

Depression Prevalence in Spinal Cord Injury: A Meta-Analysis

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September 25th, 2023

This thesis is submitted in partial fulfilment of the Honours degree of Bachelor
of Psychological Science (Honours).

Word count: 5,947

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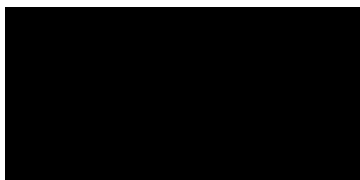
Abstract

Introduction: Estimated rates of depressive disorder following a spinal cord injury (SCI) vary drastically due to measurement differences between studies and variation among individuals' personal characteristics and injuries. **Objectives:** To consolidate research on the point prevalence of depressive disorder among adults (≥ 16 years old) who have sustained a SCI, and to identify study and sample-level factors associated with these estimates. **Methods:** A review of the CINAHL, Embase, PsycINFO, and PubMed databases was conducted to identify studies that used established diagnostic criteria to determine the prevalence of depressive disorder following SCI. Risk of bias was assessed using the JBI Prevalence Critical Appraisal Tool and proportion estimates meta-analysed using a random-effects model. Moderator analyses investigated the impact of methodological characteristics and sample-related attributes on depression prevalence. **Results:** Pooled data with a sample of 57,300 adults with SCI from 16 independent studies indicated the prevalence of depressive disorder was 14%, although the prediction interval spanned from 1 % to 73%. Prevalence estimates were similar regardless of the diagnostic criteria used ($p = .101$), study design ($p = .549$), gender ($p = .583$), injury type ($p = .285$), mean sample age ($R^2 = .38$, $p = .132$) or recruitment year ($R^2 = .00$, $p = .265$). **Discussion:** One in seven adults with SCI is diagnosed with a depressive disorder. This elevated prevalence cannot be solely explained by methodological or sample differences. Future research should prioritize the development of an appropriate screening tool for depression in SCI, with the aim of facilitating routine assessment for early identification and reduction of the negative consequences associated with depression, as well as provide detailed report of both study and sample attributes to increase reporting transparency and offer a thorough understanding of depression prevalence and its associated risk factors within the SCI population.

Keywords: Spinal Cord Injury, Depression, Prevalence

Declaration

“This thesis contains no material which has been accepted for the award of any other degree of diploma in any University, and, to the best of my knowledge, this thesis contains no material previously published except where due reference is made. I give permission for the digital version of this thesis to be made available on the web, via the University of Adelaide’s digital thesis repository, the Library Search and through web search engines, unless permission has been granted by the School to restrict access for a period of time.”



23rd September 2023

Contributor Roles

ROLE	ROLE DESCRIPTION	STUDENT	SUPERVISOR
CONCEPTUALIZATION	Ideas; formulation or evolution of overarching research goals and aims.	X	X
METHODOLOGY	Development or design of methodology; creation of models.	X	X
PROJECT ADMINISTRATION	Management and coordination responsibility for the research activity planning and execution.	X	
SUPERVISION	Oversight and leadership responsibility for the research activity planning and execution, including mentorship external to the core team.		X
RESOURCES	Provision of study materials, laboratory samples, instrumentation, computing resources, or other analysis tools.		X
SOFTWARE	Programming, software development; designing computer programs; implementation of the computer code and supporting algorithms; testing of existing code.		X
INVESTIGATION	Conducting research - specifically performing experiments, or data/evidence collection.	X	
VALIDATION	Verification of the overall replication/reproducibility of results/experiments.		X
DATA CURATION	Management activities to annotate (produce metadata), scrub data and maintain research data (including software code, where it is necessary for interpreting the data itself) for initial use and later re-use.	X	
FORMAL ANALYSIS	Application of statistical, mathematical, computational, or other formal techniques to analyse or synthesize study data.	X	
VISUALIZATION	Visualization/data presentation of the results.	X	
WRITING – ORIGINAL DRAFT	Specifically writing the initial draft.	X	
WRITING – REVIEW & EDITING	Critical review, commentary or revision of original draft		X

Introduction

Background

Spinal cord injuries (SCI), characterised by impairment of the spinal cord, disrupt the bidirectional communications between the brain and the body and lead to enduring perturbations in mobility, sensory perception, and vital physiological processes (Ahuja et al., 2017). Such injuries annually affect 250,000 to 500,000 individuals worldwide (World Health Organization, 2013), with up to 20,800 cases within Australia (SpinalCure Australia, 2020). Whilst SCI is a low prevalence condition, compared to other chronic illness, such as Alzheimer's disease (51.62 million patients worldwide; Li et al., 2022), or Multiple Sclerosis (2.8 million patients worldwide; Multiple Sclerosis Australia, 2023), it imposes substantial personal and economic costs on both the injured individual and the healthcare system (Moreno et al., 2017). Australians living with a SCI carry a lifetime burden of \$18.9 billion AUD, while the economy shoulders a substantial cost of approximately \$74.5 billion AUD, including \$31 billion AUD allocated for personal care and \$19 billion AUD delivered to address the loss of mental well-being in the SCI population (SpinalCure Australia, 2020).

The sociodemographic profile for SCI includes gender and age. A ratio of 4:1 has been documented for traumatic SCI, with men being more susceptible to injuries from motor vehicle accidents, sporting injuries, or falls (Chen et al., 2016). Age distribution presents a bimodal pattern, with the first peak occurring between adolescence and young adulthood (15 to 29 years) and a second peak seen among older age adults (>60 years old) (Singh et al., 2014; World Health Organization, 2013). Among older adults, a rise in non-traumatic SCI from intrinsic pathologies (i.e., neoplastic growths or musculoskeletal disease; Fehlings, 2013) is seen.

SCI brings with it an elevated risk of secondary medical complications, including chronic pain, deep vein thrombosis, spasms, and urinary tract infections (Selzer & Dobkin, 2008). Cognitive deficits, such as memory loss and heightened risk of dementia (Li et al., 2020), have also been noted. Equally concerning is the increased risk of developing a major psychiatric disorder after SCI, particularly depression (Craig et al., 2015; Migliorini et al., 2015; Wan et al., 2020). Up to 74% of SCI patients endorse clinical symptoms of depression at some point during their rehabilitation (Rhemah Al Abbudi et al., 2017). An earlier meta-analysis indicated that the prevalence of depressive disorder after SCI can be as high as 22% (Williams & Murray, 2015), an estimate significantly greater than the global lifetime depression prevalence of 2% - 6% among the general population (Vos et al., 2017).

Various theoretical models have been put forward to explain the onset and influence of depression among SCI patients, more recently the Spinal Cord Injury Adjustment Model; (SCIAM; Craig et al., 2022). According to the SCIAM, a combination of lowered self-efficacy (i.e., appraisals of perceived threat or perceived ability to cope) in response to the physical impairments associated with SCI, and maladaptive coping strategies (i.e., suppression, alcohol abuse) determine overall psychological adjustment (Craig et al., 2022). Individual studies also highlighted the strong relationship between psychological reactions, such as depression, and SCI secondary complications, such as bowel dysfunctions, sexual dysfunction, and pain (Cairns et al., 1996; Sipski, & Richards, 2006). Specifically, depression can reduce motivation for self-management and contribute to inconsistent self-care behaviours or self-neglect which, in turn, lead to elevated physical complications and health care utilization (Craig et al., 2019; Krueger et al., 2013). There is also evidence of “feedback loops”, wherein increased complications after depression may accentuate depression severity (Bombardier et al., 2012; Krueger et al., 2013), ultimately leading to prolonged days in bed and amplifying both financial and psychological burden (Tate et al., 1994).

Methodological considerations in SCI and depression research

Despite consensus regarding the elevated rates of depression in SCI, significant variability in estimates has been reported. Indeed, recent research has cited rates of depression ranging from 1.67% (Chang et al., 2020) to 31.6% (Peterson et al., 2019) and even 43.7% (Frank et al., 1985). This variability may be attributed to diverse research methodologies - namely construct definitions and measurement but also methods of data collection and sample characteristics.

Depression is a heterogenous disorder that includes different subtypes. Most common are Major Depressive Disorder (MDD) and Minor Depressive Disorder. Both subtypes feature a loss of interest or pleasure in activities and/or low mood most of the time, experienced at different intensities (American Psychiatric Association, 2020). There is also Seasonal Affective Disorder (SAD) – which occurs in seasonal patterns, and Persistent Depressive Disorder (PDD) – previously considered a personality disorder due to its pervasive nature (American Psychiatric Association, 2020). To minimize diagnostic heterogeneity in depression, only clinical depression (MDD and minor depression) is considered in the current study.

The two most widely used classification systems for psychiatric diagnoses, the Diagnostic and Statistical Manual of Psychiatric Disorders (DSM) and International Classification of Diseases (ICD), share content overlap but also discrepancies in their symptom focus and thresholds for determining depression severity (Andrews & Slade, 1998). For example, the ICD-10/ ICD-11 requires patients to have two out of the three symptoms (i.e., depressed mood, loss of interest, and reduction in energy), whereas the DSM-IV and DSM-V only focuses on the former two (American Psychiatric Association, 1994, 2013; World Health Organization, 2016, 2019). To date, variation in prevalence rates of depression

based on these two diagnostic systems have not been explored in SCI research, although there is evidence of potential measurement discrepancies in a general community sample with depressive symptoms (e.g., 75% using ICD-10; 90% using DSM-IV; Saito et al., 2010).

