Hogholen <i>et al</i> ³³	99				
Jain <i>et al</i> ³⁴	65				
Jensen <i>et al</i> ³⁵	117				
Jorgensen <i>et al</i> ³⁶	105	81			76
Kentar <i>et al</i> ³⁷	365		365		
Khazaeipour <i>et al</i> ³⁸	70				
Kogos <i>et al³⁹</i>	129			63	
Lamid <i>et al⁴⁰</i>	28				
Michailidou <i>et al</i> ⁴¹	96		96		
Modirian <i>et al⁴²</i>	840				
New ⁴³	68				
Nielsen <i>et al</i> ⁴⁴	41			41	
Rintala et al ⁴⁵	265				
Sauri <i>et al⁴⁶</i>	381				
Siddall <i>et al</i> ⁴⁷	59	55	43	4	
Singh <i>et al</i> ⁴⁸	21	21			
Stormer <i>et al</i> ⁴⁹	591				
Tibbett <i>et al⁵⁰</i>	19				
Turner <i>et al⁵¹</i>	315				
Vogel <i>et al</i> ⁵²	149				
Warms et al ⁵³ v1	308				
Warms v2	163				
Wen <i>et al⁵⁴</i>	23	19	6		
Wollaars et al ⁵⁵	215	155	141	67	80
Total	4901	2779	1742	398	156

ISCIP, International Spinal Cord Injury Pain; N, number.

other chronic nociceptive pain was 45% (95% CI 13% to 78%) with high heterogeneity (I^2 =98%).

The occurrence of unknown pain was not reported in any study.

Prevalence of all chronic pain types in traumatic injuries

To assess for possible sources of heterogeneity, we performed subgroup analysis based on etiology of injury (traumatic vs non-traumatic). Twelve^{21 25 30 32 37-39 42 47 48 50 54} of 37 studies included only subjects with traumatic injuries. The prevalence of pain in these 12 studies ranged from 42% to 100%. The pooled prevalence of pain among studies of patients with traumatic injuries was 69% (95% CI 60% to 78%) with high heterogeneity (I^2 =96%). Etiology of injury was not found to be a significant moderator of heterogeneity.

Certainty of prevalence estimates

Using the GRADE approach, the certainty in the prevalence estimates is judged to be low, primarily due to the high degree of heterogeneity (inconsistency). Performance of subgroup analysis according to pain category mitigated indirectness derived from differences in patient population. Given the variety of included study design and study design, we did not downgrade quality of evidence based on publication bias.

DISCUSSION

The main finding of this systematic review and meta-analysis was that the pooled prevalence of SCI-related chronic pain type overall was 68%. When the meta-analysis was performed for each ISCIP category, the prevalence rates of chronic neuropathic pain and musculoskeletal pain were 58% and 56%, respectively.

Table 3 GRADE analysis including quality assessment, summary of findings and certainty in estimates of prevalence of chronic pain in spinal cord injury

	Quality assessment					Summary of finding	s	Certainty in
ISCIP category no of studies	Limitations	Inconsistency	Indirectness	Imprecision	Publication bias	Pooled prevalence (95% CI)	No of patients	prevalence estimates
Total (all catego	ries)	<u> </u>				· · ·	•	
37	Limitations were minimal in most studies, related primarily to population sample selection and non-response bias	High degree of statistical heterogeneity (l ² =97%)	No serious indirectness	No serious imprecision	Undetected	68% (63% to 73%)	11 351	++Low
Neuropathic								
13	Limitations were minimal in most studies, related primarily to population sample selection and non-response bias	High degree of statistical heterogeneity (l ² =97%)	No serious indirectness	No serious imprecision	Undetected	58% (49% to 68%)	3512	++Low
Nociceptive								
Visceral								
8	Limitations were minimal	High degree of statistical heterogeneity (l ² =95%)	No serious indirectness	No serious imprecision	Undetected	56% (41% to 70%)	1430	++Low
Musculoskeletal								
11	Limitations were minimal in most studies, primarily related to external validity	High degree of statistical heterogeneity (l ² =98%)	No serious indirectness	No serious imprecision	Undetected	20% (11% to 29%)	2427	++Low
Other								
2	Limitations were minimal	High degree of statistical heterogeneity (I ² =98%)	No serious indirectness	Serious concern about imprecision due to small sample size	Undetected	45% (13% to 78%)	402	+Very low

GRADE, Grading of Recommendations, Assessment, Development and Evaluation; ISCIP, International Spinal Cord Injury Pain; No, number.

The prevalence of other chronic pain was 45%, and the prevalence of visceral pain was the lowest at 20%.

This is the first time that a systematic review has evaluated prevalence of chronic pain according to all categories of SCIrelated pain, using the widely accepted ISCIP criteria. The overall prevalence of chronic pain after SCI in this review is consistent with the findings of previous systematic reviews.

