

Characteristics of included studies [ordered by study ID]

Chen 2017	
Methods	<p>Trial design: prospective parallel RCT</p> <p>Year of trial: 2017</p> <p>Judgement of the quality of study: see 'Risk of bias' table</p> <p>Groups comparable at baseline: demographic characteristics in both groups was balanced at baseline with statistical analysis</p> <p>Sample size calculation: not reported</p> <p>Intention-to-treat: not performed</p> <p>Drop-off: 0% in both groups</p> <p>Compliance: not reported</p> <p>Duration of study including follow-up: 6 cycles (18 weeks) of intervention with no follow-up period</p>
Participants	<p>Ethnics: Chinese</p> <p>Number of study centres: 1</p> <p>Source: Patients from Linan People Hospital in Linan, Zhejiang Province, China</p> <p>Setting: 90 patients (47 of male) randomised into two groups [45 (CHM: Hand and foot baths of Huzhou formula) vs 45 (Vitamine B12)]</p> <p>Included: Diagnosed with gastrointestinal cancer by pathology or medical imageology; Going to receive oxaliplatin regimens (XELOX (130mg/m², 3wk/cycle for 6 cycles); Karnofsky Score > 60 scores; Life expectancy will be over three months; Signed the consent form</p> <p>Excluded: Have cardiac, hepatic or renal disorder; Have other medical conditions in nervous system or diabetes; Have received any other pharmaceutical or non-pharmaceutical treatment such as acupuncture or immunotherapy</p>
Interventions	<p>Experimental group: (CHM: Hand and foot baths of Huzhou decoction)</p> <ul style="list-style-type: none"> • route of administration – Topical wash bath • form of intervention - in the form of raw herbs • style of herbal preparation - a standard formula (Huzhou decoction) <p>composition of herbal preparation - it contains Radix Astragali (Huang Qi) 40g, Ramulus Cinnamomi (Gui Zhi) 40g, Folium Artemisiae Argyi (Ai Ye) 12g, Caulis Spatholobi (Ji Xue Teng) 30g, Radix et Rhizoma Clematidis (Wei Ling Xian) 15g, Radix et Rhizoma Salviae Miltiorrhizae (Dan Shen) 15g, Radix Paeoniae Alba (Bai Shao) 12g, Radix Angelicae Sinesis (Dang Gui) 12g, Radix Cyathulae (Niu Xi)</p>

	<p>15g, Semen Persicae (Tao Ren) 12g, Flos Carthami (Hong Hua) 10g, Radix Angelicae Pubescentis (Du Huo) 10g, Rhizoma et Radix Notopterygii (Qiang Huo) 10g.</p> <ul style="list-style-type: none">• preparation of formula: the raw herbs were cooked for decoction• time of administration: not reported, 30 mins each intervention, bid (morning and evening) for two weeks at each cycle of chemotherapy <p>Control group: Mecobalamin</p> <ul style="list-style-type: none">• route of administration - oral• form of intervention - tablets• composition of preparation: Vitamin B12 (0.5 mg)• time of administration: not reported, three times a day for 3 weeks at each cycle of chemotherapy	
Outcomes	<p>Primary outcome was measured as change in reporting of: (1) Incidence rate measured by National Cancer Institute Common Terminology Criteria for Adverse Events sensory neuropathy scale; (2) Adverse events: not reported</p> <p>Secondary outcomes were measured as change in reporting of: Nerve conduction velocity: (1) median nerve motor nerve conduction velocity (2) fibular nerve motor nerve conduction velocity (3) median nerve sensory nerve conduction velocity (4) fibular nerve sensory nerve conduction velocity</p> <p>Outcome endpoints: After six cycles of chemotherapy treatment</p>	
Notes	<p>Language: Chinese</p> <p>Country/region of study: Zhejiang province, China</p> <p>Type of publication: Journal article</p> <p>Funding source: Not reported</p>	
Risk of Bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	<p>Quote: "patients were randomly allocated using a table of random numbers."</p> <p>Comment: Probably done.</p>
Allocation concealment (selection bias)	Unclear risk	<p>Quote: "...using a table of random numbers."</p> <p>Comment: Not in detail</p>
Blinding of participants and	High risk	Participants in intervention group were given hand and foot bath, while control group were oral VitB12. Review authors believe this

personnel (performance bias) All outcomes		will introduce bias to participants and personnel.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to assess whether a risk of bias exists in outcome assessment.
Incomplete outcome data (attrition bias) All outcomes	Low risk	0/90 missing from both groups were reported.
Selective reporting (reporting bias)	Low risk	All rating scales listed in Methods were reported in Results.
Other bias	High risk	The lack of information on sample size calculation; adverse events not designed to be report in Methods