Early studies with SCI have also used the Research Diagnostic Criteria (RDC) to diagnose depression; a multidimensional questionnaire developed exclusively for research in psychiatry (Spitzer et al., 1978). Many RCD inclusion criteria map onto the earlier DSM-III (Spitzer et al., 1978). For example, both MDD and minor depression are categorised as clinical depression in the RDC and include core symptoms (depressed mood, loss of interest), alongside cognitive and behavioural symptoms (worthlessness, reoccurring suicidal thoughts, sleep difficulties, sudden weight change, lack of concentration; American Psychiatric Association, 2013; Spitzer et al., 1978). However, successive revisions of the DSM have seen higher depression prevalence estimates likely due to improved diagnostic specificity and sensitivity of depression with the DSM-IV and DSM-V (Williams & Murray, 2015).

The ‘gold standard’ clinical interview to ensure diagnostic adherence to the DSM or ICD is, however, impractical for a large-scale epidemiological study. As such, SCI studies have increasingly used self-report questionnaires to examine depression symptomatology. One notable example is the Beck Depression Inventory (BDI; Beck et al., 1987). However, the BDI may require altered scoring or interpretation given its item overlap with SCI symptoms (e.g., disrupted sleep, reduced energy, weight loss; Kaplakjian et al., 2009; Sakakibara et al., 2009). Similarly, the Depression Anxiety Stress Scales-21 (DASS-21; Lovibond & Lovibond, 1995) includes items that closely correspond to mood disorders, including Major Depressive Disorder, but has poor discriminate validity in SCI (Mitchell et al., 2008; Richards et al., 2006). The risk of socially desirability bias associated with self-reported rating tools also needs to be factored. Indeed, there is evidence that the BDI and

DASS may result in underreporting of true depression prevalence rates in SCI (Hunt et al., 2003).

Study designs may also contribute to the disparity in depression estimates within SCI research. The collection of data in prospective studies typically involves direct observations or questionnaires, whilst data in retrospective studies is often derived from administrative records or healthcare databases (Song & Chung, 2010). Prospective studies offer the advantage of a more comprehensive and specific data collection yet are vulnerable to a high dropout rate. On the other hand, retrospective studies provide immediate access to existing data but come with limitations in controlling data collection, including challenges associated with missing information (Song & Chung, 2010). The contribution of study design to depression estimates in SCI should not be underestimated, with individual studies reporting wide-ranging estimates from 1.67% (Chang et al., 2020) to 28% (Ullrich et al., 2014) based on retrospective data, and 6% (Osteraker & Levi, 2005) to 43.7% (Frank et al., 1985) among prospective designs.

Sample characteristics in SCI and depression research

Sample demographics, such as gender and age, may also confound prevalence estimates. Barbonetti et al. (2017) found that women (53.6%) with SCI are twice as likely as men (25.0%) to be diagnosed with depression, attributing this to the general proneness of females to depression (Parker & Brotchie, 2010). However, Williams and Murray (2015) did not observe a gender-based impact on depression prevalence in their meta-analysis. While for age, Lim et al. (2017) indicated that older age is associated with higher rates of depression, potentially due to the worsened physical functioning and increased complications (Alschuler et al., 2013). Yet, other studies demonstrated no significant impact of chronological age on depression prevalence (Khazaeipour et al., 2015).

Similarly, injury profiles could lead to variation in prevalence estimates. The time since SCI injury has a profound impact on depression rates (Bonanno et al., 2012). Individuals with SCI tend to experience higher levels of depression six months after injury when compared to six to eight weeks post-SCI (Craig et al., 2017). This change can be attributed to the transition from inpatient rehabilitation to community living, which often corresponds to reduced professional support and a greater need for self-management (Craig et al., 2017). Notably, previous longitudinal studies covering a span of two years post-injury document stable trajectories post SCI, with 87% showing a steady decline in depression and the remaining 13% experiencing a delayed onset of depression (Bonanno et al., 2012). Less clear is the role of other injury characteristics, particularly injury level (paraplegia vs tetraplegia). Although there is evidence that injury level does not influence depression rates post-SCI (Craig et al., 2015; Williams & Murray, 2015), a positive association between increased depression and SCI severity has also been demonstrated (e.g., Lim et al., 2017). There remains a need to consolidate these data.

Current study

In sum, the interpretation of depression prevalence in SCI necessitates careful consideration of both methodological (i.e., diagnostic criteria, study design) and sample (i.e., age, gender, injury type) disparities. This study extended on an earlier systematic review (Williams & Murray, 2015) to consolidate current data on point-in-time prevalence of depressive disorder in SCI using a comprehensive meta-analytic approach. Given the potential for measurement variations, the present review only considered studies which adhered to established and validated diagnostic criteria (Kalpakjian et al., 2009). A secondary aim was to pinpoint and reassess possible sources of methodological and sample variation associated with prevalence estimates.

Methods

Literature search

Following submission of a review protocol on 15th May 2023 (see Appendix I), a search of the CINAHL, EMBASE, PsycINFO, and PUBMED electronic databases was conducted to identify studies that reported the prevalence of depression following SCI. A list of search terms related to SCI (e.g., “spine injury”, “spinal cord laceration”, “tetraplegia”) and depression/general psychopathology (e.g., “depress”, “depressive disorder”, “mental illnesses”, “psychological adjustment”) were developed in consultation with an expert research librarian (see Appendix II). Databases were comprehensively searched from inception until June 30th, 2023.

Study eligibility criteria

Included studies involved an adult population (≥ 16 years, in accordance with the international cut-off age of 15 or below for paediatric SCI populations; Parent et al., 2011) with a clinically diagnosed traumatic or non-traumatic SCI. Studies also needed to measure depression using well-established diagnostic criteria (i.e., DSM, ICD, RCD). Eligible diagnoses included Major Depressive Disorder (MDD), Dysthymic Disorder (DD), Depressive Disorder Not Otherwise Specified (NOS), Major Depressive Episode (MDE), and Minor Depression. Only studies with an observational design, either prospective (e.g., survey) or retrospective (e.g., medical record audit), were eligible. Cross-sectional and longitudinal studies were included, given that the latter provided baseline data for point-in time prevalence of depression. Lastly, all studies were peer-reviewed with full texts available in English.

Studies were excluded if the population was demographically selective (e.g., females only, those with post-partum depression), as this type of sampling does not render

representative data. Studies which used self-report measures to screen for depression symptom severity were also excluded given that such measures are not indicative of a clinical diagnosis (Brennan et al., 2010; Subica et al., 2014). Similarly, studies using questionnaires that were not psychometrically validated with SCI (Kalpakjian et al., 2009), assessed lifetime prevalence of depression (which is vulnerable to recall bias; Kruijshaar et al., 2005; Wenze et al., 2012), or did not provide the data separately for depressive disorders were ineligible. Finally, review papers and grey literature (e.g., dissertations, government documents, conference proceedings) were excluded as the focus was on primary data that had been peer-reviewed.

Study selection

Records identified from the electronic search were uploaded to Covidence software for systematic reviews (Veritas Health Innovation, Melbourne, 2023) by the student researcher. Duplicates were automatically removed by Covidence and titles and abstracts then screened for a further full-text review. To ensure accuracy of the screening process a random sample of 100 full-text studies were screened by an independent psychology student with excellent agreement ($\kappa = .94$). The few disagreements were resolved by consensus discussion.

Data collection and extraction

This review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA; Page et al., 2020) guidelines. Information was extracted by the student researcher and reviewed by a senior researcher. Extracted data included: study characteristics (e.g., citation details, study design, setting, depression measurement), sample characteristics (e.g., sample size, demographics), SCI details (e.g., mean time since diagnosis) and effect size data in the form of proportions (i.e., number of participants meeting the diagnostic threshold for depression).

Risk of bias evaluation

The reporting quality of included studies was evaluated using The Joanna Briggs Institute Prevalence Critical Appraisal Tool (Munn et al., 2014) (see Appendix II). This 9-item checklist assesses the internal and external validity of prevalence studies based on sampling, measurement, and statistical methods (Munn et al., 2014). Each item was rated as “yes,” “no,” “unclear,” or “not applicable”. The percentage of studies that met each rating was also calculated.

The following equation was used to determine adequate sample size due to its robustness in medical or prevalence research (Pourhoseingholi et al., 2013):

$$n = \frac{Z^2 P(1 - P)}{d^2}$$

where n is the sample size, Z is the statistic for a level of confidence (set at 1.96 with $\alpha = 0.05$), $P = 22.2\%$ (the expected prevalence; based on a previous meta-analysis of depression prevalence in SCI; Williams & Murray, 2015) and d is precision (set at 0.05). Using this formula, a minimum sample size of 266 was considered as a sufficiently powered study.

Statistical analyses

Effect size data were entered into the Comprehensive Meta-Analysis (CMA) Software for statistical analysis (Version 4, Biostat Inc). The point prevalence of depression (proportion) from each study was weighted by its inverse variance to obtain a pooled estimate (Borenstein et al., 2009) – thereby ensuring that studies with a smaller variance (i.e., larger N) would be given a greater weighting due to their higher robustness and reliability. Confidence intervals were also calculated for each prevalence estimate and visually displayed using forest plots. Publication bias was then assessed using the Doi plot, developed using MetaXL software version 5.3 for Windows (www.epigear.com) The latter plots each study’s effect

size against the Z-score, providing a more robust visual assessment of asymmetry than the traditional funnel plot (Furuya-Kanamori et al., 2018). Asymmetry was then quantified with the Luis Furuya-Kanamori (LFK) index; the closer the LFK index to zero, the more symmetrical the plot.

To address between-study heterogeneity, Tau-squared (τ^2), the variance of the true effects, and I^2 , the proportion of the variance of true effects that accounted for the total observed variance, were calculated. Given that I^2 is not too discriminative in systematic reviews of prevalence (Migliavaca et al., 2020), prediction intervals, which represent the expected range of true effect estimates expected in the broader SCI literature (int Hout et al., 2016) were additionally reported.

