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# Research article

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# Comprehensive evaluation of Chinese herbal compound prescriptions for postoperative spinal cord injury: A network meta-analysis of randomized controlled trials

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## ARTICLE INFO

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## ABSTRACT

*Background:* Spinal cord injury (SCI) is a catastrophic condition associated with spinal nerve damage, which can lead to complete or partial loss of sensory and motor functions. Chinese herbal compound prescriptions (CHCP) have shown varying degrees of therapeutic effects on spinal cord injuries. However, there is a significant lack of clinical evidence-based research to substantiate these effects.

*Purpose*: This study aims to thoroughly assess the viability of CHCPs in postoperative SCI through network meta-analysis.

*Methods*: Computer searches were conducted across multiple databases, including PubMed, Cochrane Library, Embase, Web of Science, CNKI, Wanfang, VIP, and CBM, from their inception until May 2024. The meta-analysis adhered to the PRISMA guidelines and was registered in the PROSPERO database (CRD42023462686). A network meta-analysis was performed using the BUGSnet software package via R. **Study design**: A network meta-analysis of randomized clinical trials (RCTs).

*Results*: A total of 26 RCTs involving 1848 patients were ultimately included. The network metaanalysis revealed the effectiveness in improving ASIA motor score as follows: "HQGZD" > "Other Decoctions" > "BYHWD" > "TDHXD" > "THCQD" > "Surgery". For ASIA sensory score, the effectiveness ranking was: "HQGZD" > "Other Decoctions" > "BYHWD" > "TDHXD" > "THCQD" > "Surgery". Additionally, the experimental group had a higher ADL score compared to the control group, with a statistically difference [SMD = 1.08, 95 % CI = (0.88, 1.27), p < 0.05]. The experimental group had fewer adverse events compared to the control group, with a statistically difference [RR = 0.41, 95 % CI (0.22, 0.78), p < 0.05].

*Conclusion:* The findings suggest that CHCP can mprove postoperative ASIA motor and sensory scores, enhance ADL scores, and reduce adverse events following SCI surgery. Specifically, combining surgery with Huangqi Guizhi Wuwu Decoction or Buyang Huanwu Decoction may

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provide superior therapeutic effects in SCI treatment. Integrating CHCP into postoperative care for SCI patients may offer potential benefits.

## 1. Introduction

Spinal cord injury (SCI) often results from high-intensity spinal injuries such as traffic accidents, falls, and violent trauma. Additionally, SCI may stem from various other factors, including infections, tumors, spinal degenerative diseases, ischemia-reperfusion injuries, and vascular causes [1]. The condition manifest as diverse motor, sensory, and sphincter dysfunctions, accompanied by abnormal muscle tone and pathological reflexes in the affected spinal cord segment [2,3]. Moreover, the sequelae of SCI can impact multiple body systems, presenting significant challenges for patient care and rehabilitation post-injury. According to literature, the global incidence of SCI ranges from 0.7 to 1.2 million cases annually, with 20.6 million individuals living with SCI [4]. The average annual indirect cost of SCI per person in the US is \$76,327 [5].

Surgical intervention stands as a pivotal approach in treating SCI. However, variations in pathophysiological processes such as ischemic reactions, inflammatory responses, and nerve scar repair across different degrees of SCI contribute to suboptimal postsurgical recovery outcomes [6,7]. Traditional Chinese medicine (TCM) holds significant value in global medical research. Previous investigations have outlined the role and impact of TCM in SCI treatment, highlighting therapeutic effects and mechanisms of active ingredients, herbs, and compound prescriptions within TCM [8,9]. Building upon published clinical research outcomes regarding the application of Chinese herbal compound prescriptions (CHCP) in postoperative SCI, this study employs network meta-analysis (NMA) to systematically compare the efficacy and safety of various commonly used CHCP therapies for postoperative SCI patients, aiming to provide more robust evidence for clinical practice.

## 2. Methods

This meta-analysis adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Network Meta-Analyses (PRISMA-NMA) guidelines [10] and was registered on PROSPERO (CRD42023462686).

## 2.1. Search strategy

Two researchers (Z.-B.G. and K.C.) conducted a comprehensive search for randomized controlled trials (RCTs) focusing on the combination of CHCPs and surgical treatment for SCI. The search included Medline (via PubMed), EMbase, The Cochrane Library, and Web of Science, as well as Chinese databases including China National Knowledge Infrastructure (CNKI), Wanfang Digital Periodicals (Wanfang), Chinese Science and Technology Periodicals (VIP), and China Biomedical Literatures Database (CBM). The search covered studies from inception up to May 2024. The detailed study search strategy is provided in <u>Supplementary File 1</u>.

