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Moxibustion for alleviating side effects of chemotherapy or radiotherapy in people with cancer (Review)

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[Intervention Review]

Moxibustion for alleviating side effects of chemotherapy or radiotherapy in people with cancer

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ABSTRACT

Background

Moxibustion, a common treatment in traditional Chinese medicine, involves burning herbal preparations containing *Artemisia vulgaris* on or above the skin at acupuncture points. Its intended effect is to enhance body function, and it could reduce the side effects of chemotherapy or radiotherapy and improve quality of life (QoL) in people with cancer.

Objectives

To assess the effects of moxibustion for alleviating side effects associated with chemotherapy, radiotherapy or both in people with cancer.

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library, MEDLINE via Ovid, Embase via Ovid and AMED (Allied and Complementary Medicine Database) from their inception to February 2018. We also searched databases in China including the Chinese BioMedical Literature Database (CBM), Chinese Medical Current Contents (CMCC), TCMonline, Chinese Dissertation Database (CDDB), China Medical Academic Conference (CMAC) and Index to Chinese Periodical Literature from inception to August 2017. Registries for clinical trials and other resources were also searched.

Selection criteria

We included randomised controlled trials (RCTs) comparing moxibustion treatment, including moxa cone and moxa stick, versus sham, no treatment or conventional treatment.

Data collection and analysis

Two review authors (HWZ and FC) independently extracted data on study design, participants, treatment and control intervention, and outcome measures, and they also assessed risk of bias in the included studies. We performed meta-analyses, expressing dichotomous outcomes as risk ratios (RR) and continuous outcomes as mean differences (MD), with 95% confidence intervals (CI).

Main results

We included 29 RCTs involving 2569 participants. Five RCTs compared moxibustion versus no treatment, 15 compared moxibustion plus conventional treatment versus conventional treatment, one compared moxibustion versus sham moxibustion, and eight compared moxibustion versus conventional medicine. The overall risk of bias was high in 18 studies and unclear in 11 studies. Studies measured outcomes in various ways, and we could rarely pool data.

Moxibustion versus no treatment: low-certainty evidence from single small studies suggested that moxibustion was associated with higher white blood cell counts (MD 1.77 × 10^9/L; 95% CI 0.76 to 2.78; 80 participants, low-certainty evidence) and higher serum haemoglobin concentrations (MD 1.33 g/L; 95% CI 0.59 to 2.07; 66 participants, low-certainty evidence) in people with cancer, during or after chemotherapy/radiotherapy, compared with no treatment. There was no evidence of an effect on leukopenia (RR 0.50, 95% CI 0.10 to 2.56; 72 participants, low-certainty evidence) between study groups. The effects on immune function (CD3, CD4, and CD8 counts) were inconsistent.

Moxibustion versus sham moxibustion: low-certainty evidence from one study (50 participants) suggested that moxibustion improved QoL (measured as the score on the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-C30 (EORTC QLQ-C30)) compared with sham treatment (MD 14.88 points; 95% CI 4.83 to 24.93). Low-certainty evidence from this study also showed reductions in symptom scores for nausea and vomiting (MD −38.57 points, 95% CI −48.67 to −28.47) and diarrhoea (MD −13.81, 95% CI −27.52 to −0.10), and higher mean white blood cell count (MD 1.72 × 10^9/L, 95% CI 0.97 to 2.47), serum haemoglobin (MD 2.06 g/L, 95% CI 1.26 to 2.86) and platelets (MD 210.79 × 10^9/L, 95% CI 167.02 to 254.56) when compared with sham moxibustion.

Moxibustion versus conventional medicines: low-certainty evidence from one study (90 participants) suggested that moxibustion improved WBC count eight days after treatment ended compared with conventional medicines (MD 0.40 × 10^9/L; 95% CI 0.15 to 0.65). Low-certainty evidence from two studies (235 participants) suggested moxibustion improved serum haemoglobin concentrations compared with conventional medicines (MD 10.28 g/L; 95% CI 4.51 to 16.05).

Moxibustion plus conventional treatment versus conventional treatment alone: low-certainty evidence showed that moxibustion plus conventional treatment was associated with lower incidence and severity of leukopenia (WHO grade 3 to 4) (RR 0.14, 95% CI 0.01 to 2.64; 1 study, 56 participants), higher QoL scores on the EORTC QLQ-C30 (MD 8.85 points, 95% CI 4.25 to 13.46; 3 studies, 134 participants, I^2 = 26%), lower symptom scores for nausea and vomiting (RR 0.43, 95% CI 0.25 to 0.74; 7 studies, 801participants; I^2 = 19%), higher white blood cell counts (data not pooled due to heterogeneity), higher serum haemoglobin (MD 3.97 g/L, 95% CI 1.40 to 6.53; 2 studies, 142 participants, I^2 = 0%). There was no difference in platelet counts between the two groups (MD 13.48 × 10^9/L; 95% CI −16.00 to 42.95; 2 studies, 142 participants; I^2 = 34%).

Most included studies did not report related adverse events, such as burning or allergic reactions.

Authors' conclusions

Limited, low-certainty evidence suggests that moxibustion treatment may help to reduce the haematological and gastrointestinal toxicities of chemotherapy or radiotherapy, improving QoL in people with cancer; however, the evidence is not conclusive, and we cannot rule out benefits or risks with this treatment. High-quality studies that report adverse effects are needed.

PLAIN LANGUAGE SUMMARY

Moxibustion for alleviating side effects of chemotherapy or radiotherapy in people with cancer

The issue

Moxibustion is used in traditional Chinese medicine to enhance quality of life and relieve the side effects of conventional treatments for a variety of diseases. As its application involves the burning of a herbal preparation, it can also cause some undesirable side effects itself, such as allergic reactions, burns and infection.

The aim of the review

We conducted this systematic review to understand whether moxibustion can reduce common side effects of chemotherapy and radiotherapy and improve well-being in people with cancer.

Selection criteria

We reviewed 29 studies involving 2569 people with different types of cancer, receiving chemotherapy, radiotherapy or both.

What are the main findings?

We found some small single studies showing various beneficial effects of moxibustion on increasing blood cells and promoting immunological function, decreasing gastrointestinal symptoms caused by toxicity of chemotherapy or radiotherapy (such as nausea and vomiting), and improving quality of life. However, the poor reporting and high risk of bias in study methods reduced the certainty of the evidence.

What is the certainty of the evidence?

The evidence was of low or very low-certainty.

What are the conclusions?

There is presently no good evidence to support or oppose the use of moxibustion in people receiving treatment for cancer. High-quality studies are needed, which should include reporting of adverse effects.

SUMMARY OF FINDINGS

Summary of findings for the main comparison. Moxibustion versus no treatment for side effects of chemotherapy or radiotherapy in cancer patients

Moxibustion versus no treatment for side effects of chemotherapy or radiotherapy in cancer patients

Patient or population: patients receiving chemotherapy or radiotherapy for cancer treatment

Settings: hospital

Intervention: moxibustion

Comparison: no treatment

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	No treatment	Moxibustion treatment			
The incidence and severity of toxicities: leukopenia (WHO grade 3 to 4)	**111 per 1000**	**56 per 1000** (11 to 284)	**RR 0.50** (0.10 to 2.56)	72 (1 study)	⊕⊕⊖⊖ **Low**[a]
QoL	No evidence				
Patient-reported symptom: nausea/vomiting	No evidence				
Patient-reported symptom: diarrhoea	No evidence				
Objective outcome measure: WBC count (× 10^9/L)	Mean WBC counts (× 10^9/L) in the control group was **3.60**	Mean WBC counts (×10^9/L) in the intervention group was **5.37** (4.36 to 6.38)	**MD 1.77** (0.76 to 2.78)	80 (1 study)	⊕⊕⊖⊖ **Low**[a]
Objective outcome measure: haemoglobin (g/L)	Mean haemoglobin (g/L) in the control group was **10.24**	Mean haemoglobin (g/L) in the intervention groups was **11.57** (11.44 to 11.7)	**MD 1.33** (1.20 to 1.46)	66 (1 study)	⊕⊕⊖⊖ **Low**[a]
Objective outcome measure: platelets (× 10^9/L)	No evidence				

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **MD**: mean difference; **RR**: risk ratio; **WBC**: white blood cells; **WHO**: World Health Organization.

GRADE Working Group grades of evidence
High quality: further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: we are very uncertain about the estimate.

[a]Downgraded one level due to design limitations (high risk of bias) and one level due to imprecision (1 RCT of 66 to 80 participants).

Summary of findings 2. Moxibustion versus sham treatment for side effects of chemotherapy or radiotherapy in cancer patients

Moxibustion versus sham treatment for side effects of chemotherapy or radiotherapy in cancer patients

Patient or population: patients receiving chemotherapy or radiotherapy for cancer treatment

Settings: hospital

Intervention: moxibustion treatment

Comparison: sham

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	Sham	Moxibustion treatment			
The incidence and severity of chemotherapy- or radiotherapy-related toxicities	No evidence				
QoL (EORTC QLQ-C30)	Mean QoL (EORTC QLQ-C30) in the control group was **62.5**	Mean QoL (EORTC QLQ-C30) in the intervention group was **77.38** (67.33 to 87.43)	**MD 14.88** (4.83 to 24.93)	50 (1 study)	⊕⊕⊖⊖ **Low**[a]
Patient-reported symptom: nausea/vomiting (EORTC QLQ-C30)	Mean nausea/vomiting score (EORTC QLQ-C30) in the control groups was **46.67**	Mean nausea/vomiting score (EORTC QLQ-C30) in the intervention group was **8.10** (−0.2 to 18.2)	**MD −38.57** (−48.67 to −28.47)	50 (1 study)	⊕⊕⊖⊖ **Low**[a]
Patient-reported symptom: diarrhoea (EORTC QLQ-C30)	Mean diarrhoea score (EORTC QLQ-C30) in the control group was	Mean diarrhoea score (EORTC QLQ-C30) in the intervention group was **16.19** (2.48 to 29.9)	**MD −13.81** (−27.52 to −0.1)	50 (1 study)	⊕⊕⊖⊖ **Low**[a]

	30				
Objective outcome measure: WBC count (× 10^9/L)	Mean WBC count (× 10^9/L) in the control group was **4.1**	Mean WBC count (× 10^9/L) in the intervention group was **5.82** (5.07 to 6.57)	**MD 1.72** (0.97 to 2.47)	50 (1 study)	⊕⊕⊖⊖ **Low**[a]
Objective outcome measure: haemoglobin (g/L)	Mean haemoglobin (g/L) in the control group was **9.67**	Mean haemoglobin (g/L) in the intervention group was **11.73** (10.93 to 12.53)	**MD 2.06** (1.26 to 2.86)	50 (1 study)	⊕⊕⊖⊖ **Low**[a]
Objective outcome measure: platelets (× 10^9/L)	Mean platelet count (× 10^9/L) in the control group was **172.9**	Mean platelet count (× 10^9/L) in the intervention group was **383.69** (339.92 to 427.46)	**MD 210.79** (167.02 to 254.56)	50 (1 study)	⊕⊕⊖⊖ **Low**[a]

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **MD**: mean difference; **EORTC QLQ-C30**: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; **QoL**: quality of life.

GRADE Working Group grades of evidence
High quality: further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: we are very uncertain about the estimate.

[a]Downgraded one level due to design limitations (high risk of bias) and one level due to imprecision (1 RCT of 50 participants).

Summary of findings 3. Moxibustion versus conventional medicines for side effects of chemotherapy or radiotherapy in cancer patients

Moxibustion versus conventional medicines for side effects of chemotherapy or radiotherapy in cancer patients

Patient or population: patients receiving chemotherapy or radiotherapy for cancer treatment

Settings: hospital

Intervention: moxibustion treatment
Comparison: conventional medicines[a]

Outcomes	**Illustrative comparative risks* (95% CI)**		**Relative effect (95% CI)**	**No of participants (studies)**	**Certainty of the evidence (GRADE)**
	Assumed risk	**Corresponding risk**			

	conventionalmedicine	Moxibustion treatment			
The incidence and severity of toxicities: haematological toxicity	143 per 1000	81 per 1000 (21 to 315)	**RR 0.57** (0.15 to 2.20)	72 (1 study)	⊕⊕⊖⊖ **Low**[b]
QoL (Karnofsky score)	The mean Karnofsky score in the control group was 80.5	The mean Karnofsky score in the moxibustion group was 87.2 (82.9 to 91.5)	**MD 6.70** (2.37 to 11.03)	82 (1 study)	⊕⊕⊖⊖ **Low**[b]
Patient-reported symptom: nausea/vomiting	No evidence				
Patient-reported symptom: diarrhoea	No evidence				
Objective outcome measure: WBC count (× 10^9/L)	The mean WBC counts (× 10^9/L) in the control group was **5.7**	The mean WBC counts (× 10^9/L) in the intervention group was **6.10** (5.85 to 6.35)	**MD 0.40** (0.15 to 0.65)	90 (1 study)	⊕⊕⊖⊖ **Low**[b]
Objective outcome measure: haemoglobin (g/L)	The mean haemoglobin (g/L) in the control groups was **118**	The mean haemoglobin (g/L) in the intervention groups was **128.28** (122.51 to 134.05)	**MD 10.28** (4.51 to 16.05)	235 (2 studies)	⊕⊕⊖⊖ **Low**[b]
Objective outcome measure: platelets (× 10^9/L)	One study reported that moxibustion was associated with a higher platelets counts compared with ondansetron and batilol (163 participants: MD 31.99 × 10^9/L; 95% CI 16.33 to 47.65) and another found no difference in platelets counts compared with batilol, leucogen and optional G-CSF (47 participants: MD 6 × 10^9/L; 95% CI −4.86 to 16.86)		Not pooled due to high heterogeneity	210 (2 studies)	⊕⊕⊖⊖ **Low**[b]

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **G-CSF**: granulocyte-colony stimulating factor; **MD**: mean difference; **QoL**: quality of life; **RR**: risk ratio; **WBC**: white blood cells.

GRADE Working Group grades of evidence
High quality: further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: we are very uncertain about the estimate.

[a]Conventional medication: batilol, leucogen, berbamine, G-CSF and etc.
[b]Downgraded one level due to design limitations (high risk of bias) and one level due to imprecision.

Summary of findings 4. Moxibustion + conventional treatment versus conventional medicine alone for side effects of chemotherapy or radiotherapy in cancer patients

Moxibustion + conventional treatment versus conventional medicine alone for side effects of chemotherapy or radiotherapy in cancer patients

Patient or population: patients receiving chemotherapy or radiotherapy for cancer treatment

Settings: hospital

Intervention: moxibustion plus conventional treatment
Comparison: conventional treatment[a]

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	Conventional treatment	Moxibustion plus conventional treatment			
The incidence and severity of toxicities: leukopenia (WHO grade 3 to 4)	**107 per 1000**	**15 per 1000** (1 to 283)	**RR 0.14** (0.01 to 2.64)	56 (1 study)	⊕⊕⊖⊖ **Low**[b]
QoL (EORTC QLQ-c30)	The mean QoL (EORTC QLQ-c30) in the control groups was **65**	The mean QoL (EORTC QLQ-c30) in the intervention groups was **73.85** (69.25 to 78.46)	**MD 8.85** (4.25 to 13.46)	134 (3 studies)	⊕⊕⊖⊖ **Low**[b]
Patient-reported symptom: nausea/vomiting (WHO grade 3 to 4)	**152 per 1000**	**65 per 1000** (38 to 112)	**RR 0.43** (0.25 to 0.74)	801 (7 studies)	⊕⊕⊖⊖ **Low**[b]
Patient-reported symptom: diarrhoea	33 per 1000	6 per 1000 (0 to 128)	**RR 0.19** (0.01 to 3.88)	61 (1 study)	⊕⊕⊖⊖ **Low**[b]
Objective outcome measure: WBC count (× 10^9/L)	2 studies (N = 200) both reported that moxibustion was associated with a slightly higher mean white blood cell count compared with control (MD 0.5 × 10^9/L; 95% CI 0.12 to 0.88; MD 1.5 × 10^9/L; 95% CI 1.14 to 1.86). One (N = 62) found no evidence of a difference compared with control (MD 0.41 × 10^9/L; 95% CI −0.22 to 1.04).		Not pooled due to high heterogeneity	262 (3 studies)	⊕⊕⊖⊖ **Low**[a]

Objective outcome measure: haemoglobin (g/L)	The mean haemoglobin (g/L) in the control groups was **108**	The mean haemoglobin (g/L) in the intervention groups was **111.97** (109.4 to 114.53)	**MD 3.97** (1.4 to 6.53)	142 (2 studies)	⊕⊕⊖⊖ **Low**[b]
Objective outcome measure: platelet (× 10^9/L)	The mean platelet (× 10^9/L) in the control group was **170**	The mean platelet (× 10^9/L) in the intervention group was **183.48** (154 to 212.95)	**MD 13.48** (−16.00 to 42.95)	142 (2 studies)	⊕⊕⊖⊖ **Low**[b]

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **EORTC QLQ-C30**: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; **QoL**: quality of life; **RR**: risk ratio; **WBC**: white blood cells; **WHO**: World Health Organization.

GRADE Working Group grades of evidence
High quality: further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: we are very uncertain about the estimate.

[a]Conventional medication: batilol, leucogen, berbamine, G-CSF, etc.
[b]Downgraded one level due to design limitations (high risk of bias) and one level due to imprecision (1 to 7 RCTs of 56 to 801 participants).

BACKGROUND

Description of the condition

Cancer rates have steadily increased over the past few decades, placing a huge burden on health systems worldwide. The global economic burden of cancer has more than doubled over the past 30 years. Cancer is the leading causes of morbidity and mortality worldwide, with approximately 14 million new cases reported in 2012, and it is expected that annual cancer cases will rise to 22 million within the next two decades. The five most common sites of cancer diagnosed in men in 2012 were the lung, prostate, colon/rectum, stomach and liver, and in women they were the breast, colon/rectum, lung, cervix and stomach (WHO 2014).

Conventional cancer treatments include surgery, radiotherapy, chemotherapy and psychosocial support (WHO 2002). Advances in chemotherapy and radiotherapy in recent years have greatly improved treatment results (WHO 2014). However, cytotoxic drugs and ionising radiation also cause many distressing side effects. Some of these are serious enough to prompt discontinuation of treatment (Redmond 1996; Robbins 2002; WHO 2014). The side effects most commonly associated with chemotherapy and radiotherapy include fatigue, pain, and nausea and vomiting (Henry 2008; Stasi 2003). Other side effects include bone marrow suppression leading to anaemia; hair follicle cell damage leading to alopecia; gastrointestinal damage leading to diarrhoea and oral ulceration and skin reactions to radiation (Robbins 2002; WHO 2014). Although new drug development programmes have been undertaken to reduce the side effects of cancer therapy, satisfactory treatment still is not readily available to a large proportion of patients receiving chemotherapy and/or radiotherapy. New, effective treatments that can reduce chemotherapy- and radiotherapy-associated adverse effects are needed, especially non-pharmacological strategies with minimum harm (Cho 2010; Ellebaek 2008; Herrstedt 2007; Jordan 2007; Lotfi-Jam 2008; Redmond 1996).

Description of the intervention

Moxibustion is a common treatment in traditional Chinese medicine and has been used in China and other Asian countries for millenia (Cho 2009). Moxibustion involves burning herbal preparations containing *Artemisia vulgaris* (mugwort) on or above the skin at acupuncture points. Moxibustion techniques commonly used in clinical practice to treat side effects of conventional cancer treatment involve either direct moxibustion with a traditional moxa stick (stick-on moxa) (Yu 2003), or indirect moxibustion, achieved by placing insulating materials such as salt, monkshood cake, sliced ginger or garlic between the skin and a burning moxa cone (Chen 2000; Zhao 2007). The leaves of *A vulgaris* or mugwort, in Chinese called *ai ye*, are the main material used for moxibustion. Other Chinese herbs may be sometimes used in combination with mugwort. Mugwort is considered to be warm, acidic and bitter. It has the ability to warm the body's meridians, thereby promoting better circulation. According to Chinese medicine theory, the meridians are the channels inside the human body that circulate vital energy (in Chinese called *qi* and *blood*). Besides promoting the flow of vital energy through meridians, moxibustion, which stimulates some specific acupoints located along the meridians upon burning, is considered to have some specific treatment effects, such as strengthening the body's vital energy or facilitating digestion. Although practiced widely in East Asia, it is also associated with some adverse effects, such as allergic reactions, burns and infections (Chan 2014).

How the intervention might work

A systematic review demonstrated that acupuncture point stimulation, as performed through electro acupuncture and acupressure, may reduce chemotherapy-induced nausea or vomiting (Ezzo 2006). Moxibustion is widely used in China and in other East Asian countries to reduce cancer pain and fever in people with cancer and to lessen the adverse effects of radiotherapy and chemotherapy (Lee 2010; Zhang 2008). Many clinical studies of moxibustion for people with cancer receiving chemotherapy or radiotherapy have indicated that it could alleviate some of the adverse effects of treatment, such as fatigue, nausea and vomiting, diarrhoea, alopecia and pain, as well as improving quality of life (Chen 2000; Chen 2008; Gao 2010; Jiang 2002; Kim 2010; Kuai 2008; Qiu 2008; Song 2003; Shen 2008; Zhang 2008; Zhao 2007).

The clinical effects of moxibustion may be attributable to the actions of enhancing immunity, relieving bone marrow suppression and producing an anti-oxidative effect (Chen 2000; Cui 2007; Huang 1999; Jiang 2002; Pei 2007; Xu 2003a; Yu 2002a; Yu 2003; Zhao 2007). The infrared radiation peak (around 7.5 µm) of traditional indirect moxibustion with monkshood cake, ginger slices and garlic slices as the medium matches that of infrared radiation on human skin at some acupoints such as LI 4 (hegu), indicating involvement of a sympathetic vibration of infrared radiation from indirect moxibustion and the acupoints. These mechanisms of action (including thermal action, infrared radiation and sympathetic vibration) and their pharmacological effects may contribute to the therapeutic efficacy of moxibustion (Shen 2006). In addition, actions exerted on the acupoints by moxibustion may elicit systemic effects through transmission along meridians.

Why it is important to do this review

Given its potential effect, low cost and simplicity of application, moxibustion may be a valuable adjuvant treatment option for many people with cancer. However, practitioners should also consider the possible side effects related to moxibustion. A recently published systematic review on moxibustion for cancer care found limited evidence supporting the effectiveness of moxibustion for reducing cancer-related nausea and vomiting (Lee 2010). Review authors evaluated moxibustion as the sole treatment for cancer, or as an adjunct to chemotherapy or radiotherapy; however, they did not clearly specify outcome measurements. Our systematic review focuses primarily on the effects of moxibustion for alleviating the side effects of chemotherapy, radiotherapy or both in people with cancer. We used a transparent and clearly defined systematic method to comprehensively evaluate the evidence. Findings from this systematic review should help to inform medical practitioners, patients and researchers about the effectiveness and safety of moxibustion for people with cancer receiving radiotherapy, chemotherapy or both.

OBJECTIVES

To assess the effects of moxibustion for alleviating side effects associated with chemotherapy, radiotherapy or both in people with cancer.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised controlled trials (RCTs). For randomised cross-over trials, we included only phase 1 data because treatment carryover effects were likely.

Types of participants

We included participants of any age with any kind of malignant disease receiving chemotherapy, radiotherapy or both.

Types of interventions

The intervention was any type of moxibustion treatment, defined as burning moxa on or above any acupoint or at some specified region of the body. Commonly used techniques include direct and indirect moxibustion with a moxa cone or moxa stick. Direct moxibustion with a moxa cone consists of placing a small cone-shaped moxa directly on the skin and burning it; in indirect moxibustion, a medium (salt, garlic, ginger, monkshood cake or any other herbs) separates the skin and the burning cone. In moxibustion with moxa stick, a practitioner lights one end of the moxa stick, which is roughly similar to a cigar in shape and size, and holds it for several minutes or even one hour close to the area being treated until the area turns red. We also included moxibustion treatments that involve burning materials made of moxa and/or other medicinal herbs, with or without the aid of an instrument, because these approaches are considered traditional moxibustion treatments. We excluded moxa needle therapy, which consists of inserting a needle into an acupoint and wrapping the end of the needle in an ignited moxa, because this treatment method also involves acupuncture. The acupuncture treatment combined with moxibustion makes it impossible to evaluate whether the treatment effect is due only to moxibustion.

The intervention in the control group may include a sham, no treatment or other conventional treatments that are currently accepted and widely used for patients receiving chemotherapy, radiotherapy or both, and may include treatments for raising white or red blood cell counts and haemoglobin levels, or for enhancing immunity. We did not accept other herbal or complementary medicines as a control intervention when there was no validated evidence about their effectiveness.

Basic oncological treatment (chemotherapy, radiotherapy) or supportive care should be identical in the intervention and control groups. We excluded the studies with Chinese medicines as the co-administered treatment between groups because they may vary individually.