A random-effects model was deemed appropriate for these analyses, given the variation in recruitment strategies, sampling errors and depression measurement in addition to the clinical heterogeneity of SCI (Borenstein et al., 2009). For ease of data interpretation, effect sizes were initially grouped by depression measurement tool. Further subgroup analyses and meta-regressions were then conducted to examine the possible association between study methodology (i.e., diagnostic classification system, data extraction method, recruitment year) on depression prevalence and sample characteristics (i.e., gender, mean age, injury type).

Results

Study selection

A total of 10350 studies were identified through the electronic database searches (see Figure 1). Following removal of duplicates, 6105 studies were screened based on their titles and abstracts, resulting in 2538 full-text reports which were re-assessed against the exclusion criteria. During the screening process, the samples from four studies (Judd et al., 1989; Judd et al., 1991; Kishi et al., 1994; Kishi et al., 1995) were identified as overlapping and merged into two, to ensure data independence. The most representative study was selected – namely the most recent publication (Kishi et al., 1995) or the study with the largest sample size (Judd et al., 1989). The final sample resulted in a total of 16 observational studies.

Study characteristics

The final sample of 16 studies included data for 57,300 adults with SCI sourced from five countries: United States, Australia, Japan, Sweden, and Taiwan (see Table 1). Publication dates spanned the last 42 years (from 1981 to 2020). Six studies sourced their data from retrospective reviews of medical, government or insurance records (Chang et al., 2020; Matsuda et al., 2016; McDonald et al., 2018; Ullrich et al., 2014; VanDerwerker et al., 2020; Weeks et al., 2011). The remaining studies adopted a prospective design, with participants recruited from specialist SCI units and general inpatient rehabilitation centers (Bombardier et al., 2012; Craig et al., 2015; Fullerton et al., 1981; Mitchell et al., 2008; Osteraker & Levi, 2005; Radnitz et al., 1997), as well as acute hospital settings (Howell et al., 1981; Judd & Brown, 1992; Judd et al., 1989; Kishi et al., 1995). In particular, two studies provided baseline prevalence data from longitudinal datasets (Craig et al., 2015; Kishi et al., 1995).

Sample characteristics

The pooled sample had a mean age of 58 years ($SD = 6.60$, range = 16 to 90) and 47% were male, although studies did not routinely provide these data (see Table 1). Participants had been diagnosed with paraplegia (39%) or tetraplegia (61%), with both recent onset and chronic injuries represented (mean time since injury: 12.78 years, range = 1.20 months to 17 years). Additional details related to aetiology (traumatic and non-traumatic), lesion completeness, and the diagnostic criteria for SCI were either missing or not consistently reported. Socio-contextual information (educational level, income level, marital status) were also not consistently provided. Nine studies included individuals that had been prescribed with antidepressants during data collection (Chang et al., 2020; Craig et al., 2015; Fullerton et al., 1981; Matsuda et al., 2016; McDonald et al., 2018; Osteraker & Levi, 2005; Ullrich et al., 2014; VanDerwerker et al., 2020; Weeks et al., 2011).

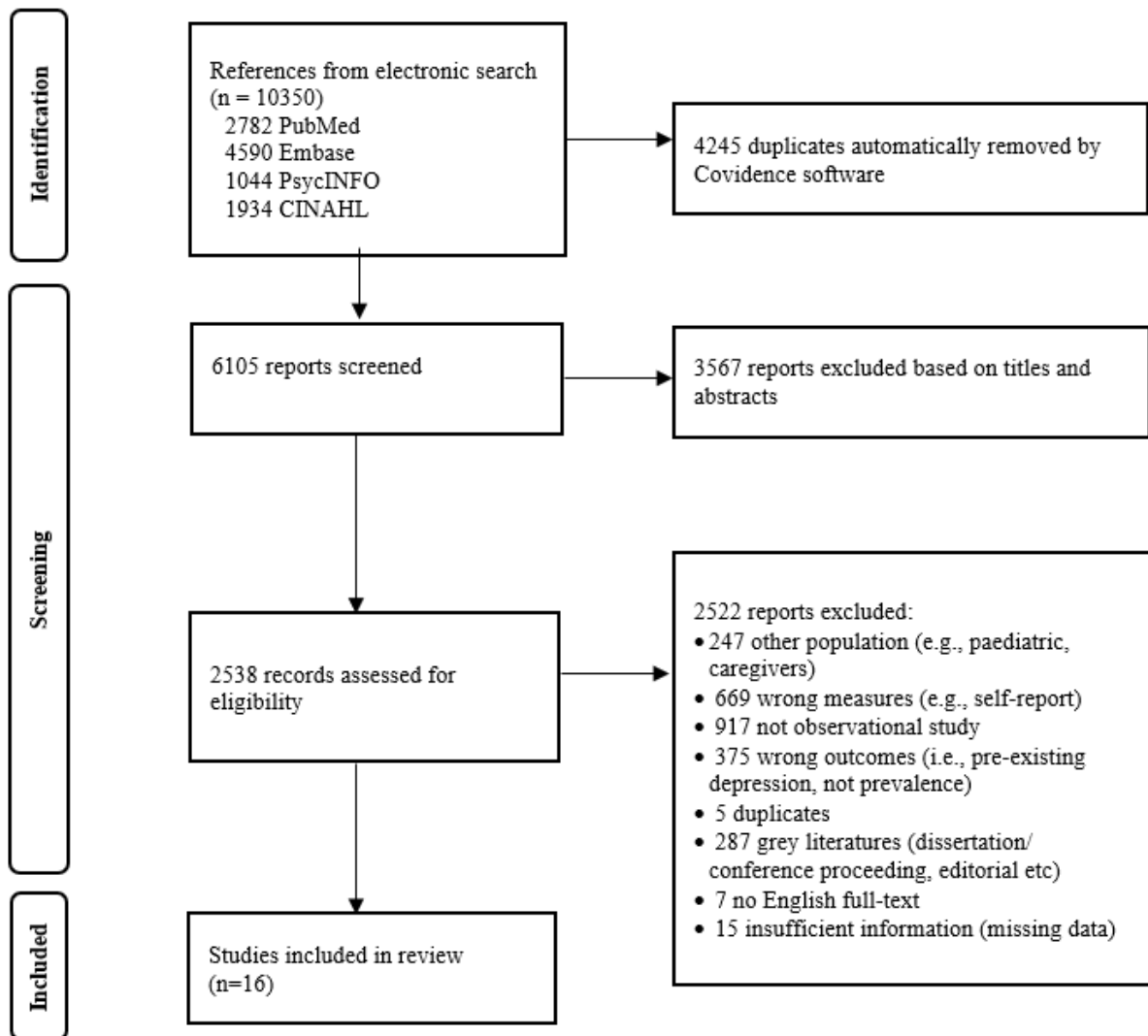
Figure 1*PRISMA Flowchart of the Study Selection Process*

Table 1*Summary of Included Studies*

Lead author (date)	Study characteristics			N	Sample characteristics		SCI details	
	Country	Design	Setting		Male : Female	Mean age (SD)	Type	Time since injury
Bombardier et al. (2012)	U.S.	Observational	Rehabilitation	142	78.2% : 21.8%	42.2 (16.6)	Paraplegia: 33.1% Tetraplegia: 66.9%	N.S.
Chang et al. (2020)	Taiwan	Retrospective	Database	11225	34.9% : 65.1%	59.7 (19.0)	N.S.	N.S.
Craig et al. (2015)	Australia	Observational	Rehabilitation & Community	88	70.5% : 29.5%	42.6 (17.8)	Paraplegia: 61% Tetraplegia: 39%	N.S.
Fullerton et al. (1981)	U.S.	Observational	Rehabilitation & University	30	90% : 10%	27.5 (N.S.)	Paraplegia: 50% Tetraplegic: 50%	1.33 years (5.14)
Howell et al. (1981)	U.S.	Observational	Hospital	22	86.4% : 13.6%	22.7 (N.S.)	Tetraplegic: 54.5% Quadriplegic: 45.5%	36.4 days (N.S.)
Judd & Brown (1992)	Australia	Observational	Hospital	227	81.9% : 18.1%	34.2 (15.9)	Paraplegia: 59.9% Tetraplegic: 40.1%	N.S.
Judd et al. (1989)	Australia	Observational	Hospital	71	73.2% : 26.8%	31.4 (N.S.)	Paraplegic: 57.7% Tetraplegic: 42.3%	N.S.
Kishi et al. (1995)	U.S.	Observational	Hospital	60	N.S.	N.S.	N.S.	N.S.
Matsuda et al. (2016)	Japan	Retrospective	Database	2266	75.6% : 24.4%	62.4 (17.8)	N.S.	N.S.
McDonald et al. (2018)	U.S.	Retrospective	Database	280	96.1%: 3.9%	58.13 (13.02)	Paraplegia: 41.4% Tetraplegia: 58.6%	16.94 years (13.30)
Mitchell et al. (2008)	Australia	Observational	Rehabilitation	40	75% : 25%	49.1 (16.7)	Paraplegia: 65% Tetraplegia: 35%	9.49 years (12.52)
Osteraker & Levi (2005)	Sweden	Observational	Rehabilitation	36	78% : 22%	40 (N.S.)	Paraplegia: 61% Tetraplegia: 39%	3 months (N.S.)
Radnitz et al. (1997)	U.S.	Observational	Rehabilitation	124	N.S.	48.8 (13.7)	Paraplegia: 41.8% Tetraplegia: 57.3%	13.1 years (N.S.)
Ullrich et al. (2014)	U.S.	Retrospective	Database	41213	N.S.	N.S.	N.S.	N.S.
VanDerwerker et al. (2020)	N.S.	Retrospective	Database	1409	67.9% : 32.1%	43.29 (15.33)	Paraplegia: 31.7% Tetraplegia: 68.3%	N.S.
Weeks et al. (2011)	N.S.	Retrospective	Database	67	61.2% : 38.8%	65.51 (N.S.)	N.S.	N.S.