Wang 2015	
Methods	<p>Trial design: prospective parallel RCT</p> <p>Year of trial: 2015</p> <p>Judgement of the quality of study: see 'Risk of bias' table</p> <p>Groups comparable at baseline: demographic characteristics in both groups was balanced at baseline with statistical analysis</p> <p>Sample size calculation: not reported</p> <p>Intention-to-treat: not performed</p> <p>Drop-off: 0% in both groups</p> <p>Compliance: not reported</p> <p>Duration of study including follow-up: 8 cycles (16 weeks) of intervention with no follow-up period</p>
Participants	<p>Ethnics: Chinese</p> <p>Number of study centres: 1</p> <p>Source: Patients from Jiangyan Chinese medicine Hospital in Taizhou, Jiangsu Province, China</p> <p>Setting: 120 patients (59 of male) randomised into four groups [30 (CHM: Hand and foot baths of Huangqiguizhiwuwu formula) vs 30 (CHM: Hand and foot baths of Huangqiguizhiwuwu formula + Ca-Mg Infusion) vs 30 (Ca-Mg Infusion) vs 30 (No additional treatment)]</p> <p>Included: Diagnosed with colorectal cancer by pathology; suitable for receiving oxaliplatin regimens (mFOLFOX 6 (85mg/m², 2wk/cycle for 8 cycles); Age between 20-75; Eastern Cooperative Oncology Group (ECOG) Score ≤ 2 scores; Life expectancy will be over three months</p> <p>Excluded: Not eligible for inclusion; Existing drug allergy to the chemotherapy; electrolyte disturbance (eg: hypermagnesemia; hypercalcemia); Have dermatologic conditions in hands and feet; unwilling to receive treatment or have poor compliance</p>
Interventions	<p>Experimental group:</p> <p>1) (CHM: Hand and foot baths of Hangqiguizhiwuwu decoction)</p> <ul style="list-style-type: none"> • route of administration – Topical wash bath • form of intervention - in the form of raw herbs • style of herbal preparation - a standard formula (Huangqiguizhiwuwu decoction) composition of herbal preparation - it contains Radix Astragali (Huang Qi) 45g, Radix Paeoniae Alba (Bai Shao) 15g, Ramulus Cinnamomi (Gui Zhi) 45g, Rhizoma Zingiberis Recens (Sheng Jiang) 20g, Fructus Jujubae (Da Zao) 10g, Caulis

	<p>Spatholobi (Ji Xue Teng) 45g, Semen Persicae (Tao Ren) 10g, Flos Carthami (Hong Hua) 10g, Radix et Rhizoma Salviae Miltiorrhizae (Dan Shen) 10g, Radix Aconiti Lateralis (Fu Zi) 10g</p> <ul style="list-style-type: none"> • preparation of formula: the raw herbs were cooked for decoction • time of administration: not reported, 30 mins each intervention, once a day for one week at each cycle of chemotherapy <p>2) CHM: Hand and foot baths of Hangqiguizhiwu decoction + Ca-Mg Infusion</p> <p>Control group:</p> <p>1) Ca-Mg infusion</p> <p>route of administration – intravenous infusion</p> <p>form of intervention - liquid</p> <p>composition of preparation: calcium gluconate 10% (10ml)+ magnesium sulfate 25% (4ml) mixing with normal saline or dextrose solution 5% (100ml)</p> <p>time of administration: not reported, two times a day when applying oxaliplatin for each cycle of chemotherapy</p> <p>2) No additional treatment</p>
Outcomes	<p>Primary outcome was measured as change in reporting of: (1) Incidence rate measured by Levi's grade; (2) Adverse events: not reported</p> <p>Secondary outcomes were measured as change in reporting of: Not reported</p> <p>Outcome endpoints: After eight cycles of chemotherapy treatment</p>
Notes	<p>Language: Chinese</p> <p>Country/region of study: Jiangsu province, China</p> <p>Type of publication: Journal article</p> <p>Funding source: Jiangsu Province Taizhou Science and Technology Bureau Grant (Taizhou Science Scheme No:2013-156)</p>

Risk of Bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were randomly allocated using a table of random numbers." Comment: Probably done.
Allocation concealment (selection bias)	Unclear risk	Quote: "...using a table of random numbers." Comment: Not in detail
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants in intervention group were given hand and foot bath (or combined with Ca/Mg iv. infusion, while control group were nothing or Ca/Mg iv. infusion. Review authors believe this will introduce bias to participants and personnel.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to assess whether a risk of bias exists in outcome assessment.
Incomplete outcome data (attrition bias) All outcomes	Low risk	0/120 missing from both groups were reported.
Selective reporting (reporting bias)	Low risk	All rating scales listed in Methods were reported in Results.
Other bias	High risk	The lack of information on sample size calculation; adverse events not designed to be report in Methods