Types of outcome measures

Primary outcomes

- Incidence and severity of chemotherapy- or radiotherapy-related toxicities, as reported according to internationally accepted criteria for common toxicities (e.g. World Health Organization (WHO) (Miller 1981), Eastern Cooperative Oncology Group (ECOG), or National Institutes of Health (NIH) criteria for adverse effects)

Secondary outcomes

- Quality of life (QoL) as measured by a validated instrument (e.g. the 36-Item Short Form Health Survey (SF-36), the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-C30 (EORTC QLQ-C30), or the World Health Organization QoL (WHOQOL)
- Patient-reported physical and psychological indices of symptom distress using a validated scale (e.g. visual analogues scale (VAS))
- Other objective outcome measures aimed at assessing side effects of chemotherapy or radiotherapy (e.g. blood cell counts, measures of immunological function)
- Modification or cessation of cancer treatments as the result of side effects or adverse effects, which may be measured as continuous or dichotomous data
- Adverse events in the treatment and control groups (including serious and moderate ones), which may or may not be related to moxibustion treatment. We compared the possible occurrence of adverse events between the moxibustion group and the control group

The above outcome measurements were collected immediately after treatment and at the end of follow-up.

Search methods for identification of studies

We searched for articles in all languages, applying no date restrictions.

Electronic searches

We searched the following databases:

- the Cochrane Central Register of Controlled Trials (CENTRAL; 2018, Issue 2), in the Cochrane Library;
- MEDLINE via Ovid (1946 to January week 4 2018);
- Embase via Ovid (1980 to 2018 week 6);
- AMED (Allied and Complementary Medicine Database) (1985 to January 2018).

We also searched trials registries and Chinese databases, including Chinese BioMedical Literature Database (CBM), Chinese Medical Current Contents (CMCC), TCMonline, Chinese Dissertation Database (CDDB), China Medical Academic Conference (CMAC) and Index to Chinese Periodical Literature from their inception time to August 2017.

The search strategies in CENTRAL, MEDLINE and Embase are in Appendix 1, Appendix 2 and Appendix 3.

We identified all relevant articles on PubMed and used the 'related articles' feature to carry out further searches for newly published articles.

Searching other resources

We searched the following registries for ongoing trials: metaregister (www.controlled-trials.com/mrct), Physicians Data Query (/www.ncbi.nlm.nih.gov), www.clinicaltrials.gov and www.cancer.gov/clinicaltrials.

To identify ongoing studies and grey literature, we searched USA CenterWatch Clinical Trials Listing Service

(www.CenterWatch.com) and OpenSIGLE (System for Information on Grey Literature in Europe).

We checked the references of all included studies and relevant reviews to find further relevant articles.

Data collection and analysis

Selection of studies

We used the search strategy described above to obtain titles and abstracts of studies that may be relevant to the review. We entered all references from electronic databases into NoteExpress and removed duplicates. Two review authors (HWZ and FC) independently reviewed these titles and abstracts, discarding studies that were not eligible for the review and retaining those with potentially relevant data or information. We retrieved full texts of potentially eligible articles for further assessment, labelling each as 'include', 'exclude' or 'unclear' on full-text review. We resolved disagreements by discussion and consensus. When the article fell into the unclear category due to unclear information or missing data, we contacted the trial authors for clarification, recording all communications.

Data extraction and management

Two review authors (HWZ and FC) independently carried out data extraction, using a pre-tested data extraction form. When we found more than one publication of a study, we grouped reports together, using the publication with the most recent and complete data to extract outcomes. When earlier reports were the only ones to publish relevant outcomes, we used these data, noting any discrepancies between published versions. A third review author (ZXL) resolved disagreements between the two review authors in consultation with them.

For included trials, HWZ abstracted the following data as recommended in Chapter 7 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

- General information: published or unpublished, author, country, publication language, publication year, journal citation.
- Trial design.
- Participants: inclusion and exclusion criteria, total number enrolled and number in each comparison group, baseline characteristics, setting.
- Interventions: administration route, timing of intervention, comparison intervention and any co-intervention, expertise of practitioner.
- Risk of bias in trials (see Assessment of risk of bias in included studies).
- Follow-up: length of follow-up, reason for and number of dropouts and withdrawals, method of analysis.
- Outcomes reported: the incidence and severity of chemotherapy- or radiotherapy-related toxicities, QoL, patient-reported physical and psychological indices of symptom distress based on a validated scale, any other objective outcome measures aimed at assessing side effects of chemotherapy or radiotherapy, modification or cessation of cancer treatments as the result of side effects or adverse effects, and incidence and types of adverse events resulting from moxibustion.
- For each outcome: outcome definition (with diagnostic criteria if relevant).
- Unit of measurement (if relevant).
- For scales: upper and lower limits, and whether high or low score is good.
- Results: number of participants allocated to each intervention group.
- For each outcome of interest: sample size and missing participants.

Data on outcomes were extracted as follows:

- For dichotomous outcomes (e.g. adverse events), we extracted the number of participants in each treatment arm who experience the outcome of interest and the number of participants assessed at endpoint to estimate a risk ratio (RR).
- For continuous outcomes (e.g. QoL), we extracted the final value and the standard deviation of the outcome of interest and the number of participants assessed at endpoint in each treatment arm at the end of follow-up to estimate the mean difference (MD) (if trials measured outcomes on the same scale) or standardised mean differences (SMD) (if trials measured outcomes on different scales) between treatment arms and standard error.

Assessment of risk of bias in included studies

Two review authors (HWZ and FC) independently assessed the risk of bias in the included studies, resolving any discrepancies by discussion and reaching conclusions by consensus. If disagreements persisted, a third review author (ZXL) helped to make the final decision.

To detect potential selection bias, performance bias, detection bias, attrition bias and reporting bias, we addressed the following six domains in the assessment of risk of bias.

- Selection bias.
  - Random sequence generation.
  - Allocation concealment.
- Performance bias.
  - Blinding of participants and personnel (participants and treatment providers) on subjective and objective outcomes.
- Detection bias.
  - Blinding of outcome assessment.
- Attrition bias.
  - Incomplete outcome data: we recorded the proportion of participants whose outcomes were not reported at the end of the study, coding a satisfactory level of loss to follow-up for each outcome, such as:
    - ☐ Low risk of bias, if fewer than 20% of participants were lost to follow-up, and reasons were similar in both treatment arms.
    - ☐ High risk of bias, if more than 20% of participants were lost to follow-up, or reasons for loss to follow-up differed between treatment arms.
    - ☐ Unclear risk of bias, if authors did not report loss to follow-up.
- Reporting bias.
  - Selective reporting of outcomes.
- Other possible sources of bias.
  - Baseline characteristics.

We categorised the risk of bias for each outcome, within and across included studies, into three levels: low, unclear and high risk of bias. On the basis of this assessment, we used the GRADE system to further evaluate the certainty of evidence for each individual outcome (Higgins 2009). This involved consideration not only of risk of bias (methodological quality) but also of directness of evidence, heterogeneity, precision of effect estimates and risk of publication bias. The empirical evidence for each individual outcome was graded into four levels: high, moderate, low or very low certainty in accordance with the GRADE approach.

Measures of treatment effect

We used the following measures of the effect of treatment.

- For dichotomous outcomes, we used the RR with 95% confidence interval (CI). To help determine the applicability of the results to individual participants, we planned to calculate the number needed to treat for a beneficial outcome (NNTB) across a range of assumed control risks if needed.
- For continuous outcomes, we used the mean difference between treatment arms (with its 95% CI).

Unit of analysis issues

We analysed outcomes based on randomised participants. In the case of multiple intervention groups within a study, we performed pair-wise comparisons relevant to the study objective. If necessary, we combined relevant groups to make a single comparison or split them to make multiple comparisons.

Dealing with missing data

Conducting available case analysis, we considered the potential impact of missing data in the 'Risk of bias' table and in interpretation of the results. We did not impute missing outcome data for any of the outcomes.

Assessment of heterogeneity

We assessed heterogeneity between studies through visual inspection of forest plots, by estimation of the percentage of heterogeneity between trials that cannot be ascribed to sampling variation (Higgins 2003), by a formal statistical test of the significance of the heterogeneity (Deeks 2001), and, if possible, by subgroup analyses. When heterogeneity was present, we first reviewed study components such as participants, interventions and outcomes to decide whether the heterogeneity was substantial. If that were the case, we investigated and reported on possible reasons.

Assessment of reporting biases

Due to the widespread comparisons in the included studies, we did not undertake funnel plot analysis as planned.

Data synthesis

When clinically similar studies were available, we pooled their results in meta-analyses.

- For any dichotomous outcomes, we calculated the RR for each trial and then as a pooled effect estimate.
- For continuous outcomes, we pooled the MDs between treatment arms at the end of follow-up if all trials measured the outcome on the same scale.

We used random-effects models with inverse variance weighting for all meta-analyses (DerSimonian 1986).

Subgroup analysis and investigation of heterogeneity

We undertook post hoc subgroup analysis based on the different conventional medicines in the control group. We did not conduct the planned subgroup analyses based on type of cancer, indirect or direct moxibustion, age of participants and duration of moxibustion treatment due to the widespread comparisons and limited number of included studies.

Sensitivity analysis

We planned a sensitivity analysis to explore the influence of adequate sequence generation and blinding as well as the possible influence of including data from the first period in a cross-over study, but we were not able to carry this out due to the paucity of relevant included studies.

Summary of findings table

Based on the methods described in Chapter 11 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011), we prepared a 'Summary of findings' table to present the review findings. We presented results for the following outcomes.

- Incidence and severity of chemotherapy- or radiotherapy-related toxicities.
- QoL (EORTC QLQ-C30).
- Patient-reported physical and psychological indices of symptom distress.
  - Nausea/vomiting (EORTC QLQ-C30, WHO grade 3 to 4).
  - Diarrhoea (EORTC QLQ-C30).
- Objective outcome measures aimed at assessing side effects of chemotherapy or radiotherapy.
  - Leukopenia (WHO grade 3 to 4).
  - WBC count ($\times 10^9$/L).
  - Haemoglobin (g/L).
  - Platelets ($\times 10^9$/L).

We used the GRADE system to rate the certainty of the evidence (Schünemann 2011), downgrading for inconsistency, design limitations (risk of bias), imprecision, indirectness and other factors, such as publication bias, where appropriate. Where the evidence was based on single studies, or where there was no evidence on a specific outcome, we included the pre-specified outcome in the 'Summary of findings' tables and graded or explained accordingly. Two review authors (HWZ and FC) performed the grading, resolving differences by discussion and, if necessary, by involving a third review author (ZXL).

RESULTS

Description of studies

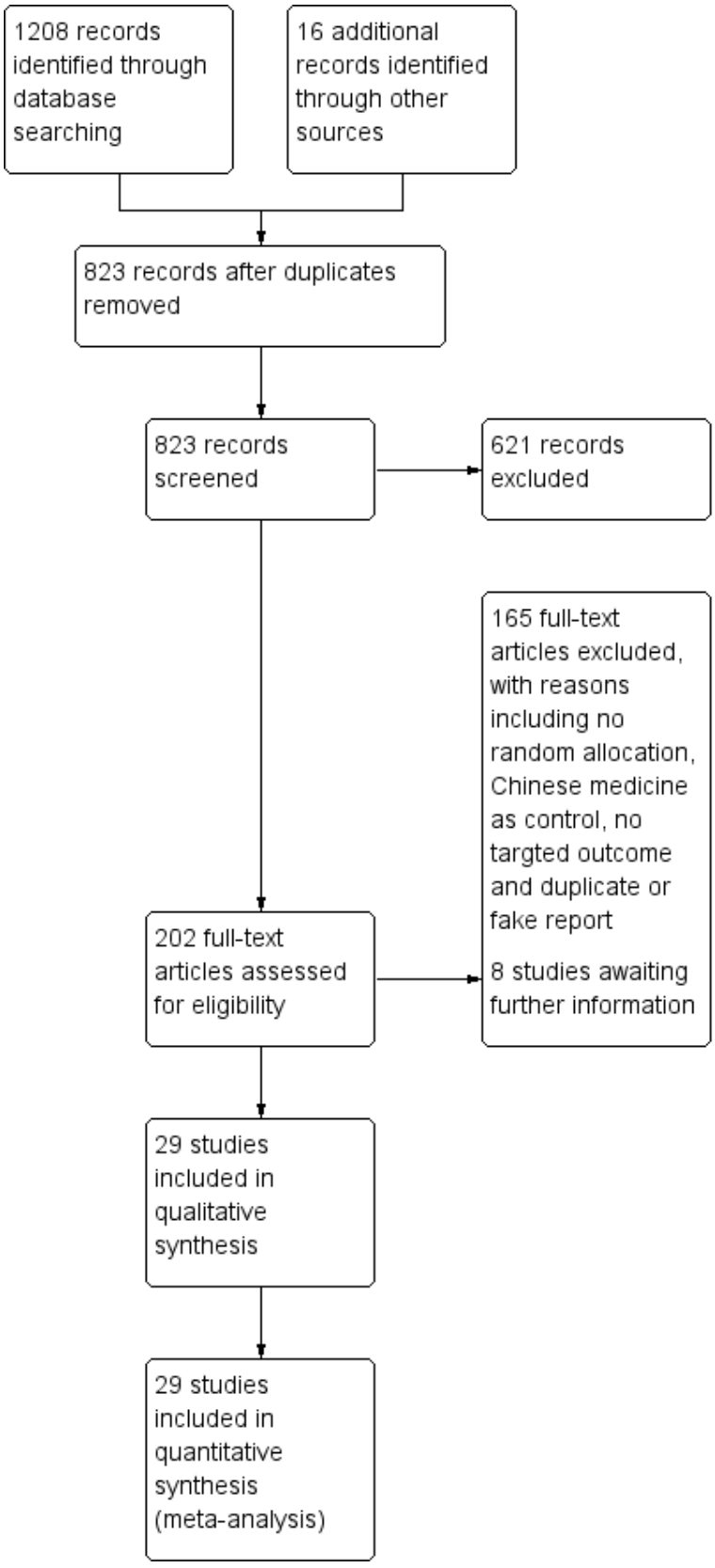
See Characteristics of included studies; Characteristics of excluded studies; and Characteristics of studies awaiting classification.

Results of the search

Our searches yielded 1224 records. After removing duplicates, we screened the titles or abstracts of 823 records. We read the full texts of 202 records and finally included 29 RCTs in the review (Chen 2000;

Chen 2015; Cheng 2005; Cheng 2016; Enkhtuya 2010; Fan 2001; Gao 2013; Hao 2014; Li 2011; Li 2012; Li 2014a; Li 2015; Li 2016; Liang 2002; Mo 2016; Ruan 2014; Tian 2015; Wang 2014; Wu 2013; Xu 2014a; Xu 2014b; Yang 2014; Yin 2013; Yu 2004; Yuan 2014; Zhang 2013 Zhang 2016a; Zhang 2016b; Zhu 2017). Eight of the full texts contained insufficient or ambiguous information (Cui 2010; Lan 2013; Li 2014b; Liang 2012; Qiu 2015; Zhang 2014b; Zhang 2014c; Zhang 2014d), justifying their inclusion in the Characteristics of studies awaiting classification section, pending responses from the investigators (Figure 1). After careful comparison, we considered two records to pertain to the same study as Zhang 2013, while eight pertained to Yu 2004.

Figure 1. Study flow diagram.



Included studies

We included 29 studies involving 2569 participants. The sample sizes ranged from 24 to 332 participants. All studies were reported in Chinese; 28 were conducted in Chinese hospitals, whereas Enkhtuya 2010 took place in a Mongolian hospital. The participants had a variety of cancers, including nasopharyngeal carcinoma, gastric cancer, respiratory system cancer, primary non-small cell lung cancer, breast cancer and cervical cancer. All but two studies, Fan 2001 and Liang 2002, reported participant gender, and overall, 1279 (49.8%) of participants in these studies were men.

In 2 studies, participants received simultaneous chemotherapy and radiotherapy plus moxibustion (Chen 2000; Cheng 2005); in 19 studies, participants received simultaneous moxibustion plus chemotherapy (Chen 2015; Cheng 2016; Enkhtuya 2010; Hao 2014; Li 2011; Li 2014a; Li 2015; Liang 2002; Ruan 2014; Wang 2014; Wu 2013; Xu 2014a; Xu 2014b; Yang 2014; Yin 2013; Yuan 2014; Zhang 2013; Zhang 2016b; Zhu 2017); in 1 study, participants received moxibustion before and after chemotherapy (Fan 2001); in 6 studies, participants received moxibustion after chemotherapy and/or radiotherapy (Gao 2013; Li 2012; Li 2016; Mo 2016; Tian 2015; Zhang 2016a); and in 1 study, participants received simultaneous moxibustion with radiotherapy (Yu 2004).

Fifteen studies compared moxibustion plus conventional treatment versus conventional treatment alone (Chen 2000; Chen 2015; Enkhtuya 2010; Gao 2013; Hao 2014; Li 2015; Li 2016; Ruan 2014; Xu 2014a; Yang 2014; Yin 2013; Yuan 2014; Zhang 2013; Zhang 2016b; Zhu 2017); eight compared moxibustion versus conventional medicines (Cheng 2005; Cheng 2016; Fan 2001; Li 2012; Li 2014a; Mo 2016; Tian 2015; Wang 2014); five compared moxibustion versus no treatment (Li 2011; Liang 2002; Wu 2013; Yu 2004; Zhang 2016a); and one compared moxibustion versus sham moxibustion (Xu 2014b).

In four studies (Enkhtuya 2010; Li 2011; Zhang 2013; Zhang 2016b), practitioners placed at least three continuous moxa cones directly on acupoints RN4 (guanyuan) or bilateral BL17 (geshu) and BL19 (danshu), and the treatment duration ranged from 5 to 10 days. Three studies used a direct grain-sized moxa cone placed on the acupoints ST36 (zusanli), DU14 (dazhui), BL13 (feishu) or RN4 (guanyuan) with continuous 5, 9 or 18 cones, and the treatment duration ranged from 12 to 42 days (Gao 2013; Xu 2014a; Zhang 2016a). In two studies, a specially made direct moxa box on was used on acupoints RN13 (shangwan), RN12 (zhongwan), RN10 (xiawan), ST25 (tianshu), PC6 (neiguan), and ST36 (zusanli) (Cheng 2016; Li 2015). In seven studies, an indirect moxa cone was placed on salt on acupoint RN8 (shenque), or on ginger placed on the acupoints DU14 (dazhui), BL17 (geshu), BL20 (pishu), BL21 (weishu), ST36 (zusanli) or RN12 (zhongwan), with treatment duration ranging from 3 to 65 days (Chen 2000; Chen 2015; Cheng 2005; Li 2011; Li 2014a; Xu 2014b; Yuan 2014). Nine studies used a moxa stick (Fan 2001; Hao 2014; Liang 2002; Li 2016; Mo 2016; Tian 2015; Yang 2014; Yin 2013; Yu 2004), generally for about 10 to 30 minutes on acupoints ST36 (zusanli), SP6 (sanyinjiao) and RN8 (shenque) for 5 to 50 days. One study used moxa stick on acupoints RN8 (shenque), on a paste of grounded herbs (chaihu (Bupleuri Radix), chuanxiong (Chuanxiong Rhizoma), dangshen (Codonopsis Radix), maidong (Ophiopogonis Radix), wuweizi (Schisandrae Chinensis Fructus), danggui (Angelicae Sinensis Radix), huangqi (Astragali Radix) and shexiang (Moschus) for about 2 hours per treatment and 3 times per week, with duration of 126 days (Wu 2013). One study used indirect moxa box on ginger, which was placed on the bilateral acupoints ST36 (zusanli) and KI 1 (yongquan) (Zhu 2017). Only three studies used complementary acupoints based on syndrome differentiation, according to Chinese medicine theory (Hao 2014; Liang 2002; Yang 2014).

The conventional medicines used in the control group included leucogen, batilol, berbamine or recombinant human granulocyte colony-stimulating factor (G-CSF) injection. The conventional treatments administered in both groups were generally supportive and symptomatic ones, including granisetron for the prevention of vomiting.

In Xu 2014b, a moxa cone was placed on a slice of ginger in the treatment arm, and for the sham moxibustion, a piece of board in thickness of 0.6 mm was placed on a slice of ginger between the skin and moxa cone to insulate the heat of burned moxa cone.

Excluded studies

The main reasons for excluding studies were lack of random allocation (Chen 2010), moxibustion combined with other therapy (Chen 2006), Chinese medicine as the control intervention (Liu 2002), no targeted outcome (Chen 1991), varied conventional treatment depending on the symptoms in the control group or both groups (Liang 2014; Zhang 2014a; Zhong 2014), no chemotherapy or radiotherapy (Wang 2016), and duplicate or fake reports (Xu 2002a).

Most relevant studies took place in China, and many authors used self-developed scales or national criteria to assess the treatment outcome (Zheng 2002).

Risk of bias in included studies

See Figure 2; Figure 3

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

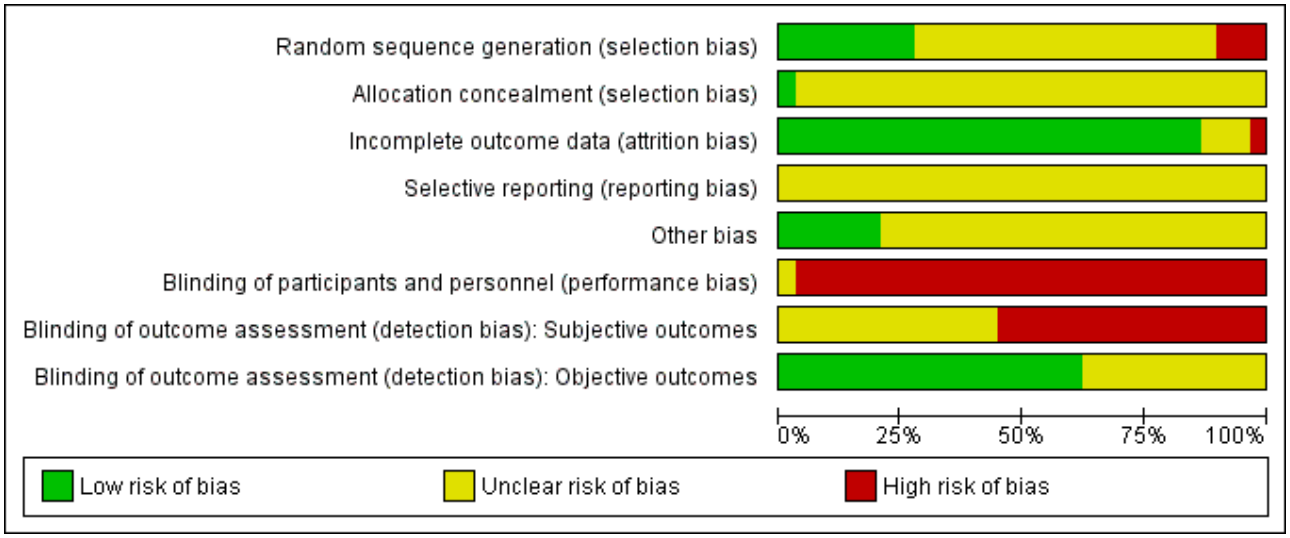


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

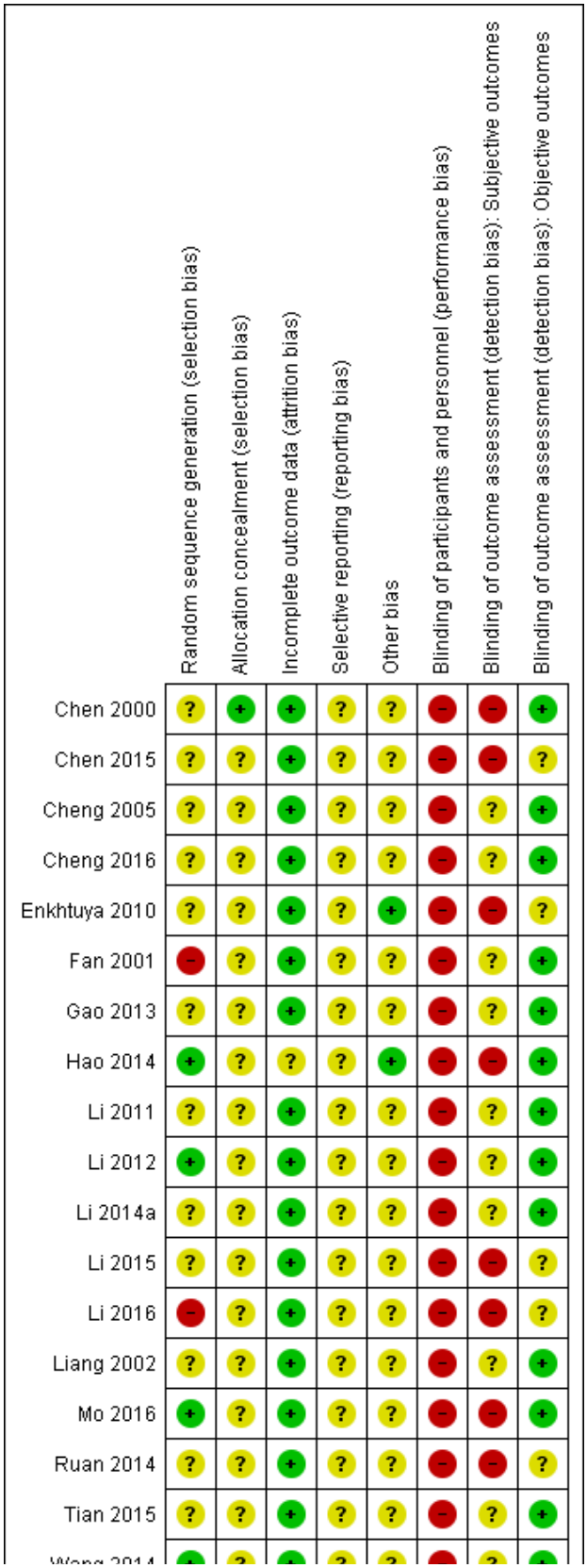


Figure 3. (Continued)

Allocation

Only nine studies reported using a random number table or computer programme (Hao 2014; Li 2012; Li 2016; Mo 2016; Ruan 2014; Wang 2014; Xu 2014a; Xu 2014b; Zhang 2016a). Other studies mentioned only the random allocation without any further information. In three studies, there was a high imbalance in the number of cases between groups (Fan 2001; Li 2016; Yu 2004), which we considered conferred high risk of bias. One study reported using an envelop during random allocation. Only Chen 2000 reported adequate procedures for allocation concealment.