Abbreviations. SCI: spinal cord injury; N: sample size; SD: standard deviation; U.S.: United States; N.S.: not specified

Assessment of depression in SCI

Most studies relied on the DSM to diagnose depression (Bombardier et al., 2012; Craig et al., 2015; Judd & Brown, 2002; Judd et al., 1989; Kishi et al., 1995; McDonald et al., 2018; Osteraker & Levi, 2005; Radnitz et al., 1997), or a combination of the DSM and ICD classification systems (Chang et al., 2020; Mitchell et al., 2008). Only two studies used the Research Diagnostic Criteria (RDC; Fullerton et al., 1981; Howell et al., 1981), with ICD employed in the remaining studies (see Table 2). Prospective data were obtained using semi-structured interview guides, administered by psychologists, psychiatrists, or trained research assistants, to provide an objective evaluation of depressive symptoms. Examples included: the Structured Clinical interview for DSM-III/IV (Bombardier et al., 2012; Judd et al., 1989; Radnitz et al., 1997) (SCID; First & Gibbon, 2004; Spitzer et al., 1990), the Mini International Neuropsychiatric Interview (Craig et al., 2015; Mitchell et al., 2008) (MINI; Sheehan et al., 1998), Schedule for Affective Disorders and Schizophrenia (Fullerton et al., 1981; Howell et al., 1981) (SADS-L; Endicott & Spitzer, 1978), and the Present State Examination (Kishi et al., 1995), which evaluates symptoms associated with 17 psychological states, including depression (Wing et al., 1974).

Risk of bias assessment

Quality ratings for each independent study are summarized (see Appendix III) and between-study ratings are graphically presented in Figure 2. Overall, there was a moderate risk of bias across the 16 studies. Internal validity was a methodological strength, primarily attributed to the stringent inclusion criteria employed for this review. Specifically, the use of standardised diagnostic criteria to diagnose depression (criterion 6b: 100% met) was rigorously adhered to. Statistical analyses were also highly appropriate as all studies provided point prevalence estimates of depressive disorder (criterion 8: 100% met). Most studies also

described their samples in some detail (criterion 4: 94% met), thereby facilitating comparison with the broader SCI population.

Table 2

Depression Diagnostic Criteria used by Included Studies

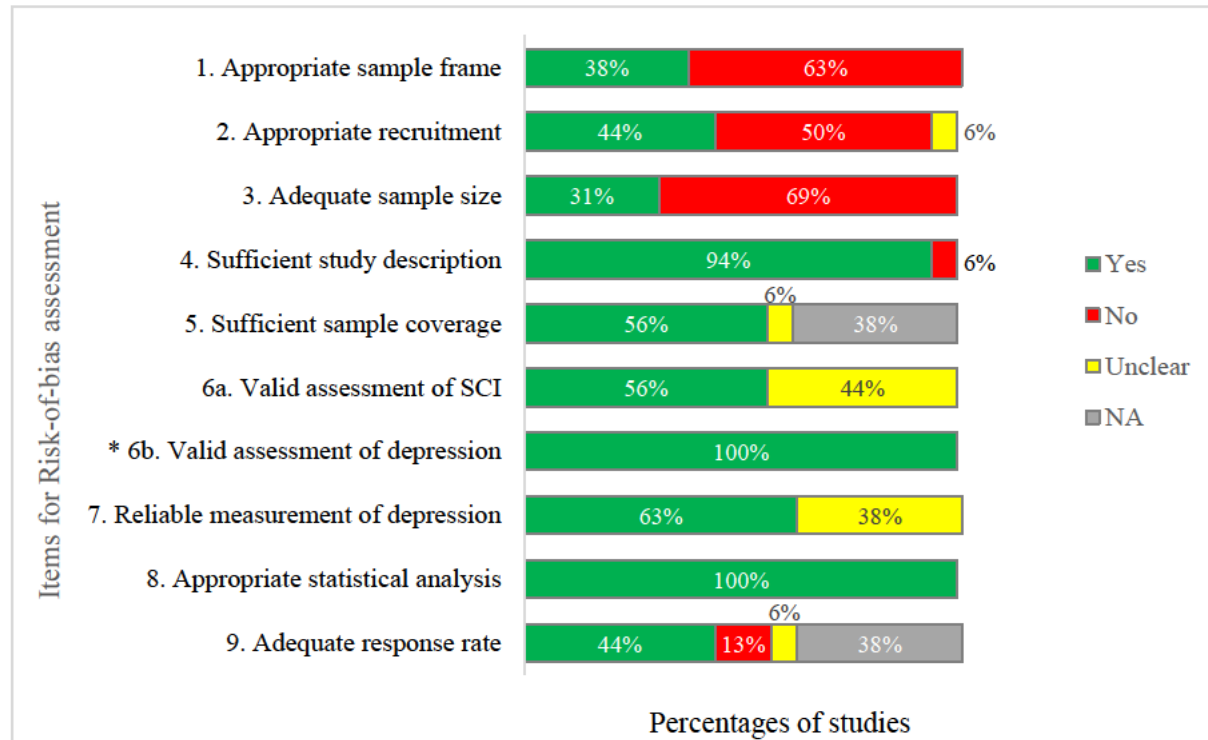
Lead author (date)	Criteria	Diagnosis (definition of depression)
Bombardier et al. (2012)	DSM-IV	Depressive Disorders (major)
Chang et al. (2020)	DSM-IV ICD-9	Major Depression Disorder (MDD)
Craig et al. (2015)	DSM-IV	Depressive disorders (major), including depression caused by a medical condition or substance use
Fullerton et al. (1981)	RDC	Major and Minor Depression
Howell et al. (1981)	RDC	Major and minor depression
Judd & Brown (1992)	DSM-III	Major Depressive Episode (MDE)
Judd et al. (1989)	DSM-III	Major Depressive Disorder (MDD)
Kishi et al. (1995)	DSM-III	Major and minor depression
Matsuda et al. (2016)	ICD-10	Depressive episodes Major Depressive Disorder (MDD, recurrent)
McDonald et al. (2018)	DSM-IV	Depressive Disorders
Mitchell et al. (2008)	DSM-IV ICD-10	Major Depressive Episode (MDE) Dysthymia Disorder (DD)
Osteraker & Levi (2005)	DSM-IV	Major Depressive Episode (MDE)
Radnitz et al. (1997)	DSM-III	Major Depressive Episode (MDE)
Ullrich et al. (2014)	ICD-9	Major Depressive Disorder (MDD) Dysthymic Disorder (DD) Depressive Disorder Not Otherwise Specified (NOS)
VanDerwerker et al. (2020)	ICD-9	Major Depressive Disorder (MDD)
Weeks et al. (2011)	ICD-9	Major Depressive Disorder (MDD, recurrent) Depressive Disorder Not Otherwise Specified (NOS)

Abbreviations. DSM: Diagnostic and Statistical Manual of Mental Disorders; ICD:

International Classification of Diseases; RCD: Research diagnostic criteria

Figure 2.

Percentages of the Included Studies Meeting Each Criterion from the Joanna Briggs Institute Critical Appraisal Checklist for Studies Reporting Prevalence Data (Munn et al., 2014)



* Eligibility criterion in the current meta-analysis

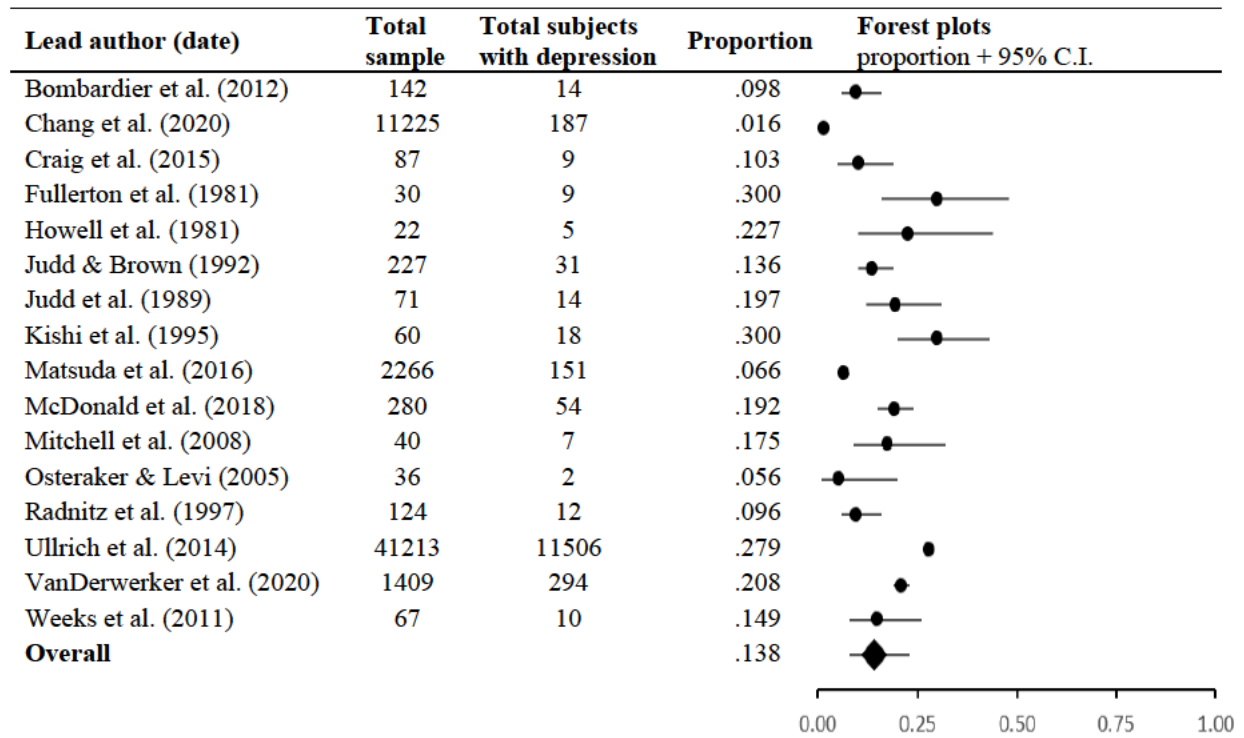
However, the risk of bias assessment also highlighted significant threats to external validity. Studies predominantly used convenience samples (criterion 2: 50% not meet) or sample frames that failed to accurately represent the SCI population (criterion 1: 63% not met), limiting the generalisability of the pooled findings. Additionally, a substantial portion of studies were underpowered ($N > 266$; as per Pourhoseingholi et al., 2013, criterion 3: 69% not met). The validity of SCI assessment (criterion 6a, 44% unclear), and the assessors' (researchers') qualifications to determine the reliability of depression diagnosis (criterion 7; 38% unclear) were also unclear. Similarly, the occurrence of coverage bias (i.e., inconsistent response rate between a sample's subgroups (criterion 5), and the overall response rate

(criterion 9), could not be determined from the few studies which retrospectively analysed data obtained from medical or insurance records (Chang et al., 2020; Matsuda et al., 2016; McDonald et al., 2018; Ullrich et al., 2014; VanDerwerker et al., 2020; Weeks et al., 2011).