Deng 2014	
Methods	<p>Trial design: prospective parallel RCT</p> <p>Year of trial: 2014</p> <p>Judgement of the quality of study: see 'Risk of bias' table</p> <p>Groups comparable at baseline: demographic characteristics in both groups was balanced at baseline with statistical analysis</p> <p>Sample size calculation: not reported</p> <p>Intention-to-treat: not performed</p> <p>Drop-off: 18.0% in both groups (15.6% in intervention group; 20.3% in control group)</p> <p>Compliance: not reported</p> <p>Duration of study including follow-up: 6 cycles (12 weeks) of intervention with no follow-up period</p>
Participants	<p>Ethnics: Chinese</p> <p>Number of study centres: 1</p> <p>Source: inpatients and clinic patients from Beijing Chinese medicine Hospital Affiliated to Capital University of Medical Sciences, Beijing, China</p> <p>Setting: 128 patients (57 of male) randomised into four groups [64 (CHM: Hand and foot baths of Wenyangtongluo decoction) vs 64 (Hand and foot baths of warm water)]</p> <p>Included: Diagnosed with gastrointestinal cancer; Going to receive oxaliplatin regimens (FOLFOX4 -85mg/m² or FOLFOX 6 -100mg/m² (2wk/cycle for 8 cycles); XELOX -130mg/m² or L-OHP+S1 -100mg/m² (3wk/cycle for 8 cycles); Age ≤ 70; Karnofsky Score ≥ 70 scores; Have no cardiovascular, respiratory, hepatic, renal and nervous system disorder; Consent to participating the study</p> <p>Excluded: Not eligible for the study; Have central or peripheral nervous system conditions; Have diabetes that may impair peripheral nerve function</p>
Interventions	<p>Experimental group: (CHM: Hand and foot baths of Yangxuewenjingtongluo decoction)</p> <ul style="list-style-type: none"> • route of administration – topical wash bath • form of intervention - in the form of raw herbs • style of herbal preparation - a standard formula (Yangxuewenjingtongluo decoction) composition of herbal preparation - it contains Radix Astragali (Huang Qi), Radix Angelicae Sinesis (Dang Gui), Flos Carthami (Hong Hua), Radix Aconiti (Chuan Wu), Caulis Spatholobi (Ji Xue Teng), etc (dosage not available) • preparation of formula: the raw herbs were cooked for decoction

	<ul style="list-style-type: none"> time of administration: not reported, 20 mins each intervention, twice a day during each cycle of chemotherapy <p>Control group: No additional treatment</p>
Outcomes	<p>Primary outcome was measured as change in reporting of: (1) Incidence rate measured by WHO sensory neuropathy scale; (2) Adverse events</p> <p>Secondary outcomes were measured as change in reporting of: (1) Toronto Clinical Scoring System (TCSS); (2) cumulative oxaliplatin dosage by the onset of grade ≥ 2 peripheral neuropathy</p> <p>Outcome endpoints: At baseline and after eight cycles of chemotherapy treatment</p>
Notes	<p>Language: Chinese</p> <p>Country/region of study: Beijing, China</p> <p>Type of publication: Master degree thesis</p> <p>Funding source: Not reported</p>

Risk of Bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were randomly allocated using a table of random numbers." Comment: Probably done.
Allocation concealment (selection bias)	High risk	Quote: "...using a table of random numbers." Comment: Probably not done.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants in intervention group were given hand and foot bath, while control group were nothing. Review authors believe this will introduce bias to participants and personnel.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to assess whether a risk of bias exists in outcome assessment.
Incomplete outcome data (attrition bias) All outcomes	Low risk	10/54 missing from intervention groups (4 due to 'discontinuation in chemotherapy'), 7/54 missing from placebo group due to 'discontinuation in chemotherapy'
Selective reporting (reporting bias)	Low risk	All rating scales listed in Methods were reported in Results.
Other bias	Unclear risk	Insufficient information to assess whether an important risk of bias exists;

Huang 2010	
Methods	<p>Trial design: prospective parallel RCT</p> <p>Year of trial: 2010</p> <p>Judgement of the quality of study: see 'Risk of bias' table</p> <p>Groups comparable at baseline: demographic characteristics in both groups was balanced at baseline with statistical analysis</p> <p>Sample size calculation: not reported</p> <p>Intention-to-treat: not performed</p> <p>Drop-off: 0% in both groups</p> <p>Compliance: not reported</p> <p>Duration of study including follow-up: 4 cycles (8 weeks) of intervention with no follow-up period</p>
Participants	<p>Ethnics: Chinese</p> <p>Number of study centres: 2</p> <p>Source: Patients from Wenzhou Chinese medicine Hospital and the First Affiliated Hospital to Wenzhou Medical School in Wenzhou, Zhejiang Province, China</p> <p>Setting: 60 patients (43 of male) randomised into two groups [30 (CHM: Hand and foot baths of Huangqiguizhiwuwu formula) vs 30 (No additional treatment)]</p> <p>Included: Diagnosed with colorectal cancer by pathology or cytology; suitable for receiving oxaliplatin regimens; Age between 28-76; Karnofsky Score > 60 scores; Life expectancy will be over three months; Signed the consent form</p> <p>Excluded: Not eligible for inclusion; Have other medical conditions in nervous system or diabetes; Have dermatologic conditions in hands and feet or drug allergy</p>
Interventions	<p>Experimental group: (CHM: Hand and foot baths of Hangqiguizhiwuwu decoction)</p> <ul style="list-style-type: none"> • route of administration – Topical wash bath • form of intervention - in the form of raw herbs • style of herbal preparation - a standard formula (Huangqiguizhiwuwu decoction) composition of herbal preparation - it contains Radix Astragali (Huang Qi) 100g, Radix Paeoniae Alba (Bai Shao) 30g, Ramulus Cinnamomi (Gui Zhi) 20g, Rhizoma Zingiberis Recens (Sheng Jiang) 10g, Fructus Jujubae (Da Zao) 10g • preparation of formula: the raw herbs were cooked for decoction • time of administration: not reported, 30 mins each intervention,