At least two previous systematic reviews have reported the prevalence of chronic pain based on two of the subcategories. The prevalence of chronic neuropathic pain was reported in a systematic review that involved 17 studies.⁵⁶ Criteria for study inclusion required evidence that a working definition of neuropathic pain was used which encompassed use of the ISCIP classification system. The overall point prevalence of neuropathic pain was 53% (95% CI 39% to 67%).⁵⁶ The 58% prevalence of neuropathic pain reported in our study is within the 95% CI of the Burke et al study.⁵⁶ For the ISCIP subcategories of at-level and below-level neuropathic pain, the prevalence rates were 19% (95% CI 13% to 26%) and 27% (95% CI 20% to 35%), respectively. High levels of heterogeneity ($I^2 = 84\% - 93\%$) were reported for all prevalence calculations.⁵⁶ In a separate systematic review that involved eight studies, the prevalence of chronic musculoskeletal pain was 49% (95% CI 44% to 55%).⁵⁷ The prevalence of chronic back pain was 47% (95% CI 43% to 50%) and the prevalence of chronic low back pain was 49% (95% CI 44% to 55%).⁵⁷ The type of back and low back pain could not be further differentiated due to insufficient evidence.⁵⁷ These prevalence rates are lower than the 56% prevalence identified

herein, but our review included information from an additional five studies.

Assessment of heterogeneity

All pooled prevalence rates were confounded by high levels of heterogeneity. Despite use of subgroup and meta-regression analyses, which are recommended approaches for identifying sources of heterogeneity,58 59 high levels of heterogeneity remained unexplained. High levels of heterogeneity have been reported in systematic reviews of prevalence studies.⁶⁰ Although a computational analysis of the $I^{\bar{2}}$ statistic is beyond the scope of this review, it may be described as a measure of inconsistency among included studies, and not necessarily as a threshold tool for conduction of meta-analysis. The value of I² increases with the number of subjects in the studies comprising the metaanalysis.^{61 62} If the underlying eligibility criteria are considered to be sound, restricting studies based on statistical heterogeneity introduces bias. The decision to conduct a meta-analysis should not be solely based on the I² statistic; rather, the decision to pool studies should also incorporate an assessment of other relevant sources of heterogeneity.⁶² Other potential sources of heterogeneity were considered but inadequate data were available to conduct subgroup analyses based on pain intensity, temporal changes in pain, cervical versus lumbar SCI or duration of injury.

Other systematic reviews of SCI-related pain prevalence have also found high degrees of statistical heterogeneity. The primary aim of a systematic review that involved 82 studies was to identify sources of heterogeneity in pain prevalence studies.⁴ In this

Study	Cases	Total	Prevalence	95% C.I.	Weight (Randon
Adriaansen 2013	121	139	87.05	[80.31; 92.14]	2.79
Adriaansen 2016	179	282	63.48	[57.56; 69.10]	2.79
Andresen 2016	392	537	73.00	[69.03; 76.71]	2.89
Barrett 2003	66	88	75.00	[64.63; 83.62]	2.59
Cragg 2015	937	1493	62.76	[60.25; 65.22]	2.89
Craig 2013	65	70	92.86	[84.11; 97.64]	2.79
Cruz-Almeida 2005	75	123	60.98	[51.77; 69.64]	2.69
Cudeiro-Blanco 2017	169	253	66.80	[60.63; 72.57]	2.7
Figoni 2015	85	178	47.75	[40.23; 55.36]	2.69
Finnerup 2001	255	330	77.27	[72.37; 81.68]	2.7
Finnerup 2008	107	193	55.44	[48.13; 62.58]	2.69
Finnerup 2016	61	81	75.31	[64.47; 84.22]	2.5
Gironda 2004	345	669	51.57	[47.71; 55.42]	2.89
Grabher 2015	6	14	42.86	[17.66; 71.14]	1.59
Hogholen 2018	99	105	94.29	[87.98; 97.87]	2.79
Jain 2010	65	93	69.89	[59.50; 78.97]	2.59
Jensen 2005	117	147	79.59	[72.17; 85.79]	2.7
Jorgensen 2017	105	123	85.37	[77.86; 91.09]	2.79
Kentar 2018	365	451	80.93	[77.00; 84.45]	2.89
Khazaeipour 2017	70	140	50.00	[41.44; 58.56]	2.69
Kogos 2005	129	261	49.43	[43.20; 55.66]	2.79
Lamid 1985	28	64	43.75	[31.37; 56.72]	2.49
Michailidou 2018	96	219	43.84	[37.16; 50.68]	2.79
Modirian 2010	840	1295	64.86	[62.19; 67.47]	2.89
New 2016	68	150	45.33	[37.20; 53.66]	2.69
Nielsen 2017	41	125	32.80	[24.67; 41.77]	2.6
Rintala 2005	265	348	76.15	[71.32; 80.53]	2.79
Sauri 2017	381	831	45.85	[42.42; 49.31]	2.89
Siddall 2003	59	73	80.82	[69.92; 89.10]	2.69
Singh 2010	21	50	42.00	[28.19; 56.79]	2.3
Stormer 1997	591	901	65.59	[62.39; 68.70]	2.89
Tibbett 2019	19	20	95.00	[75.13; 99.87]	2.59
Turner 2001	315	384	82.03	[77.82; 85.74]	2.89
Vogel 2002	149	216	68.98	[62.35; 75.08]	2.79
Warms 2002 v1	308	388	79.38	[75.01; 83.30]	2.89
Warms 2002 v2	163	215	75.81	[69.52; 81.38]	2.79
Wen 2013	23	23	100.00	[85.18; 100.00]	2.79
Wollaars 2007	215	279	77.06	[71.67; 81.86]	2.7
Random effects model		11351	67.89	[63.17; 72.61]	100.09
Heterogeneity: $I^{2} = 97\%$, $\tau^{2} =$	0.0206. y	. = 1181	.36 (p < 0.01)		