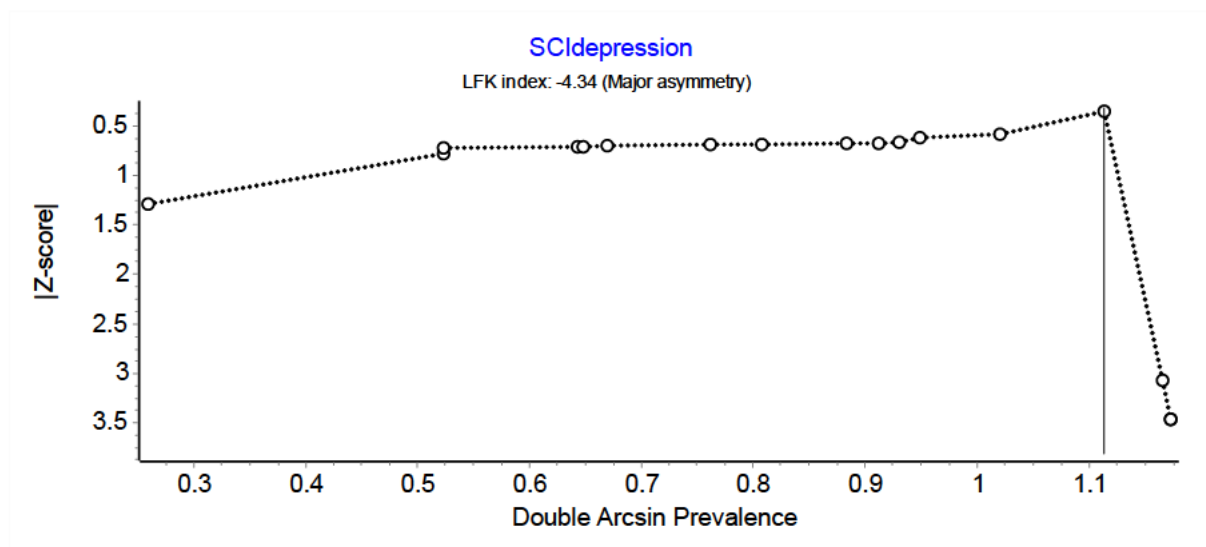
Overall prevalence of depression in SCI

The pooled overall prevalence estimate for depressive disorder across the 16 studies was 14% (95% CI [8%, 23%]), although the prediction interval suggested that the true population prevalence lay within the range of 1% to 73% (see Figure 3). Substantial between-study heterogeneity was noted ($\tau^2 = 1.636$ log units, $I^2 > 90\%$). Smaller N studies, in particular, were characterised by imprecise prevalence estimates with large confidence intervals (i.e., Fullerton et al., 1981; Howell et al., 1981).

A one-study removed analysis indicated the absence of statistical outliers; no single study contributed a disproportionate amount to the overall pooled prevalence estimate. The Doi plot did, however, suggest gross evidence of publication bias with major asymmetry (see Figure 4), with studies spreading out towards the left (LKF index of -4.34).

Figure 3*Forest Plot of the Effect Sizes*

Abbreviation: C.I.: Confidence Interval

Figure 4*Publication Bias assessed by Doi Plot and LFK Index*

Subgroup analyses

Within group data for key methodological, demographic and injury characteristics are summarised in Table 3. Depression prevalence estimates were similar, regardless of the diagnostic criteria used (DSM or ICD) ($Q_B [1] = 6.221, p = 0.101$), or data extraction method (prospective data via interview vs. retrospective data via database records) ($Q_B [1] = 0.360, p = 0.549$). Estimates were also similar among the few studies that provided data separately for gender ($Q_B [1] = 0.301, p = 0.583$), and injury type ($Q_B [1] = 1.142, p = 0.285$).

Meta-regressions

A series of univariate meta-regressions did not identify any statistically significant covariates. Neither the mean sample age ($R^2 = .38, p = .132$) nor the year of recruitment ($R^2 = .00, p = .265$) explained the variance in effect sizes. Scatterplots for these regression models are provided in Appendix V.

Table 3*Subgroup Analysis Examining Methodological, Demographic and Injury Variables*

Variable	<i>k</i>	Prevalence (%)	95% CI		PI		Heterogeneity	
			Lower	Upper	Lower	Upper	<i>I</i> ²	<i>Tau</i> ²
Diagnostic criteria								
DSM	8	14.6	10.7	19.6	5.4	33.9	71.2	0.17
ICD	4	16.0	8.1	29.0	0.5	88.2		0.58
DSM/ICD	2	5.5	0.5	40.8	NA	NA		3.11
RCD	2	27.1	16.7	40.7	NA	NA		0.00
Data extraction								
Prospective -Interview	10	15.7	11.5	21.1	5.7	36.7	66.4	0.21
Retrospective - Records	6	11.6	4.2	28.2	0.2	88.6		1.85
Gender								
Female	5	10.4	3.4	27.9	0.2	89.1	98.2	4.83
Male	5	10.1	3.4	26.0	0.1	90.1		1.22
Injury Type								
Paraplegia	5	17.6	12.7	23.7	NA	NA	0.00	0.00
Tetraplegia	5	21.8	16.8	27.8	NA	NA		0.00

Abbreviations. *k* = number of studies included for calculation; 95% CI: 95% confidence interval;

DSM: Diagnostic and Statistical Manual of Mental Disorders; ICD: International Classification of Diseases; NA: Not Applicable; PI: prediction interval; RCD: Research diagnostic criteria;

*Tau*² = estimated variance of the true effect

Notes. P.I. is not provided when there is minimal heterogeneity across studies.

Discussion

The present meta-analysis consolidated data from 16 observational studies spanning a 43-year period to estimate the prevalence of depressive disorder within the global SCI population. The mean prevalence of depressive disorder estimated in this review (14%) is notably lower than the reported prevalence in an earlier meta-analysis (22%; Williams & Murray, 2015). This discrepancy can be attributed to the inclusion of non-peer-reviewed studies (i.e., doctoral dissertation), and studies reliant on self-reported depressive symptomatology. It is crucial to underscore that the current meta-analysis did not identify study-level moderators that may influence prevalence estimates – specifically, *diagnostic criteria, methods of data extraction, gender, and SCI type*. Limited data also hampered the interpretation of additional socio-contextual factors (i.e., marital status, educational level, race, time since injury and lesion level), which are known to impact on depression in SCI (Arango-Lasprilla et al., 2011; Kaur et al., 2022; Khazaeipour et al., 2015; Krause et al., 2000; Lim et al., 2017).

Furthermore, the current findings were characterised by significant between-study heterogeneity in prevalence estimates (ranging from 1% - 73%), indicating imprecision in the estimates. This finding is perhaps expected given the heterogeneity of depression (Migliavaca et al., 2020), especially within a clinical population such as SCI (Gupta et al., 2019). The current results do, however, need to be interpreted carefully due to the presence of publication bias, which generally leads to an overestimation of effect sizes and the dissemination of false-positive results (Rothstein et al., 2005).

Methodological characteristics and depression in SCI

Comparable depression prevalence rates were observed regardless of the diagnostic criteria utilized, further affirming diagnostic concordance or at least overlap in depression

definition between DSM and ICD (Andrews & Slade, 1998; Lopez Ibor et al., 1994). That is, the diagnosis of clinically significant depression in DSM and ICD involves similar symptoms (e.g., depressed mood or loss of interest, increased fatigue, disrupted sleep etc) and duration (i.e., symptoms persisting for at least 2 weeks; Andrews & Slade, 1998). Notably, both the DSM and ICD do not account for the overlap of physical signs and symptoms between MDD and SCI (Kalpakjian et al., 2009), eventually leading to a similar depression rate measured. Whilst a substantially high depression rate (27.1%) was noted based on RDC diagnosis, no firm conclusions can be drawn about the RDC given that this analysis was underpowered.

Depression prevalence estimates were also high irrespective of the study design. Rates derived from prospective clinical interviews (15.7%) aligned closely with those extracted from retrospective reviews of large databases (11.6%). It is argued that prospective studies have superior accuracy in data collection compared to retrospective medical records, due to fewer instances of missing data (Nagurney et al., 2005). Despite this advantage, retrospective studies in this study (Chang et al., 2020; Matsuda et al., 2016; McDonald et al., 2018; VanDerwerker et al., 2020), included more robust sample sizes (≥ 266) than the prospective studies ($N = 22$ to 227). This discrepancy in sample size led to reduced statistical power and, potentially, an overestimation of depression prevalence based on prospective data alone (Serdar et al., 2021).