	twice a day for five days at each cycle of chemotherapy Control group: No additional treatment	
Outcomes	Primary outcome was measured as change in reporting of: (1) Incidence rate measured by Levi’s grade; (2) Adverse events: not reported Secondary outcomes were measured as change in reporting of: Nerve conduction velocity: (1) median nerve motor nerve conduction velocity (2) fibular nerve motor nerve conduction velocity (3) median nerve sensory nerve conduction velocity (4) fibular nerve sensory nerve conduction velocity Outcome endpoints: After four cycles of chemotherapy treatment	
Notes	Language: Chinese Country/region of study: Zhejiang province, China Type of publication: Journal article Funding source: Zhejiang Province Wenzhou Medical Science research Grant (No:2009B054)	
Risk of Bias		
Bias	Authors’ judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “patients were randomly allocated using a table of random numbers.” Comment: Probably done.
Allocation concealment (selection bias)	Unclear risk	Quote: “...using a table of random numbers.” Comment: Not in detail
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants in intervention group were given hand and foot bath, while control group were nothing. Review authors believe this will introduce bias to participants and personnel.
Blinding of outcome assessment	Unclear risk	Insufficient information to assess whether a risk of bias exists in outcome

(detection bias) All outcomes		assessment.
Incomplete outcome data (attrition bias) All outcomes	Low risk	0/60 missing from both groups were reported.
Selective reporting (reporting bias)	Low risk	All rating scales listed in Methods were reported in Results.
Other bias	High risk	The lack of information on sample size calculation; adverse events not designed to be report in Methods

Wang 2014	
Methods	<p>Trial design: prospective parallel RCT</p> <p>Year of trial: 2014</p> <p>Judgement of the quality of study: see 'Risk of bias' table</p> <p>Groups comparable at baseline: demographic characteristics in both groups was balanced at baseline with statistical analysis</p> <p>Sample size calculation: not reported</p> <p>Intention-to-treat: not performed</p> <p>Drop-off: 4.3% in both groups (2.9% in intervention group; 5.7% in control group)</p> <p>Compliance: not reported</p> <p>Duration of study including follow-up: 6 cycles (12 weeks) of intervention with no follow-up period</p>
Participants	<p>Ethnics: Chinese</p> <p>Number of study centres: 1</p> <p>Source: inpatients and clinic patients from Department of Oncology, Zhejiang province, China</p> <p>Setting: 70 patients (29 of male) randomised into two groups [35 (CHM: Hand and foot baths of Wengjinghuoxue decoction) vs 35 (No additional treatment)]</p> <p>Included: Diagnosed with gastrointestinal cancer by pathology or cytology; Suitable for receive oxaliplatin regimens (135mg/m²; 2wk/cycle for 6 cycles); Age between 18-75; Karnofsky Score ≥ 60 scores and life expectancy ≥ six months; Preclude from any reasons inducing peripheral neuropathy (eg. diabetes, poisoning, infection); Have no cardiac, hepatic, renal and nervous system disorder; Consent to participating the study</p> <p>Excluded: Not eligible for the study; Have neurological system conditions; Have hands and feet skin diseases and drug allergy to any composition of herbal medicine; Receiving other neurotoxic chemotherapy or radiotherapy; During pregnancy or Lactation period; Have poor compliance</p>
Interventions	<p>Experimental group: (CHM: Hand and foot baths of Wengjinghuoxue decoction)</p> <ul style="list-style-type: none"> • route of administration – topical wash bath • form of intervention - in the form of raw herbs • style of herbal preparation - a standard formula (Wengjinghuoxue decoction) composition of herbal preparation - it contains Ramulus Cinnamomi (Gui Zhi) 12g, Herba Ephedrae (Ma Huang) 6g, Radix Paeoniae Alba (Bai Shao) 12g, Flos Carthami (Hong Hua) 9g, Radix