Blinding

No included study reported any procedure for undertaking blinding of participants or doctors, even the study using sham moxibustion. We considered all of the studies except Xu 2014b to be at high risk of performance bias. Xu 2014b used sham moxibustion, but there was no description of blinding measures. The risk of performance bias was unclear in this study. For detection bias, no study reported information on blinding. Because we thought the lack of blinding had less influence on the objective compared to subjective outcomes, we considered objective outcomes to be at unclear risk of bias and subjective ones to be at high risk.

Incomplete outcome data

All but three of the included studies reported complete data (Xu 2014b; Yu 2004; Zhang 2016a). In Xu 2014b, data were missing for 2/27 participants in both groups. In Yu 2004, data were missing for 2/38 and 9/30 participants, with no explanation for the reason. In Zhang 2016a, there were no data for 2/35 participants in the treatment group and 3/35 in the control group.

Selective reporting

There were no protocols available for included studies, but the review outcomes described in the Methods were generally reported, so we considered the risk of reporting bias to be unclear.

Other potential sources of bias

Eight studies presented baseline data, which were comparable between groups (Enkhtuya 2010; Hao 2014; Ruan 2014; Xu 2014a; Xu 2014b; Yang 2014; Zhang 2016a; Zhu 2017). The other studies reported only that some baseline data between groups were comparable without any detailed information, or they provided no information about comparability.

We assessed the overall risk of bias as unclear in 11 studies (Cheng 2005; Cheng 2016; Gao 2013; Li 2011; Li 2012; Li 2014a; Liang 2002; Tian 2015; Wang 2014; Wu 2013; Zhang 2016a) and high in 18 others (Chen 2000; Chen 2015; Enkhtuya 2010; Fan 2001; Hao 2014; Li 2015; Li 2016; Mo 2016; Ruan 2014; Xu 2014a; Xu 2014b; Yang 2014; Yin 2013;Yu 2004; Yuan 2014; Zhang 2013; Zhang 2016b; Zhu 2017).

Effects of interventions

See: **Summary of findings for the main comparison** Moxibustion versus no treatment for side effects of chemotherapy or radiotherapy in cancer patients; **Summary of findings 2** Moxibustion versus sham treatment for side effects of chemotherapy or radiotherapy in cancer patients; **Summary of findings 3** Moxibustion versus conventional medicines for side effects of chemotherapy or radiotherapy in cancer patients; **Summary of findings 4** Moxibustion + conventional treatment versus conventional medicine alone for side effects of chemotherapy or radiotherapy in cancer patients

Moxibustion versus no treatment

Five trials contributed data to this comparison (Liang 2002; Li 2011; Yu 2004; Wu 2013; Zhang 2016a), but most analyses comprised only one or two trials.

Incidence and severity of chemotherapy- or radiotherapy-related toxicities: leukopenia

Liang 2002 found no difference between intervention and control groups in the incidence of WHO grade 3 or 4 leukopenia (RR 0.50; 95% CI 0.10 to 2.56; 1 study, 80 participants; Analysis 1.1; low-certainty evidence, downgraded due to design limitations and imprecision).

Other objective outcome measures aimed at assessing side effects of chemotherapy or radiotherapy

WBC counts

In Li 2011, mean WBC count was higher in the moxibustion group compared with the control group (MD 1.77 × 10^9/L; 95% CI 0.76 to 2.78; 1 study, 80 participants; Analysis 1.2; low-certainty evidence, downgraded due to design limitations and imprecision).

Haemoglobin concentration

One trial reported this outcome (Yu 2004). Mean serum haemoglobin concentration was higher in the moxibustion group compared with the control group (MD 1.33 g/L; 95% CI 0.59 to 2.07; 1 study, 66 participants; Analysis 1.3; low-certainty evidence, downgraded due to design limitations and imprecision).

Lymphocyte counts

In Yu 2004, moxibustion increased total lymphocyte count (CD3) compared with control (MD 5.30 g/L; 95% CI 1.46 to 9.14; 1 study, 57 participants; Analysis 1.5; low-certainty evidence, downgraded due to design limitations and imprecision).

Meta-analysis of Wu 2013 and Yu 2004 showed that moxibustion increased T-helper cell (CD4) counts (MD 5.42 g/L; 95% CI 3.01 to 7.82; Analysis 1.6; 2 studies, 113 participants; I^2 = 0; low-certainty evidence, downgraded due to design limitations and imprecision), but the results in cytotoxic T cell (CD8) counts were inconsistent (Analysis 1.7).

Platelets

Mean platelet count was slightly higher with moxibustion than no treatment (MD 30.80 × 10^9/L; 95% CI 8.03 to 53.57; Analysis 1.4; 1 study, 65 participants; low-certainty evidence, downgraded due to design limitations and imprecision).

Immunoglobulin (Ig) count

Results of Wu 2013 and Yu 2004 in IgA (Analysis 1.8), IgM (Analysis 1.9) and IgG (Analysis 1.10) were all inconsistent. We did not perform meta-analysis due to the high heterogeneity.

The differences in moxibustion duration and participants between Wu 2013 and Yu 2004 may have contributed substantially to the high heterogeneity found in the meta-analyses involving data from these trials.

Moxibustion versus sham moxibustion

Only one trial contributed data to this comparison (Xu 2014b). We graded all evidence as being of low certainty due to design limitations and imprecision.

Quality of life

Karnofsky score

A Karnofsky score is based on a performance index of physical ability; higher scores indicate better health and well-being. Moxibustion was associated with a higher mean Karnofsky score compared with sham one (MD 10.86 points; 95% CI 5.1 to 16.62; 1 study, 50 participants; Analysis 2.1).

EORTC QLQ-C30

Moxibustion was associated with higher QoL scores, assessed by EORTC QLQ-C30 (version 3.0), compared with sham one (MD 14.88 points; 95% CI 4.83 to 24.93; 1 study, 50 participants; Analysis 2.2).

Patient-reported physical and psychological indices of symptom distress

Nausea/vomiting

Moxibustion was associated with lower nausea and vomiting scores than the sham treatment, as assessed by EORTC QLQ-C30 (version 3.0) (Analysis 2.3; 1 study, 50 participants: MD −38.57 points; 95% CI −48.67 to −28.47).

Diarrhoea

Similarly, in Xu 2014b, moxibustion was associated with lower scores for diarrhoea only of borderline significance, assessed by EORTC QLQ-C30 (version 3.0), compared with sham one (MD −13.81; 95% CI −27.52 to −0.1; 1 study, 50 participants; Analysis 2.4).

Other objective outcome measures aimed at assessing side effects of chemotherapy or radiotherapy

WBC count

Moxibustion was associated with a higher mean white blood cell count compared with sham control (MD 1.72 × 10^9/L; 95% CI 0.97 to 2.47; 1 study, 50 participants; Analysis 2.5).

Haemoglobin

The mean serum haemoglobin concentration was higher with moxibustion than with sham control (MD 2.06 g/L; 95% CI 1.26 to 2.86; 1 study, 50 participants; Analysis 2.6).

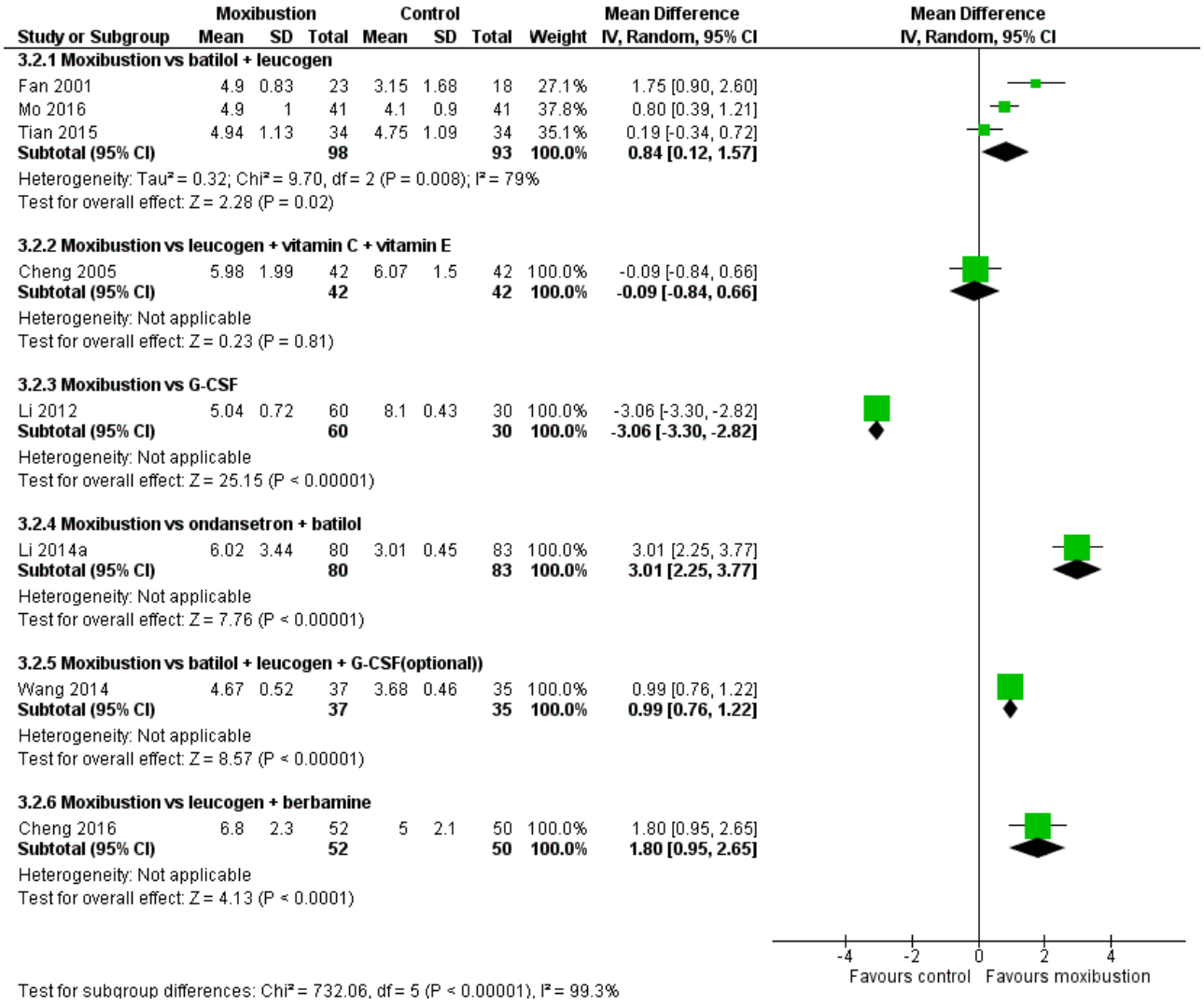
Platelets

Mean platelet count was higher with moxibustion than sham treatment (MD 210.79 × 10^9/L; 95% CI 167.02 to 254.56; 1 study, 50 participants; Analysis 2.7).

Moxibustion versus conventional medicines

Eight trials contributed data to this comparison. We graded all evidence as being of low certainty due to design limitations (high risk of bias) and inconsistency (heterogeneity) (Figure 4). The different conventional medicines used as controls and heterogeneity of participant populations contributed to inconsistent findings.

Figure 4. Forest plot of comparison: 3 Moxibustion treatment vs conventional medicine, outcome: 3.1 WBC counts (× 10^9/L) after treatment.



Incidence and severity of chemotherapy- or radiotherapy-related toxicities: haematological toxicity

Wang 2014 found no clear difference in the risk of haematological toxicity (assessed by the WHO grading system) due to chemotherapy when comparing moxibustion versus batilol plus leucogen plus optional G-CSF, which was administered to those with neutropenia (RR 0.57; 95% CI 0.15 to 2.20; 1 study, 72 participants; Analysis 3.1).

Quality of life: Karnofsky score

Mo 2016 reported that moxibustion was associated with a higher Karnofsky score compared with oral batilol plus legucogen (MD 6.70 points; 95% CI 2.37 to 11.03; 1 study, 82 participants; Analysis 3.6).

Other objective outcome measures aimed at assessing side effects of chemotherapy or radiotherapy

WBC count

Due to the high heterogeneity, we did not conduct a meta-analysis of eight trials reporting WBC counts (Cheng 2005; Cheng 2016; Fan 2001; Li 2012; Li 2014a; Mo 2016; Tian 2015; Wang 2014). The subgroup analysis based on the conventional medicines in the control group is shown on the forest plot (Analysis 3.2). The pooled results of Fan 2001, Mo 2016 and Tian 2015 show that moxibustion was associated with higher WBC count compared with oral batilol and legucogen (MD 0.84 × 10^9/L; 95% CI 0.12 to 1.57; 3 studies, 191 participants; Analysis 3.2; I^2 = 79%). Cheng 2005 found no difference in WBC count when comparing moxibustion versus leucogen plus vitamin C plus vitamin E (MD −0.09 × 10^9/L; 95% CI −0.84 to 0.66; 1 study, 84 participants; Analysis 3.2). Li 2012 reported that G-CSF increased WBC count more than moxibustion, but was associated with fever, sore muscle, fatigue and abnormally high WBC counts (MD −3.06 × 10^9/L; 95% CI −3.3 to −2.82; 1 study, 90 participants; Analysis 3.2) at the end of nine-day treatment; however, eight days after the end of treatment, the moxibustion group had a higher mean WBC count than the G-CSF group (MD 0.40 × 10^9/L; 95% CI 0.15 to 0.65; 1 study, 90 participants; Analysis 3.3). Li 2014a reported that moxibustion was associated with higher WBC count compared with ondansetron plus batilol (MD 3.01 × 10^9/L; 95% CI 2.25 to 3.77; 1 study, 163 participants; Analysis 3.2), and Wang 2014 reported that

moxibustion was associated with higher WBC count compared with batilol plus leucogen plus optional G-CSF (MD 0.99 × 10^9/L; 95% CI 0.76 to 1.22; 1 study, 72 participants; Analysis 3.2). Cheng 2016 reported that moxibustion was associated with a higher WBC count compared with leucogen plus berbamine (MD 1.8 × 10^9/L; 95% CI 0.95 to 2.65; 1 study, 102 participants; Analysis 3.2).

Haemoglobin

In a meta-analysis of two trials (Li 2014a; Wang 2014), moxibustion was associated with higher serum haemoglobin concentrations compared with conventional treatment (MD 10.28 g/L; 95% CI 4.51 to 16.05; 2 studies, 235 participants; Analysis 3.4; I^2 = 63%).

Platelets

Li 2014a reported that moxibustion was associated with higher platelet counts compared with ondansetron plus batilol (MD 31.99 × 10^9/L; 95% CI 16.33 to 47.65; 1 study, 163 participants; Analysis 3.5). Wang 2014 found no difference in platelets counts compared with batilol plus leucogen plus optional G-CSF (MD 6.00 × 10^9/L; 95% CI −4.86 to 16.86; 1 study, 47 participants; Analysis 3.5).

CD counts

Meta-analysis of Cheng 2005 and Li 2014a found no clear difference in CD3 counts (MD 0.69 g/L; 95% CI −0.64 to 2.02; 2 studies, 247 participants; Analysis 3.7; I^2 = 0) without heterogeneity. However, their results on CD4 and CD8 varied, with high heterogeneity, so we did not pool these data. Cheng 2005 reported that moxibustion was associated with higher CD4 counts than leucogen plus vitamin C plus vitamin E (MD 15.18 g/L; 95% CI 13 to 17.36; 1 study, 84 participants; Analysis 3.8). Li 2014a reported that there was no difference in CD4 counts between moxibustion versus ondansetron plus batilol (MD 2.11 g/L; 95% CI −0.44 to 4.66; 1 study, 163 participants; Analysis 3.8).

Cheng 2005 reported that moxibustion was associated with higher CD8 counts than leucogen plus vitamin C plus vitamin E (MD 10.76 g/L; 95% CI 9.02 to 12.50; 1 study, 84 participants; Analysis 3.9). Li 2014a also reported that moxibustion was associated with higher CD8 counts compared with ondansetron and batilol (MD 4.06 g/L; 95% CI 1.85 to 6.27; 1 study, 163 participants; Analysis 3.9).

Immunoglobulin (Ig) count

Fan 2001 reported increases in IgA (MD 2.84 g/L; 95% CI 2.3 to 3.38; 41 participants; Analysis 3.10), IgG (MD 7.31 g/L; 95% CI 6.05 to 8.57; 41 participants; Analysis 3.11) and IgM (MD 2.06 g/L; 95% CI 1.66 to 2.46; 41 participants; Analysis 3.12) with moxibustion compared with conventional medicine.

Moxibustion plus conventional medicine versus conventional medicine

Fifteen trials contributed data to this comparison. We graded all evidence as being of low certainty due to design limitations (high risk of bias) and imprecision.

Incidence and severity of chemotherapy- or radiotherapy-related toxicities: leukopenia

Chen 2000 found no difference in the incidence of severe haematologic toxicity of chemotherapy as assessed by WHO grade 3 to 4 leukopenia between moxibustion plus conventional medicine versus conventional medicine alone (RR 0.14; 95% CI 0.01 to 2.64; 1 study, 56 participants; Analysis 4.1).

Quality of life

Karnofsky score

Meta-analysis included four trials (Xu 2014a; Yang 2014; Zhang 2013; Zhang 2016b). Moxibustion combined with conventional medicine was associated with a higher mean Karnofsky score compared with conventional treatment (MD 7.21 points; 95% CI 5.74 to 8.68; 4 studies, 252 participants; Analysis 4.8; I^2 = 0%).

EORTC QLQ-C30, FACT-G 4.0, FACT-L 4.0

Meta-analysis included three trials (Enkhtuya 2010; Xu 2014a; Zhu 2017). Moxibustion plus conventional medicine was associated with higher QoL (EORTC QLQ-C30) scores compared with controls (MD 8.85 points; 95% CI 4.25 to 13.46; 3 studies, 134 participants; Analysis 4.9; I^2 = 26%).

Li 2016 reported that moxibustion plus conventional medicine increased QoL, as assessed by FACT-G 4.0 (Functional Assessment of Cancer Therapy - General) compared with the control group (MD 11.51 points; 95% CI 10.64 to 12.38; 1 study, 332 participants; Analysis 4.10). Zhang 2016b also reported increased QoL, as assessed by FACT-L 4.0 (Functional Assessment of Cancer Therapy - Lung) (MD 10.04 points; 95% CI 7.63 to 12.45; 1 study, 60 participants; Analysis 4.11).

Physical well-being

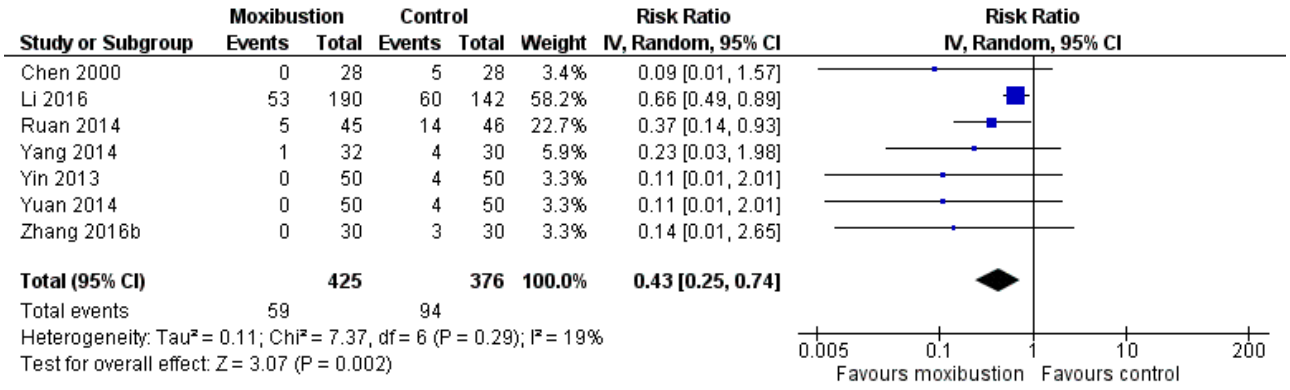
Chen 2015 reported that moxibustion combined with conventional medicine increased physical well-being compared with the control group, as assessed by FACT-L 4.0 (MD −4.33 points; 95% CI −6.25 to −2.41; Analysis 4.12; 72 participants).

Patient-reported physical and psychological indices of symptom distress

Nausea/vomiting

Meta-analysis included seven trials (Chen 2000; Li 2016; Ruan 2014; Yang 2014; Yin 2013; Yuan 2014; Zhang 2016b). Moxibustion plus conventional medicine was associated with a reduced risk of severe nausea and vomiting (WHO grade 3 to 4) compared with the control group (RR 0.43; 95% CI 0.25 to 0.74; 7 studies, 801 participants; Analysis 4.3; I^2 = 19%; Figure 5).

Figure 5. Forest plot of comparison: 4 Moxibustion treatment + conventional medicine vs conventional medicine, outcome: 4.3 Nausea/vomiting (WHO grade 3 to 4).



Li 2015 reported severe vomiting (Common Terminology Criteria for Adverse Events (CTCAE) v3.0 grade 3 to 5) and found no clear difference in this outcome between intervention and control groups (RR 0.07; 95% CI 0.00 to 1.14; 169 participants; Analysis 4.4).

Diarrhoea

Hao 2014 found no difference in the incidence of severe diarrhoea (WHO grade 3 to 4) with moxibustion plus conventional medicine compared with the control group (RR 0.19; 95% CI 0.01 to 3.88; 61 participants; Analysis 4.5).

Other objective outcome measures aimed at assessing side effects of chemotherapy or radiotherapy

WBC count

The results on WBC count varied amongst three trials (Gao 2013; Yang 2014; Zhang 2013). Gao 2013 reported that moxibustion was associated with a slightly higher mean WBC count compared with control (MD 0.50 × 10^9/L; 95% CI 0.12 to 0.88; 1 study, 120 participants; Analysis 4.2). Yang 2014 found no difference between groups (MD 0.41 × 10^9/L; 95% CI −0.22 to 1.04; 1 study, 62 participants; Analysis 4.2). Zhang 2013 reported that moxibustion was associated with a higher mean white blood cell count compared with control (MD 1.5 × 10^9/L; 95% CI 1.14 to 1.86; 1 study, 80 participants; Analysis 4.2).

Haemoglobin

Meta-analysis included two trials (Yang 2014; Zhang 2013). Mean haemoglobin concentration was higher with moxibustion plus conventional medicine than with conventional treatment alone (MD 3.97 g/L; 95% CI 1.4 to 6.53; 2 studies, 142 participants; Analysis 4.6; I^2 = 0%).

Platelets

Meta-analysis included two trials (Yang 2014; Zhang 2013). There was no clear difference in mean platelet counts between groups (MD 13.48 g/L; 95% CI −16.00 to 42.95; 2 studies, 142 participants; Analysis 4.7; I^2 = 34%).

Immunoglobulin (Ig) count

Hao 2014 reported that moxibustion plus conventional medicine treatment increased IgA (MD 0.55 g/L; 95% CI 0.21 to 0.89; 61 participants; Analysis 4.13), IgG (MD 2.11 g/L; 95% CI 1.19 to 3.03; 61 participants; Analysis 4.14) and IgM (MD 0.40 g/L; 95% CI 0.19 to 0.61; 61 participants; Analysis 4.15) compared with conventional treatment.