Interestingly, the recruitment years spanning four decades did not significantly affect depression prevalence in the SCI population. This finding aligns with the consistently elevated depression rates reported in studies encompassing participants recruited during the years 1994 to 2014 (Lim et al., 2017). Despite the advancements in diagnostic accuracy (Williams & Murray, 2015), as well as improvements in study design and reporting quality since the 1980s, depression remains highly prevalent within the SCI population, irrespective of changes in study designs (i.e., sample size, sampling methods, diagnostic criteria) or

sample characteristics (i.e. age, injury profiles) across studies. This finding underscores the chronic and pervasive nature of depression in the SCI population (Arango-Lasprilla et al., 2011; Kennedy & Rogers, 2000). That said, this study lacked studies conceptualising depression using the current DSM-5 criteria, highlighting the need for further research to employ the most updated diagnostic criteria (i.e., DSM-5, ICD-11) to shed light on potential shift or time trends by meta-analysing depression prevalence estimates from longitudinal studies.

Sample characteristics and depression in SCI

The absence of disparity in the prevalence of depression between males (10.1%) and females (10.4%) also contradicted a substantial body of cross-sectional research highlighting higher depression rates among females with SCI (Khazaeipour et al., 2015; Krause et al., 2000; Sauri et al., 2017), a trend commonly attributed to the higher vulnerability to depression in women than in men (Fann et al., 2011). There are some evidence of comparable depression rates between males and females with SCI (Bombardier et al., 2004, as cited in Khazaeipour et al., 2015), albeit without explanatory insights. The data in this review were, however, based on a sample which comprised of 47% male – potentially reflecting the increased incidence of traumatic SCI seen among females (McCaughey et al., 2016). Further population-based studies investigating the potential role of diverse racial groups and time since injury can better elucidate the complex relationship between gender and depression in SCI. In an early study, Krause et al. (2000) underscored the importance of considering the higher risk of depression faced by minority women, even after controlling for their level of education and income. The odds of developing a depressive disorder among females with SCI also appears to increase over time, with an elevated diagnosis seen among females at 5 years post-injury, but not at 1-year post-injury (Arango-Lasprilla et al., 2011).

Depression prevalence estimates between SCI patients with paraplegia and tetraplegia were also comparable in the present review. Previous research has typically attributed depression post-SCI to the limited physical abilities and increased dependency on others seen in tetraplegic patients (Gioia et al., 2006; Khazaeipour et al., 2015). Notably, Khandelwal et al. (2022) identified higher depression rates among individuals with paraplegia and incomplete injuries, although their findings were limited by an inadequate sample size ($N = 49$). Nonetheless, this finding highlights the need for further research to not only report but also examine key sample parameters such as SCI type and lesion completeness.

Depression in SCI also remained unaffected by chronological age, consistent with the findings of Khazaeipour et al. (2015) and Migliorini et al. (2008). Where positive correlations between depression rates and age have been reported (e.g., Krause et al., 2000; Lim et al., 2017), these correlations have often been explained by the decline of physical functioning and elevated complications in SCI symptoms typically seen with increased aged (Alschuler et al., 2013). However, a U-shaped association might also be present, whereby middle-aged individuals with SCI exhibit the highest depression rates compared to younger or older peers. This could be due to a large disparity between actual level of functioning and high-performance expectations, from society, in middle age (Alschuler et al., 2013). Nonetheless, the finding of this meta-analysis confirms the complexity of chronologic age as a construct. Age has always acted as a proxy, if not, directly affected by the time since SCI injury (Krause et al., 2000). Past research has shown that depression levels decline over time since injury, from 12% at 1-year post-SCI to 10% at 5-years post injury (Arango-Laprillaa et al., 2011), speculating that individuals with SCI needed time to reorganize their values and perceptions of themselves as to cope and accept their new status (Decker & Schulz, 1985).

Clinical implications and future directions

This study marks a significant milestone in SCI research, being the first review to strictly require depression diagnosis based on the “gold standard” clinical interview and involving a sample of over 40,000 adults with SCI. The findings highlight the elevated depression rates in SCI patients with diverse characteristics (age, gender, injury type), in different settings (community, rehabilitation, or hospital), and at varying time points post injury (Arango-Lasprilla et al., 2011), underscoring the urgent need for early, accurate and routine assessment of depression among SCI patients.

Early detection of depression allows for timely treatment, mitigating potential adverse impacts associated with a diagnosis of MDD (Cacheda et al., 2019; Picardi et al., 2016) - including prolonged rehabilitation length of stay, compromised physical and functional recovery, increased pain (Fann et al., 2011), and sleep disruptions (Craig et al., 2022). To date, however, mental health resources to recognise and treat depression in SCI populations remain limited. A mere 34% depressed individuals with SCI receive antidepressant treatment or counselling, not accounting for those who resist depression assessments due to stigma (Fann et al., 2011). There remains a need to increase mental health resources to facilitate routine depression assessment across the spectrum of SCI care (Craig et al., 2015; Migliorini et al., 2015; Williams & Murray, 2015).

However, clinical interviews, while effective, are inherently time-consuming and resource-intensive in mental health practices. Thus, a pressing need for a rapid yet accurate screening tool arises. One potential tool, which incorporates DSM-IV depression diagnostic criteria into a brief self-report tool, is the Patient Health Questionnaire-9 (PHQ-9; Kroenke et al., 2001). PHQ-9 is selected as the depression screening tool with highest diagnostic accuracy and feasibility of implementation among SCI populations in the recent systematic review (Titman et al., 2019). However, studies in the general and SCI population, have not been consistent in reporting cut-off scores to determine depression “caseness” based on the

PHQ-9 (e.g., Bombardier et al., 2012; Manea et al., 2012; Titman et al., 2019). This highlights a need for further research to validate and calibrate the PHQ-9 with different cut-off scores and in different settings of the SCI population.

Methodological considerations

The current meta-analysis demonstrated several methodological strengths, particularly in terms of high internal validity. The selected studies were carefully chosen through stringent inclusion criteria, excluding studies that lacked robust measurements (i.e., does not use clinical interviews for diagnosing clinical depression, inaccurate use of statistical methods). Moreover, this study adhered to contemporary guidelines for analysis and results reporting. Notably, a Doi plot was used instead of the traditional funnel plot analysis, a deliberate choice based on its proven robustness in visual assessment of publication bias (Furuya-Kanamori et al., 2018). Furthermore, this study reported prediction intervals, representing the range wherein the true values were likely to lie, alongside with I^2 to elucidate between-study heterogeneity (int Hout et al., 2016; Migliavaca et al., 2022).

Despite these notable contributions, methodological limitations were encountered during data extraction, affecting the external validity. The overemphasis on SCI studies within developed countries (i.e., United States, Australia) and the absence of studies from low and middle-income countries raise concerns about the applicability of prevalence estimates to the global SCI population. Moreover, the sex ratio in the current study was 1:1 (male to female), which was not representative of the male-dominated SCI population (Lee et al., 2014). Convenience sampling, rather than rigorous random sampling procedures, was also adopted in most studies which further diminished the generalizability of the findings to the broader SCI population. The presence of publication bias further emphasises the need for

careful interpretation of study outcomes. Future observational studies can address these limitations by enhancing their sample size and by adopting random sampling approaches.

Additionally, study-level variables regarded as potential sources of variation in depression estimates among SCI – namely, time since injury, patient demographics (i.e., race, employment, and educational level), and injury characteristics (i.e., completeness of lesion) were inconsistently reported across studies. Unfortunately, this crucial information was often absent, particularly within retrospective databases. Future research needs to improve the transparency of data reporting by documenting critical sample characteristics such as age, gender, income, and educational attainment, while also standardising the reporting of SCI characteristics using established nomenclature (e.g., American Spinal Injury Association classification system to report types of SCI; Betthausen et al., 2023). Doing so will help to shed light on potential risk factors and moderators influencing depression following SCI.

Conclusion

The current meta-analysis represents a comprehensive synthesis of research spanning four decades and provides critical insights into the prevalence of depressive disorder following SCI. One in seven adults with SCI is diagnosed with major or minor depression. Prevalence estimates are high across diverse study methodologies (diagnostic system used, study design, recruitment year) and sample characteristics (gender, age, injury type). Future research needs to prioritize the development of an appropriate screening tool to enhance the diagnostic accuracy for depression for use with large population-based studies, with the goal of providing timely treatments to mitigate the detrimental consequences associated with depression. Future research should also report study and sample characteristics in detail to enhance reporting transparency and provide comprehensive insights into depression prevalence and its associated risk factors in the SCI population.

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Appendices

Appendix A: Research Proposal for Depression in SCI Patients

Psychology Honours Project 2023 – Research Plan

Student ID: ██████████

Study Information

1. Title: Prevalence of clinically diagnosed depression following spinal cord injury: a meta-analysis
2. Target Journal: *Spinal Cord* (a multi-disciplinary journal) or *Rehabilitation Psychology*
3. Research Aim/s: The aim of this study is to investigate the point prevalence of depressive disorder among adults (> 16 years – consistent with the cut-off age of 15 or below for paediatric populations in the international literature; Parent et al., 2011) with a spinal cord injury (SCI). A secondary aim is to example potential sample and methodological characteristics that may impact prevalence estimates.
4. Research Question/s: What is the prevalence of depressive disorder for patients following a SCI?
5. Use of Theory: Not applicable

Design Plan

6. Tradition (optional): Frequentist
7. Study Design: A systematic review with meta-analysis
8. Study Measures (optional): The primary outcome is depressive disorder, obtained from a clinical diagnosis and/or medical record audit using well-established classification systems (i.e., Diagnostic and Statistical Manual of Mental Disorders, International Statistical Classification of Diseases and Related Problems). This criterion may be refined depending on the available data (noting that clinically diagnosed depression has varying subtypes and symptom severity - ranging from dysthymia to major depressive disorder).
9. Study Materials (optional):
Covidence systematic review software (Veritas Health Innovation, Melbourne, 2023).
Comprehensive Meta-analysis Software (Version 4, Biostat).
10. Study Procedure:
Consistent with PRISMA (2020) guidelines:
 - (1) A review protocol will be registered on the Open Science Framework
 - (2) A list of search terms will be developed in consultation with an expert subject librarian.
 - (3) Eligible studies will be identified from database searches of: Embase, PsycINFO, PubMed, CINAHL
 - (4) Records will be uploaded into Covidence software and screened using pre-specified inclusion and exclusion criteria. A manual search of their respective reference sections will also be completed.