	<p>Chuanxiong (Chuan Xiong) 30g, Radix Aconiti Lateralis (Fu Zi) 6g, Radix et Rhizoma Glycyrrhizae (Gan Cao) 6g</p> <ul style="list-style-type: none">• preparation of formula: the raw herbs were cooked for decoction• time of administration: not reported, 40 mins each intervention, once a day for five days at each cycle of chemotherapy <p>Control group: No additional treatment</p>	
Outcomes	<p>Primary outcome was measured as change in reporting of: (1) Incidence rate measured by Levi’s sensory neuropathy scale; (2) Adverse events</p> <p>Secondary outcomes were measured as change in reporting of: (1) Incidence of peripheral neuropathy when oxaliplatin dose ≥ 900mg/m²</p> <p>Outcome endpoints: At baseline and after two/four/six cycles of chemotherapy treatment</p>	
Notes	<p>Language: Chinese</p> <p>Country/region of study: Zhejiang province, China</p> <p>Type of publication: Master degree thesis</p> <p>Funding source: Not reported</p>	
Risk of Bias		
Bias	Authors’ judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	<p>Quote: “patients were randomly allocated using a table of random numbers.”</p> <p>Comment: Probably done.</p>
Allocation concealment (selection bias)	Unclear risk	<p>Quote: “...using a table of random numbers.”</p> <p>Comment: Not in detail</p>
Blinding of participants and personnel (performance bias) All outcomes	High risk	<p>Participants in intervention group were given hand and foot bath, while control group were nothing. Review authors believe this will introduce bias to participants and personnel.</p>

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to assess whether a risk of bias exists in outcome assessment.
Incomplete outcome data (attrition bias) All outcomes	Low risk	1/35 missing from intervention group due to 'side effects of treatment'; 2/35 missing from control group (1 due to 'side effects of treatment')
Selective reporting (reporting bias)	Low risk	All rating scales listed in Methods were reported in Results.
Other bias	Unclear risk	Insufficient information to assess whether an important risk of bias exists;

Zhang 2017	
Methods	<p>Trial design: prospective parallel RCT</p> <p>Year of trial: 2017</p> <p>Judgement of the quality of study: see 'Risk of bias' table</p> <p>Groups comparable at baseline: demographic characteristics in both groups was balanced at baseline with statistical analysis</p> <p>Sample size calculation: not reported</p> <p>Intention-to-treat: not performed</p> <p>Drop-off: 4.5% in both groups (0% in intervention group; 9.1% in control group)</p> <p>Compliance: not reported</p> <p>Duration of study including follow-up: 4 cycles (8 weeks) of intervention with no follow-up period</p>
Participants	<p>Ethnics: Chinese</p> <p>Number of study centres: 1</p> <p>Source: Patients from Department of Oncology, Henan Provincial Hospital, Henan Province, China</p> <p>Setting: 44 patients (28 of male) randomised into four groups [22 (CHM: Hand and foot baths of Huangqiguizhiwuwu formula) vs 22 (No additional treatment)]</p> <p>Included: Diagnosed with colorectal cancer by pathology or cytology; suitable for receiving oxaliplatin regimens (FOLFOX4 or FOLFOX 6 (85mg/m², 2wk/cycle for 12 cycles); Age between 18-75; Life expectancy will be over nine months; Joined the study voluntarily and signed the consent form</p> <p>Excluded: Not eligible for inclusion; Have mental disorder or poor compliance; Have other medical conditions in nervous system; Have drug allergy to herbal medicine or mecobalamin; Have participated in other similar clinical studies.</p>
Interventions	<p>Experimental group: (CHM: Hand and foot baths of Huangwuteng decoction) + mecobalamin</p> <p>Hand and foot baths of Huangwuteng decoction:</p> <ul style="list-style-type: none"> • route of administration – Topical wash bath • form of intervention - in the form of raw herbs • style of herbal preparation - a standard formula (Huangwuteng decoction) composition of herbal preparation - it contains Radix Astragali (Huang Qi) 30g, Caulis Spatholobi (Ji Xue Teng) 30g, Caulis Trachelospermi (Luo Shi Teng) 30g, Radix Tinosporae (Jin Guo Lan) 30g, Ramulus Mori (Sang Zhi) 30g, Radix Angelicae Sinesis (Dang Gui)