#1 MeSH Terms: "chinese medicine" OR "traditional Chinese medicine" OR "Chinese Traditional Medicine".

#2 MeSH Terms: "spinal cord injury" OR "spinal cord trauma" OR "spinal cord transection" OR "spinal cord laceration" OR "spinal cord contusion".

#3 MeSH Terms: "RCT" OR "randomized controlled trial".

#4 #1 AND #2 AND #3.

Two researchers (Z.-B.G. and K.C.) autonomously screened the studies using predefined inclusion and exclusion criteria. Discrepancies were resolved through consensus discussions, and if necessary, consultation with a third independent researcher (W.-X.S.) was sought.

# 2.2. Study selection criteria

## 2.2.1. Eligibility criteria

Eligibility criteria are developed in accordance with the PICOS principle. (P) Participants must be diagnosed with SCI, irrespective of injury time, segment, severity, race, sex, or age. (I) The experimental group is administered CHCP and surgical treatments. CHCP is defined as orally administered prescriptions comprising a minimum of two traditional Chinese medicines, available in forms such as decoctions and pills. (C) The control group should receive routine treatment and surgical intervention. (O) The study must include at least one of the following outcome indicators: (a) American Spinal Cord Injury Association Neurological Function Score (ASIA Score), encompassing ASIA motor score or ASIA sensory score; (b) Activities of daily living (ADL) sore: including Barthel index and functional independence measure (FIM) score. (c) Number of adverse events. (S) The study design must be a RCT.

## 2.2.2. Exclusion criteria

- (a) The experimental group received treatment with traditional Chinese patent drugs or non-oral traditional Chinese drugs.
- (b) Case reports, case series, reviews, editorials, and animal studies.
- (c) Repeated publications of studies.
- (d) Studies with incomplete or non-standard original text.

(e) Articles lacking clear outcome indicators or complete information, where authors could not be contacted for access, with inconsistent data format, and an inability to convert research data.

## 2.3. Data extraction

Two evaluators (Z.-B.G. and K.C.) independently screened the studies based on the eligibility and exclusion criteria. Any discrepancies were resolved through discussion with a third evaluator (W.-X.S.). Additionally, the references cited in the included studies were systematically screened.

Basic information from the screened studies was extracted, including the title, author, publication year, patient age, gender, intervention measures, CHCP name, included outcome indicators, and quality evaluation methods. In the event of missing data, the original corresponding author would be contacted via email to obtain the necessary information.

## 2.4. Risk of bias and GRADE assessment

Two researchers assessed the studies' risk of bias using the Cochrane Collaboration's tool, covering seven domains: allocation concealment, random sequence generation, incomplete outcome data, selective outcome reporting, blinding of participants and personnel, blinding of outcome assessment, and other biases. The GRADE system tool was employed to appraise the quality of evidence for outcome indicators, considering five aspects: risk of bias, inconsistency, indirectness, imprecision, and publication bias. Based on the quality evaluation results, the studies are categorized as high, medium, low, or extremely low quality. To assess bias, a funnel plot was also generated for each outcome.

## 2.5. Statistical analysis

Network Meta-Analysis (NMA) was executed using the BUGSnet software package (version 1.1.0) through R (version 4.3.2) (www. r-project.org) and JAGS (Just Another Gibbs Sampler, version 4.3.1). BUGSnet utilizes a generalized linear model simulated by Markov

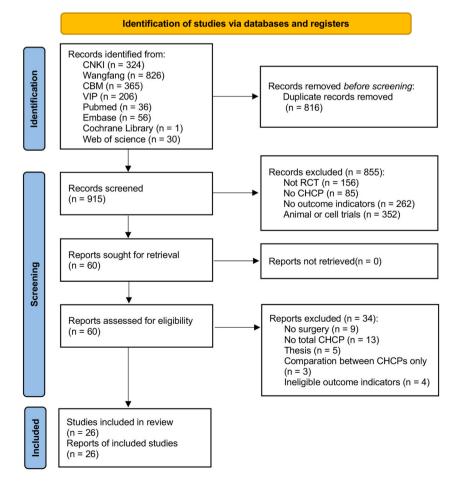


Fig. 1. Flow chart of studies search and selection process.