Figure 2 Pooled prevalence of chronic pain in spinal cord injury, all pain types.

particular review, the precision of clinical criteria used to diagnose chronic pain (mild, moderate or high) was reported to be an important source of heterogeneity. Another reported source of heterogeneity included whether a study was primarily focused on pain; the prevalence of chronic pain was 14%-25% higher in studies that had a primary pain focus. The higher prevalence among pain-focused studies was postulated to be due to (1) selection bias (patients without pain less likely to participate); (2) publication bias (studies reporting high prevalence rates more likely to be published) and (3) higher sensitivity of diagnostic tools in pain-focused studies.⁴ In a second systematic review that involved 42 studies, the prevalence of chronic pain ranged from 26% to 96%.³ Although a formal meta-analysis was not performed due to high levels of heterogeneity, the mean prevalence rate was reported to be 62%.³ In both reviews,^{3 4} the use of uniform research methods for conducting prevalence studies of SCI pain was recommended as an approach to reduce heterogeneity in future studies. Although improved methodological heterogeneity will not necessarily improve the I² statistic, this is a laudable goal for conduction of further prevalence studies.

Based on the finding that whether a study's primary focus was on pain was a significant moderator of heterogeneity, we also performed subgroup analysis based on this characteristic. Thirty-two^{20–25} 28–31 34–45 47–55 63</sup> of 37 studies had a primary pain focus. The prevalence of pain in these 32 studies ranged from 33% to 100%. The pooled prevalence of pain in pain-focused studies was 68% (95% CI 63% to 73%) with high heterogeneity

 $(I^2=97\%)$. Pain as the primary study focus was not found to be a significant moderator of heterogeneity.

In summary, we have reported the I^2 statistic as a measure of statistical heterogeneity, which was high across all subgroups as has been observed in other systematic review of prevalence studies. Three study design characteristics including risk of bias, etiology of injury and whether pain was the primary focus of the study were all considered, and none were found to be significant moderators of statistical heterogeneity. Other systematic reviews have highlighted the importance of methodological heterogeneity as contributing to variability across studies. We have endeavored to address the problem of clinical heterogeneity through study design stratifying chronic SCI-related pain according to type of pain as defined by the ISCIP categories.

Limitations

This systematic review has limitations. By restricting our search to English language only, we may have excluded prevalence studies relevant to our objective. This introduces intrinsic bias to our results against manuscripts not published in English. There is also the question of appropriateness of meta-analysis given the statistical heterogeneity of the data. Although our preceding discussion addressed our rationale for conducting meta-analysis despite high levels of statistical heterogeneity in the meta-regression, there is a reasonable argument to be made that qualitative analysis would be sufficient for presentation of results. Given the known high degrees of statistical heterogeneity



Musculoskeletal Pain





Figure 3 Pooled prevalence of chronic pain in spinal cord injury, subgroup analysis based on ISCIP categories. ISCIP, International Spinal Cord Injury Pain.

among prevalence studies in general, we felt that proceeding with meta-analysis was reasonable given the reported data among the identified studies. We felt that our results were sufficiently comparable to justify calculation of pooled prevalence of chronic SCI-related pain stratified according to the ISCIP categories, thereby decreasing the problem of clinical heterogeneity among this complex patient population.

Conclusion

This systematic review and meta-analysis extends the findings of previous studies by reporting the prevalence of chronic pain after SCI based on the ISCIP classification system. Pain is common after SCI and ongoing population-based prevalence studies using the ISCIP classification system are needed to accurately determine the prevalence of chronic pain in this important patient population.

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Contributors All authors have made substantial contributions to the conception or design of the work, or the acquisition, analysis or interpretation of data; and have participated in drafting the work or revising it critically for important intellectual content. All have submitted final approval of the version published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Patient consent for publication Not required.