	<p>30g, Ramulus Cinnamomi (Gui Zhi) 10g, Radix Gentianae Macrophyllae (Qin Jiao) 10g, Radix Cyathulae (Niu Xi) 10g, Radix Chuanxiong (Chuan Xiong) 20g, Cortex Phellodendri Chinensis (Huang Bo) 15g, Herba Taraxaci (Pu Gong Ying) 30g, Radix Aconiti (Chuan Wu) 20g, Radix Aconiti Kusnezoffii (Cao Wu) 20g</p> <ul style="list-style-type: none"> • preparation of formula: the raw herbs were cooked for decoction • time of administration: not reported, 30 mins each intervention, twice a day, daily during each cycle of chemotherapy <p>Mecobalamin:</p> <ul style="list-style-type: none"> • route of administration - oral • form of intervention - tablets • composition of preparation: Vitamin B12 (0.5 mg) • time of administration: not reported, three times a day for one week for each cycle of chemotherapy <p>Control group: mecobalamin (As above)</p>
Outcomes	<p>Primary outcome was measured as change in reporting of: (1) Incidence rate measured by NCI-CTC sensory neuropathy scale; (2) Adverse events: not reported</p> <p>Secondary outcomes were measured as change in reporting of: (1) Activities of Daily Living (ADL) Score; (2) cumulative oxaliplatin dosage when PN occurred; (3) sensory median nerve conduction velocity</p> <p>Outcome endpoints: At baseline and after four/eight/twelve cycles of chemotherapy treatment</p>
Notes	<p>Language: Chinese</p> <p>Country/region of study: Henan province, China</p> <p>Type of publication: Master degree thesis</p> <p>Funding source: Not reported</p>

Risk of Bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	<p>Quote: "patients were randomly allocated using a table of random numbers."</p> <p>Comment: Probably done.</p>
Allocation concealment (selection bias)	High risk	<p>Quote: "...using a table of random numbers."</p>

		Comment: Probably not done.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants in intervention group were given hand and foot bath, while control group were oral VitB12. Review authors believe this will introduce bias to participants and personnel.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to assess whether a risk of bias exists in outcome assessment.
Incomplete outcome data (attrition bias) All outcomes	Low risk	0/22 missing from the intervention group; 2/22 missing from the control group due to 'discontinuation in chemotherapy'
Selective reporting (reporting bias)	Low risk	All rating scales listed in Methods were reported in Results.
Other bias	High risk	The lack of information on sample size calculation; adverse events not designed to be report in Methods

Li 2010	
Methods	<p>Trial design: prospective parallel RCT</p> <p>Year of trial: 2010</p> <p>Judgement of the quality of study: see 'Risk of bias' table</p> <p>Groups comparable at baseline: demographic characteristics in both groups was balanced at baseline with statistical analysis</p> <p>Sample size calculation: not reported</p> <p>Intention-to-treat: not performed</p> <p>Drop-off: 0% in both groups</p> <p>Compliance: not reported</p> <p>Duration of study including follow-up: 6 cycles (12 weeks) of intervention with no follow-up period</p>
Participants	<p>Ethnics: Chinese</p> <p>Number of study centres: 1</p> <p>Source: Patients from Guangdong Provincial Chinese Medicine Hospital, Guangdong Province, China</p> <p>Setting: 90 patients (49 of male) randomised into two groups [45 (CHM: Hand and foot baths of Wenjinghuoxue formula) vs 45 (No additional treatment)]</p> <p>Included: Diagnosed with gastrointestinal cancer (gastric cancer; esophageal cancer; colorectal cancer) with pathology evidence; suitable for receiving L-OHP regimen and concomitant medications do not include any other neurotoxic drugs; Age between 18-75; Eastern Cooperative Oncology Group (ECOG) Score: 0-2 scores; Life expectancy will be over three months; Have no cardiac, hepatic, renal and bone marrow disorders; First time to use L-HOP; Signed the participant consent form</p> <p>Excluded: Those who are allergic to this drug; those with original nervous system diseases; those with neurological compression symptoms caused by brain metastasis or limb metastasis; those with neurological diseases caused by alcohol or heavy metal poisoning and other systemic diseases (such as severe diabetes); electrolyte disorders such as hypercalcemia or hypomagnesemia; people who are using digitalis or thiazide diuretics; those with history of hands and feet skin problems or allergy to drug exposure</p>
Interventions	<p>Experimental group: (CHM: Hand and foot baths of Wenjingtongluo decoction)</p> <ul style="list-style-type: none"> • route of administration – Topical wash bath • form of intervention - in the form of raw herbs • style of herbal preparation - a standard formula (Wenjingtongluo

	<p>decoction) composition of herbal preparation - it contains Aconiti Lateralis Radix Praeparata (Fu Zi) 40g, Cinnamomi Ramulus (Gui Zhi) 60g, Glycyrrhizae Radix et Rhizoma (Gan Cao) 20g, Herba Lycopodii (Shen Jin Cao) 60g</p> <ul style="list-style-type: none">• preparation of formula: the raw herbs were cooked for decoction• time of administration: not reported, 20 mins each intervention, once a day during each cycle of chemotherapy <p>Control group: No additional treatment</p>	
Outcomes	<p>Primary outcome was measured as change in reporting of: (1) Incidence rate measured by Levi’s grade; (2) Adverse events: not reported</p> <p>Secondary outcomes: Not reported</p> <p>Outcome endpoints: After each cycles of chemotherapy treatment</p>	
Notes	<p>Language: Chinese</p> <p>Country/region of study: Guangdong Province, China</p> <p>Type of publication: Journal article</p> <p>Funding source: N/A</p>	
Risk of Bias		
Bias	Authors’ judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	<p>Quote: “patients were randomly allocated using a table of random numbers.”</p> <p>Comment: Probably done.</p>
Allocation concealment (selection bias)	Unclear risk	<p>Quote: “...using a table of random numbers.”</p> <p>Comment: Not in detail</p>
Blinding of participants and personnel (performance bias) All outcomes	High risk	<p>Participants in intervention group were given hand and foot bath, while control group were nothing. Review authors believe this will introduce bias to participants and personnel.</p>