Adverse effects

Only one study reported that a single participant with lung cancer presented fever and sore throat after receiving direct grain-size moxibustion, but the symptoms resolved after 24 hours, and there was no relapse (Zhang 2016a). Only two studies reported that no participants experienced any obvious adverse effects of moxibustion during the study period (Hao 2014; Li 2014a). The other studies provided no information about any adverse events related to moxibustion.

DISCUSSION

Summary of main results

This review includes 29 studies on moxibustion treatment for alleviating side effects of chemotherapy or radiotherapy in people with cancer. Five compared moxibustion versus no treatment, 15 compared moxibustion plus conventional treatment versus conventional treatment alone, 1 compared moxibustion versus sham treatment, and 8 compared moxibustion versus conventional medicines.

Single studies reported that compared with no treatment, moxibustion increased white blood cell count and haemoglobin in people with cancer receiving or after receiving chemotherapy/radiotherapy, but its effect on immunological function was inconsistent. A single study reported that moxibustion improved QoL; reduced the symptoms of nausea/vomiting and diarrhoea; and increased mean white blood cell count, mean haemoglobin concentration and mean platelet counts when compared with sham moxibustion.

When comparing moxibustion versus conventional medicines, there was no clear difference in mean white blood cell count, platelets, or CD count; however, moxibustion was associated with higher mean haemoglobin and immunoglobulin concentrations compared with conventional medicines. When moxibustion was added to conventional medicine, it helped decrease the symptoms of nausea/vomiting, improve QoL, increase white blood cell count and haemoglobin, and increase immunoglobulin. The overall risk of bias was high in 18 studies and unclear in 11 studies.

Overall, limited evidence suggests some promising effects of moxibustion in people undergoing chemotherapy or radiotherapy, such as improved haematological and immunological profiles, improved gastrointestinal symptom scores and improved QoL. However, due to the generally low quality and poor reporting of included studies, no high-certainty evidence supports the use of moxibustion in people undergoing chemotherapy or radiotherapy.

Overall completeness and applicability of evidence

Some included studies assessed patient-reported physical and psychological indices of symptom distress using self-developed scales. They reported no modification or cessation of cancer treatment due to moxibustion. Most included studies provided no information on the adverse effects.

Twenty-eight studies took place in China and one in Mongolia. The moxibustion treatment varied amongst included studies; furthermore, the proper procedures of moxibustion treatment were not adequately standardised. Although no studies reported the adverse events related to moxibustion, this treatment is well known to be related to some adverse effects such as allergic reactions, burns and infections (Chan 2014). These issues raise questions about the applicability of evidence in other countries or regions.

Quality of the evidence

The review included 29 studies involving 2569 people with cancer receiving chemotherapy or/and radiotherapy. The certainty of the included studies was generally low due to poor reporting and methodological design flaws. There were three main problems with study methodology. Firstly, most included studies provided no proper description on random number generation, allocation concealment or baseline characteristics. An imbalance between groups in three included studies introduced doubt on baseline comparability. Secondly, the lack of blinding measurement undertaken for participants or outcome assessors can introduce bias during the study period and outcome data collection, especially for subjective outcomes. Thirdly, the treatment outcomes were not assessed adequately. Some included studies used self-developed scales to assess toxicity and participants' symptoms. We used the GRADE approach to assess certainty of evidence, downgrading once or twice for inconsistency or risk of publication bias. The different participants and chemotherapy or radiotherapy regimens may contribute much to the high heterogeneity among the included studies. Most studies reported positive results. Although we did not undertake funnel plot analysis due to the insufficient data, it is not possible to rule out the risk of publication bias (GRADE 2015).

Potential biases in the review process

We undertook a comprehensive search strategy with clear and rigid inclusion criteria to screen a large amount of articles. Some studies did not assess any of the reviewed outcomes. Other reviews might have included these studies; however, we considered that studies evaluating other outcomes were beyond the scope of this review, and we excluded them. Type I errors may also exist in the analysis of several subgroups when moxibustion is compared to conventional medicines.

Agreements and disagreements with other studies or reviews

Lee 2010 included five RCTs employing moxibustion as an adjuvant treatment for conventional medicine in people with any type of cancer. It found limited evidence to suggest moxibustion was an effective supportive therapy for nausea and vomiting in cancer. The findings remain similar to this review. Our study has a more comprehensive scope, but it was not possible to establish stronger evidence due to the sparse comparisons and low certainty in the included studies.

AUTHORS' CONCLUSIONS

Implications for practice

Limited, low-certainty evidence suggests that moxibustion may help to reduce the haematological and gastrointestinal toxicities of chemotherapy or radiotherapy and improve QoL in people with cancer; however, the evidence is not conclusive, and we cannot rule out benefits or risks with this treatment. High-quality studies are needed, which should include reporting of adverse effects.

Implications for research

Based on this review of current available studies, we suggest that future randomised controlled trials adhere to CONSORT guidelines, including:

1. proper description of random number generation and allocation concealment;
2. proper sample size to ensure sufficient power to detect difference between groups;
3. blinding outcome assessors, participants, and doctors by using reliable sham moxibustion (Zhao 2006);
4. clear description of any adverse effect observed during the study;
5. proper controlled intervention to examine the specific effect of moxibustion other than heat.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Chen 2000

Methods	Design: parallel RCT Randomisation method: not reported Blinding: no Power calculation: no Dropouts/withdrawals: no
Participants	Patients with nasopharyngeal carcinoma (stage TNM III and IVa), Karnofsky > 60 Number (treatment/control): 56 (28/28) Mean age (range): 43.7 (18-71) Gender (M/F): 30/26 Country: Guangdong province, China Setting: hospital

Interventions	Indirect moxa cone on salt + conventional treatment vs conventional treatment
	Treatment group
	• Indirect moxa cone on salt
	  * 10 continuous indirect moxa cones on salt on the acupoint RN8 (shenque), once per day
	  * Treatment duration: 30 days
	• Chemotherapy with doxorubicin and cisplatin for 1 course
	• Radiotherapy for 7 to 8 weeks
	• Conventional treatment
	Control group
	• Chemotherapy with doxorubicin and cisplatin for 1 course
	• Radiotherapy for 7 to 8 weeks
	• Conventional treatment
	Conventional treatment
	• Symptomatic treatment

Outcomes	WHO Recommendations for Grading of Acute and Subacute Toxicity (1981) at the end of treatment • Haemoglobin • WBC • Platelets • Nausea/vomiting • Oral mucosa • Hair loss
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described

Chen 2000 *(Continued)*

Allocation concealment (selection bias)	Low risk	Envelope was used for random allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	There was no loss to follow-up. All participants were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Few outcome measures were reported
Other bias	Unclear risk	It was mentioned that the groups were comparable, but no baseline characteristics data were presented.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	No blinding; however, objective outcomes detected by machine were not influenced substantially

Chen 2015

Methods	Design: parallel RCT Randomisation method: not reported Blinding: no Power calculation: no Dropouts/withdrawals: no
Participants	People with non-small cell lung cancer who were receiving chemotherapy Number (treatment/control): 72 (36/36) Mean age (range): 58.53 (42-72) Gender (M/F): 43/29 Country: Shanghai city, China Setting: hospital

Interventions	Indirect moxa cone on ginger + conventional medicine vs conventional medicine
	Treatment group
	• Indirect moxa cone
	  * Indirect moxa cone on ginger placed on the acupoints ST36 zusanli) and RN12 (zhongwan) continuous 3 cones, once per day
	  * Treatment duration: 10 days

Chen 2015 *(Continued)*

	• Chemotherapy with docetaxel + cisplatin (TP)/gemcitabine + cisplatin (GP)/toxal + cisplatin (NP) for 8 days • Conventional treatment **Control group** • Chemotherapy with TP/GP/NP for 8 days • Conventional treatment • Treatment duration: 10 days Conventional treatment • Granisetron hydrochloride 3 mg and dexamethasone 5 mg, iv, 1/d
Outcomes	FACT-L4.0 (PWB) at the end of treatment
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	No relevant description
Incomplete outcome data (attrition bias) All outcomes	Low risk	There was no loss to follow-up. All participants were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Limited outcome measures were reported.
Other bias	Unclear risk	There was a statement about group similarity but without baseline characteristics data presented
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	No objective outcome was reported.

Cheng 2005

Methods	Design: parallel RCT Randomisation method: not reported

Cheng 2005 *(Continued)*

	Blinding: no Power calculation: no Dropouts/withdrawals: no
Participants	People with advanced nasopharyngeal carcinoma (stage III and IV), Karnofsky > 60 Number (treatment/control): 84 (42/42) Mean age (range): 45.9 (21-78) Gender (M/F): 45/39 Country: Guangdong province, China Setting: hospital

Interventions	Indirect moxa cone on salt vs conventional medicine
	Treatment group
	• Indirect moxa cone on salt
	  * Indirect moxa cone on salt on the acupoint RN8 (Shenque), once per day
	  * Treatment duration: 30 days
	• Chemotherapy with doxorubicin and 5-Fu for 5 times
	• Radiotherapy for 7 to 8 weeks
	Control group
	• conventional medicine
	  * Oral leucogen 20 mg, vitamin C 0.2 g and vitamin E 20 mg, 3 times per day
	• Chemotherapy with doxorubicin and 5-Fu for 5 times
	• Radiotherapy for 7 to 8 weeks

Outcomes	WBC count at the end of treatment
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	No relevant description
Incomplete outcome data (attrition bias) All outcomes	Low risk	There was no loss to follow-up. All participants were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Limited outcome measures were reported.
Other bias	Unclear risk	There were no baseline characteristics data presented and no statement of group similarity.

Cheng 2005 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	No subjective outcome was reported.
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	No blinding However, the objective outcomes detected by machine were generally not influenced substantially.

Cheng 2016

Methods	Design: parallel RCT Randomisation method: not reported Blinding: no Power calculation: no Dropouts/withdrawals: no
Participants	Cancer patients who were receiving chemotherapy Number (treatment/control): 102 (52/50) Mean age (range): not reported (37-72) Gender (M/F): 71/31 Country: Zhejiang province, China Setting: hospital

Interventions	Direct moxa box vs conventional medicine
	Treatment group
	• Direct moxa box
	  * Direct moxa box on the acupoint ST36 (Zusanli) for 15 minutes, once per day
	  * Treatment duration: 21 days (beginning at the same day of chemotherapy)
	• Chemotherapy
	• Conventional treatment
	Control group
	• conventional medicine
	  * Oral leucogen 20 mg, and Berbamine 112 mg, 3 times per day
	• Chemotherapy
	• Conventional treatment
	Conventional treatment
	• G-CSF 150μg, 2 times per day, was provided when WBC is less than $2*10^9$/L or neutrophil granulocyte is less than $1*10^9$/L. It was stopped when WBC was more than $2*10^9$/L after 2 days.

Cheng 2016 *(Continued)*

Outcomes	WBC count at the end of treatment
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	No relevant description
Incomplete outcome data (attrition bias) All outcomes	Low risk	There was no loss to follow-up. All participants were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Limited outcome measures were reported.
Other bias	Unclear risk	It was mentioned that the groups were comparable, but no baseline characteristics data were presented.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	No subjective outcome was reported.
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	No blinding; however, machine-measured objective outcomes were not influenced substantially

Enkhtuya 2010

Methods	Design: parallel RCT Randomisation method: not reported Blinding: no Power calculation: no Dropouts/withdrawals: no
Participants	People with primary gastric cancer (stage IIIA and IIIB), with expected survival time of more than 3 months and Karnofsky ≥ 60 Number (treatment/control): 24 (12/12) Mean age (range): 61.6 (36-77) Gender (M/F): 13/11

Enkhtuya 2010 *(Continued)*

	Country: Mongolia Setting: hospital

Interventions	Direct moxa cone + conventional medicine vs conventional medicine
	Treatment group
	• direct moxa cone
	  * Direct moxa cone on the acupoints RN4 (guanyuan), continuous 5 to 9 cones, once per day
	  * Treatment duration: 5 days
	• Chemotherapy with 5-FU and CDDP
	Control group
	• Chemotherapy with 5-FU and CDDP
	Conventional medicine
	• Symptomatic treatment, including ondansetron and dexamethasone

Outcomes	EORTC QLQ-C30 at the end of treatment
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	No relevant description
Incomplete outcome data (attrition bias) All outcomes	Low risk	There was no loss to follow-up. All participants were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Limited outcome measures were reported.
Other bias	Low risk	Baseline characteristics data were comparable.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	No objective outcome was reported.

Fan 2001

Methods	Design: parallel RCT Randomisation method: not reported Blinding: no Power calculation: no Dropouts/withdrawals: no
Participants	The participants with respiratory and digestive system cancer receiving combination chemotherapy Number (treatment 1/treatment 2/control): 63 (23/22/18) Mean age (range): not reported Gender (M/F): not reported Country: Jiangsu province, China Setting: hospital

Interventions	Moxa stick vs acupoint injection vs conventional medicine
	Treatment group 1:
	• Moxa stick
	  * Moxa stick treatment for about 20 to 30 minutes on the acupoints ST36 (zusanli) and SP6 (sanyinjiao), once/d
	  * Treatment duration: 18 days (5 days before chemotherapy til 7 days after chemotherapy)
	• Chemotherapy
	  * Combination chemotherapy including cyclophosphamide, adriamycin, vincristine, vepeside, cisplatin, methotrexate, and 5-FU
	Treatment group 2:
	• Acupoint injection
	  * Huangqi injection on acupoints ST36 (zusanli) and SP6 (sanyinjiao), 4 mL, once/d
	  * Treatment duration: 18 days (5 days before chemotherapy til 7 days after chemotherapy)
	• Chemotherapy (same as group 1)
	Control group
	• Conventional medicine
	  * Oral batilol 100 mg and leucogen 20 mg, 3 times/d
	  * Treatment duration: 18 days
	• Chemotherapy (same as group1)

Outcomes	WBC count IgG IgA IgM Outcomes measured at the end of treatment
Notes	—
Risk of bias	

Fan 2001 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not described; there was imbalance on the number of participants between groups.
Allocation concealment (selection bias)	Unclear risk	No relevant description
Incomplete outcome data (attrition bias) All outcomes	Low risk	There was no loss to follow-up. All participants were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Limited outcome measures were reported.
Other bias	Unclear risk	There was no baseline characteristics data presented and no statement of group similarity.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	No subjective outcome was reported.
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	No blinding; however, machine-measured objective outcomes were not influenced substantially

Gao 2013

Methods	Design: parallel RCT Randomisation method: not reported Blinding: no Power calculation: no Dropouts/withdrawals: no
Participants	People with cancer after chemotherapy or radiotherapy with leukopenia (WBC count < 4×10^9); expected survival time of more than 6 months; Karnofsky ≥ 70 Number (treatment/control): 120 (60/60) Mean age (range): 45.2 (19-76) Gender (M/F): 58/62 Country: Jiangsu province, China Setting: hospital
Interventions	Direct grain-sized moxa cone + conventional medicine vs conventional medicine

Gao 2013 *(Continued)*

Treatment group

- Direct moxa cone
  - Direct grain-sized moxa cone on the acupoints ST36 (zusanli), RN4 (guanyuan) and DU14 (dazhui), 5 continuous cones, once per day
- Conventional treatment
  - Oral leucogen, batilol and vitamin B4
- Treatment duration: 12 days

Control group

- Conventional treatment
  - Oral leucogen, batilol and vitamin B4
- Treatment duration: 12 days

Conventional treatment

- Granisetron hydrochloride 3 mg and dexamethasone 5 mg, iv, 1/d

Outcomes	WBC count at the end of treatment
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	No relevant description
Incomplete outcome data (attrition bias) All outcomes	Low risk	There was no loss to follow-up. All participants were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Limited outcome measures were reported.
Other bias	Unclear risk	There was no baseline characteristics data presented and no statement of group similarity.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	No subjective outcome was reported.
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	No blinding; however, machine-measured objective outcomes were not influenced substantially

Hao 2014

Methods	Design: parallel RCT Randomisation method: random number table Blinding: no Power calculation: no Dropouts/withdrawals: no
Participants	The participants with gastrointestinal tract and gynaecological cancer with expected survival time of more than 3 months; Karnofsky ≥ 60 Number (treatment/control): 61 (31/30) Mean age (range): 61.13 (35-80) Gender (M/F): 37/24 Country: Jiangsu province, China Setting: hospital

Interventions	Moxa stick + conventional medicine vs conventional medicine
	Treatment group
	• Moxa stick
	  * Moxa stick on the acupoints RN8 (shenque) and bilateral ST36 (zusanli) for 15 minutes per acupoint, with additional acupoint RN6 (qihai) for those with syndrome of qi deficiency, SP10 (xuehai) for those with syndrome of blood stagnation, RN12 (zhongwan) for those with digestive reactions and SP6 (sanyinjiao) for those with gynaecological tumours, 30 minutes per treatment, once per day, 6 times per week
	  * Treatment duration: 60 days (beginning at the same day of chemotherapy)
	• Conventional treatment
	  * Dexamethasone and cimetidine, promethazine, tropisetron, and G-CSF
	• Chemotherapy
	Control group
	• Conventional treatment
	  * Dexamethasone and cimetidine, promethazine, tropisetron, and G-CSF
	• Chemotherapy

Outcomes	IgA, IgG, IgM, diarrhoea (WHO grade 3 to 4) at the end of treatment
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number table
Allocation concealment (selection bias)	Unclear risk	No relevant description
Incomplete outcome data (attrition bias)	Unclear risk	1 participant in treatment, and 2 in control group were lost to follow-up. Such attrition was not considered to bias the results substantially.

Hao 2014 *(Continued)*

All outcomes		
Selective reporting (reporting bias)	Unclear risk	Limited outcome measures were reported.
Other bias	Low risk	Baseline characteristic data were comparable.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	No blinding; however, machine-measured objective outcomes were not influenced substantially

Li 2011

Methods	Design: parallel RCT Randomisation method: not reported Blinding: no Power calculation: no Dropouts/withdrawals: no
Participants	Patients with primary non-small cell lung cancer (stage IIIa, IIIb and IV) with expected survival time of more than 3 months, Karnofsky > 60 Number (treatment/control): 80 (40/40) Mean age (range): not reported (41-65) Gender (M/F): 51/29 Country: Guangdong province, China Setting: hospital

Interventions	Direct moxa cone vs no treatment
	Treatment group
	• direct moxa cone
	  * Direct moxa cone on the acupoints sihua (bilateral BL17 (geshu) and BL19 (danshu)), continuous 3 cones, once per day
	  * Treatment duration: 8 days
	• Chemotherapy with PDD and NVB
	Control group
	• Chemotherapy with PDD and NVB

Li 2011 *(Continued)*

Outcomes	WBC count at the end of treatment
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	No relevant description
Incomplete outcome data (attrition bias) All outcomes	Low risk	There was no loss to follow-up. All participants were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Limited outcome measures were reported.
Other bias	Unclear risk	There were no baseline characteristics data presented and no statement of group similarity.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	No subjective outcome was reported.
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	No blinding; however, machine-measured objective outcomes were not influenced substantially

Li 2012

Methods	Design: parallel RCT Randomisation method: random number table Blinding: no Power calculation: no Dropouts/withdrawals: no
Participants	Cancer patients with leukopenia **after** having received chemotherapy Number (treatment/control): 90 (60/30) Mean age: 63.8 Gender (M/F): 53/37 Country: Henan province, China

Li 2012 *(Continued)*

	Setting: hospital
Interventions	Indirect moxa cone on ginger vs conventional medicine **Treatment group** • Indirect moxa cone * Indirect moxa cone on ginger placed on the acupoints DU14 (dazhui), BL17 (geshu), BL20 (pishu) and BL21 (weishu) companied with other complementary acupoints, continuous 7 cones, once per day * Treatment duration: 9 days **Control group** • conventional medicine * G-CSF (recombinant human granulocyte colony-stimulating factor injection), 100 μg, subcutaneous injection, once per day * Treatment duration: 7 days
Outcomes	WBC count at the end of treatment and 8 days after the end of treatment
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number table
Allocation concealment (selection bias)	Unclear risk	No relevant description
Incomplete outcome data (attrition bias) All outcomes	Low risk	There was no loss to follow-up. All participants were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Limited outcome measures were reported.
Other bias	Unclear risk	There was a statement about group similarity but without baseline characteristics data presented
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	No subjective outcome was reported.
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	No blinding; however, machine-measured objective outcomes were not influenced substantially

Li 2014a

Methods	Design: parallel RCT Randomisation method: not reported Blinding: no Power calculation: no Dropouts/withdrawals: no
Participants	Cancer patients receiving chemotherapy Number (treatment/control): 163 (80/83) Mean age (range): 67.83 (32-75) Gender (M/F): 96/67 Country: Guangdong province, China Setting: hospital

Interventions	Indirect moxa cone on ginger vs conventional medicine
	Treatment group
	• Indirect moxa cone
	  * Indirect moxa cone on ginger placed on the bilateral acupoints BL43 (gaohuangshu), BL17 (geshu), BL20 (pishu), BL21 (weishu) and BL23 (shenshu), continuous 3 cones, once per day
	• Chemotherapy
	• Treatment duration: 14 days
	Control group
	• Conventional medicine
	  * Ondansetron hydrochloride 8 mg, intravenous push, 1/d or oral batilol 50 mg, 3/d, continuous 3 days, depending on the symptoms
	• Chemotherapy

Outcomes	WBC count, Hb, platelets, CD3, CD4, CD8 at the end of treatment
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	No relevant description
Incomplete outcome data (attrition bias) All outcomes	Low risk	There was no loss to follow-up. All participants were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Limited outcome measures were reported.

Li 2014a *(Continued)*

Other bias	Unclear risk	There was a statement about group similarity but without baseline characteristics data presented
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	No subjective outcome was reported.
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	No blinding; however, machine-measured objective outcomes were not influenced substantially

Li 2015

Methods	Design: parallel RCT Randomisation method: not reported Blinding: no Power calculation: no Dropouts/withdrawals: no
Participants	Cancer patients who could accept the smell of moxibustion Number (treatment/control): 169 (85/84) Mean age (range): 53.8 (40-88) Gender (M/F): 89/80 Country: Guangdong province, China Setting: hospital

Interventions	Direct moxa box + conventional medicine vs conventional medicine
	Treatment group
	• Direct moxa cone
	  * Direct moxa box on the acupoints RN13 (shangwan), RN12 (zhongwan), RN10 (xiawan), ST25 (tianshu), PC6 (neiguan), ST36 (zusanli), complemented by SP15 (daheng), RN6 (qihai), ST25 (guanyuan), and ST21 (liangmen) depended on the syndrome differentiation, 20 to 30 minutes for the whole treatment, twice per day
	  * Treatment duration: 8 days (beginning at the same day of chemotherapy)
	• Conventional treatment
	  * Tropisetron hydrochloride 5 mg, iv, 1/d, through 3 courses chemotherapy
	• Chemotherapy containing platinum for 3 courses
	Control group
	• Conventional treatment
	  * Tropisetron hydrochloride 5 mg, iv, 1/d, through 3 courses chemotherapy

Li 2015 *(Continued)*

	• Chemotherapy containing platinum for 3 courses
Outcomes	Vomiting (CTCAE 3.0 grade 3 to 5) at the end of treatment
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	No relevant description
Incomplete outcome data (attrition bias) All outcomes	Low risk	There was no loss to follow-up. All participants were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Limited outcome measures were reported.
Other bias	Unclear risk	There was no statement about group similarity.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	No objective outcome was reported.

Li 2016

Methods	Design: parallel RCT Randomisation method: random number table Blinding: no Power calculation: no Dropouts/withdrawals: no
Participants	Cancer patients with symptoms of nausea and vomiting after receiving chemotherapy. Number (treatment/control): 332 (190/142) Mean age (range): not reported (26-87) Gender (M/F): 189/143

Li 2016 *(Continued)*

	Country: Henan province, China Setting: hospital

Interventions	Moxa stick + conventional medicine vs conventional medicine
	
	Treatment group
	
	• Moxa stick
	  * Moxa stick on the acupoints RN4 (guanyuan), RN6 (qihai) and bilateral ST36 (zusanli) and EX-HN5 (Taiyangxue) for about 20 minutes, twice per day
	  * Treatment duration: 14 days
	• Conventional treatment
	  * Oral metoclopramide tablet, 5 mg, 3 times per day
	
	Control group
	
	• Conventional treatment
	  * Oral metoclopramide tablet, 5 mg, 3 times per day

Outcomes	Nausea/vomiting (WHO grade 3 to 4), FACT-G 4.0 (Functional Assessment of Cancer Therapy - General) at the end of treatment
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Random number table was used, but there was high imbalance between groups
Allocation concealment (selection bias)	Unclear risk	No relevant description
Incomplete outcome data (attrition bias) All outcomes	Low risk	There was no loss to follow-up. All participants were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Limited outcome measures were reported.
Other bias	Unclear risk	Baseline characteristic data were comparable.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	No objective outcome was reported.