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Appendix A: Detailed Search Strategy

Ovid

Database(s): EBM Reviews - Cochrane Central Register of Controlled Trials July 2019, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to August 15, 2019, Embase 1974 to 2019 August 19, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to August 19, 2019 Search Strategy:

#	Searches	Results
1	exp Spinal Cord Injuries/	120073
2	exp Paraplegia/	34241
3	exp Quadriplegia/	24269
4	("brown presentation" or "brown sequard disease" or "Brown Sequard syndrome" or "Brown-Sequards syndrome" or "central cord syndrome" or "central spinal cord syndrome" or "medullary transverse lesion*" or Paraplegia* or "Post Traumatic Myelopath*" or Quadriplegia* or "Spinal Cord Contusion*" or "Spinal Cord Injur*" or "Spinal Cord Laceration*" or "Spinal Cord Transection*" or "spinal cord transsection*" or "spinal cord transverse lesion*" or "Spinal Cord Trauma*" or "transverse cord lesion*" or "transverse lesion*" or "transverse spinal cord lesion*" or "Traumatic Myelopath*").ti,ab,hw,kw.	175374
5	1 or 2 or 3 or 4	196091
6	exp chronic pain/	71621
7	(((chronic* or persist* or recur* or reocur* or "re-ocur*") adj5 pain*) or "back ache*" or "back pain*" or backache* or backpain* or "diskogenic pain*" or dorsalgia* or lumbago or "musculoskeletal pain*" or "musculo-skeletal pain*" or "neuropathic pain*" or "nociceptive pain*" or "vertebrogenic pain*" or "Visceral Pain*" or "widespread pain*").ti,ab,hw,kw.	459067
8	6 or 7	459067
9	5 and 8	11165
10	epidemiology.fs.	2568733
11	exp prevalence/	971841
12	(epidemiol* or frequency or frequent* or incidence* or ocurrence* or prevalence* or prevalent or rate or rates).ti,ab,hw,kw.	13053650
13	10 or 11 or 12	14022601
14	9 and 13	2860
15	exp meta analysis/	273593
16	exp Meta-Analysis as Topic/	59185
17	exp "systematic review"/	326644
18	exp controlled study/	7033396
19	exp Randomized Controlled Trial/	1054076
20	exp triple blind procedure/	229

Supplemental material

21 e	exp Double-Blind Method/	449590
22 e	exp Single-Blind Method/	82970
23 e	exp latin square design/	363
24 e	exp Placebos/	398188
25 e	exp Placebo Effect/	11605
26 e	exp Cross-Sectional Studies/	618379
27 e	exp Cross-Over Studies/	141642
28 e	exp Cohort Studies/	2528441
29 e	exp longitudinal study/	389871
30 e	exp retrospective study/	1584263
31 e	exp prospective study/	1142249
32 e	exp clinical trial/	2255158
33 c	clinical study/	157797
34 e	exp correlational study/	38403
35 e	exp confidence interval/	166318
36 e	exp regression analysis/	853991
37 e	exp proportional hazards model/	165610
38 e	exp multivariate analysis/	527342
() 5 6 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7	((meta adj analys*) or metaanalys* or (systematic* adj3 review*) or (control* adj3 study) or (control* adj3 trial) or (randomized adj3 study) or (randomized adj3 trial) or (randomised adj3 study) or (randomised adj3 trial) or "pragmatic clinical trial" or (random* adj1 allocat*) or (doubl* adj blind*) or (doubl* adj mask*) or (singl* adj blind*) or (singl* adj mask*) or (tripl* adj blind*) or (tripl* adj mask*) or (trebl* adj blind*) or (trebl* adj mask*) or "latin square" or placebo* or nocebo* or nultivariate or "cross-sectional study" or "cross-sectional analysis" or "prevalence analysis" or "prevalence survey" or "disease frequency study" or "disease frequency analysis" or "disease frequency survey" or crossover or "cross-over" or cohort* or "longitudinal study" or "longitudinal survey" or "longitudinal analysis" or "longitudinal evaluation" or longitudinal* or ((retrospective or "ex post facto") adj3 (study or survey or analysis or design)) or retrospectiv* or "incidence study" or "incidence survey" or "incidence analysis" or ("follow-up" or followup) adj (stud* or survey or analysis)) or "clinical study" or "clinical trial" or (("phase 0" or "phase 1" or "phase 1" or "phase 2" or "phase 11" or "phase 3" or "phase 11" or 'phase 4" or "longi trial or "confidence interval" or "regression analysis" or 'least square" or "least squares" or (hazard* adj (model* or analys* or regression or ratio or ratios)) or "Cox model" or "Cox survival analyses" or "Cox survival analysis" or "Cox survival model" or "prevalence study" or "prevalence survey" or "prevalence analysis" or "Cox survival analyses" or "Cox survival analysis" or "Cox survival model" or "prevalence study" or "prevalence survey" or "prevalence analysis").mp,t.	17576398