- (5) The reporting quality of each study will be assessed using a well-established tool for prevalence studies (selection of this tool is still to be determined; <https://www.equator-network.org>)
- (6) Study data will be tabulated using a purposely designed Excel sheet for transparency.

Sampling Plan

- 11. Existing Data
- 12. Data Collection Procedures:
Peer-reviewed studies that are published in English and adopt an observational design to examine an adult population with spinal cord injury (traumatic or non-traumatic onset) will be sourced from electronic databases in psychology, medicine, and health. The study screening process will be double-checked by another researcher (i.e., a postgraduate psychology student and/or the project supervisor), as will data extraction. Corresponding authors of individual studies will be contacted for additional information if data are not present, or not clearly reported, in their published study.
- 13. Type of Data Collected:
For each included study, the total sample size and number of patients diagnosed with a depressive disorder will be extracted. In addition, data relating to sample characteristics (e.g., mean age, gender ratio, time since SCI) and methodological characteristics (e.g., method of depression diagnosis) will be obtained from each study.
- 14. Sample Size:
At least 10 independent studies are required to ensure sufficient statistical power, including subgroup analyses and meta-regression, for a meta-analysis (Borenstein et al., 2011).
- 15. Stopping Rule:
Not applicable.

Analysis Plan

- 16. Data Analyses:
The prevalence rate of depression from each study, measured using proportions, will be calculated, and then pooled across studies. The pooled mean prevalence rate will be deducted from the inverse variance method, so that studies with smaller variance will be weighted higher due to their higher robustness and reliability. The formula for this calculation is as follows (Barendregt et al., 2013):

$$P = \frac{\sum_i \frac{p_i}{Var(p_i)}}{\sum_i \frac{1}{Var(p_i)}}$$

Confidence intervals will also be calculated for each effect estimate and visually displayed in a forest plot to demonstrate the distribution of prevalence estimates and to identify possible statistical outliers. Additionally, a funnel plot analysis and I^2 will be calculated to investigate the presence of bias and between-study heterogeneity, respectively.

Other

- 17. Other (Optional):
Not applicable

Appendix B: Tables for Search Terms

Table B1

Search Terms for Pubmed

Depression	Spinal cord injuries
“Depression”[mh] OR “Depressive disorder”[mh] OR depress*[tiab] OR depressive symptom*[tiab] OR mental health illness*[tiab] OR mental illness*[tiab] OR psychopatholog*[tiab] OR Mood disorder*[tiab] OR distress[tiab] OR emotion*[tiab] OR psychological outcome*[tiab] OR neurotic outcome*[tiab] OR psychosocial outcome*[tiab] OR psychological adjustment*[tiab] OR internalizing symptom*[tiab] OR internalising symptom* OR affective disorder*[tiab]	“spinal cord injuries”[mh] OR spinal cord injur*[tiab] OR spine injur*[tiab] OR spinal injur*[tiab] OR spinal cord trauma*[tiab] OR spinal cord laceration*[tiab] OR spinal cord lesion*[tiab] OR spinal cord damage*[tiab] OR spinal cord disease*[tiab] OR spinal fracture*[tiab] OR “paraplegia”[majr] OR “quadriplegia”[majr] OR parapleg*[tiab] OR quadripleg*[tiab] OR tetrapleg*[tiab]

Table B2*Search Terms for Embase*

Depression	Spinal cord injury
Depression.sh OR depression.ti,ab OR depress*.ti,ab OR depressive symptom*.ti,ab OR Mental health illness*.ti,ab OR mental illness*.ti,ab OR psychopatholog*.ti,ab OR mood disorder*.ti,ab OR distress.ti,ab OR emotion*.ti,ab OR ((psychological OR neurotic OR psychosocial) adj4 (outcome* OR adjustment*)).ti,ab OR internalizing symptom*.ti,ab OR affective disorder*.ti,ab	spinal cord injury.sh OR spinal cord injur*.ti,ab OR spine injur*.ti,ab OR spinal injur*.ti,ab OR spinal cord trauma*.ti,ab OR spinal cord laceration*.ti,ab OR spinal cord lesion*.ti,ab OR spinal cord damage*.ti,ab OR spinal cord disease*.ti,ab OR spinal fracture*.ti,ab OR parapleg*.ti,ab OR quadripleg*.ti,ab OR tetrapleg*.ti,ab

Table B3*Search Terms for PsycINFO*

Depression	Spinal cord injury
Major depression.sh OR “depression (emotion)”.sh OR depress*.ti,ab OR depressive symptom*.ti,ab OR mental health illness*.ti,ab OR mental illness*.ti,ab OR psychopatholog*.ti,ab OR mood disorder*.ti,ab OR distress.ti,ab OR emotion*.ti,ab OR psychological outcome*.ti,ab OR neurotic outcome*.ti,ab OR psychosocial outcome*.ti,ab OR psychological adjustment*.ti,ab OR internalizing symptom*.ti,ab OR affective disorder*.ti,ab	spinal cord injuries.sh OR spinal cord injur*.ti,ab OR spine injur*.ti,ab OR spinal injur*.ti,ab OR spinal cord trauma*.ti,ab OR spinal cord laceration*.ti,ab OR spinal cord lesion*.ti,ab OR spinal cord damage*.ti,ab OR spinal cord disease*.ti,ab OR spinal fracture*.ti,ab OR parapleg*.ti,ab OR quadripleg*.ti,ab OR tetrapleg*.ti,ab

Table B4*Search Terms for CINALH*

Depression	Spinal cord injuries
<p>MH Depression+</p> <p>OR TI (depression OR “depressive disorder*” OR depress* OR “depressive symptom*” OR “mental health illness*” OR “mental illness*” OR psychopatholog* OR “Mood disorder*” OR distress OR emotion* OR “psychological outcome*” OR “neurotic outcome*” OR “psychosocial outcome*” OR “psychological adjustment*” OR “internalizing symptom*” OR “affective disorder”)</p> <p>OR AB (depression OR “depressive disorder*” OR depress* OR “depressive symptom*” OR “mental health illness*” OR “mental illness*” OR psychopatholog* OR “Mood disorder*” OR distress OR emotion* OR “psychological outcome*” OR “neurotic outcome*” OR “psychosocial outcome*” OR “psychological adjustment*” OR “internalizing symptom*” OR “affective disorder”)</p>	<p>MH “spinal cord injuries+” OR MH “spinal injuries+”</p> <p>OR TI (“spinal cord injur*” OR “spinal injur*” OR “spine injur*” OR “spinal cord trauma*” OR “spinal cord laceration*” OR “spinal cord lesion*” OR “spinal cord damage*” OR “spinal cord disease*” OR “spinal cord fracture*” OR “spinal fracture*” OR parapleg* OR quadripleg* OR tetrapleg*)</p> <p>OR AB (“spinal cord injur*” OR “spinal injur*” OR “spine injur*” OR “spinal cord trauma*” OR “spinal cord laceration*” OR “spinal cord lesion*” OR “spinal cord damage*” OR “spinal cord disease*” OR “spinal cord fracture*” OR “spinal fracture*” OR parapleg* OR quadripleg* OR tetrapleg*)</p>

Appendix C: Quality Ratings for Individual Studies

Table C

Within-study Risk-of-bias Assessment (Munn et al., 2014)

Lead author (date)	1. Appropriate sampling frame	2. Appropriate recruitment	3. Adequate sample size	4. Sufficient study description	5. Sufficient sample coverage	6a. Valid assessment of SCI	6b. Valid assessment of depression (eligibility criterion)	7. Reliable measurement of depression	8. Appropriate statistical analysis	9. Adequate response rate
Bombardier et al. (2012)	●	●	●	●	●	●	●	●	●	●
Chang et al. (2020)	●	●	●	●	●	●	●	●	●	●
Craig et al. (2015)	●	●	●	●	●	●	●	●	●	●
Fullerton et al. (1981)	●	●	●	●	●	●	●	●	●	●
Howell et al. (1981)	●	●	●	●	●	●	●	●	●	●
Judd & Brown (1992)	●	●	●	●	●	●	●	●	●	●
Judd et al. (1989)	●	●	●	●	●	●	●	●	●	●
Kishi et al. (1995)	●	●	●	●	●	●	●	●	●	●
Matsuda et al. (2016)	●	●	●	●	●	●	●	●	●	●
McDonald et al. (2018)	●	●	●	●	●	●	●	●	●	●
Mitchell et al. (2008)	●	●	●	●	●	●	●	●	●	●
Osteraker & Levi (2005)	●	●	●	●	●	●	●	●	●	●
Radnitz et al. (1997)	●	●	●	●	●	●	●	●	●	●
Ullrich et al. (2014)	●	●	●	●	●	●	●	●	●	●
VanDerwerker et al. (2020)	●	●	●	●	●	●	●	●	●	●
Weeks et al. (2011)	●	●	●	●	●	●	●	●	●	●