chain Monte Carlo to enable NMA through Bayesian comparison [11]. The outcome indicators included ASIA motor and sensory scores, as well as adverse reactions. The light touch score and pinprick score will be combined and calculated to derive the ASIA sensory score using StatsToDo (www.StatsToDo.com/MakeTable.php). The surface under the cumulative ranking (SUCRA) curve and Rankogram plot presented the ranking of each treatment method. SUCRA values range from 0 to 1, with 1 indicating the best intervention effect and 0 indicating the worst intervention effect. In the Rankogram plot, lighter colors indicate better intervention effects. To evaluate the model fit, we used leverage plots and the deviance information criterion (DIC) to decide whether to use a fixed-effect model or a random-effect model. The DIC value is the primary criterion for selection, and we typically choose the model

## Table 1

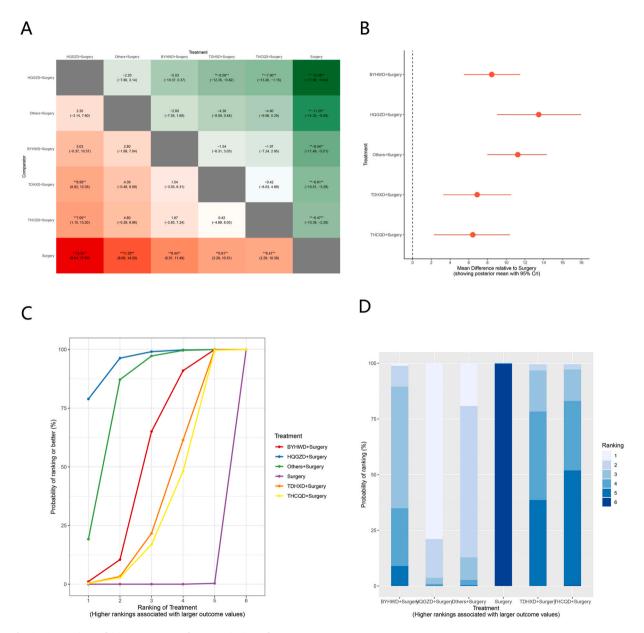
## Characteristics of included studies.