40 or/15-39	17792379
41 14 and 40	1517
limit 41 to ("all adult (19 plus years)" or "young adult (19 to 24 years)" or "adult (19 to 44 years)" or "young adult and adult (19-24 and 19-44)" or "middle age (45 to 64 years)" or "middle aged (45 plus years)" or "all aged (65 and over)" or "aged (80 and over)") [Limit not valid in CCTR,CDSR,Embase; records were retained]	1428
 limit 42 to (adult <18 to 64 years> or aged <65+ years>) [Limit not valid in 43 CCTR,CDSR,Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained] 	1005
 limit 41 to ("all infant (birth to 23 months)" or "all child (0 to 18 years)" or "newborn infant (birth to 1 month)" or "infant (1 to 23 months)" or "preschool child (2 to 5 years)" or "child (6 to 12 years)" or "adolescent (13 to 18 years)") [Limit not valid in CCTR,CDSR,Embase; records were retained] 	1226
limit 44 to (embryo or infant or child or preschool child <1 to 6 years> or school child <7 to 12 years> or adolescent <13 to 17 years>) [Limit not valid in CCTR,CDSR,Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained]	250
46 45 not 43	37
47 41 not 46	1480
 limit 47 to (conference abstract or editorial or erratum or note or addresses or autobiography or bibliography or biography or blogs or comment or dictionary or directory or interactive tutorial or interview or lectures or legal cases or legislation or news or newspaper article or overall or patient education handout or periodical index or portraits or published erratum or video-audio media or webcasts) [Limit not valid in CCTR,CDSR,Embase,Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained] 	166
49 from 48 keep 1-2	2
50 (47 not 48) or 49	1316
51 limit 50 to yr="1980 -Current"	1305
52 remove duplicates from 51	999

<u>Scopus</u>

- 1 TITLE-ABS-KEY("brown presentation" or "brown sequard disease" or "Brown Sequard syndrome" or "Brown-Sequards syndrome" or "central cord syndrome" or "central spinal cord syndrome" or "medullary transverse lesion*" or Paraplegia* or "Post Traumatic Myelopath*" or Quadriplegia* or "Spinal Cord Contusion*" or "Spinal Cord Injur*" or "Spinal Cord Laceration*" or "Spinal Cord Transection*" or "spinal cord transsection*" or "spinal cord transverse lesion*" or "Spinal Cord Trauma*" or "transverse cord lesion*" or "transverse lesion*" or "transverse spinal cord lesion*" or "Traumatic Myelopath*")
- 2 TITLE-ABS-KEY(((chronic* or persist* or recur* or reocur* or "re-ocur*") W/5 pain*) OR "back ache*" OR "back pain*" OR backache* OR backpain* OR "diskogenic pain*" OR dorsalgia* OR lumbago OR "musculoskeletal pain*" OR "musculo-skeletal pain*" OR "neuropathic pain*" OR "nociceptive pain*" OR "vertebrogenic pain*" OR "Visceral Pain*" OR "widespread pain*")
- 3 TITLE-ABS-KEY(epidemiol* OR frequency OR frequent* OR incidence* OR ocurrence* OR prevalence* OR prevalent OR rate OR rates)
- 4 TITLE-ABS-KEY((meta W/1 analys*) OR metaanalys* OR (systematic* W/3 review*) OR (control* W/3 study) OR (control* W/3 trial) OR (randomized W/3 study) OR (randomized W/3 trial) OR (randomised W/3 study) OR (randomised W/3 trial) OR "pragmatic clinical trial" OR (random* W/1 allocat*) OR (doubl* W/1 blind*) OR (doubl* W/1 mask*) OR (singl* W/1 blind*) OR (singl* W/1 mask*) OR (tripl* W/1 blind*) OR (tripl* W/1 mask*) OR (trebl* W/1 blind*) OR (trebl* W/1 mask*) OR "latin square" OR placebo* OR nocebo* OR multivariate OR "cross-sectional study" OR "cross-sectional analysis" OR "cross-sectional survey" OR "cross-sectional design" OR "prevalence study" OR "prevalence analysis" OR "prevalence survey" OR "disease frequency study" OR "disease frequency analysis" OR "disease frequency survey" OR crossover OR "crossover" OR cohort* OR "longitudinal study" OR "longitudinal survey" OR "longitudinal analysis" OR "longitudinal evaluation" OR longitudinal* OR ((retrospective OR "ex post facto") W/3 (study OR survey OR analysis OR design)) OR retrospectiv* OR "prospective study" OR "prospective survey" OR "prospective analysis" OR prospectiv* OR "incidence study" OR "incidence survey" OR "incidence analysis" OR (("follow-up" or followup) W/1 (stud* or survey or analysis)) OR "clinical study" OR "clinical trial" OR (("phase 0" or "phase 1" or "phase I" or "phase 2" or "phase II" or "phase 3" or "phase III" or "phase 4" or "phase IV") W/5 (trial or study)) OR "multicenter study" OR "multi-center study" OR "odds ratio" OR "confidence interval" OR "regression analysis" OR "least square" OR "least squares" OR (hazard* W/1 (model* OR analys* OR regression or ratio or ratios)) OR "Cox model" OR "Cox multivariate analyses" OR "Cox multivariate analysis" OR "Cox regression" OR "Cox survival analyses" OR "Cox survival analysis" OR "Cox survival model" OR "prevalence study" OR "prevalence survey" OR "prevalence analysis")
- 5 PUBYEAR AFT 1979
- 6 1 and 2 and 3 and 4 and 5
- 7 TITLE-ABS-KEY(newborn* or neonat* or infant* or toddler* or child* or adolescent* or paediatric* or pediatric* or girl or girls or boy or boys or teen or teens or teenager* or preschooler* or "pre-schooler*" or preteen or preteens or "pre-teen" or "pre-teens" or youth or youths) AND NOT TITLE-ABS-KEY(adult or adults or "middle age" or "middle aged" OR elderly OR geriatric* OR "old people" OR "old person*" OR "older people" OR "older person*" OR "very old")
- 8 6 and not 7
- 9 DOCTYPE(ab) OR DOCTYPE(ed) OR DOCTYPE(bk) OR DOCTYPE(er) OR DOCTYPE(no) OR DOCTYPE(sh)
- 10 8 and not 9