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to assess whether a risk of bias exists in outcome assessment.
Incomplete outcome data (attrition bias) All outcomes	Low risk	0/90 missing from both groups were reported.
Selective reporting (reporting bias)	Low risk	All rating scales listed in Methods were reported in Results.
Other bias	High risk	The lack of information on sample size calculation; adverse events not designed to be report in Methods

Yang 2015	
Methods	<p>Trial design: prospective parallel RCT</p> <p>Year of trial: 2015</p> <p>Judgement of the quality of study: see 'Risk of bias' table</p> <p>Groups comparable at baseline: demographic characteristics in both groups was balanced at baseline with statistical analysis</p> <p>Sample size calculation: not reported</p> <p>Intention-to-treat: not performed</p> <p>Drop-off: 4.2% in both groups (2.7% in intervention group; 5.6% in control group)</p> <p>Compliance: not reported</p> <p>Duration of study including follow-up: 6 cycles (12 weeks) of intervention with no follow-up period</p>
Participants	<p>Ethnics: Chinese</p> <p>Number of study centres: 1</p> <p>Source: in patients from Department of Oncology, Beijing Chinese Medicine Hospital, Beijing, China</p> <p>Setting: 72 patients (38 of male) randomised into four groups [35 (CHM: Hand and foot baths of Wenyangtongluo decoction) vs 34 (No additional treatment)]</p> <p>Included: Diagnosed with gastrointestinal cancer by validated criteria; initial receiving oxaliplatin regimens (FOLFOX4 (85mg/m², 2wk/cycle for 6 cycles); Age between 18-75; Karnofsky Score \geq 60 scores; Life expectancy will be over three months</p> <p>Excluded: Have mental disorder or poor compliance; During pregnancy or Lactation period; Have other medical conditions in nervous system or diabetes; Have drug allergy to any composition of herbal medicine</p>
Interventions	<p>Experimental group: (CHM: Hand and foot baths of Wenyangtongluo decoction):</p> <ul style="list-style-type: none"> • route of administration – Topical wash bath • form of intervention - in the form of raw herbs • style of herbal preparation - a standard formula (Wenyangtongluo decoction) composition of herbal preparation - it contains Radix Astragali (Huang Qi) 50g, Radix Aconiti Lateralis (Fu Zi) 15g, Radix Angelicae Sinesis (Dang Gui) 10g, Flos Carthami (Hong Hua) 10g, Caulis Polygoni Multiflori (Shou Wu Teng) 15g, Caulis Spatholobi (Ji Xue Teng) 15g, Radix Aconiti (Chuan Wu) 10g, Radix Aconiti Kusnezoffii (Cao Wu) 10g, Pheretima (Di Long) 15g, Hirudo (Shui Zhi)

	<p>6g, Fructus Liquidambaris (Lu Lu Tong) 15g, Folium Artemisiae Argyi (Ai Ye) 15g, etc.</p> <ul style="list-style-type: none">• preparation of formula: the raw herbs were cooked for decoction• time of administration: not reported, 30 mins each intervention, twice a day for a week at each cycle of chemotherapy <p>Control group: No additional treatment</p>	
Outcomes	<p>Primary outcome was measured as change in reporting of: (1) Incidence rate measured by Levi’s sensory neuropathy scale; (2) Adverse events</p> <p>Secondary outcomes were measured as change in reporting of: (1) Quality of Life (Karnofsky Score (KPS))</p> <p>Outcome endpoints: At baseline and after each of chemotherapy treatment</p>	
Notes	<p>Language: Chinese</p> <p>Country/region of study: Beijing, China</p> <p>Type of publication: Master degree thesis</p> <p>Funding source: Not reported</p>	
Risk of Bias		
Bias	Authors’ judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	<p>Quote: “patients were randomly allocated using a table of random numbers.”</p> <p>Comment: Probably done.</p>
Allocation concealment (selection bias)	High risk	<p>Quote: “...using a table of random numbers.”</p> <p>Comment: Probably not done.</p>
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants in intervention group were given hand and foot bath, while control group were nothing. Review authors believe this will introduce bias to participants and personnel.
Blinding of outcome assessment (detection	Unclear risk	Insufficient information to assess whether a risk of bias exists in outcome assessment.