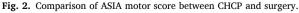
Included trials	Sample sizes (T/ C)	Age (T/C)	Intervention (T)	Intervention (C)	Time	Outcome indicators
Shen Q 2004	16/17	$\begin{array}{c} 44.3 \pm 7.85 \\ /45.1 \pm 12.8 \end{array}$	#Routine + Surgery + Placebo	#Routine + Surgery + Others	60d	126
Dai Z 2012	24/24	$37.8 \pm 11.2$ $/37.1 \pm 10.9$	#Routine + Surgery	#+THCQD	1y	023
Zhang G 2014	31/32	33.6	#Routine + Surgery	#+BYHWD	24w	12
Zhang Y 2014	18/18	38.6	#Routine + Surgery	#+BYHWD	12m	26
Chen J 2015	30/30	$35.36\pm5.32$	#Routine+ Surgery	#+BYHWD	3m	00
Deng Z 2016	52/53	$48.5 \pm 5.7$ /48.9 $\pm 5.3$	#Routine + Surgery	BYHWD	22w	00
Guo X 2015	36/36	$33.4 \pm 6.9$ /34.3 ± 7.2	#Routine + Surgery	BYHWD	24w	00
Lu G 2015	42/42	$36.80 \pm 9.70/37.60 \pm 10.10$	#Routine + Surgery	#+BYHWD	12w	1278
Meng X 2017	32/32	$\begin{array}{c} 10.10\\ 41.86 \pm 4.97\\ /42.38 \pm 5.14 \end{array}$	#Routine+ Surgery	#+TDHXD	5w	00
Yang W 2017	31/31	$44.50 \pm 1.76$ $/42.00 \pm 1.23$	#Routine+ Surgery	BYHWD	20w	10
Du H 2019	40/39	$36.55 \pm 3.88$ $35.55 \pm 3.54$	#Routine+ Surgery + MP	#+THCQD	6m	1236
Li Y 2019	42/42	$37.45 \pm 3.33$ $37.45 \pm 3.33$ $37.56 \pm 3.14$	#Routine+ Surgery	#+Others	3m	123
Zhao P 2019	21/21	$37.2 \pm 2.6/36.9 \pm 2.3$	#Routine + Surgery	#+TDHXD	5w	00
Zhang M	35/35	$43.59 \pm 3.61$	#Routine+	#+Others	1m	035
2020	00,00	$/46.23 \pm 4.81$	Surgery	"   Others		000
Zhang Y 2020	41/41	42.5 ± 7.1 /42.1 ± 6.8	#Routine+ Surgery	#+TDHXD	4w	157890
Cheng Z 2021	42/40	$39.25 \pm 8.03$ $/37.94 \pm 7.91$	#Routine+ Surgery	#+TDHXD	4w	1791
Deng Z 2021	40/40	$49.21 \pm 5.34$ /48.67 $\pm 5.88$	#Routine+ Surgery	#+Others	2w	00
Jiang X 2021	45/45	$41.25 \pm 3.64$	#Routine+ Surgery	#+Others	3m	00
Yan K 2021	48/48	$39.23 \pm 5.72$ /37.89 $\pm$ 6.43	#Routine+ Surgery	#+Others	8w	1351
Ren F 2022	40/40	$34.86 \pm 4.97$ $/35.02 \pm 4.82$	#Routine + Surgery	#+HQGZD	4w	12345
Wang K 2022	48/48	$48.29 \pm 1.38$ $48.25 \pm 1.36$	#Routine+ Surgery	#+TDHXD	1m	1267890
Zhang H 2022	36/36	$34.74 \pm 5.08$ $/34.19 \pm 5.47$	#Routine+ Surgery	#+BYHWD	3m	12378
Cheng Y 2023	32/32	$34.19 \pm 3.47$ $48.88 \pm 7.84$ $/47.38 \pm 8.94$	#Routine + Surgery+ Joint movement therapy	#+Others	8w	124790
Wang Y 2023	50/50	$43.92\pm 6.28$	#Routine+	#+HQGZD	60d	1235678
Wu R 2023	42/42	$egin{array}{c} /44.16 \pm 5.73 \ 50.14 \pm 2.48 \ /50.27 \pm 2.51 \end{array}$	Surgery #Routine+	#+THCQD	1m	06
Xu R 2023	10/10	$(50.2) \pm 2.51$ 42.52 $\pm$ 7.08 $(42.12 \pm 5.98)$	Surgery #Routine+	#+Others	12w	1590
Zhao P 2019	21/21	$742.12 \pm 5.98$ $37.2 \pm 2.6$ $736.9 \pm 2.3$	Surgery #Routine + Surgery	#+TDHXD	5w	00
2019 Lu G 2015	42/42	$736.9 \pm 2.3$ $36.80 \pm 9.70$ $737.60 \pm 10.10$	#Routine+ Surgery	#+BYHWD	12w	0278

\* ①ASIA motor score; ②ASIA sensory score; ③ASIA grade; ④JOA score; ③ADL score; ⑥Adverse event; ⑦SEP amplitude; ⑧MEP amplitude; ⑨SEP incubation; ⑩VAS score; BYHWD: Buyang Huwanwu Decoction; HQGZD: Huangqi Guizhi Wuwu Decoction; TDHXD: Tongdu Huoxu Decoction; THCQD: Taohe Chengqi Decoction; Others: Chinese herbal compound prescriptions with less than 3 included studies; #: routine treatment; y: year; m: month; w: week; d: day.

with the lower DIC value. If the DIC values differ by 5 or less, both models are acceptable. We also considered the number of outliers in the leverage plots as a secondary criterion for model selection. To assess the presence of inconsistency, we fitted leverage plots, selected the model with a lower DIC value, and observed the simplicity of the leverage plots. Additionally, we plotted the posterior mean deviation contribution of individual data points for both the consistency model and the inconsistency model to highlight the differences between the two models.

If the number of included studies is insufficient for a NMA, only a meta-analysis will be conducted. The meta-analysis was conducted using RevMan (version 5.4) from the Cochrane Collaboration, Oxford, UK. The outcome indicators included ADL score and adverse event. For dichotomous variables, risk ratio (RR) and 95 % confidence interval (CI) were estimated. For continuous variables, we calculated the standard mean difference (SMD) and its 95 % CI as the statistical measure. If  $I^2 \le 50$  % and p > 0.05, it indicates non-significant heterogeneity between studies, and a fixed-effects model is employed for meta-analysis. In cases where  $I^2 > 50$  % and  $p \le 0.05$ , indicating significant heterogeneity between studies, a random-effects model is utilized for meta-analysis. p < 0.05 suggests a