Liang 2002

Methods	Design: parallel RCT Randomisation method: not reported Blinding: no Power calculation: no Dropouts/withdrawals: no
Participants	Cancer patients receiving chemotherapy Number (treatment/control): 72 (36/36) Mean age (range): not reported Gender (M/F): not reported Country: Shandong province, China Setting: hospital

Interventions	Moxa stick vs no treatment
	Treatment group
	• Moxa stick
	  * Moxa stick on the bilateral acupoints ST36 (zusanli) and RN12 (zhongwan), 15 minutes, once per day
	  * Treatment duration: 14 days (beginning at the same day of chemotherapy)
	• Chemotherapy
	Control group
	• Chemotherapy

Outcomes	Leukocytes (WHO grade 3 to 4) at the end of treatment
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	No relevant description
Incomplete outcome data (attrition bias) All outcomes	Low risk	There was no loss to follow-up. All participants were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Limited outcome measures were reported.
Other bias	Unclear risk	There was no statement about group similarity.

Liang 2002 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	No subjective outcome was reported.
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	No blinding; however, machine-measured objective outcomes were not influenced substantially

Mo 2016

Methods	Design: parallel RCT Randomisation method: random number table Blinding: no Power calculation: no Dropouts/withdrawals: no
Participants	Cancer patients after chemotherapy with expected survival time of more than 6 months, Karnofsky ≥ 60, and WBC count less than 4×10^9/L; diagnosed with the Chinese medicine syndrome of qi and blood insufficiency Number (treatment/control): 82 (41/41) Mean age (range): 55.5 (34-69) Gender (M/F): 48/34 Country: Guangdong province, China Setting: hospital

Interventions	Moxa stick vs conventional medicine
	Treatment group
	• Moxa stick
	  * Moxa stick on the acupoints RN4 (guanyuan), RN8 (shenque), RN6 (qihai) and bilateral ST36 (zusanli), once per day, 20 minutes each treatment, 6 times per week
	• Treatment duration: 21 days
	Control group
	• conventional medicine
	  * Oral batilol 40 mg, 3/d and leucogen 20 mg, 3/d
	• Treatment duration: 21 days

Outcomes	WBC count and Karnofsky score at the end of treatment
Notes	—

Mo 2016 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number table
Allocation concealment (selection bias)	Unclear risk	No relevant description
Incomplete outcome data (attrition bias) All outcomes	Low risk	There was no loss to follow-up. All participants were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Limited outcome measures were reported.
Other bias	Unclear risk	There was no statement about group similarity.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	No blinding; however, machine-measured objective outcomes were not influenced substantially

Ruan 2014

Methods	Design: parallel RCT Randomisation method: random number table Blinding: no Power calculation: no Dropouts/withdrawals: no
Participants	People with gastric cancer with expected survival time of more than 3 months; Karnofsky ≥ 60 Number (treatment/control): 91 (45/46) Mean age: 48.35 Gender (M/F): 52/39 Country: Zhejiang province and Shanghai city, China Setting: hospital
Interventions	Indirect moxa cone on herbal paste + conventional medicine vs conventional medicine

Ruan 2014 *(Continued)*

Treatment group

- Indirect moxa cone on herbal paste
  - Indirect moxa cone on herbal paste, made from Pinelliae Rhizoma (banxia), Citri Reticulatae Pericarpium (chenpi), Bambusae Caulis in Taenias (zhuru), Coptidis Rhizoma (huanglian), Euodiae Fructus (wuzhuyu) and Caryophylli Flos (dingxiang), was placed on the acupoints RN12 (zhongwan), RN4 (guanyuan), ST36 (zusanli), ST25 (tianshu), PC6 (neiguan), and SP15 (daheng), continuous 4 cones, once per day
  - Treatment duration: 14 days (beginning at the same day of chemotherapy)
- Conventional treatment
  - Ondansetron hydrochloride 8 mg and dexamethasone 5 mg, iv, 1/d, for day 1 to day 3
  - Omeprazole 40 mg, iv, 1/d, for day 1 to day 3
  - Oral metoclopramide tablet, 10 mg, 3/d, for day 4 to day 7
- Chemotherapy
  - Oxaliplatin
  - Gimeracil and oteracil potassium capsules
  - Treatment duration: 14 days

Control group

- Conventional treatment
  - Ondansetron hydrochloride 8 mg and dexamethasone 5 mg, iv, 1/d, for day 1 to day 3
  - Omeprazole 40 mg, iv, 1/d, for day 1 to day 3
  - Oral metoclopramide tablet, 10 mg, 3/d, for day 4 to day 7
- Chemotherapy
  - Oxaliplatin
  - Gimeracil and oteracil potassium capsules
  - Treatment duration: 14 days

Outcomes	Vomiting (WHO grade 3 to 4) at the end of treatment
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	No relevant description
Incomplete outcome data (attrition bias) All outcomes	Low risk	There was no loss to follow-up. All participants were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Limited outcome measures were reported.
Other bias	Unclear risk	Baseline characteristics data were comparable.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding

Ruan 2014 *(Continued)*

Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	No objective outcome was reported.

Tian 2015

Methods	Design: parallel RCT Randomisation method: not reported Blinding: no Power calculation: no Dropouts/withdrawals: no
Participants	Cancer patients after chemotherapy with expected survival time of > 3 months, Karnofsky ≥ 60, and WBC count less than 4×10^9/L Number (treatment/control): 68 (34/34) Mean age (range): 51.6 (32-76) Gender (M/F): 41/27 Country: Guangdong province, China Setting: hospital

Interventions	Moxa stick vs conventional medicine
	Treatment group
	• Moxa stick
	  * Moxa stick on the acupoints RN4 (guanyuan), ST36 (zusanli) and RN6 (qihai), once per day, 15 minutes each treatment
	• Treatment duration: 14 days
	Control group
	• Conventional medicine
	  * Oral batilol 50 mg, 3/d and leucogen 20 mg, 3/d
	• Treatment duration: 14 days

Outcomes	WBC count at the end of treatment
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described

Tian 2015 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	No relevant description
Incomplete outcome data (attrition bias) All outcomes	Low risk	There was no loss to follow-up. All participants were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Limited outcome measures were reported.
Other bias	Unclear risk	There was a statement about group similarity but without baseline characteristics data presented
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	No subjective outcome was reported.
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	No blinding; however, machine-measured objective outcomes were not influenced substantially

Wang 2014

Methods	Design: parallel RCT Randomisation method: random number table Blinding: no Power calculation: no Dropouts/withdrawals: no
Participants	People with gastric cancer with expected survival time of > 3 months; Karnofsky ≥ 60 They also needed to meet the criteria of Chinese medicine syndrome of insufficiency of heart and spleen. Number (treatment/control): 72 (37/35) Mean age: 52.7 Gender (M/F): 42/30 Country: Zhejiang province and Shanghai city, China Setting: hospital
Interventions	Indirect moxa cone on herbal paste vs conventional medicine **Treatment group** • Indirect moxa cone on herbal paste * Indirect moxa cone on herbal paste, made from Astragali Radix (huangqi), Angelicae Sinensis Radix (dangdui), Ginseng Radix et Rhizoma (renshen), Atractylodis mMacrocephalae Rhizoma (baizhu), Poria (fuling), Glycyrrhizae Radix et Rhizoma Praeparata cum Melle (zhigancao), Spatholobi Caulis

Wang 2014 *(Continued)*

(jixueteng), Psoraleae Fructus (buguzhu), Polygonati Rhizoma (huangjing), and Rehmanniae Radix Praeparata (shudi), was placed on the acupoints RN4 (guanyuan), ST36 (zusanli), SP6 (sanyinjiao), SP10 (xuehai) and RN8 (shenque), continuous 4 cones, once per day
  * Treatment duration: 14 days (beginning at the same day of chemotherapy)
- Chemotherapy

Control group

- Conventional treatment
  * Oral batilol 50 mg, 3/d and leucogen 20 mg, 3/d
  * G-CSF, subcutaneous injection for agranulemia
- Chemotherapy

Chemotherapy

- Oxaliplatin
- Gimeracil and oteracil potassium capsules
- Treatment duration: 14 days

Outcomes	Hematologic (adults) (WHO grade 3 to 4), WBC count, Hb, platelets at the end of treatment
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number table
Allocation concealment (selection bias)	Unclear risk	No relevant description
Incomplete outcome data (attrition bias) All outcomes	Low risk	There was no loss to follow-up. All participants were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Limited outcome measures were reported.
Other bias	Unclear risk	It was mentioned that the groups were comparable, but no baseline characteristics data were presented.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	No subjective outcome was reported.
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	No blinding; however, machine-measured objective outcomes were not influenced substantially

Wu 2013

Methods	Design: parallel RCT Randomisation method: random number table Blinding: no Power calculation: no Dropouts/withdrawals: no
Participants	Patients with breast cancer receiving chemotherapy following radical mastectomy, diagnosed with syndrome of deficiency in spleen and kidney based on Chinese medicine theory Number (treatment/control): 60 (30/30) Mean age (range): 50.1 (36-67) Gender (M/F): F Country: Shandong province, China Setting: hospital

Interventions	Indirect moxa stick on herbs vs no treatment
	Treatment group
	• Indirect moxa stick
	  * Indirect moxa stick on the acupoints shenque (RN8), which was pasted by grounded herbs (chaihu, chuanxiong, dangshen, maidong, wuweizi, danggui, huangqi and shexiang), for about 2 hours per treatment, 3 times per week
	  * Treatment duration: 126 days
	• Chemotherapy
	  * CAF protocol: granisetron, cyclophosphamide, doxorubicin, vitamin B6 and calcium folinate
	  * Treatment duration: 126 days (21 days per course, and consecutive 6 courses)
	Control group
	• Chemotherapy (same as treatment group)

Outcomes	CD4, CD8, IgA, IgM, IgG at the end of treatment
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	No relevant description
Incomplete outcome data (attrition bias) All outcomes	Low risk	There was no loss to follow-up. All participants were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Limited outcome measures were reported.

Wu 2013 *(Continued)*

Other bias	Unclear risk	It was mentioned that the groups were comparable, but no baseline characteristics data were presented.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	No subjective outcome was reported.
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	No blinding; however, machine-measured objective outcomes were not influenced substantially

Xu 2014a

Methods	Design: parallel RCT Randomisation method: random number table Blinding: no Power calculation: no Dropouts/withdrawals: no
Participants	Patients with gynaecology malignancy who had received at least 2 courses of chemotherapy Number (treatment/control): 50 (25/25) Mean age (range): 53.8 (35-73) Gender (M/F): 0/50 Country: Jiangsu province, China Setting: hospital

Interventions	Direct grain-sized moxa cone + conventional medicine vs conventional medicine
	Treatment group
	• Direct moxa cone
	  * Direct grain-sized moxa cone on the acupoints ST36 (zusanli) and DU14 (dazhui), continuous 18 cones on each acupoint, once per day
	• Treatment duration: 14 days (beginning at the same day of chemotherapy, continuous 7 days for 1 course and totally 2 treatment courses)
	• Conventional treatment
	  * Cimetidine 0.4 g and dexamethasone 20 mg, iv, 30 minutes before chemotherapy
	  * Proazamine 25 mg, im, before chemotherapy
	  * Ondansetron 8 mg and inosine 0.1 g, intravenous injection
	  * Ringer's solution 500 mL, iv
	• Chemotherapy
	Control group
	• Conventional treatment

Xu 2014a *(Continued)*

	• * Cimetidine 0.4 g and dexamethasone 20 mg, iv, 30 minutes before chemotherapy * Proazamine 25 mg, im, before chemotherapy * Ondansetron 8 mg and inosine 0.1 g, intravenous injection * Ringer's solution 500 mL, iv • Chemotherapy
Outcomes	Karnofsky score, EORTC QLQ-C30 V3.0 (Chinese version) at the end of treatment
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number table
Allocation concealment (selection bias)	Unclear risk	No relevant description
Incomplete outcome data (attrition bias) All outcomes	Low risk	There was no loss to follow-up. All participants were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Limited outcome measures were reported.
Other bias	Low risk	The baseline characteristics data were presented with good comparability.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	No objective outcome was reported.

Xu 2014b

Methods	Design: parallel RCT Randomisation method: random number table Blinding: unclear Power calculation: no Dropouts/withdrawals: yes (2 participants in each group)
Participants	Cancer patients with expected survival time of more than 3 months; Karnofsky ≥ 60 Number (treatment/control): 54 (27/27)

Xu 2014b *(Continued)*

	Mean age (range): 48 (37-67) Gender (M/F): 29/25 Country: Hong Kong, China Setting: clinic and hospital

Interventions	Indirect moxa cone on ginger vs sham moxibustion
	Treatment group
	• Indirect moxa cone on ginger
	  * Indirect moxa cone (Happyall moxibustion) on ginger on the acupoints guanyuan (RN4), bilateral ST36 (zusanli) and BL20 (Pishu), for about 20 minutes per treatment, 3 times per week
	• Treatment duration: 65 days (5 days before the chemotherapy)
	• Chemotherapy
	Control group
	• Sham moxibustion
	  * Indirect moxa cone with a layer of cardboard between the apparatus and ginger to prevent heat from passing through, sham on the acupoints guanyuan (RN4), bilateral ST36 (zusanli) and BL20 (Pishu), for about 20 minutes per treatment, 3 times per week
	• Treatment duration: 65 days (5 days before the chemotherapy)
	• Chemotherapy

Outcomes	Karnofsky score, EORTC QLQ-C30 version 3.0 (QoL, nausea and vomiting, diarrhoea) at the end of treatment
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number table
Allocation concealment (selection bias)	Unclear risk	No relevant description
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	2 participants in each group were lost to follow-up.
Selective reporting (reporting bias)	Unclear risk	Limited outcome measures were reported.
Other bias	Low risk	The baseline characteristics data were presented with good comparability.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Sham moxibustion similar to the real one was used, but there was no assessment for the degree of blinding.
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	No blinding

Xu 2014b *(Continued)*

Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	No objective outcome was reported.

Yang 2014

Methods	Design: parallel RCT Randomisation method: not reported Blinding: no Power calculation: no Dropouts/withdrawals: no
Participants	Cancer patients with expected survival time of more than 3 months; Karnofsky ≥ 60 Number (treatment/control): 62 (32/30) Mean age (range): not reported Gender (M/F): 35/27 Country: Jiangsu province, China Setting: hospital

Interventions	Moxa stick + conventional medicine vs conventional medicine
	Treatment group
	• Moxa stick
	  * Moxa stick on the acupoints RN8 (shenque) and bilateral ST36 (zusanli) for 15 minutes per acupoint, additional acupoint RN6 (qihai) for those with syndrome of qi deficiency or acupoint RN12 (zhongwan) for those with nausea and vomiting, once per day, 5 times per week
	  * Treatment duration: 30 days (beginning at the same day of chemotherapy)
	• Conventional treatment
	  * Dexamethasone and ondansetron
	• Chemotherapy
	Control group
	• Conventional treatment
	  * Dexamethasone and ondansetron
	• Chemotherapy

Outcomes	WBC count, Hb, platelet, vomiting (WHO grade 3 to 4), Karnofsky score at the end of treatment
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described

Yang 2014 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	No relevant description
Incomplete outcome data (attrition bias) All outcomes	Low risk	None lost to follow-up
Selective reporting (reporting bias)	Unclear risk	Limited outcome measures were reported.
Other bias	Low risk	Baseline characteristic data were comparable.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	No blinding; however, machine-measured objective outcomes were not influenced substantially

Yin 2013

Methods	Design: parallel RCT Randomisation method: not reported Blinding: no Power calculation: no Dropouts/withdrawals: no
Participants	People with non-small lung cancer receiving chemotherapy, with Karnofsky ≥ 70 Number (treatment/control): 100 (50/50) Mean age (range): 55.5 (35-67) Gender (M/F): 44/56 Country: Shanghai city, China Setting: hospital

Interventions	Moxa stick + conventional medicine vs conventional medicine
	Treatment group
	• Moxa stick
	  * Moxa stick on the acupoints RN8 (shenque) for 30 minutes, twice per day
	  * Treatment duration: 5 days (beginning at the same day of chemotherapy)

Yin 2013 *(Continued)*

- Conventional treatment
  - Metoclopramide 20 mg, intramuscular injection, 1/d, 30 minutes before chemotherapy
  - Tropisetron hydrochloride 5 mg, iv, 1/d
  - Dexamethasone 10 mg, intramuscular injection on acupoint ST36 (zusanli)
- Chemotherapy

Control group

- Conventional treatment
  - Metoclopramide 20 mg, intramuscular injection, 1/d, 30 minutes before chemotherapy
  - Tropisetron hydrochloride 5 mg, iv, 1/d
- Chemotherapy

Outcomes	Vomiting (WHO grade 3 to 4) at the end of treatment
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number table
Allocation concealment (selection bias)	Unclear risk	No relevant description
Incomplete outcome data (attrition bias) All outcomes	Low risk	None lost to follow-up.
Selective reporting (reporting bias)	Unclear risk	Limited outcome measures were reported.
Other bias	Unclear risk	It was mentioned that the groups were comparable, but no baseline characteristics data were presented.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	No objective outcome was reported.

Yu 2004

Methods	Design: parallel RCT Randomisation method: not reported Blinding: no

Yu 2004 *(Continued)*

	Power calculation: no Dropouts/withdrawals: yes
Participants	The patients with cervical cancer (stage I, II and III) with Karnofsky score > 80 Number (treatment/control): 68 (38/30) Mean age (range): 58 (38-81) Gender (M/F): F Country: Jiangsu province, China Setting: hospital

Interventions	Moxa stick vs no treatment
	Treatment group
	• Moxa stick
	  * Moxa stick on RN8 (shenque), bilateral SP6 (sanyinjiao), and additional bilateral ST36 (zusanli) for those with syndrome of Qi deficiency, 10 minutes for each acupoint, once every other day
	  * Treatment duration: 8 weeks
	• Radiotherapy
	Control group
	• Radiotherapy

Outcomes	IgG, IgA, IgM, Hb, CD3, CD4, CD8 at the end of treatment
Notes	The studies Yu 2011, Yuan 2003, Yu 2002, Yu 2003a, Yu 2003b, Xu 2002, Xu 2003 and Zhu 2003 were considered to be reports of the same study as Yu 2004. The additional data from these studies were incorporated into Yu 2004.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not described; there was an imbalance in the number of participants between groups
Allocation concealment (selection bias)	Unclear risk	No relevant description
Incomplete outcome data (attrition bias) All outcomes	High risk	There were participants lost to follow-up.
Selective reporting (reporting bias)	Unclear risk	Limited outcome measures were reported.
Other bias	Unclear risk	It was mentioned that the groups were comparable, but no baseline characteristics data were presented.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding

Yu 2004 *(Continued)*

Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	No subjective outcome was reported.
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	No blinding; however, machine-measured objective outcomes were not influenced substantially

Yuan 2014

Methods	Design: parallel RCT Randomisation method: not reported Blinding: no Power calculation: no Dropouts/withdrawals: no
Participants	Cancer patients receiving chemotherapy Number (treatment/control): 100 (50/50) Mean age (range): 54.3 Gender (M/F): 39/61 Country: Shanghai city, China Setting: hospital

Interventions	Indirect moxa cone on ginger + conventional medicine vs conventional medicine
	Treatment group
	• Indirect moxa cone on ginger
	  * Indirect moxa cone on ginger was placed on the acupoints RN8 (shenque), continuous 2-3 cones, once per day
	  * Treatment duration: 3 days (beginning at the same day of chemotherapy)
	• Conventional treatment
	  * Ondansetron hydrochloride 8 mg, iv, 1/d
	  * Treatment duration: 3 days (beginning at the same day of chemotherapy)
	• Chemotherapy
	Control group
	• Conventional treatment
	  * Ondansetron hydrochloride 8 mg, iv, 1/d
	  * Treatment duration: 3 days (beginning at the same day of chemotherapy)
	• Chemotherapy

Outcomes	Vomiting (WHO grade 3 to 4) at the end of treatment
Notes	—
Risk of bias	

Yuan 2014 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	No relevant description
Incomplete outcome data (attrition bias) All outcomes	Low risk	There was no loss to follow-up.
Selective reporting (reporting bias)	Unclear risk	Limited outcome measures were reported.
Other bias	Unclear risk	It was mentioned that the groups were comparable, but no baseline characteristics data were presented.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	No objective outcome was reported.

Zhang 2013

Methods	Design: parallel RCT Randomisation method: not reported Blinding: no Power calculation: no Dropouts/withdrawals: no
Participants	The patients with original non-small cell lung cancer (stage III and IV) with expected survival time of more than 3 months, Karnofsky > 60 Number (treatment/control): 80 (40/40) Mean age (range): 57 (41-65) Gender (M/F): 41/39 Country: Guangdong province, China Setting: hospital
Interventions	Direct moxa cone + conventional medicine vs conventional medicine **Treatment group**

Zhang 2013 *(Continued)*

- Direct moxa cone
  - Direct moxa cone on the acupoints Sihua (bilateral BL17 (geshu) and BL19 (danshu)), continuous 3 cones, once per day
  - Treatment duration: 10 days
- Chemotherapy with PDD and NVB

Control group

- Chemotherapy with PDD and NVB

Conventional medicine

- Symptomatic treatment, including granisetron for the prevention of vomiting

Outcomes	Karnofsky score, WBC count, Hb, platelets at the end of treatment
Notes	Some data from Lin 2012 were added into the study Zhang 2013. They were considered to be reports of the same study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	No relevant description
Incomplete outcome data (attrition bias) All outcomes	Low risk	There was no loss to follow-up. All participants were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Limited outcome measures were reported.
Other bias	Unclear risk	It was mentioned that the groups were comparable, but no baseline characteristics data were presented.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	No blinding; however, machine-measured objective outcomes were not influenced substantially

Zhang 2016a

Methods	Design: parallel RCT Randomisation method: computer programme

Zhang 2016a *(Continued)*

	Blinding: no Power calculation: no Dropouts/withdrawals: yes (2 in treatment group/3 in control group)
Participants	People with non-small cell lung cancer who had received chemotherapy after pulmonary lobectomy Number (treatment/control): 70 (35/35) Mean age: 55.55 (available participants) Gender (M/F): 42/23 (available participants) Country: Beijing city, China Setting: hospital

Interventions	Direct grain-sized moxa cone vs no treatment
	Treatment group
	• Direct grain-sized moxa cone
	  * Direct grain-sized moxa cone on the bilateral acupoints ST36 (zusanli) and BL13 (feishu), continuous 9 cones, once per day
	  * Treatment duration: 42 days
	Control group
	• No treatment

Outcomes	Platelet at the end of treatment
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer programme
Allocation concealment (selection bias)	Unclear risk	No relevant description
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	2 participants dropped out in the treatment group and 3 in the control group.
Selective reporting (reporting bias)	Unclear risk	Limited outcome measures were reported.
Other bias	Low risk	Baseline characteristic data were comparable.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias)	Unclear risk	No subjective outcome was reported.

Zhang 2016a *(Continued)*

Subjective outcomes		
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	No blinding; however, machine-measured objective outcomes were not influenced substantially

Zhang 2016b

Methods	Design: parallel RCT Randomisation method: not reported Blinding: no Power calculation: no Dropouts/withdrawals: no
Participants	The patients with original non-small cell lung cancer (stage IIIa, IIIb and IV) with expected survival time of > 3 months, Karnofsky > 60 Number (treatment/control): 60 (30/30) Mean age (range): 57.22 (42-70) Gender (M/F): 31/29 Country: Guangdong province, China Setting: hospital

Interventions	Direct moxa cone + conventional medicine vs conventional medicine
	Treatment group
	• Direct moxa cone
	  * Direct moxa cone on the acupoints sihua (bilateral BL17 (geshu) and BL19 (danshu)), continuous 3 cones, once per day
	  * Treatment duration: 10 days
	• Conventional medicine
	  * Symptomatic treatment including granisetron and dexamethasone
	• Chemotherapy with paclitaxel and cisplatin
	Control group
	• Conventional medicine
	  * Symptomatic treatment including granisetron and dexamethasone
	• Chemotherapy with paclitaxel and cisplatin

Outcomes	FACT-L, Karnofsky score, nausea/vomiting (WHO grade 3 to 4) at the end of treatment
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described

Zhang 2016b *(Continued)*

Allocation concealment (selection bias)	Unclear risk	No relevant description
Incomplete outcome data (attrition bias) All outcomes	Low risk	There was no loss to follow-up. All participants were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Limited outcome measures were reported.
Other bias	Unclear risk	It was mentioned that the groups were comparable, but no baseline characteristics data were presented.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	No objective outcome was reported.