bias) All outcomes		
Incomplete outcome data (attrition bias) All outcomes	Low risk	1/36 missing from intervention groups due to 'discontinuation in chemotherapy'; 2/36 missing from placebo group due to 'discontinuation in chemotherapy'
Selective reporting (reporting bias)	Low risk	All rating scales listed in Methods were reported in Results.
Other bias	High risk	The lack of information on sample size calculation; adverse events not designed to be report in Methods

Yuan 2015	
Methods	<p>Trial design: prospective parallel RCT</p> <p>Year of trial: 2015</p> <p>Judgement of the quality of study: see 'Risk of bias' table</p> <p>Groups comparable at baseline: demographic characteristics in both groups was balanced at baseline with statistical analysis</p> <p>Sample size calculation: not reported</p> <p>Intention-to-treat: not performed</p> <p>Drop-off: 8.3% in both groups (10% in intervention group; 6.7% in control group)</p> <p>Compliance: not reported</p> <p>Duration of study including follow-up: 6 cycles (12 weeks) of intervention with no follow-up period</p>
Participants	<p>Ethnics: Chinese</p> <p>Number of study centres: 1</p> <p>Source: inpatients and clinic patients from Department of Oncology, Dalian Chinese Medicine Hospital, Dalian, Liaoning province, China</p> <p>Setting: 60 patients (29 of male) randomised into four groups [30 (CHM: Hand and foot baths of Huoxuetongjing decoction) vs 30 (Hand and foot baths of warm water)]</p> <p>Included: Diagnosed with gastrointestinal cancer by pathology or cytology; going to receive oxaliplatin regimens (FOLFOX4 -85mg/m² or FOLFOX 6 -100mg/m² 2wk/cycle for 4 cycles; XELOX -130 mg/m² or L-OHP+S1 100mg/m² -3wk/cycle for 4 cycles) and consent to participating the study; Age between 18-70; Karnofsky Score \geq 70 scores; Have no cardiac, hepatic, renal and nervous system disorder; Have no other skin issues; Life expectancy \geq four months</p> <p>Excluded: Have drug allergy to any composition of herbal medicine; Not eligible for the study; Had serious adverse events which excluded from clinical observation; Pre-existing other medical conditions in neurological, skeletal and peripheral nerves system; Have diabetes or any other medical condition that may impair peripheral nerve function; Have poor compliance</p>
Interventions	<p>Experimental group: (CHM: Hand and foot baths of Huoxuetongjing decoction)</p> <p>Hand and foot baths of Hangwuteng decoction:</p> <ul style="list-style-type: none"> route of administration – topical wash bath form of intervention - in the form of raw herbs style of herbal preparation - a standard formula (Huoxuetongjing decoction) composition of herbal preparation - it contains Radix Astragali (Huang Qi), Semen Persicae (Tao Ren), Flos Carthami (Hong Hua), Radix

	<p>Paeoniae Rubra (Chi Shao), Rhizoma Curcumae (E Zhu), Radix et Rhizoma Clematidis (Wei Ling Xian), Herba Erodii (Lao Guan Cao), Caulis Spatholobi (Ji Xue Teng), etc (dosage not available)</p> <ul style="list-style-type: none">• preparation of formula: the raw herbs were cooked for decoction• time of administration: not reported, 30 mins each intervention, twice a day during each cycle of chemotherapy <p>Control group: Hand and foot baths of warm water</p> <ul style="list-style-type: none">• route of administration – topical wash bath• time of administration: not reported, 30 mins each intervention, twice a day during each cycle of chemotherapy	
Outcomes	<p>Primary outcome was measured as change in reporting of: (1) Incidence rate measured by WHO sensory neuropathy scale; (2) Adverse events</p> <p>Secondary outcomes were measured as change in reporting of: (1) cumulative oxaliplatin dosage by the onset of grade >=2 peripheral neuropathy</p> <p>Outcome endpoints: At baseline and after four cycles of chemotherapy treatment</p>	
Notes	<p>Language: Chinese</p> <p>Country/region of study: Dalian, Liaoning province, China</p> <p>Type of publication: Master degree thesis</p> <p>Funding source: Not reported</p>	
Risk of Bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	<p>Quote: “patients were randomly allocated using a table of random numbers.”</p> <p>Comment: Probably done.</p>
Allocation concealment (selection bias)	High risk	<p>Quote: “...using a table of random numbers.”</p> <p>Comment: Probably not done.</p>
Blinding of participants and personnel (performance bias) All	High risk	<p>Participants in intervention group were given hand and foot bath of herbal formula, while control group were hand and foot bath of warm water. Review authors believe this will introduce bias to participants and personnel.</p>

outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to assess whether a risk of bias exists in outcome assessment.
Incomplete outcome data (attrition bias) All outcomes	Low risk	3/30 missing from intervention groups (2 due to 'discontinuation in chemotherapy'), 2/30 missing from placebo group (1 due to 'discontinuation in chemotherapy')
Selective reporting (reporting bias)	Low risk	All rating scales listed in Methods were reported in Results.
Other bias	Unclear risk	Insufficient information to assess whether an important risk of bias exists;