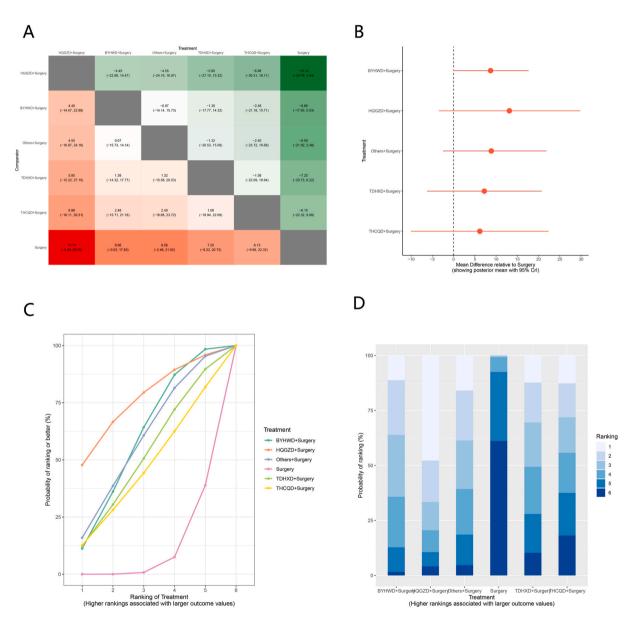
\*A: League table heatmap of ASIA motor score; \*\* means statistically significant (p < 0.05); B: Mean Difference of ASIA motor score; C: SCURA curve of ASIA motor score; D: Rankogram plot of ASIA motor score; BYHWD: Buyang Huwanwu Decoction; HQGZD: Huangqi Guizhi Wuwu Decoction; TDHXD: Tongdu Huoxu Decoction; THCQD: Taohe Chengqi Decoction; Others: Chinese herbal compound prescriptions with less than 3 included studies.

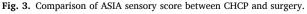
statistically significant difference in outcome measures.

## 3. Results

# 3.1. Study characteristics

There were 1731 articles in the initial search, and after screening, 26 studies [12–37] were finally included. These studies reported on a total of 1848 patients, with 924 in the experimental group and 924 in the control group. All studies were in Chinese. Among the included studies, with 8 studies [15,22,24,25,27,35–37] related to Buyang Huanwu Decoction (BYHWD), 2 studies [12,16] to Huangqi Guizhi Wuwu Decoction (HQGZD), 3 studies [26,30,32] to Taohe Chengqi Decoction (THCQD), 5 studies [14,17,20,21,34] to Tongdu Huoxue Decoction (TDHXD), and 8 studies [13,18,19,23,28,29,31,33] to other decoctions. The studies screening process is illustrated in Fig. 1, while the basic information of the included studies is summarized in Table 1. Supplementary Figs. 1–3 provide the network





\*A: League table heatmap of ASIA sensory score, \*\* means statistically significant (p < 0.05); B: Mean Difference of ASIA motor score; C: SCURA curve of ASIA sensory score; D: Rankogram plot of ASIA sensory score; BYHWD: Buyang Huwanwu Decoction; HQGZD: Huangqi Guizhi Wuwu Decoction; TDHXD: Tongdu Huoxu Decoction; THCQD: Taohe Chengqi Decoction; Others: Chinese herbal compound prescriptions with less than 3 included studies.

relationship diagram and baseline characteristics. Supplemental Fig. 4 presents the risk of bias.

#### 3.2. Consistency check

The included studies exclusively compared surgery combined with CHCP to surgery alone, lacking direct comparisons between various intervention measures. This gap prevented the formation of a closed loop. The random-effect model for both the ASIA motor score and the ASIA sensory score is superior to the fixed-effect model, as both have lower DIC values and fewer outliers in the leverage plots (Supplemental Figs. 5 and 6).

The DIC values for the consistency models of both the ASIA motor score and the ASIA sensory score are smaller, and the leverage plots of the consistency models appear cleaner (Supplemental Figs. 7 and 8). Most data points are located on or near the (y = x) line, except for a few outliers, indicating that the consistency between the two models is roughly the same (Supplemental Fig. 9). Consequently, this suggests that we should use the more parsimonious consistency model.