- 11 INDEX(embase) OR INDEX(medline) OR PMID(0* OR 1* OR 2* OR 3* OR 4* OR 5* OR 6* OR 7* OR 8* OR 9*)
- 12 10 and not 11

Study	Selection - 1. Does the patient(s) represent(s) the whole experience of the investigator (centre) or is the selection method unclear to the extent that other patients with similar presentation may not have been reported?	Ascertainment - 2. Was the exposure adequately ascertained?	Ascertainment - 3. Was the outcome adequately ascertained?	Reporting - 8. Is the case(s) described with sufficient details to allow other investigators to replicate the research or to allow practitioners make inferences related to their own practice?
Adriaansen ¹¹ 2013	Y	Y	Y	Ŷ
Adriaansen ¹² 2016	Y	Y	Y	Y
Andresen ¹³ 2016	Y	N	Y	Y
Barrett ¹⁴ 2003		N.		
Cragg ¹⁵ 2015	Y V	Y V	Y	Y N
Craig ¹⁶ 2013			V	V V
Cruz-Almeida ¹⁷ 2005	V	V	V	V I
Cudeiro-Blanco ¹⁸ 2017	I V	N	N	Y
Figoni ¹⁹ 2015	Y	Y	Y	Y Y
Finnerun ²⁰ 2001	Y	N	N	Y
Finnerup ²¹ 2008	Y	N	N	Y
Finnerup ²² 2016	Y	N	N	Y
Gironda ²³ 2004	Y	N	N	Y
Grabher ²⁴ 2015	N	Y	Y	Y
Hogholen ²⁵ 2018	Y	Y	Y	Y
Jain ²⁶ 2010	Y	Y	Y	Y
Jensen ²⁷ 2005	Y	Y	Y	Y
Jorgensen ²⁸ 2017	Y	Y	Y	Y
Kentar ²⁹ 2018	Y	Y	Y	Y
Khazaeipour ³⁰ 2017	Y	Y	Y	Y
Kogos ³¹ 2005	Y	Y	Y	Y
Lamid ³² 1985	N	Y	Ν	Y

	Selection - 1. Does the patient(s) represent(s) the whole experience of the investigator (centre) or is the selection method unclear to the extent that other patients with similar presentation may not have	Ascertainment - 2. Was the exposure adequately ascertained?	Ascertainment - 3. Was the outcome adequately ascertained?	Reporting - 8. Is the case(s) described with sufficient details to allow other investigators to replicate the research or to allow practitioners make inferences related to their own practice?
Study	been reported?			
Michailido ³³ 2018	Ν	Y	Y	Y
Modirian ³⁴ 2010	Y	Y	Y	Y
New ³⁵ 2016	Y	Y	Y	Y
Nielsen ³⁶ 2017	N	Y	Y	Y
Rintala ³⁷ 2005	N	Y	Y	Y
Sauri ³⁸ 2017	N	Y	Y	Y
Siddall ³⁹ 2003	N	Y	Y	Y
Singh ⁴⁰ 2010	Y	Y	Y	Y
Stormer ⁴¹ 1997	Y	Y	Y	Y
Tibbett ⁴² 2019	N	Y	Y	Y
Turner ⁴³ 2001	Y	Y	Y	Y
Vogel ⁴⁴ 2002	N	Y	Y	Y
Warms ⁴⁵ 2002	Y	Y	Y	Y
Wen ⁴⁶ 2013	N	Y	Y	Y
Wollaars ⁴⁷ 2007	Y	Y	Y	Y