● Yes ● No ● Unclear ● Not Applicable

Appendix D: Scoring for the Risk of Bias Assessment Tool

Table D

Joanna Briggs Institute Prevalence Critical Appraisal Instrument (Munn et al., 2014)

Risk of bias item	Criteria for answers (please circle one option)	Additional notes and studies examples
1. Was the sample frame appropriate to address the target population?	<p>Yes (Low risk): The sample frame is a close representation of the target population in relation to the characteristics, demographics or injury profiles, such as sex, occupation, injury types.</p> <p>No (High risk): The sample frame is not a close representation, for example, only males are recruited despite the overall target population including all genders.</p> <p>Unclear: Demographics or injury profiles of the sample is not provided.</p> <p>NA: The study requires no sample.</p>	<p>The study covers approximately 100% of the SCI population in Taiwan (Chang et al., 2020). The answer is: Yes (Low risk).</p> <p>Although the study recruits participants from only the rehabilitation setting, the sample has an age distribution, diverse race, and a sex ratio (Male : Female = 4:1) similar to the overall SCI population (Bombardier et al., 2012). The answer is: Yes (Low risk).</p> <p>The study only recruits participants from one hospital, with 90% males, without other information about their race, social status (Fullerton et al., 1981). The answer is: No (High risk).</p>
2. Were study participants sampled in an appropriate way?	<p>Yes (Low risk): Appropriate sampling (i.e., random sampling, cluster sampling) is employed or a census is undertaken.</p> <p>No (High risk): Convenience samples are used, such as street surveys or interviews, instead of a random selection of a sample.</p> <p>Unclear: Sampling methods are not provided.</p> <p>NA: The study requires no sampling.</p>	<p>The study covers nearly 100% of the SCI population in Taiwan due to the usage of government database (Chang et al., 2020). The answer is: Yes (Low risk).</p> <p>The study recruits SCI patients from rehabilitation and community setting and include all patients admitted from April 2010 to December 2012 (Craig et al., 2015). The answer is: Yes (Low risk).</p> <p>The study only samples from the University of Wisconsin Hospital (Howell et al., 1981). The answer is: No (High risk).</p> <p>The study recruits participants from a larger study and does not specify the sampling process (Radnitz et al., 1997). The answer is: Unclear (U).</p>
3. Was the sample size adequate?	<p>Yes (Low risk): Sample size ≥ 266 (calculations are shown in the next column).</p> <p>No (High risk): Sample size < 266.</p> <p>Unclear: When the sample size is not provided.</p> <p>NA: The study requires no sample.</p>	<p>The calculation for the minimum sample size is based on the formula (Pourhoseingholi et al., 2013) below:</p> $n = \frac{Z^2 P(1 - P)}{d^2}$ <p>$Z = 1.96$, $P = 22.2\%$ (Williams & Murray, 2015), $d = 0.05$ Thus, $n = 266$</p>
4. Were the study subjects	<p>Yes (Low risk): The sample is described in detail (i.e., sex ratio, sociodemographic</p>	<p>Detailed information of the SCI sample is provided, including age, years since</p>

and the setting described in detail?	variables between countries) so other researchers can determine whether the sample is comparable to the population of interest.	SCI, sex, race, SCI etiology and level of injury. The answer is: Yes (Low risk) .
	No (High risk): Sample demographics are not sufficiently provided.	Descriptions of the SCI sample only include sex ratio and mean age (Weeks et al., 2011). The answer is: No (High risk) .
	Unclear: It is unclear if the provided demographic details are relevant to the sample.	
	NA: The study requires no description of the sample.	
5. Was the data analysis conducted with sufficient coverage of the identified sample?	Yes (Low risk): Limited coverage bias is shown as not all subgroups of the identified sample respond at the same rate.	No participants drop out, resulting in a full response among different subgroups (Judd & Brown, 1992). The answer is: Yes (Low risk) .
	No (High risk): Presence of coverage bias is observed.	Despite drop-outs, the study does not evaluate the demographics differences between the drop-outs and participating SCI patients, so it is unclear whether it includes sufficient coverage of the sample. The answer is: Unclear (U) .
	Unclear: It is unclear of the response rate of the subgroups.	
	NA: The study does not involve any response from the sample.	This question is not applicable (NA) for retrospective studies as it involves no response rates (Chang et al., 2020).
6a. Were valid methods used for the identification of spinal cord injury?	Yes (Low risk): Spinal Cord Injury is assessed based on standardised diagnostic criteria instead of observer-report or self-report scales. No or little measurement or classification bias is observed.	Diagnosis on SCI is based on ICD code 805.0 to 806.9 (Chang et al., 2020). The answer is: Yes (Low risk) .
	No (High risk): Spinal cord injury is based on a self-report scale, or a non-validated measurement.	No information is provided for the spinal cord injury diagnosis, such as ICD codes, CT scans, or whether it is assessed by professionals (Judd et al., 1989). The answer is: No (High risk) .
	Unclear: It is unclear how spinal cord injury is measured.	
	NA: This study does not involve the identification of spinal cord injury.	
b. Were valid methods used for the identification of depression?	Yes (Low risk): Depression is assessed based on standardised diagnostic criteria instead of observer-report or self-report scales. No or little measurement or classification bias is observed.	One of the eligibility criteria of this study. The answer is: Yes (Low risk) for all studies.
	No (High risk): Depression is based on a self-report scale, or a non-validated measurement.	
	Unclear: It is unclear how depression is measured.	
	NA: This study does not involve the identification of depression.	

7. Was the condition measured in a standard, reliable way for all participants?	<p>Yes (Low risk): Studies provide information regarding who conduct the interview or assess the interrater reliability for the depression diagnosis.</p> <p>No (High risk): Interviewer is not properly trained, with low interrater reliability for the depression diagnosis.</p> <p>Unclear: No information regarding the person implementing the interviews is provided.</p> <p>NA: The study does not involve any assessments or interviews.</p>	<p>Trained professions, psychologists and psychiatrists, conducted the measurement (i.e., Bombardier et al, 2012; Craig et al., 2015). The answer is: Yes (Low risk).</p> <p>It is unclear who and how the data is collected from retrospective medical, government or insurance database (i.e., Chang et al., 2020; Matsuda et al., 2016). The answer is: Unclear.</p> <p>Some studies do not mention who has collected the data. (i.e., Kishi et al., 1995). The answer is: Unclear.</p>
8. Was there appropriate statistical analysis?	<p>Yes (Low risk): A detailed methods section is provided and the appropriate analytical technique to used to measure the variable of interest.</p> <p>No (High risk): Numerators and denominators are incorrectly used and reported. Statistics are not fully reported, such as missing confidence intervals.</p> <p>Unclear: The statistical analyses are not clearly stated.</p> <p>NA: The study involves no statistical analyses.</p>	<p>All studies either list the number of participants diagnosed with depression or present depression rates as proportions. The answer is: Yes (Low risk).</p>
9. Was the response rate adequate, and if not, was the low response rate managed appropriately?	<p>Yes (Low risk): The response rates are appropriate, with no or few dropouts and refusals are properly managed.</p> <p>No (High risk): Dropout rates are not properly managed, such as a lack of analysis comparing responders and non-responders that show no differences in demographics between the two.</p> <p>Unclear: The study does not mention anything related to response rates.</p> <p>NA: The study requires no sample, thereby response rates.</p>	<p>Only 6% refused to participate in the study with no dropouts (Judd et al., 1989). The answer is: Yes (Low risk).</p> <p>22% dropout rates without proper management (Osteraker et al., 2005). The answer is: No (High risk).</p> <p>Data from Chang et al. (2020) are based on a Taiwanese government database. The answer is: NA.</p>

Abbreviations: NA: not applicable; SCI: Spinal Cord Injury.

Appendix E: Scatterplots for the Regression Models

Figure E1.

Scatterplot showing the Association between Depression Rate and Mean Age

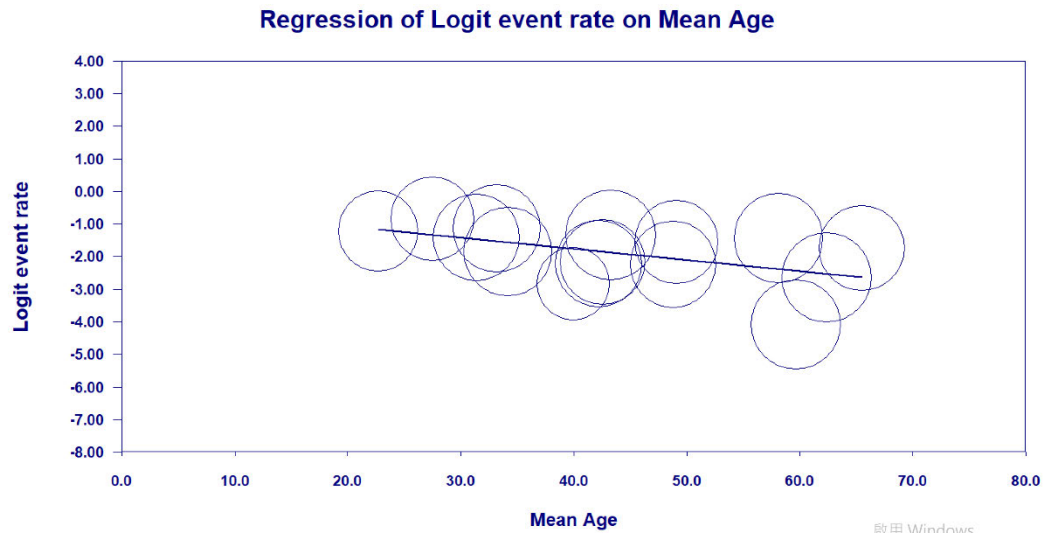


Figure E2.

Scatterplot showing the Association between Depression Rate and Recruitment Year