## 3.3. ASIA motor score

A total of 25 studies [12–24,26–37] reported on the ASIA motor score, involving 1812 patients. The results (Fig. 2A and B) demonstrated that, compared with routine treatment combined with surgery, the combination of HQGZD showed a statistically improvement (p < 0.05) in motor function [MD = 13.46, 95 % CI (9.04, 17.99)]. The combination of BYHWD also showed a statistically improvement (p < 0.05) [MD = 8.44, 95 % CI (5.51, 11.49)], as did the combination of TDHXD [MD = 6.91, 95 % CI (3.29, 10.51)]. Additionally, the combined use of THCQD was statistically in improving motor function (p < 0.05) [MD = 6.47, 95 % CI (2.29, 10.39)]. According to the SUCRA curve (Fig. 2C) and Rankogram plot (Fig. 2D), the effectiveness in improving motor function is as follows: "HQGZD" > "Other Decoctions" > "BYHWD" > "TDHXD" > "THCQD" > "Surgery"; The two most effective measure for improving motor function is "HQGZD" and "BYHWD", while the least effective is "Surgery".

## 3.4. ASIA sensory score

A total of 20 studies [12–16,21–30,33–37] reported on the ASIA sensory score, involving 1414 patients. The results (Fig. 3A and B) indicated that, compared with routine treatment combined with surgery, the combination of BYHWD showed a statistically difference (p < 0.05) in improving sensory function [MD = 8.71, 95 % CI (0.22, 17.44)]. The combination of HQGZD showed no statistically difference in improving sensory function [MD = 13.07, 95%CI (-3.02, 29.20)]. Similarly, the combination of TDHXD also showed no statistically difference [MD = 7.28, 95 % CI (-5.75, 20.20)], There was no statistically difference in improving sensory function with the combination of THCQD [MD = 6.15, 95 % CI (-9.57, 21.97)]. According to the SUCRA curve (Fig. 3C) and Rankogram plot (Fig. 3D), the effectiveness in improving sensory function is as follows: "HQGZD" > "Other Decoctions" > "BYHWD" > "TDHXD" > "THCQD" > "Surgery". The two most effective measures to improve sensory function are "BYHWD" and " HQGZD ", while the least measure is "Surgery".

## 3.5. ADL score

A total of 6 studies [12,16,18–20,31] reported ADL score, involving 448 patients. The results indicated low heterogeneity ( $I^2 < 50$ %), so a fixed-effect model was used for the meta-analysis. The results (Fig. 4) show that the experimental group had a higher ADL score compared to the control group, with a statistically difference [SMD = 1.08, 95 % CI = (0.88, 1.27), p < 0.05].

## 3.6. Adverse event

A total of 6 studies [12,14,23,25,30,32] reported adverse event, with a total of 12 adverse events (5.6 %) in the experimental group and 30 adverse events (14.0 %) in the control group. The results indicated low heterogeneity ( $I^2$ <50 %), so a fixed-effect model was used for the meta-analysis. The results (Fig. 5) show that the experimental group had fewer adverse events compared to the control group, with a statistically significant difference [RR = 0.41, 95 % CI (0.22, 0.78), p < 0.05]. The most common adverse event in both groups was gastrointestinal dysfunction. The specific adverse event reporting details are shown in Table 2.

	C	ontrol		Exp	perimer	nt		Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Ren F 2022	58.43	8.09	40	52.39	6.79	40	19.1%	0.80 [0.34, 1.26]	
Wang Y 2023	85.23	4.68	50	79.64	4.87	50	22.0%	1.16 [0.74, 1.59]	
Xu R 2023	59.14	7.1	10	51.4	6.22	10	4.3%	1.11 [0.15, 2.07]	
Yan K 2021	65.13	12.76	48	53.24	11.83	48	22.1%	0.96 [0.54, 1.38]	
Zhang M 2020	69.95	9.46	35	56.02	10.36	35	14.4%	1.39 [0.86, 1.91]	
Zhang Y 2020	59.12	7.12	41	51.38	6.24	41	18.1%	1.15 [0.68, 1.61]	
Total (95% CI)			224			224	100.0%	1.08 [0.88, 1.27]	◆
Heterogeneity: Chi <sup>2</sup> =	3.30, df =	= 5 (P =	0.65);	$ ^2 = 0\%$				-	
Test for overall effect: Z = 10.58 (P < 0.00001)							-2 -1 0 1 2 Favours [control] Favours [experimental]		

Fig. 4. ADL score Forest plot.