Study	Prevalence	95% C.I.	
highrob = n			
Adriaansen 2013	87.05	[80.31: 92.14]	
Adriaansen 2016	63.48	[57.56: 69.10]	
Andresen 2016	73.00	[69.03: 76.71]	-
Barrett 2003	75.00	[64.63: 83.62]	
Craig 2013	92.86	[84.11: 97.64]	
Cruz-Almeida 2005	60.98	[51 77: 69 64]	
Figoni 2015	47.75	[40 23: 55 36]	
Grabber 2015	42.86	[17 66: 71 14]	
Hogholen 2018	94.29	[87.98: 97.87]	
Jain 2010	69.89	159 50 78 971	
Jensen 2005	79 59	[72 17: 85 79]	
Jorgensen 2017	85 37	[77 86: 91 09]	
Kentar 2018	80.93	[77 00: 84 45]	
Khazaeinour 2017	50.00	[41 44: 58 56]	
Kogos 2005	49.43	[43 20: 55 66]	
Michailidou 2018	43.45	[37 16: 50 68]	2 m
Modirian 2010	64.86	[62 10: 67 47]	
New 2016	45 33	[37 20: 53 66]	
Nielsen 2017	32.80	[24 67: 41 77]	
Pintolo 2005	76 15	[71 22: 80 52]	
Sauri 2017	45.85	[71.32, 60.33]	
Siddall 2003	40.00	[42.42, 49.31]	
Singh 2010	42.00	[09.32, 05.10]	
Stormor 1007	42.00	[20.19, 50.79]	
Tibbett 2010	05.09	[02.39, 00.70]	
Turper 2001	95.00	[77.02: 95.07]	
Vagel 2002	62.03	[77.02, 05.74]	
Warma 2002 v1	70.20	[02.35, 75.00]	
Warma 2002 v1	79.30	[75.01, 05.50]	
Wantis 2002 v2	100.00	[09.52, 01.30]	
Wellager 2007	77.06		
Wollaars 2007	11.00	[/1.0/, 01.00]	
Kandom enects model	09.22	[04.02; 74.45]	
Heterogeneity: $I = 9T \gamma_0, \tau = 0$	1.0204, X ₃₀ = 11	J14.31 (D ≤ 0.01)	
highrob = y			
Cragg 2015	62.76	[60.25; 65.22]	-
Cudeiro-Blanco 2017	66.80	[60.63; 72.57]	
Finnerup 2001	77.27	[72.37; 81.68]	
Finnerup 2008	55.44	[48.13; 62.58]	
Finnerup 2016	75.31	[64.47; 84.22]	
Gironda 2004	51.57	[47.71; 55.42]	-
Lamid 1985	43.75	[31.37; 56.72]	
Random effects model	62.07	[51.16; 72.98]	
Heterogeneity: $I^2 = 94\%, \tau^2 = 0$	$0.0204, \chi_6^2 = 95$.34 ($p \le 0.01$)	
Random effects model	67.90	[63.20; 72.59]	i
Heterogeneity: $I^2 = 97\%$, $\tau^2 = 0$	0.0204, $\chi^2_{37} = 1^{\circ}$	181.36 (p < 0.01)	
Residual heterogeneity: $J^2 = 97$	$\%, \chi^2_{36} = 1109$.65 (p < 0.01) 0	20 40 60 80 100 Prevalence of All Pain

Study	Prevalence	95% C.I.	
primarypain = n			1
Cudeiro-Blanco 2017	66.80	[60.63; 72.57]	
Figoni 2015	47.75	[40.23; 55.36]	
Grabher 2015	42.86	[17.66; 71.14]	
Hogholen 2018	94.29	[87.98; 97.87]	
Sauri 2017	45.85	[42.42; 49.31]	-
Random effects model	61.20	[47.77; 74.63]	
Heterogeneity: $l^2 = 99\%$, $\tau^2 =$	$0.0206, \chi_4^2 = 30$	9.53 (p < 0.01)	
primarypain = y			
Adriaansen 2013	87.05	[80.31; 92.14]	
Adriaansen 2016	63.48	[57.56: 69.10]	
Andresen 2016	73.00	[69.03: 76.71]	-
Barrett 2003	75.00	[64.63; 83.62]	÷
Cragg 2015	62.76	[60.25; 65.22]	-
Craig 2013	92.86	[84.11: 97.64]	
Cruz-Almeida 2005	60.98	[51.77: 69.64]	
Finnerup 2001	77.27	[72.37: 81.68]	i - -
Finnerup 2008	55.44	[48.13: 62.58]	
Finnerup 2016	75.31	[64.47: 84.22]	
Gironda 2004	51.57	[47.71: 55.42]	-
Jain 2010	69.89	[59.50: 78.97]	
Jensen 2005	79.59	[72.17: 85.79]	
Jorgensen 2017	85.37	[77.86: 91.09]	
Kentar 2018	80.93	[77.00: 84.45]	-
Khazaeipour 2017	50.00	[41.44: 58.56]	
Kogos 2005	49.43	[43.20: 55.66]	
Lamid 1985	43.75	[31.37: 56.72]	
Michailidou 2018	43.84	[37.16: 50.68]	
Modirian 2010	64.86	[62,19: 67,47]	-
New 2016	45.33	[37.20: 53.66]	
Nielsen 2017	32.80	[24.67: 41.77]	
Rintala 2005	76.15	[71.32: 80.53]	
Siddall 2003	80.82	[69.92: 89.10]	
Singh 2010	42.00	[28.19; 56.79]	
Stormer 1997	65.59	[62.39: 68.70]	-
Tibbett 2019	95.00	[75.13; 99.87]	·
Turner 2001	82.03	[77.82: 85.74]	-
Vogel 2002	68.98	[62.35; 75.08]	
Warms 2002 v1	79.38	[75.01; 83.30]	-
Warms 2002 v2	75.81	[69.52: 81.38]	- -
Wen 2013	100.00	[85.18; 100.00]	
Wollaars 2007	77.06	[71.67; 81.86]	
Random effects model	68.84	[63.79; 73.88]	+
Heterogeneity: $I^2 = 96\%$, $\tau^2 =$	$0.0206, \chi^2_{32} = 83$	37.51 (p < 0.01)	
Random effects model	67.89	[63.17; 72.62]	-
Heterogeneity: $I^2 = 97\%$, $\tau^2 =$	$0.0206, \chi^2_{37} = 1$	181.36 (p < 0.01)	
Residual heterogeneity: I ² = 9	97%, χ ₃₆ ² = 1147.	.04 (p < 0.01) 0	20 40 60 80 100 Prevalence of All Pain