Zhu 2017

Methods	Design: parallel RCT Randomisation method: not reported Blinding: no Power calculation: no Dropouts/withdrawals: no
Participants	People with primary liver cancer who were eligible for receiving transarterial chemoembolization (TACE), and were diagnosed with Chinese medicine syndrome of stagnation of liver qi and spleen deficiency Number (treatment/control): 60 (30/30) Mean age: 47.84 Gender (M/F): 44/16 Country: Guangxi province, China Setting: hospital
Interventions	Indirect moxa box on ginger + conventional medicine vs conventional medicine **Treatment group**

Zhu 2017 *(Continued)*

- Indirect moxa box on ginger
  - Indirect moxa box on ginger was placed on the bilateral acupoints ST36 (zusanli) and KI 1 (yongquan), 30 minutes, once per day
  - Treatment duration: 8 days (1 day before TACE)
- Conventional treatment
  - Symptomatic treatment
- TACE

Control group

- Conventional treatment
  - Symptomatic treatment
- TACE

Outcomes	QoI (EORTC QLQ-c30) at the end of treatment
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	No relevant description
Incomplete outcome data (attrition bias) All outcomes	Low risk	There was no loss to follow-up. All participants were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Limited outcome measures were reported.
Other bias	Unclear risk	Baseline characteristic data were comparable.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	No objective outcome was reported.

5-FU: fluorouracil; **CD3**: lymphocyte count; **CD4**: T-helper cell; **CD8**: cytotoxic T cell; **CTCAE**: Common Terminology Criteria for Adverse Events; **EORTC QLQ-C30**: European Organization for Research and Treatment of Cancer QoL Questionnaire; **FACT-G 4.0**: Functional Assessment of Cancer Therapy - General; **G-CSF**: granulocyte-colony stimulating factor; **Hb**: haemoglobin; **Ig**: immunoglobulin; **im**: intramuscular; **iv**: intravenous; **NVB**: vinorelbine; **PDD**: cis-platinum (II) diamminedichloride; **PWB**: physical well-being; **QoL**: quality of life; **RCT**: randomised controlled trial; **WBC**: white blood cells; **WHO**: World Health Organization.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Chen 1991	No relevant outcome measure was available in the study report
Chen 2006	Moxibustion plus acupuncture treatment was used as the treatment intervention.
Chen 2010	There was no random allocation for intervention assignment.
Chen 2012	No relevant outcome measure was available in the study report.
Ding 2008	Although random allocation was mentioned in the abstract, sequence of admission to hospital determined group assignment.
Fan 2011	Although random allocation was mentioned in the abstract, visiting order determined group assignment.
Ge 2011	No relevant outcome measure was available in the study report.
Guo 2011	No relevant outcome measure was available in the study report.
Huang 2015	No relevant outcome measure was available in the study report.
Jiang 2002	Acupressure was applied after moxibustion in the treatment group.
Jin 2003	Acupuncure was used together with moxibustion in the treatment group.
Li 2007	No relevant outcome measure was available in the study report.
Liang 2014	The conventional medicine in 2 groups varied depending on the symptoms.
Liu 2001	The treatment duration was different between the comparison groups.
Liu 2002	The combination treatment of chemotherapy and Chinese herbal medicine was used as the control intervention.
Liu 2006	The treatment group assignment was determined by the patient preference.
Liu 2013	The treatment information about chemotherapy was not provided.
Long 2012	It was a cross-over study, but no phase I study data were available.
Ou 1992	No information about the outcome data was provided.
Qiu 2008	Acupressure was administered with moxibustion in the treatment group.
Shao 2012	No relevant outcome measure was available in the study report.
Shen 2002	No relevant outcome measure was available in the study report.
Shen 2010	It has the same results on some outcomes as Fan 2001. It was possibly a fake article.
Shen 2011	No relevant outcome measure was available in the study report.
Song 2003	No relevant outcome measure was available in the study report.

Study	Reason for exclusion
Tang 2011	Warm needle moxibustion was used as the treatment intervention.
Wang 2016	The patients with cancer pain might not receive chemotherapy or radiotherapy.
Xiang 2011	Acupressure was administered with moxibustion in the treatment group.
Xu 2008	No random allocation
Yao 1998	The sequential balanced coefficient method was used for intervention assignment.
Zhang 2014a	The dose of G-CSF in the control group varied.
Zhong 2011	Acupressure was administered with moxibustion in the treatment group.
Zhong 2014	The conventional medicine in the control group varied according to the side effects of chemotherapy.

G-CSF: granulocyte-colony stimulating factor.

Characteristics of studies awaiting assessment *[ordered by study ID]*

Cui 2010

Methods	Cross-over RCT
Participants	Patients with lung cancer, Karnofsky > 60
Interventions	Moxa stick + conventional treatment vs conventional treatment
Outcomes	WHO Recommendations for Grading of Acute and Subacute Toxicity (Vomiting) (Miller 1981)
Notes	Information on the number of participants in the treatment and control group in phase I and II trial study was not reported. No response has been received after sending enquiry mail at the time of drafting the review.

Lan 2013

Methods	RCT
Participants	Cancer patients receiving chemotherapy
Interventions	Indirect moxibustion on ginger + conventional treatment vs conventional treatment
Outcomes	Nause and vomiting assessed by a problematic grading criteria
Notes	Description on the outcome assessment time was unclear. No response has been received to enquiry mail at the time of drafting the review.

Li 2014b

Methods	RCT
Participants	Cancer patients receiving chemotherapy
Interventions	Moxa stick treatment + chemotherapy vs chemotherapy
Outcomes	Incidence and grading of chemotherapy-induced diarrhoea
Notes	The treatment duration was not reported. No response has been received after sending enquiry mail at the time of drafting the review.

Liang 2012

Methods	RCT
Participants	The digestive people with cancer receiving chemotherapy
Interventions	Moxa stick treatment on herbal paste + chemotherapy vs chemotherapy
Outcomes	Grading of toxic effect, WBC, blood platelet
Notes	The treatment duration was not reported. No response has been received after sending enquiry mail at the time of drafting the review.

Qiu 2015

Methods	RCT
Participants	People with cervical cancer receiving radiotherapy
Interventions	Moxa stick treatment + conventional medicine vs conventional medicine
Outcomes	Radiation Therapy Oncology Group (lower GI)
Notes	The moxibustion treatment lasted during the whole period of radiotherapy; however, no information about the treatment duration was reported. No response has been received to enquiry mail at the time of drafting the review.

Zhang 2014b

Methods	RCT
Participants	Cancer patients receiving radiotherapy
Interventions	Indirect moxa cone on ginger + conventional medicine vs conventional medicine
Outcomes	WBC count, Hb, platelets
Notes	The moxibustion treatment duration was not provided. No response has been received to enquiry mail at the time of drafting the review.

Zhang 2014c

Methods	RCT
Participants	Cancer patients receiving chemotherapy
Interventions	Direct grain-size moxibustion + chemotherapy vs chemotherapy
Outcomes	WBC count
Notes	The information about treatment duration was unclear. No response has been received to enquiry mail at the time of drafting the review.

Zhang 2014d

Methods	RCT
Participants	Cancer patients receiving chemotherapy with expected survival time of more than 3 months and Karnofsky > 60
Interventions	Indirect moxa cone on ginger vs conventional medicine
Outcomes	WBC count, Hb, platelets, Karnofsky score
Notes	The information about treatment duration was unclear. No response has been received to enquiry mail at the time of drafting the review.

GI: gastrointestinal; **Hb**: haemoglobin; **RCT**: randomised controlled trial; **WBC**: white blood cells; **WHO**: World Health Organization.

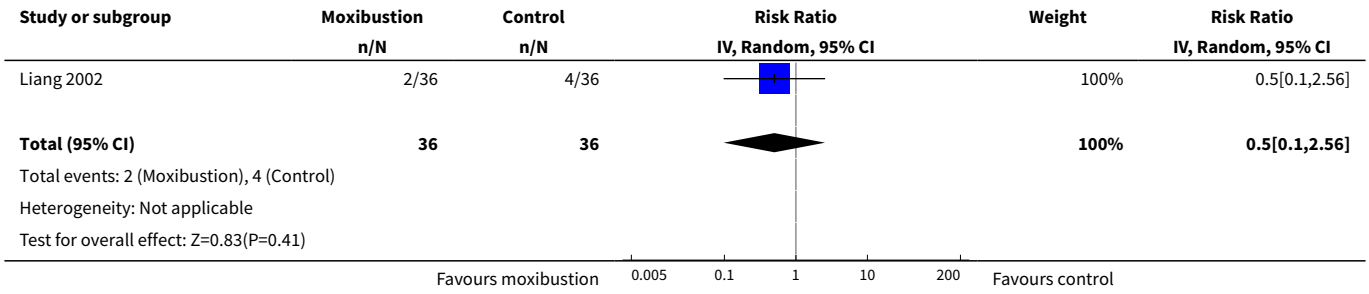
DATA AND ANALYSES

Comparison 1. Moxibustion treatment vs no treatment

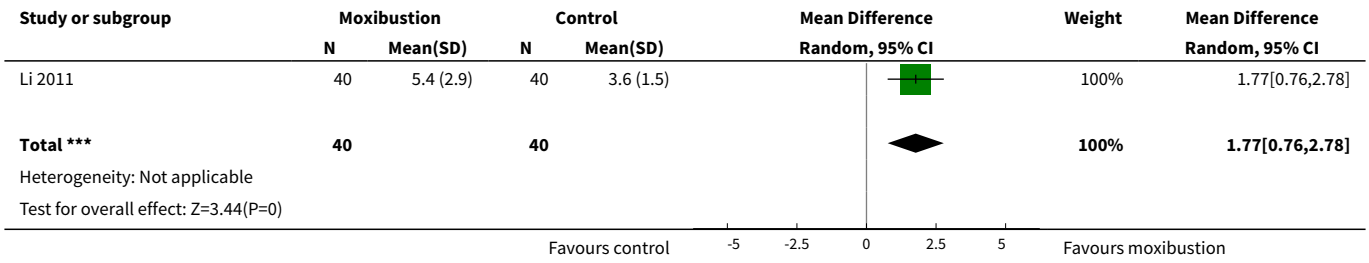
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Leukopenia (WHO grade 3 to 4)	1	72	Risk Ratio (IV, Random, 95% CI)	0.5 [0.10, 2.56]
2 WBC count (× 10^9/L)	1	80	Mean Difference (IV, Random, 95% CI)	1.77 [0.76, 2.78]
3 Haemoglobin (g/L)	1	66	Mean Difference (IV, Random, 95% CI)	1.33 [0.59, 2.07]
4 Platelets (× 10^9/L)	1	65	Mean Difference (IV, Fixed, 95% CI)	30.80 [8.03, 53.57]
5 CD3 (g/L)	1	57	Mean Difference (IV, Random, 95% CI)	5.30 [1.46, 9.14]
6 CD4 (g/L)	2	113	Mean Difference (IV, Random, 95% CI)	5.42 [3.01, 7.82]
7 CD8 (g/L)	2		Mean Difference (IV, Random, 95% CI)	Subtotals only

Outcome or sub-group title	No. of studies	No. of partici-pants	Statistical method	Effect size
8 IgA (g/L)	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
9 IgM (g/L)	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
10 IgG (g/L)	2		Mean Difference (IV, Random, 95% CI)	Subtotals only

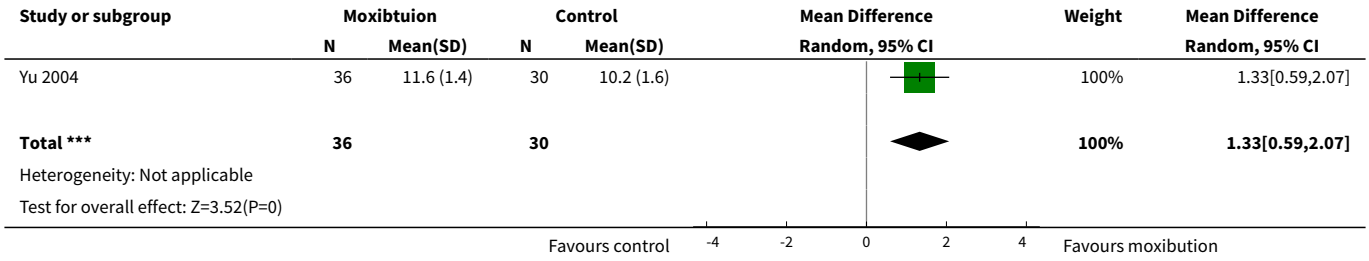
Analysis 1.1. Comparison 1 Moxibustion treatment vs no treatment, Outcome 1 Leukopenia (WHO grade 3 to 4).



Analysis 1.2. Comparison 1 Moxibustion treatment vs no treatment, Outcome 2 WBC count (× 10^9/L).

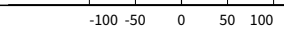


Analysis 1.3. Comparison 1 Moxibustion treatment vs no treatment, Outcome 3 Haemoglobin (g/L).



Analysis 1.4. Comparison 1 Moxibustion treatment vs no treatment, Outcome 4 Platelets (× 10^9/L).

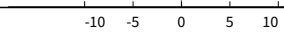
Study or subgroup	Moxibustion N	Moxibustion Mean(SD)	Control N	Control Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Zhang 2016a	33	212.8 (49.3)	32	182 (44.3)		100%	30.8[8.03,53.57]
Total ***	**33**		**32**			**100%**	**30.8[8.03,53.57]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.65(P=0.01)							



Favours control — Favours moxibustion

Analysis 1.5. Comparison 1 Moxibustion treatment vs no treatment, Outcome 5 CD3 (g/L).

Study or subgroup	Moxibustion N	Moxibustion Mean(SD)	Control N	Control Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Yu 2004	36	75.4 (7)	21	70.1 (7.2)		100%	5.3[1.46,9.14]
Total ***	**36**		**21**			**100%**	**5.3[1.46,9.14]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.71(P=0.01)							



Favours control — Favours moxibustion

Analysis 1.6. Comparison 1 Moxibustion treatment vs no treatment, Outcome 6 CD4 (g/L).

Study or subgroup	Moxibustion N	Moxibustion Mean(SD)	Control N	Control Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Wu 2013	30	25.8 (5.8)	30	20.1 (5.3)		73.82%	5.67[2.87,8.47]
Yu 2004	35	44.9 (8.2)	18	40.2 (8.3)		26.18%	4.7[0,9.4]
Total ***	**65**		**48**			**100%**	**5.42[3.01,7.82]**
Heterogeneity: Tau^2=0; Chi^2=0.12, df=1(P=0.73); I^2=0%							
Test for overall effect: Z=4.42(P<0.0001)							

Favours control — Favours moxibustion

Analysis 1.7. Comparison 1 Moxibustion treatment vs no treatment, Outcome 7 CD8 (g/L).

Study or subgroup	Moxibustion N	Moxibustion Mean(SD)	Control N	Control Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Wu 2013	30	20.6 (3.4)	30	18.2 (3)		0%	2.45[0.82,4.08]
Yu 2004	36	22.1 (6.1)	21	24.4 (6.5)		0%	-2.3[-5.72,1.12]

Favours control — Favours moxibustion

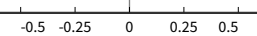
Analysis 1.8. Comparison 1 Moxibustion treatment vs no treatment, Outcome 8 IgA (g/L).

Study or subgroup	Moxibustion		Control		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
Wu 2013	30	0.8 (0.2)	30	0.8 (0.1)		0%	0.02[-0.05,0.09]
Yu 2004	36	1.1 (0.1)	30	1.2 (0.1)		0%	-0.14[-0.19,-0.09]

Favours control — Favours moxibustion

Analysis 1.9. Comparison 1 Moxibustion treatment vs no treatment, Outcome 9 IgM (g/L).

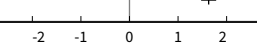
Study or subgroup	Moxibustion		Control		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
Wu 2013	30	1.1 (0.2)	30	1.2 (0.2)		0%	-0.09[-0.19,0.01]
Yu 2004	36	1.2 (0.2)	30	0.9 (0.1)		0%	0.24[0.17,0.31]



Favours control — Favours moxibustion

Analysis 1.10. Comparison 1 Moxibustion treatment vs no treatment, Outcome 10 IgG (g/L).

Study or subgroup	Moxibustion		Control		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
Wu 2013	60	9.9 (1.5)	60	9.9 (1.5)		0%	0.07[-0.48,0.62]
Yu 2004	36	8.3 (0.3)	30	6.6 (0.3)		0%	1.63[1.48,1.78]

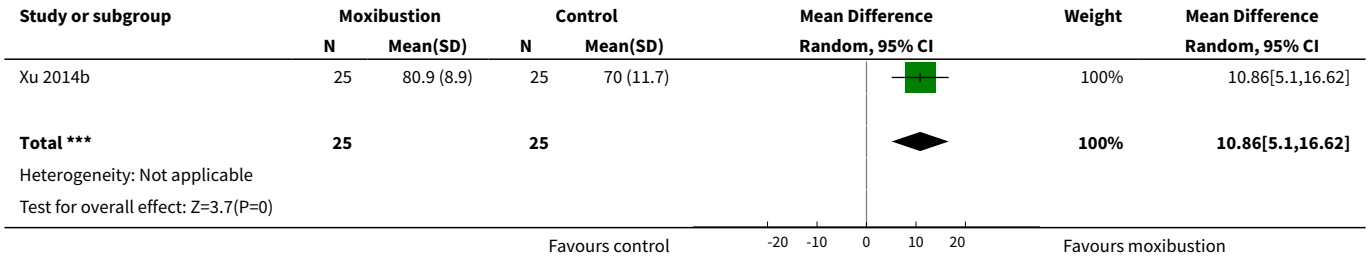


Favours control — Favours moxibustion

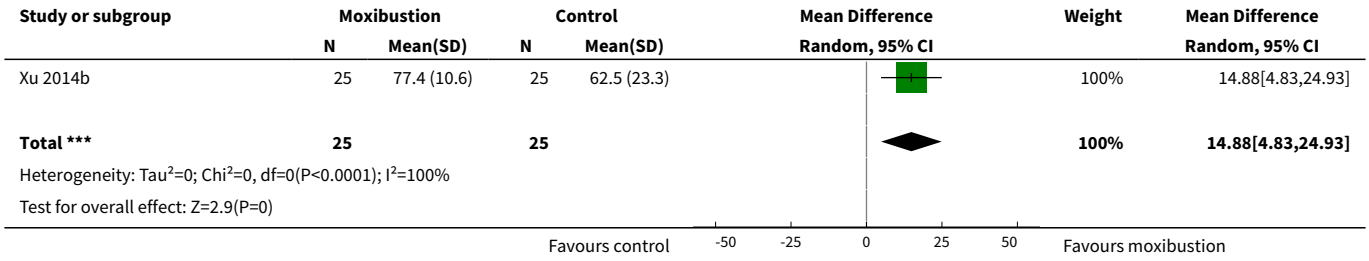
Comparison 2. Moxibustion treatment vs sham moxibustion

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Karnofsky score	1	50	Mean Difference (IV, Random, 95% CI)	10.86 [5.10, 16.62]
2 QoL (EORTC QLQ-C30) (version 3.0)	1	50	Mean Difference (IV, Random, 95% CI)	14.88 [4.83, 24.93]
3 Nausea/vomiting (EORTC QLQ-C30) (version 3.0)	1	50	Mean Difference (IV, Random, 95% CI)	-38.57 [-48.67, -28.47]
4 Diarrhoea (EORTC QLQ-C30) (version 3.0)	1	50	Mean Difference (IV, Random, 95% CI)	-13.81 [-27.52, -0.10]
5 WBC count (× 10^9/L)	1	50	Mean Difference (IV, Random, 95% CI)	1.72 [0.97, 2.47]
6 Haemoglobin (g/L)	1	50	Mean Difference (IV, Random, 95% CI)	2.06 [1.26, 2.86]
7 Platelets (× 10^9/L)	1	50	Mean Difference (IV, Random, 95% CI)	210.79 [167.02, 254.56]

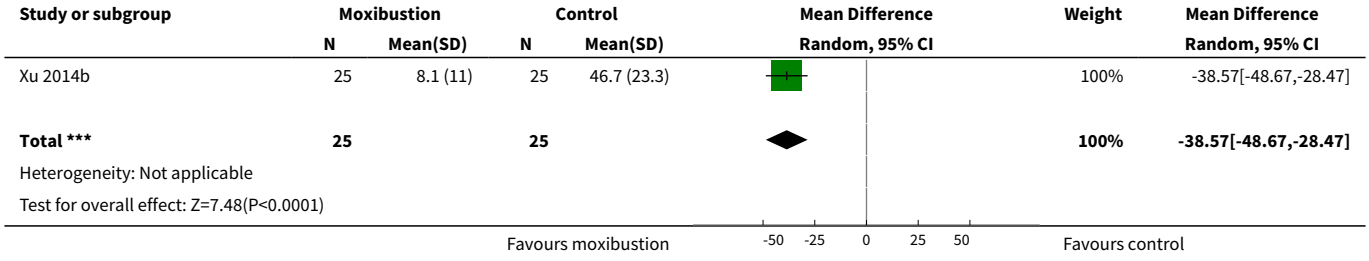
Analysis 2.1. Comparison 2 Moxibustion treatment vs sham moxibustion, Outcome 1 Karnofsky score.



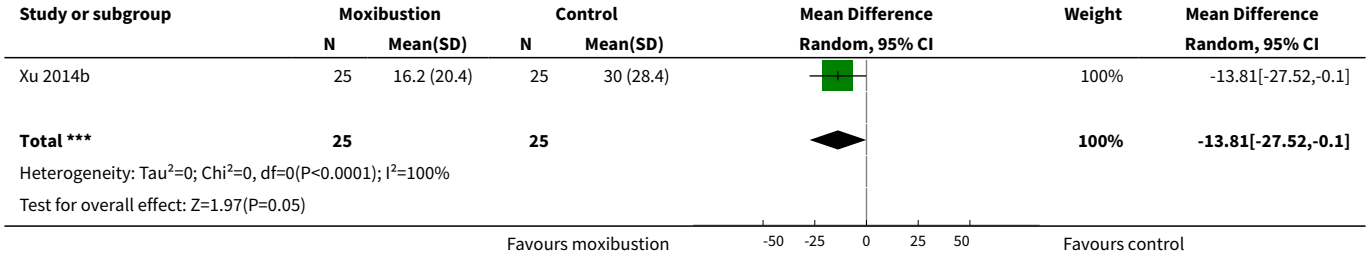
Analysis 2.2. Comparison 2 Moxibustion treatment vs sham moxibustion, Outcome 2 QoL (EORTC QLQ-C30) (version 3.0).



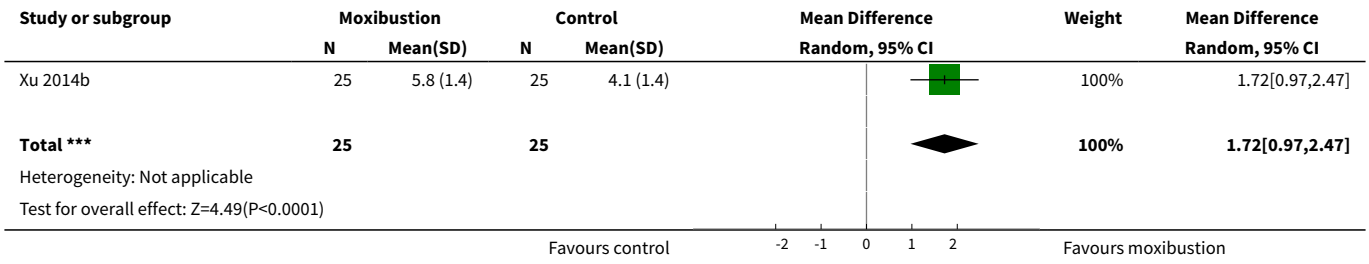
Analysis 2.3. Comparison 2 Moxibustion treatment vs sham moxibustion, Outcome 3 Nausea/vomiting (EORTC QLQ-C30) (version 3.0).



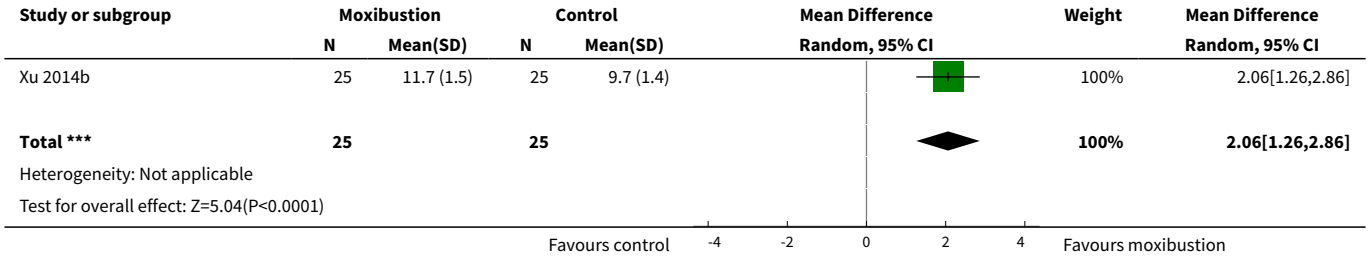
Analysis 2.4. Comparison 2 Moxibustion treatment vs sham moxibustion, Outcome 4 Diarrhoea (EORTC QLQ-C30) (version 3.0).



