

Appendix

Systematic review and network meta-analysis comparing Chinese herbal injections with chemotherapy for treating patients with esophageal cancer

PRISMA checklist for network meta-analysis:

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review incorporating a network meta-analysis (or related form of meta-analysis).	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: Background: main objectives Methods: data sources; study eligibility criteria, participants, and interventions; study appraisal; and synthesis methods, such as network meta-analysis. Results: number of studies and participants identified; summary estimates with corresponding confidence/credible intervals; treatment rankings may also be discussed. Authors may choose to summarize pairwise comparisons against a chosen treatment included in their analyses for brevity. Discussion/Conclusions: limitations; conclusions and implications of findings. Other: primary source of funding; systematic review registration number with registry name.	1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known, including mention of why a network meta-analysis has been conducted	2

Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	2
METHODS			
Protocol and registration	5	Indicate if a review protocol exists and if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	/
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. Clearly describe eligible treatments included in the treatment network, and note whether any have been clustered or merged into the same node (with justification).	3-4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	3
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	3
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	4
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	4
Geometry of the network	12	Describe methods used to explore the geometry of the treatment network under study and potential biases related to it. This should include how the evidence base has been graphically summarized for presentation, and what characteristics were compiled and used to describe the evidence base to readers	4-5
Risk of bias within individual studies	13	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	4
Summary measures	14	State the principal summary measures (e.g., risk ratio, difference in means). Also describe the use of additional summary measures assessed, such as treatment rankings and surface under the cumulative ranking curve (SUCRA) values, as well as modified approaches used to present summary findings from meta-analyses.	4-5
Planned methods of analysis	15	Describe the methods of handling data and combining results of studies for each network meta-analysis. This should include, but not be limited to: Handling of multigroup trials; Selection of variance structure; Selection of prior distributions in Bayesian analyses; and Assessment of model fit.	4-5
Assessment of inconsistency	16	Describe the statistical methods used to evaluate the agreement of direct and indirect evidence in the treatment network(s) studied. Describe efforts taken to address its presence when found.	5

Risk of bias across studies	17	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies)	4
Additional analyses	18	Describe methods of additional analyses if done, indicating which were prespecified. This may include, but not be limited to, the following: Sensitivity or subgroup analyses; Meta-regression analyses; Alternative formulations of the treatment network; and Use of alternative prior distributions for Bayesian analyses (if applicable).	4-5
RESULTS			
Study selection	19	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	5-7
Presentation of network structure	20	Provide a network graph of the included studies to enable visualization of the geometry of the treatment network.	7
Summary of network geometry	21	Provide a brief overview of characteristics of the treatment network. This may include commentary on the abundance of trials and randomized patients for the different interventions and pairwise comparisons in the network, gaps of evidence in the treatment network, and potential biases reflected by the network structure.	5-6
Study characteristics	22	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	6-7
Risk of bias within studies	23	Present data on risk of bias of each study and, if available, any outcome level assessment.	7
Results of individual studies	24	For all outcomes considered (benefits or harms), present, for each study: 1) simple summary data for each intervention group, and 2) effect estimates and confidence intervals. Modified approaches may be needed to deal with information from larger networks.	7-9
Synthesis of results	25	Present results of each meta-analysis done, including confidence/credible intervals. In larger networks, authors may focus on comparisons versus a particular comparator (e.g., placebo or standard care), with full findings presented in an appendix. League tables and forest plots may be considered to summarize pairwise comparisons. If additional summary measures were explored (such as treatment rankings), these should also be presented.	7-9
Exploration for inconsistency	26	Describe results from investigations of inconsistency. This may include such information as measures of model fit to compare consistency and inconsistency models, P values from statistical tests, or summary of inconsistency estimates from different parts of the treatment network.	/
Risk of bias across studies	27	Present results of any assessment of risk of bias across studies for the evidence base being studied.	10
Results of additional analyses	28	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression analyses, alternative network geometries studied, alternative choice of prior distributions for Bayesian analyses, and so forth).	10
DISCUSSION			

Summary of evidence	29	Summarize the main findings, including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., health care providers, researchers, and policymakers).	10-11
Limitations	30	Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias). Comment on the validity of the assumptions, such as transitivity and consistency. Comment on any concerns regarding network geometry (e.g., avoidance of certain comparisons).	12
Conclusions	31	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	12
FUNDING			
Funding	32	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. This should also include information regarding whether funding has been received from manufacturers of treatments in the network and/or whether some of the authors are content experts with professional conflicts of interest that could affect use of treatments in the network.	13