Study	Prevalence	95% C.I.	
traumatic = non			1
Adriaansen 2013	87.05	[80.31: 92.14]	- - -
Adriaansen 2016	63.48	[57,56: 69,10]	- -
Barrett 2003	75.00	[64.63: 83.62]	
Cragg 2015	62.76	[60.25: 65.22]	
Craig 2013	92.86	[84.11: 97.64]	
Cudeiro-Blanco 2017	66.80	[60.63: 72.57]	
Figoni 2015	47.75	[40.23: 55.36]	and the second s
Finnerup 2001	77.27	[72.37: 81.68]	
Finnerup 2008	55.44	[48.13: 62.58]	
Gironda 2004	51.57	[47.71: 55.42]	-
Hogholen 2018	94.29	[87.98: 97.87]	
Jain 2010	69.89	[59.50: 78.97]	
Jensen 2005	79.59	[72.17: 85.79]	
Jorgensen 2017	85.37	[77.86: 91.09]	
Lamid 1985	43 75	[31 37: 56 72]	
Michailidou 2018	43.84	[37 16: 50 68]	
New 2016	45.33	[37,20: 53,66]	
Nielsen 2017	32.80	[24.67: 41.77]	
Rintala 2005	76.15	[71.32: 80.53]	
Sauri 2017	45 85	[42 42: 49 31]	-
Stormer 1997	65.59	[62 39: 68 70]	-
Turner 2001	82.03	[77.82: 85.74]	
Vogel 2002	68.98	[62.35: 75.08]	
Warms 2002 v1	79.38	[75.01: 83.30]	1
Warms 2002 v2	75.81	[69.52: 81.38]	
Wollaars 2007	77.06	[71.67: 81.86]	
Random effects model	67.34	[61.60: 73.09]	
Heterogeneity: $I^2 = 97\%$, $\tau^2 =$	$0.0213, \chi^2_{25} = 88$	39.25 (p < 0.01)	
traumatic = trauma			
Andresen 2016	73.00	[69 03· 76 71]	-
Cruz-Almeida 2005	60.98	[51 77: 69 64]	
Finnerun 2016	75.31	[64 47: 84 22]	
Grabber 2015	42.86	[17 66: 71 14]	
Kentar 2018	80.93	[77 00: 84 45]	
Khazaeipour 2017	50.00	[41.44: 58.56]	
Kogos 2005	49.43	[43.20: 55.66]	
Modirian 2010	64.86	[62.19: 67.47]	
Siddall 2003	80.82	[69.92: 89.10]	
Singh 2010	42.00	[28.19: 56.79]	
Tibbett 2019	95.00	[75.13: 99.87]	
Wen 2013	100.00	[85,18: 100,00]	
Random effects model	69.12	[60,40: 77,83]	
Heterogeneity: $l^2 = 96\%$, $\tau^2 =$	$0.0213, \chi^2_{11} = 20$	30.06 (p < 0.01)	
Random effects model	67.88	[63.08; 72.68]	
Heterogeneity: $I^2 = 97\%$, $\tau^2 =$	$= 0.0213, \chi^2_{37} = 1$	181.36 (p < 0.01)	
Residual heterogeneity: $I^2 =$	97%, χ ₃₆ ² = 1169	.31 (p < 0.01) 0	20 40 60 80 100 Prevalence of All Pain