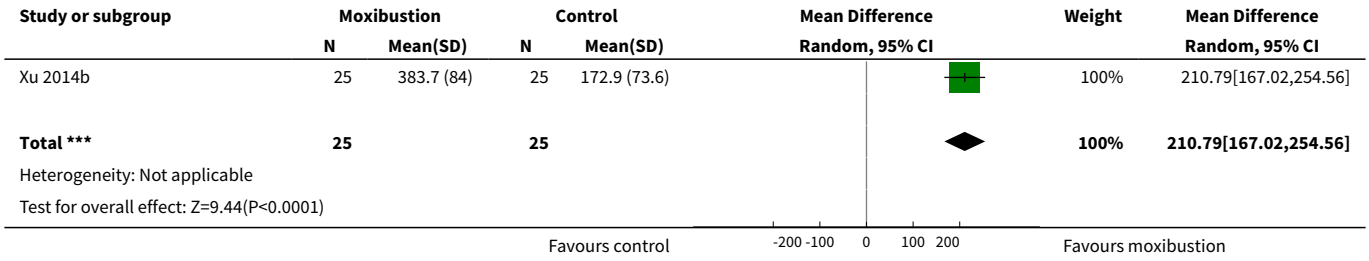
Analysis 2.5. Comparison 2 Moxibustion treatment vs sham moxibustion, Outcome 5 WBC count (× 10^9/L).



Analysis 2.6. Comparison 2 Moxibustion treatment vs sham moxibustion, Outcome 6 Haemoglobin (g/L).



Analysis 2.7. Comparison 2 Moxibustion treatment vs sham moxibustion, Outcome 7 Platelets (× 10^9/L).



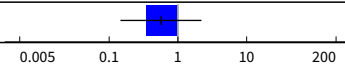
Comparison 3. Moxibustion treatment vs conventional medicines

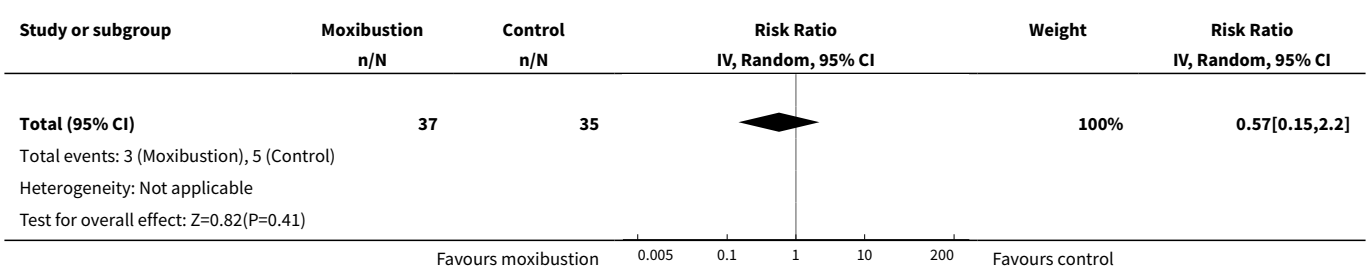
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Haematologic (adults) (WHO grade 3 to 4)	1	72	Risk Ratio (IV, Random, 95% CI)	0.57 [0.15, 2.20]
2 WBC count (× 10^9/L) at the end of treatment	8		Mean Difference (IV, Random, 95% CI)	Subtotals only
2.1 Moxibustion vs batilol + leucogen	3	191	Mean Difference (IV, Random, 95% CI)	0.84 [0.12, 1.57]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.2 Moxibustion vs leucogen + vitamin C + vitamin E	1	84	Mean Difference (IV, Random, 95% CI)	-0.09 [-0.84, 0.66]
2.3 Moxibustion vs G-CSF	1	90	Mean Difference (IV, Random, 95% CI)	-3.06 [-3.30, -2.82]
2.4 Moxibustion vs ondansetron + batilol	1	163	Mean Difference (IV, Random, 95% CI)	3.01 [2.25, 3.77]
2.5 Moxibustion vs batilol + leucogen + G-CSF(optional))	1	72	Mean Difference (IV, Random, 95% CI)	0.99 [0.76, 1.22]
2.6 Moxibustion vs leucogen + berbamine	1	102	Mean Difference (IV, Random, 95% CI)	1.80 [0.95, 2.65]
3 WBC count (× 10^9/L) after follow-up (8 days)	1	90	Mean Difference (IV, Random, 95% CI)	0.40 [0.15, 0.65]
4 Haemoglobin (g/L)	2	235	Mean Difference (IV, Random, 95% CI)	10.28 [4.51, 16.05]
5 Platelets (× 10^9/L)	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
6 Karnofsky score	1	82	Mean Difference (IV, Random, 95% CI)	6.70 [2.37, 11.03]
7 CD3 (g/L)	2	247	Mean Difference (IV, Random, 95% CI)	0.69 [-0.64, 2.02]
8 CD4 (g/L)	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
9 CD8 (g/L)	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
10 IgA (g/L)	1	41	Mean Difference (IV, Random, 95% CI)	2.84 [2.30, 3.38]
11 IgG (g/L)	1	41	Mean Difference (IV, Random, 95% CI)	7.31 [6.05, 8.57]
12 IgM (g/L)	1	41	Mean Difference (IV, Random, 95% CI)	2.06 [1.66, 2.46]

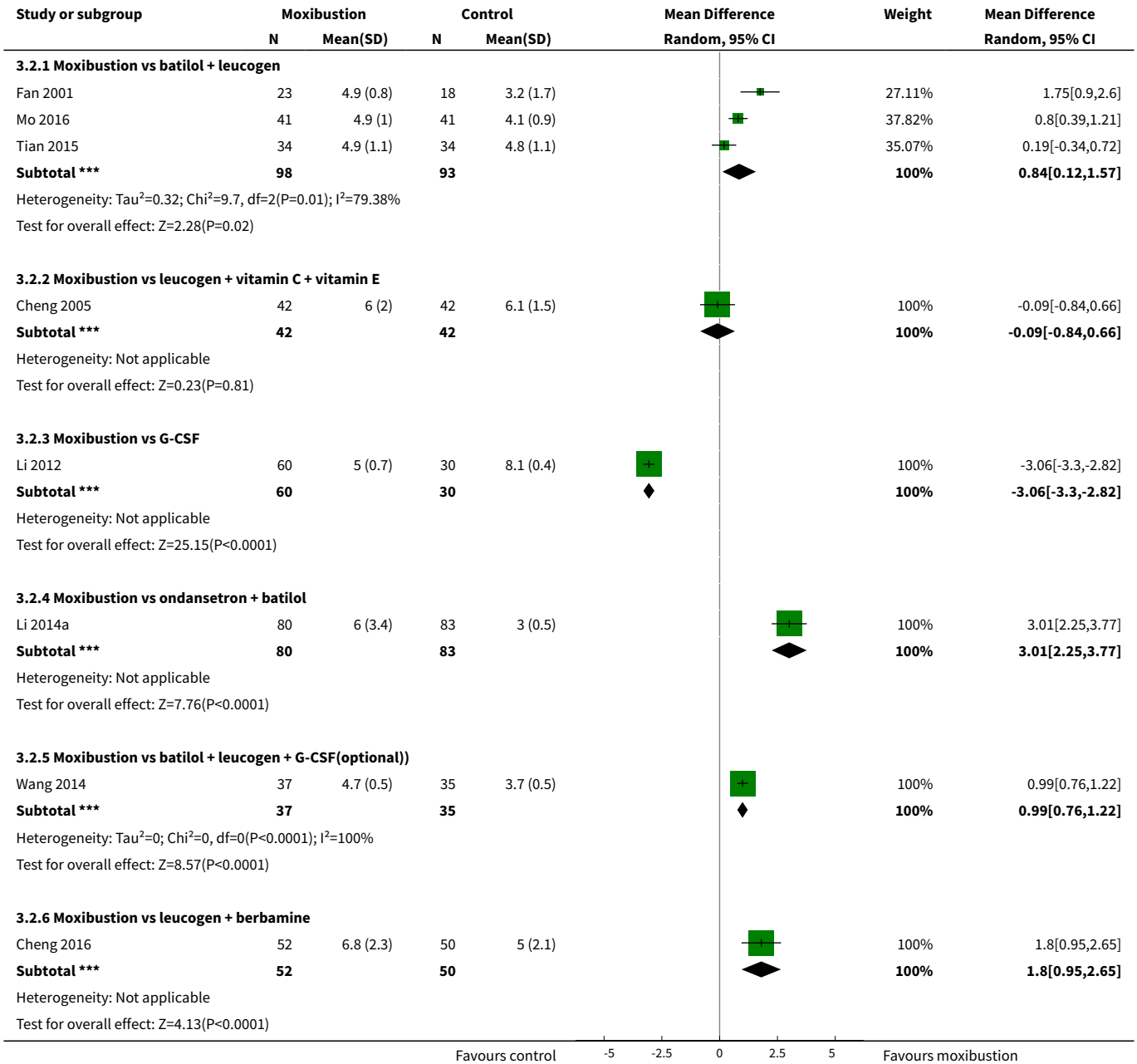
Analysis 3.1. Comparison 3 Moxibustion treatment vs conventional medicines, Outcome 1 Haematologic (adults) (WHO grade 3 to 4).

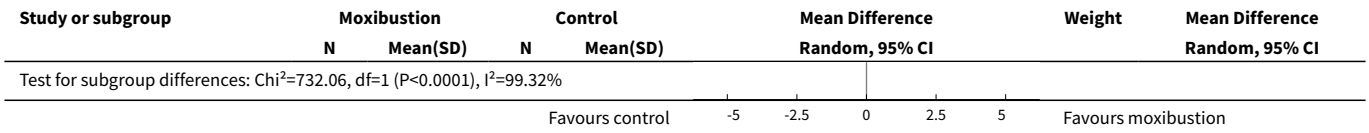
Study or subgroup	Moxibustion n/N	Control n/N	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
Wang 2014	3/37	5/35		100%	0.57[0.15,2.2]



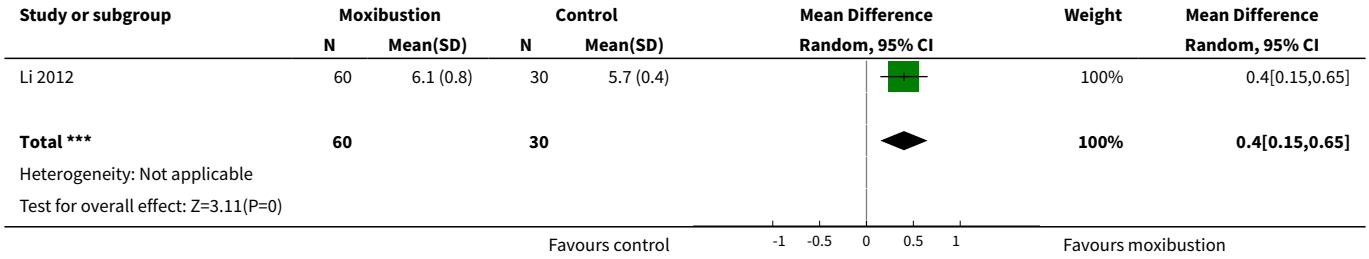


Analysis 3.2. Comparison 3 Moxibustion treatment vs conventional medicines, Outcome 2 WBC count (× 10^9/L) at the end of treatment.

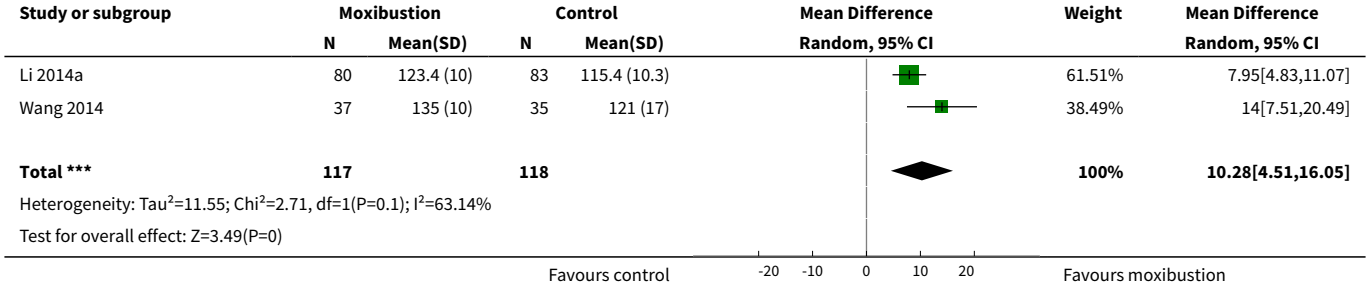




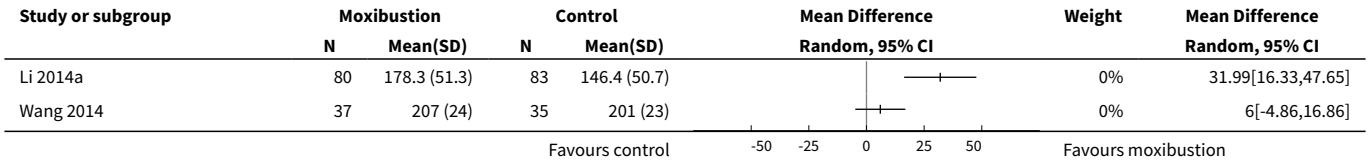
Analysis 3.3. Comparison 3 Moxibustion treatment vs conventional medicines, Outcome 3 WBC count (× 10^9/L) after follow-up (8 days).



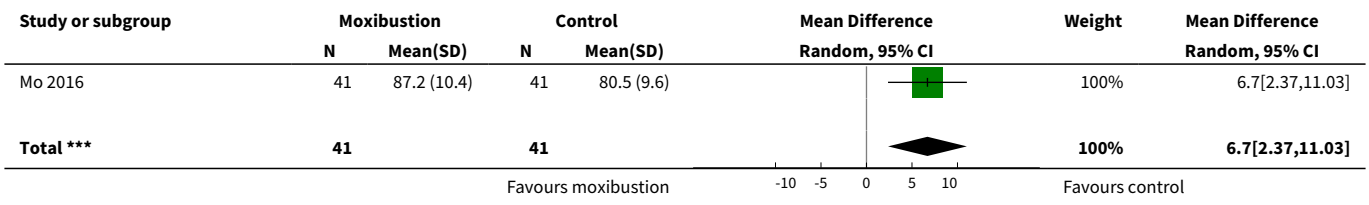
Analysis 3.4. Comparison 3 Moxibustion treatment vs conventional medicines, Outcome 4 Haemoglobin (g/L).

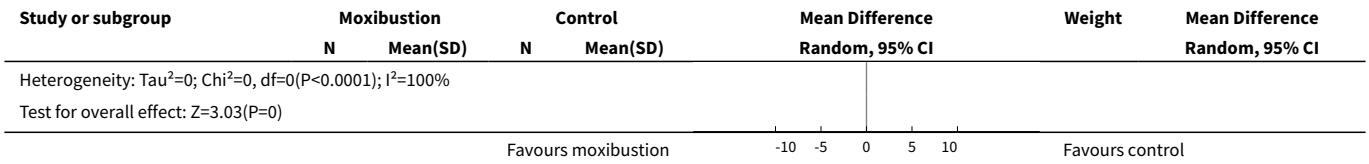


Analysis 3.5. Comparison 3 Moxibustion treatment vs conventional medicines, Outcome 5 Platelets (× 10^9/L).

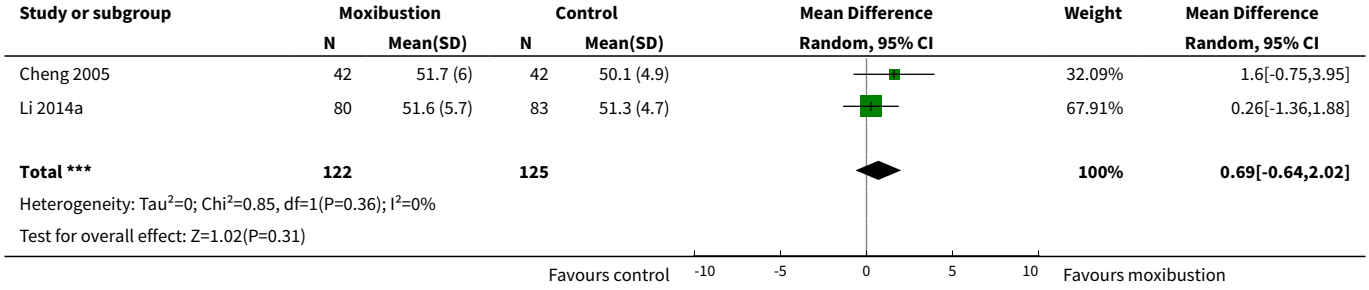


Analysis 3.6. Comparison 3 Moxibustion treatment vs conventional medicines, Outcome 6 Karnofsky score.

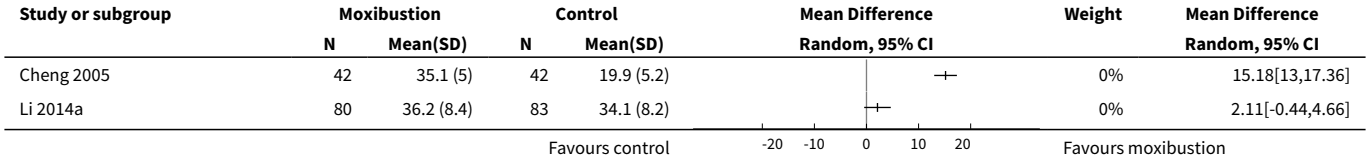




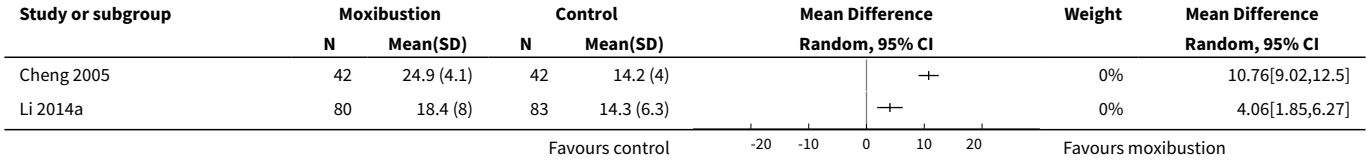
Analysis 3.7. Comparison 3 Moxibustion treatment vs conventional medicines, Outcome 7 CD3 (g/L).



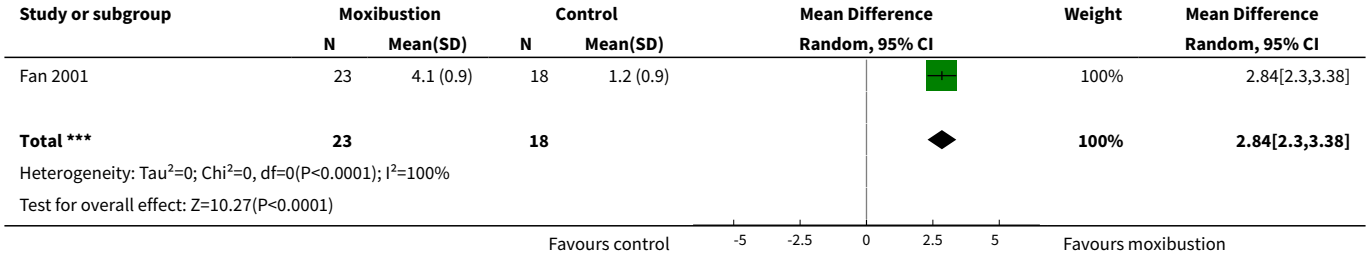
Analysis 3.8. Comparison 3 Moxibustion treatment vs conventional medicines, Outcome 8 CD4 (g/L).



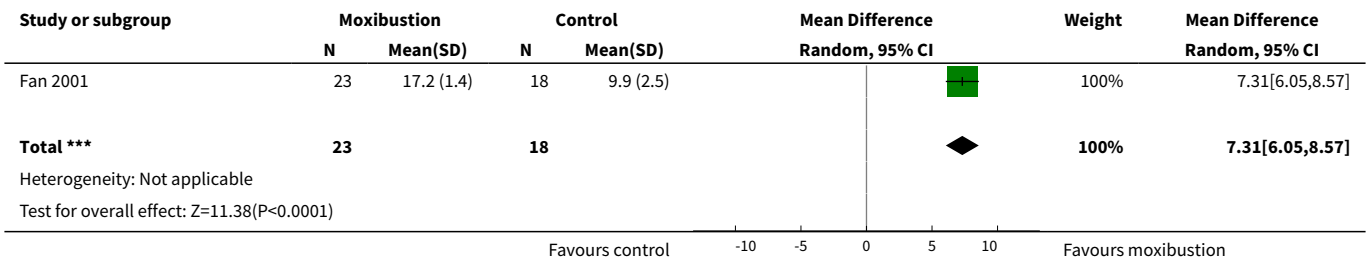
Analysis 3.9. Comparison 3 Moxibustion treatment vs conventional medicines, Outcome 9 CD8 (g/L).



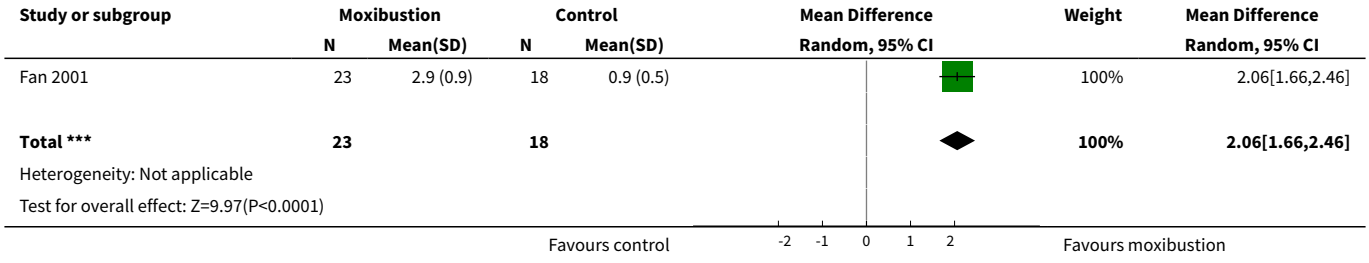
Analysis 3.10. Comparison 3 Moxibustion treatment vs conventional medicines, Outcome 10 IgA (g/L).



Analysis 3.11. Comparison 3 Moxibustion treatment vs conventional medicines, Outcome 11 IgG (g/L).



Analysis 3.12. Comparison 3 Moxibustion treatment vs conventional medicines, Outcome 12 IgM (g/L).



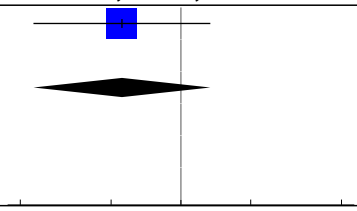
Comparison 4. Moxibustion treatment + conventional medicine vs conventional medicine

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Leukopenia (WHO grade 3 to 4)	1	56	Risk Ratio (IV, Random, 95% CI)	0.14 [0.01, 2.64]
2 WBC count (× 10^9/L)	3		Mean Difference (IV, Random, 95% CI)	Subtotals only
3 Nausea/vomiting (WHO grade 3 to 4)	7	801	Risk Ratio (IV, Random, 95% CI)	0.43 [0.25, 0.74]
4 Vomiting (CTCAE v3.0 grade 3 to 5)	1	169	Risk Ratio (IV, Random, 95% CI)	0.07 [0.00, 1.14]
5 Diarrhoea (WHO grade 3 to 4)	1	61	Risk Ratio (IV, Random, 95% CI)	0.19 [0.01, 3.88]
6 Haemoglobin (g/L)	2	142	Mean Difference (IV, Random, 95% CI)	3.97 [1.40, 6.53]
7 Platelets (×10^9/L)	2	142	Mean Difference (IV, Random, 95% CI)	13.48 [-16.00, 42.95]
8 Karnofsky score	4	252	Mean Difference (IV, Random, 95% CI)	7.21 [5.74, 8.68]
9 QoL (EORTC QLQ-c30)	3	134	Mean Difference (IV, Random, 95% CI)	8.85 [4.25, 13.46]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
10 QoL (FACT-G)	1	332	Mean Difference (IV, Random, 95% CI)	11.51 [10.64, 12.38]
11 QoL (FACT-L)	1	60	Mean Difference (IV, Fixed, 95% CI)	10.04 [7.63, 12.45]
12 Physical well-being (FACT-L)	1	72	Mean Difference (IV, Random, 95% CI)	-4.33 [-6.25, -2.41]
13 IgA (g/L)	1	61	Mean Difference (IV, Random, 95% CI)	0.55 [0.21, 0.89]
14 IgG (g/L)	1	61	Mean Difference (IV, Random, 95% CI)	2.11 [1.19, 3.03]
15 IgM (g/L)	1	61	Mean Difference (IV, Random, 95% CI)	0.40 [0.19, 0.61]

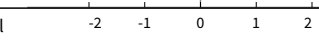
Analysis 4.1. Comparison 4 Moxibustion treatment + conventional medicine vs conventional medicine, Outcome 1 Leukopenia (WHO grade 3 to 4).