More details about the product information of CHIs

CHI name	Raw materials	Labeled efficacy	Indications
Compound kushen injection	<i>Sophorae Flavescentis</i> <i>Radix, Smilacis Glabrae</i> <i>Rhizoma</i>	Clearing away hot, removing dampness, cooling blood, removing toxin, resolving hard mass, and relieving pain	Cancer pain, bleeding
Shenqifuzheng injection	<i>Astragali Radix, Ligustri Lucidi Fructus</i>	Tonifying Qi and nourishing Yin	Fatigue, lack of strength, vertigo caused by asthenia of pulmonosplenic Qi; auxiliary treatment of the above symptoms for lung cancer and gastric cancer
Aidi injection	<i>Mylabris, Ginseng Radix Et Rhizoma, Astragali Radix, Acanthopanacis Senticosi Radix Et Rhizoma Seu Caulis</i>	Clearing away hot, removing toxin, resolving stagnation and dispersing masses	Primary liver cancer, lung cancer, rectal cancer, malignant lymphoma, gynecological malignant tumors, etc.
Kangai injection	<i>Astragali Radix, Ginseng Radix Et Rhizoma, Sophorae Flavescentis Radix</i>	Tonifying Qi and strengthening body resistance	Primary liver cancer, lung cancer, rectal cancer, malignant lymphoma, gynecological malignant tumors; neutropenia and thrombocytopenia; chronic hepatitis B from various causes.
Huachansu injection	<i>Bufois Corium</i>	Removing toxin, detumescence, and relieving pain	Middle and advanced cancer, chronic hepatitis B etc..
Kanglaite injection	<i>Jobstears Seed Oil</i>	Tonifying Qi, nourishing Yin, and resolving mass	Unfavorable operation of Qi and yin deficiency, spleen deficiency and dampness retention with primary non-small cell lung cancer and primary liver cancer; has anti cachexia and analgesic effects in patients with advanced cancer
Javanica emulsion injection	oil <i>Bruceae Fructus</i>	Anticarcinogen	Lung cancer, brain metastasis of lung cancer and digestive system neoplasms
Xiaoaiping injection	<i>Marsdenia tenacissima Caul</i>	Clearing away heat and toxic material, resolving phlegmand softening hard masses	Esophageal cancer, gastric cancer, lung cancer, liver cancer; combination with radiotherapy and chemotherapy as adjuvant therapy
Delisheng	<i>Radix Ginseng, Astragalus, venenum</i>	Supplementing Qi and strengthening the body resistance, eliminating	Syndromes of Qi deficiency stasis on middle-late stage primary liver cancer, abdominal

injection	<i>bufonis, cantharides</i>	inflammation and dissipating stasis	mass in right rib, pain of fixed location, abdominal distension, fatigue.
Elemene injection	β -, γ -, δ -elemene mixture	/	Combined with routine regimen of radiotherapy and chemotherapy to enhance the curative effect and reduce the toxic and side effects for treating lung cancer, liver cancer, esophageal cancer, nasopharyngeal cancer, brain tumor, bone metastasis cancer and other malignant tumors; interventional therapy, intracavitary chemotherapy and treatment of carcinomatous hydrothorax and ascites; as first-line treatment for malignant pleural effusion, ascites, brain tumors, respiratory tract and digestive tract tumors; as second-line therapy for gynecologic cancer, breast cancer, skin cancer, bone metastasis, lymphoma, leukemia, etc..
Shenmai injection	<i>Radix Ginseng Rubra, Radix Ophiopogonis</i>	Tonifying Qi and preventing exhaustion, nourishing Yin and generating body fluid, activating pulse	Shock, coronary heart disease, viral myocarditis, chronic pulmonary heart disease and neutropenia with deficiency of Qi and Yin; improve the immune function of patients with tumors, combined with chemotherapy to enhance the curative effect and reduce the toxic and side effects
Disodium cantharidinate and vitamin B6 injection	Disodium cantharidinate and vitamin B6	Anticarcinogen	Advanced primary liver cancer and advanced lung cancer
Chansu injection	<i>Venenum bufonis</i>	Heat-clearing and detoxicating	Acute and chronic suppurative infection; as adjuvant drug for malignant tumors
Lentinan injection	Lentinan	Immunomodulator	Adjuvant therapy for malignant tumors
Ginseng polysaccharide injection	Ginseng polysaccharide	Immunomodulator	Alleviate the side effects of radiotherapy and chemotherapy, adjuvant therapy for tumors; improve the immune function, acute and chronic hepatitis and liver injuries, chronic infections, diabetes and immunological disease
Shenfu injection	<i>Radix Ginseng, Radix Carmichaeli</i>	Reviving Yang for resuscitation, tonifying Qi and preventing exhaustion	Desertion syndrome caused by excessive Yang Qi desertion (infectious, hemorrhagic and fluid loss shock); deficiency of Yang or Qi with palpitation, cough, stomachache, diarrhea, rheumatism, etc.
Astragalus polysaccharides	Astragalus polysaccharides	Supplementing Qi and tonifying deficiency	Fatigue, spontaneous sweating, shortness of breath, anorexia of Qi deficiency syndrome; patients with aleucocytosis, low quality of life, and immunocompromise

injection				after chemotherapy
Astragalus injection	<i>Astragali Radix</i>		Tonifying Qi and strengthening body resistance, pulse invigorating and heart nourishing, fortifying spleen and disinhibiting dampness	Insufficiency of the heart-qi and blood stasis syndrome of viral myocarditis, cardiac insufficiency; hepatitis with spleen deficiency and dampness syndrome
Tongkenging injection	<i>Equisetum hiemale, Selaginella tamariscina</i>		Heat-clearing and detoxifying, expelling stagnation and relaxing vein	Adjuvant therapy for malignant tumor-induced pain
Wutou injection	<i>Radix Aconiti, Radix Aconiti Kusnezoffii</i>		tranquilizing and relieving pain	Stomach cancer, liver cancer and other advanced cancers-induced pain
Polyporus polysaccharide injection	Grifola polysaccharide		Immunomodulator	Combined with antineoplastic drugs, it can enhance the curative effect and a decrease side reactions
Yuanqinzhitong injection	<i>Corydalis ambigua Ch., Radix Aconiti Praeparata, Fraxinus bungeana, Radices Stephaniae Tetrandrae, Chelidonium majus L.</i>		Promoting Qi to activate blood, activating meridians to stop pain	Moderate cancerous pain caused by Qi stagnation and blood stasis
Placental polypeptides injection	Placental peptide	/		Reduced or dysregulated cellular immunity-induced disease, postoperative healing, viral infection-induced disease, leucopenia caused by various reasons