	Experin	nent	Contr	ol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	M-H, Fixed, 95% Cl
Du H 2019	1	40	7	39	24.4%	0.14 [0.02, 1.08]	
Shen Q 2004	0	16	0	17		Not estimable	
Wang K 2022	2	48	5	48	17.2%	0.40 [0.08, 1.96]	
Wang Y 2023	8	50	10	50	34.4%	0.80 [0.34, 1.86]	
Wu R 2023	1	42	7	42	24.1%	0.14 [0.02, 1.11]	
Zhang Y 2014	0	18	0	18		Not estimable	
Total (95% CI)		214		214	100.0%	0.41 [0.22, 0.78]	•
Total events	12		29				
Heterogeneity: Chi <sup>2</sup> = 4	4.48, df = 3	3 (P = 0	.21); l <sup>2</sup> = 3				
Test for overall effect: Z = 2.73 (P = 0.006)						0.01 0.1 1 10 100 Favours [experimental] Favours [control]	

Fig. 5. Adverse event Forest plot.

Table 2
Adverse event report Form.

Adverse event	Experimental group ( $n=214$ )	Control group ( $n=214$ )
Gastrointestinal dysfunction	6 ( 2.8 % )	14 ( 6.5 % )
Urinary infection	1 ( 0.5 % )	1 ( 0.5 % )
Dysuria	2 ( 0.9 % )	3 ( 1.4 % )
Vomiting	1 ( 0.5 % )	3 ( 1.4 % )
Headache	1 ( 0.5 % )	2 ( 0.5 % )
Unknown reasons	1 ( 0.5 % )	7 ( 3.3 % )
Total	12 ( 5.6 % )	30 ( 14.0 % )

#### 3.7. Publication bias and quality of evidence

A publication bias evaluation was performed on clinical studies with more than 10 included articles, and the results (Supplementary Fig. 10) indicated that most studies in the funnel plot were concentrated on both sides, centered on the vertical line, suggesting acceptable symmetry. The factors influencing symmetry may be associated with the lower quality of the included studies. The GRADE system tool was employed to assess the outcome indicators, and the results (Supplementary Table 1) revealed that all the outcome indicators were of low quality, lacking evidence of high quality.

## 4. Discussion

The prognosis for neurological function recovery in SCI patients varies, primarily contingent upon the initial severity of neurological injury and medical management [38]. Among these considerations, patients exhibit a heightened concern for the recovery of motor function. Previous literatures have affirmed that TCM serves as an effective and safe adjuvant therapy for SCI, contributing to the enhancement of ASIA scores, encompassing both motor and sensory scores [39]. A study has found that CHCP Du Huo Ji Sheng Decoction (DHJSD) alleviates neuroinflammation and neuropathic pain by inhibiting M1 polarization of microglia through network pharmacology [40]. Some researchers have observed the effects of using DHJSD in patients with cervical, thoracic, and lumbar multi-segment spinal canal stenosis combined with SCI after undergoing segmental spinal canal decompression surgery. They found that it yielded good results and suggested that the use of Chinese medicine post-SCI surgery might lead to better therapeutic outcomes [41].

To our knowledge, this study represents the first network meta-analysis assessing the feasibility of TCM treatment for SCI. Within this NMA, we compared the efficacy and safety of four commonly used CHCPs for postoperative SCI patients. Our findings highlight Huangqi Guizhi Wuwu Decoction and Buyang Huanwu Decoction as optimal choices, as both demonstrated superior efficacy in promoting motor function recovery compared to surgery alone. BYHWD also showed a statistically difference in promoting sensory function recovery compared to surgery alone. Additionally, the use of CHCP resulted in fewer adverse events compared to surgery alone, although the limited number of included studies prevented a comprehensive NMA.

Our research findings align with previous reviews. From a methodological standpoint, NMA has surpassed the constraints of traditional meta-analysis regarding the number of intervention measures, addressing the dearth of direct comparison evidence across various TCM interventions [42]. Therefore, it can categorize the included TCM interventions more precisely, aligning with the TCM treatment plans' concept of "Treating the same disease with different methods". We contribute new evidence by conducting a thorough analysis of the therapeutic effects of commonly used CHCPs. Our findings establish that HQGZD and BYHWD stand out as the optimal choices in Chinese medicine post-SCI surgery. Currently, the sole expert consensus recommendation for SCI in the realm of TCM advocates for the use of BYHWD [43]. This aligns, in part, with our research findings.

BYHWD first appeared in "*Correcting Mistakes in the Medical Forest*" compiled during the Qing Dynasty. For centuries, BYHWD has been employed in China to treat SCI, with clinical trials demonstrating its capacity to enhance the prognosis of SCI [44]. The primary active ingredients in BYHWD encompass quercetin, kaempferol, and  $\beta$ -sitosterol. These components exert therapeutic effects on SCI by intervening with targets like TP53, AKT1, MAPK1, RELA, and signaling pathways such as MAPK, PI3K-Akt, Fox O, TLRs, and TNF [45]. BYHWD can promote neural recovery in rats with SCI by improving motor function and neuron survival in the nucleus. The neuroprotective effects of BYHWD are likely related to its influence on the mTOR signaling pathway and autophagy [46]. HQGZD originates

from "*Synopsis Golden Chamber*" and possesses the effects of tonifying *Qi*, warming meridians, and promoting blood circulation to unblock obstruction. It is a classic prescription with key information published by the National Administration of TCM in China. Currently, modern research on HQGZD primarily centers on clinical and pharmacological mechanisms of action. However, research on its material basis is relatively scarce and not comprehensive. A study has demonstrated that the total effective rate of HQGZD in treating SCI with ASIA neural function grading is 88.89 %, markedly superior to the total effective rate of 61.11 % in the conventional group [47]. HQGZD can effectively reduce the levels of pain-inducing and inflammatory factors, promote vertebral function repair, and alleviate clinical symptoms in patients with SCI [16,48,49]. Another study has shown that HQGZD can regulate Caspase-3 and improve spinal cord damage in rats [50].

While this study yielded positive results, some limitations should be considered: (a) Blinding Issues: The majority of included studies did not specify blinding methods for allocation concealment, blinding implementation processes, or outcome evaluation. Only one study mentioned the use of blinding methods, which reduces the reliability of CHCP effectiveness evaluation. (b) Diversity in CHCPs: The CHCPs in the experimental group comprised both classic and empirical decoctions. Some of these decoctions lacked detailed specifications, leading to a diversification of intervention measures within the experimental group. (c) Geographic Limitation: All included studies were conducted in China, in which has abundant TCM resources and extensive research and clinical practice. However, SCI is a globally relevant condition, and the results obtained may carry language and publication biases. (d) Short Trial Cycles: Most studies had short trial cycles and lacked long-term prognostic efficacy evaluations.

However, existing research often concentrates on the effects of CHCP on SCI through clinical observation, lacking rigorous experimental design, quality management, and in-depth mechanistic exploration. This poses obstacles and limitations for the broader application of TCM in SCI. Therefore, this study systematically assessed the promotional effect of CHCP on spinal cord function recovery post-SCI surgery and mitigated adverse events. The findings indicate that CHCP significantly enhances AISA motor and sensory scores post-SCI surgery, subsequently improving patients' quality of life while minimizing the occurrence of adverse events.

Due to the generally low methodological quality of the studies included in this research, there is a lack of uniformity among the experimental groups, control groups, and outcome indicators, affecting the evidence strength of meta-analysis. Therefore, future research requires high-quality RCTs conducted across multiple centers, with long-term follow-up and large sample sizes. Additionally, further investigations into potential therapeutic mechanisms, optimal administration routes, and dosages based on clinical trials are warranted. Moreover, validating TCM theory through modern mechanistic research methods is essential to uncover the contemporary mechanisms of relevant treatment principles and methods in traditional theory. This approach aims to enhance the quality of evidence-based medicine and facilitate the widespread application of TCM in treatment.

## 5. Conclusion

Chinese herbal compound prescriptions have demonstrated the ability to improve postoperative ASIA motor and sensory scores, enhance ADL scores, and reduce adverse events following SCI surgery. The combination of surgery with HQGZD or BYHWD have shown superior therapeutic effects in SCI treatment. Integrating CHCP into postoperative care for SCI patients may offer potential benefits.

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## Data availability statement

The original data and supplementary materials for this research have been stored at https://osf.io/d38nc/. For additional data access requests, please contact the first author at 523066306@qq.com.

#### CRediT authorship contribution statement

**Wen-xi Sun:** Writing – original draft, Methodology, Investigation, Formal analysis, Data curation. **Zi-bo Gao:** Methodology, Investigation, Formal analysis. **Ao-wei Tan:** Resources, Methodology. **Bo-lai Chen:** Supervision, Funding acquisition. **Li-ming Lu:** Writing – review & editing, Supervision, Methodology, Funding acquisition, Conceptualization. **Yong-peng Lin:** Writing – review & editing, Supervision, Methodology, Funding acquisition.

## Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:Yong-peng Lin reports financial support was provided by Guangdong Second Traditional Chinese Medicine Hospital. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e37058.

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