Study or subgroup	Moxibustion n/N	Control n/N	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
Chen 2000	0/28	3/28		100%	0.14[0.01,2.64]
Total (95% CI)	**28**	**28**		**100%**	**0.14[0.01,2.64]**
Total events: 0 (Moxibustion), 3 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.31(P=0.19)					



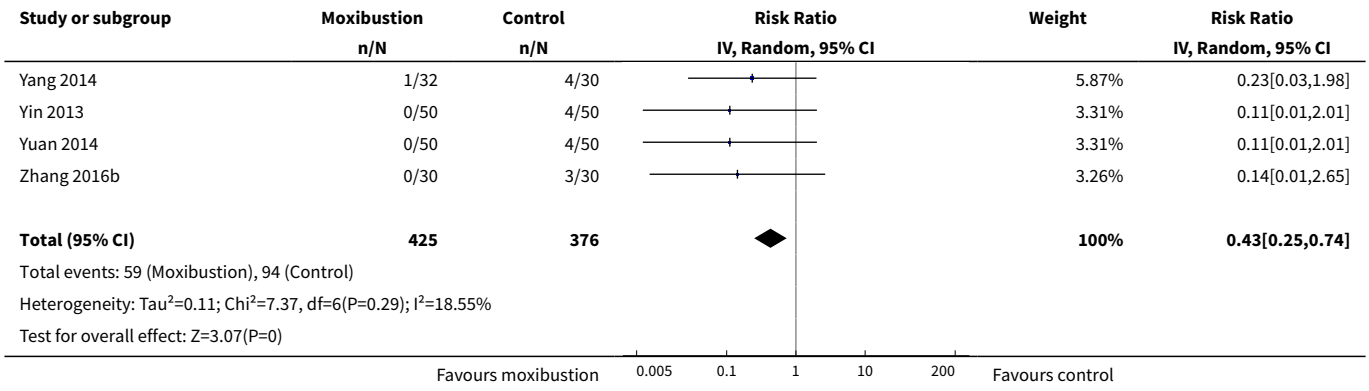
Analysis 4.2. Comparison 4 Moxibustion treatment + conventional medicine vs conventional medicine, Outcome 2 WBC count (× 10^9/L).

Study or subgroup	Moxibustion N	Moxibustion Mean(SD)	Control N	Control Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Gao 2013	60	4.8 (1.1)	60	4.3 (1)		0%	0.5[0.12,0.88]
Yang 2014	32	4.8 (1.2)	30	4.4 (1.3)		0%	0.41[-0.22,1.04]
Zhang 2013	40	5.2 (1)	40	3.7 (0.6)		0%	1.5[1.14,1.86]

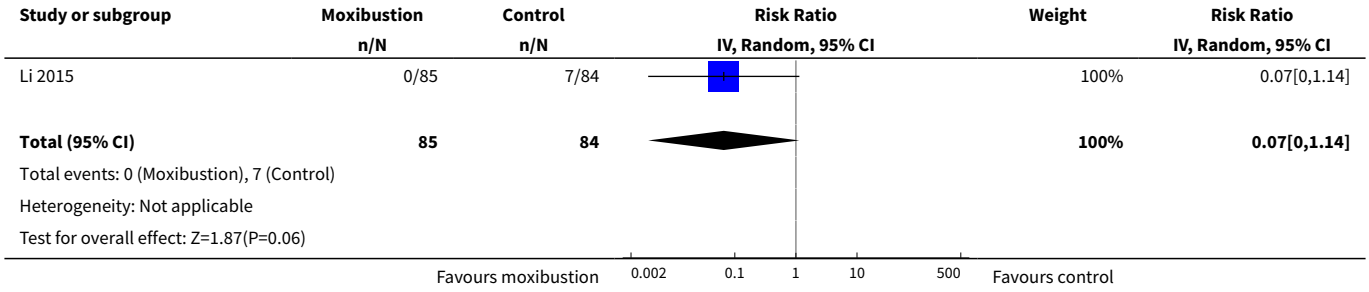


Analysis 4.3. Comparison 4 Moxibustion treatment + conventional medicine vs conventional medicine, Outcome 3 Nausea/vomiting (WHO grade 3 to 4).

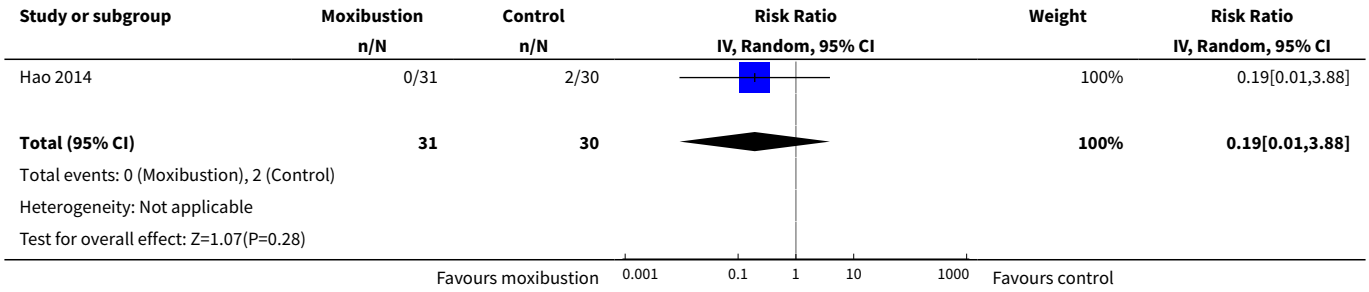
Study or subgroup	Moxibustion n/N	Control n/N	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
Chen 2000	0/28	5/28		3.42%	0.09[0.01,1.57]
Li 2016	53/190	60/142		58.16%	0.66[0.49,0.89]
Ruan 2014	5/45	14/46		22.67%	0.37[0.14,0.93]



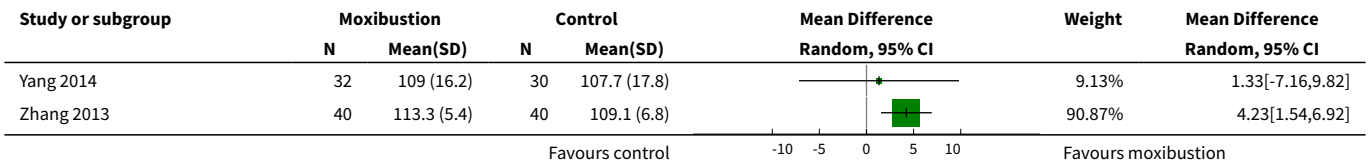
Analysis 4.4. Comparison 4 Moxibustion treatment + conventional medicine vs conventional medicine, Outcome 4 Vomiting (CTCAE v3.0 grade 3 to 5).

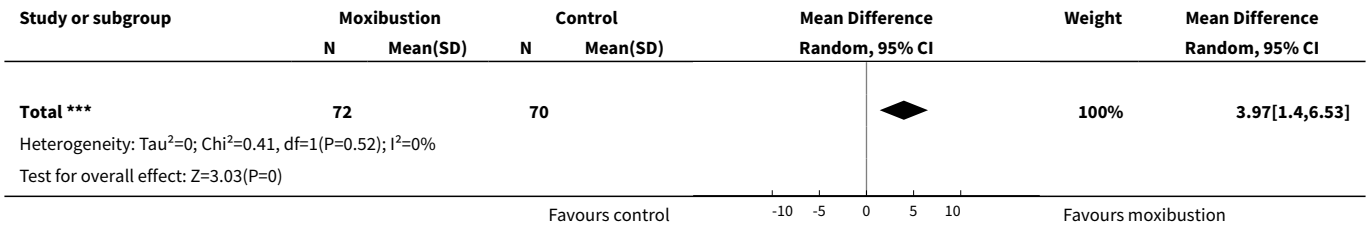


Analysis 4.5. Comparison 4 Moxibustion treatment + conventional medicine vs conventional medicine, Outcome 5 Diarrhoea (WHO grade 3 to 4).

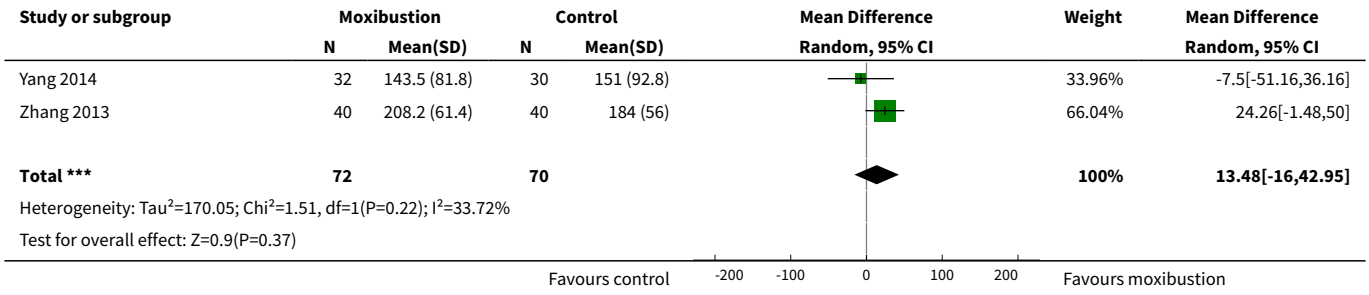


Analysis 4.6. Comparison 4 Moxibustion treatment + conventional medicine vs conventional medicine, Outcome 6 Haemoglobin (g/L).

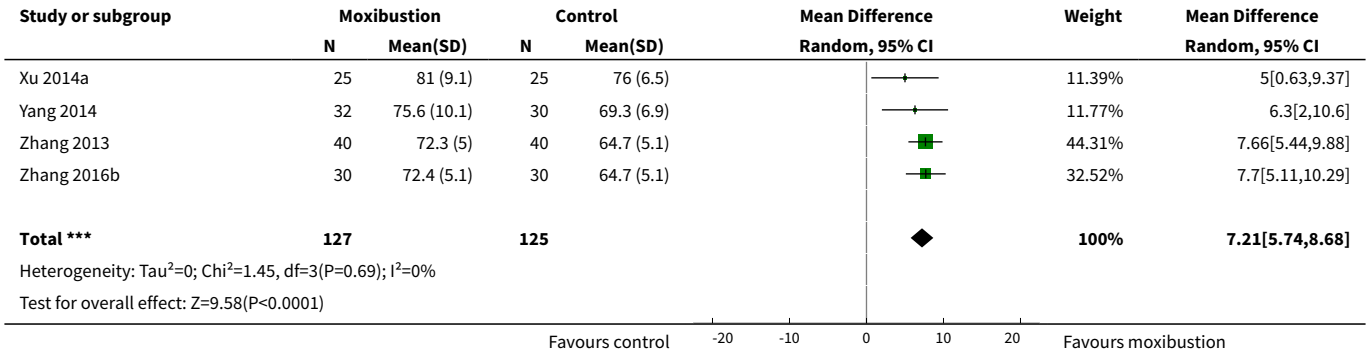




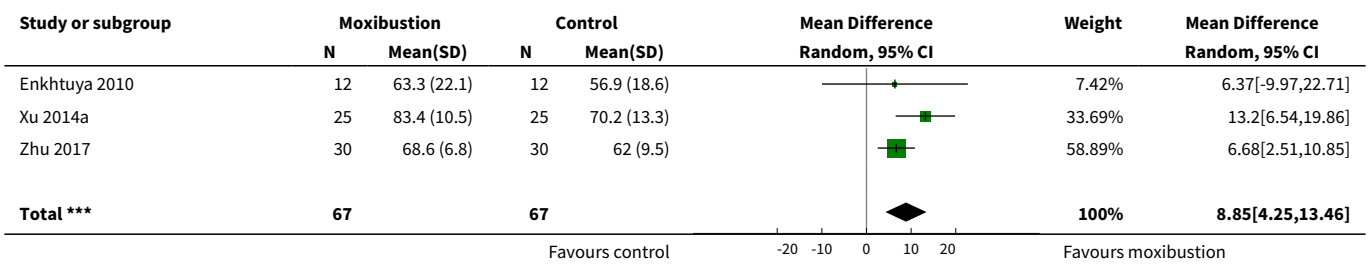
Analysis 4.7. Comparison 4 Moxibustion treatment + conventional medicine vs conventional medicine, Outcome 7 Platelets (×10⁹/L).

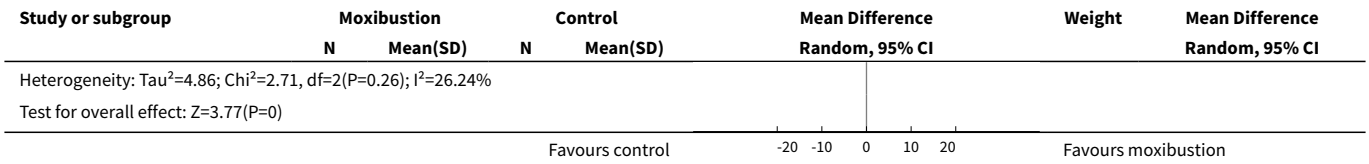


Analysis 4.8. Comparison 4 Moxibustion treatment + conventional medicine vs conventional medicine, Outcome 8 Karnofsky score.

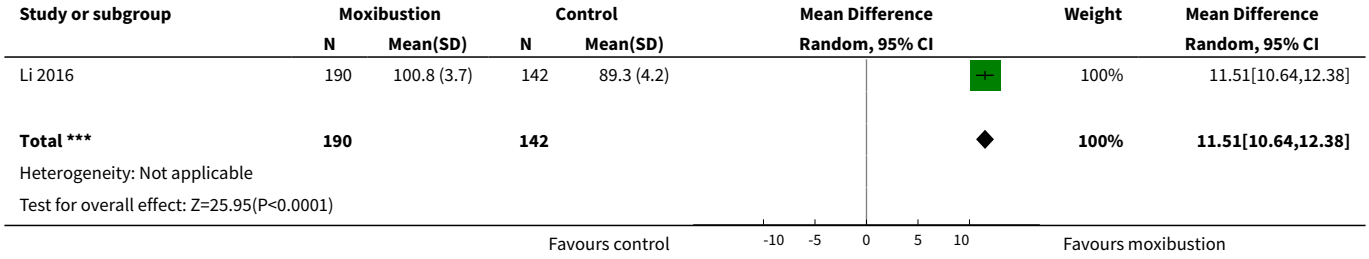


Analysis 4.9. Comparison 4 Moxibustion treatment + conventional medicine vs conventional medicine, Outcome 9 QoL (EORTC QLQ-c30).

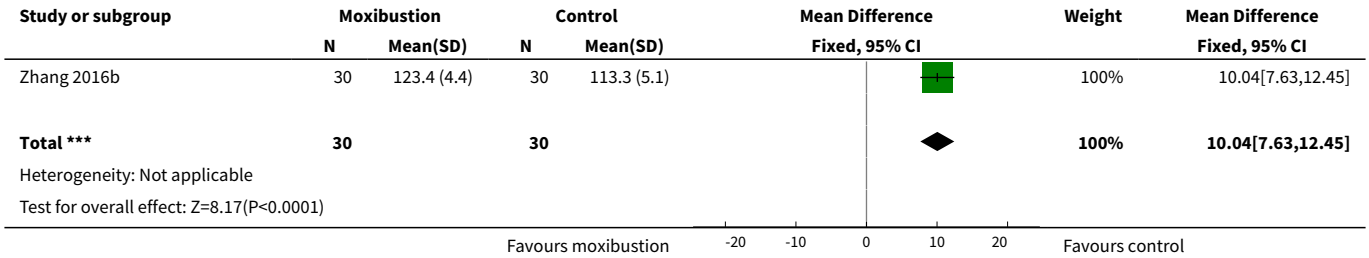




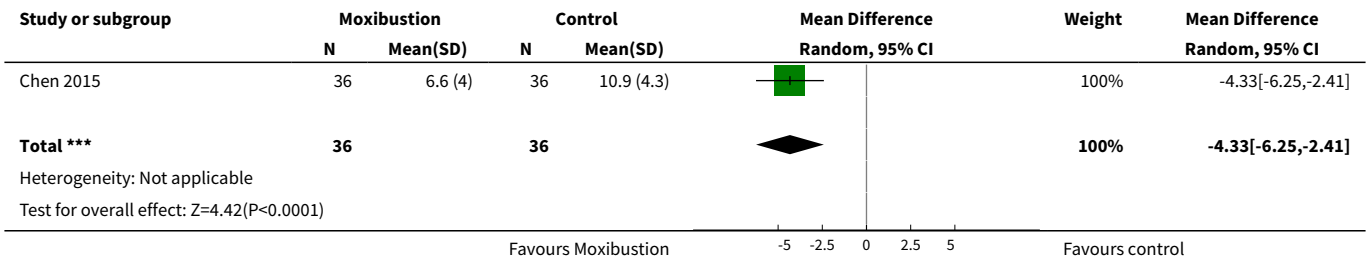
Analysis 4.10. Comparison 4 Moxibustion treatment + conventional medicine vs conventional medicine, Outcome 10 QoL (FACT-G).



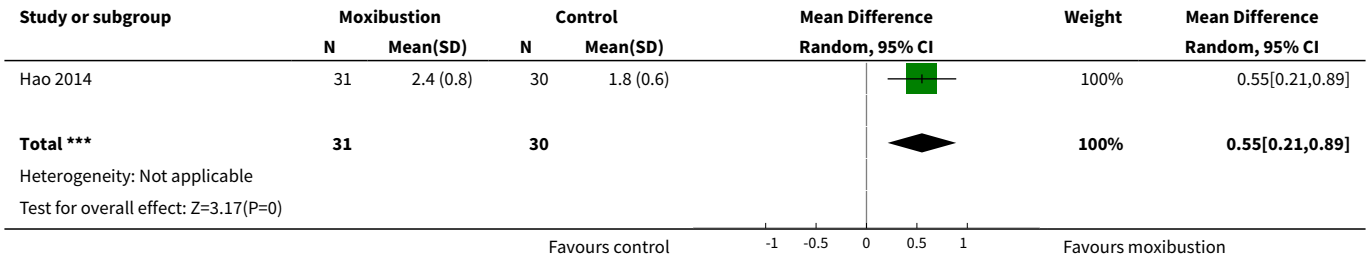
Analysis 4.11. Comparison 4 Moxibustion treatment + conventional medicine vs conventional medicine, Outcome 11 QoL (FACT-L).



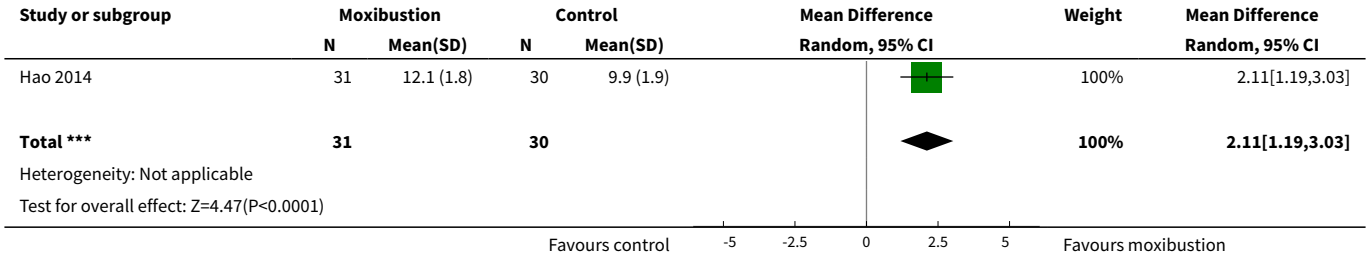
Analysis 4.12. Comparison 4 Moxibustion treatment + conventional medicine vs conventional medicine, Outcome 12 Physical well-being (FACT-L).



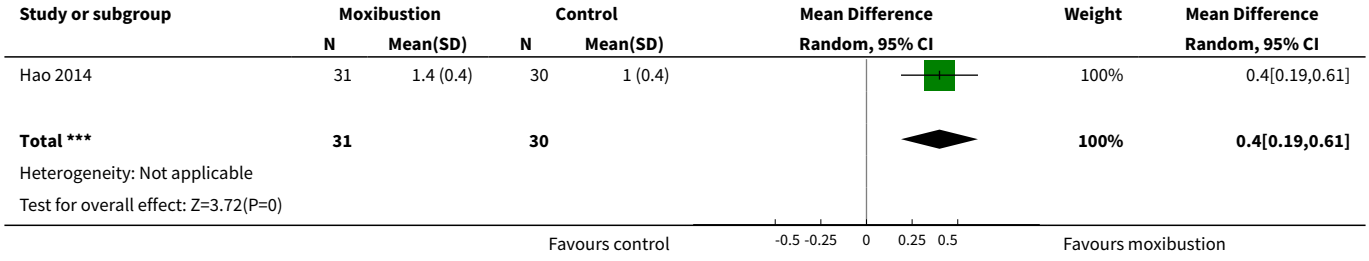
Analysis 4.13. Comparison 4 Moxibustion treatment + conventional medicine vs conventional medicine, Outcome 13 IgA (g/L).



Analysis 4.14. Comparison 4 Moxibustion treatment + conventional medicine vs conventional medicine, Outcome 14 IgG (g/L).



Analysis 4.15. Comparison 4 Moxibustion treatment + conventional medicine vs conventional medicine, Outcome 15 IgM (g/L).



APPENDICES

Appendix 1. MEDLINE search strategy

1. Moxibustion/
2. (moxa or moxibustion).mp.
3. 1 or 2
4. exp Radiotherapy/
5. (radiotherap* or radiation).mp.
6. (chemoradi* or radiochemo*).mp.
7. radiotherapy.fs.
8. exp Antineoplastic Agents/

9. Antineoplastic Combined Chemotherapy Protocols/
10.chemotherap*.mp.
11.drug therapy.fs.
12.4 or 5 or 6 or 7 or 8 or 9 or 10 or 11
13.3 and 12
14.exp Neoplasms/
15.(cancer* or tumor* or tumour* or malignan*or carcinoma* or neoplas*).mp.
16.14 or 15
17.13 and 16
18.(animals not (humans and animals)).sh.
19.17 not 18

Key:

mp = title, original title, abstract, name of substance word, subject heading word, unique identifier
fs = floating subheading
sh = subject heading

Appendix 2. CENTRAL search strategy

#1 MeSH descriptor: [Moxibustion] this term only
#2 moxa or moxibustion
#3 #1 or #2
#4 MeSH descriptor: [Radiotherapy] explode all trees
#5 radiotherap* or radiation
#6 chemoradi* or radiochemo*
#7 Any MeSH descriptor with qualifier(s): [Radiotherapy - RT]
#8 MeSH descriptor: [Antineoplastic Agents] explode all trees
#9 MeSH descriptor: [Antineoplastic Combined Chemotherapy Protocols] explode all trees
#10 chemotherap*
#11 Any MeSH descriptor with qualifier(s): [Drug therapy - DT]
#12 #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11
#13 #3 and #12
#14 MeSH descriptor: [Neoplasms] explode all trees
#15 cancer* or tumor* or tumour* or malignan* or carcinoma* or neoplas*
#16 #14 or #15
#17 #13 and #16

Appendix 3. Embase search strategy

1 moxibustion/
2 (moxa or moxibustion).mp.
3 1 or 2
4 exp radiotherapy/
5 (radiotherap* or radiation).mp.
6 (chemoradi* or radiochemo*).mp.
7 rt.fs.
8 exp chemotherapy/
9 exp antineoplastic agent/
10 dt.fs.
11 chemotherap*.mp.
12 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11
13 3 and 12
14 exp neoplasm/
15 (cancer* or tumor* or tumour* or malignan* or carcinoma* or neoplas*).mp.
16 14 or 15
17 13 and 16
18 (exp animal/ or nonhuman/ or exp animal experiment/) not human/
19 17 not 18

key:

mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword
fs=floating subheading

CONTRIBUTIONS OF AUTHORS

- Drafting of the protocol: HWZ, ZXL, WCC
- Study selection: HWZ, FC
- Extraction of data from studies: HWZ, FC
- Entry of data into RevMan/check of data entry: HWZ, FC
- Carrying out the analysis: HWZ, FC
- Interpreting the analysis: HWZ, JLT, ZXL
- Drafting of the final review: HWZ, ZXL, WCC, JLT
- Disagreement resolution: ZXL
- Updating of the review: HWZ, FC, ZXL

DECLARATIONS OF INTEREST

Hong Wei Zhang: none known.
Zhi Xiu Lin: none known.
Fan Cheung: none known.
William Chi-Shing Cho: none known.
Jin-Ling Tang: none known.

SOURCES OF SUPPORT

Internal sources

- The Chinese University of Hong Kong, Hong Kong.

External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We did not conduct the planned subgroup, sensitivity analyses and reporting bias assessment due to the heterogeneous comparisons and limited number of included studies. We undertook post hoc subgroup analysis based on the different conventional medicines in the control group.

With regard to study selection, we excluded studies with Chinese medicines as the co-administered treatment between groups because they may vary individually, which may bias the comparison results between groups.

We changed the outcome 'quality of life' from a primary outcome to a secondary outcome.

We added the plan for a 'Summary of findings' table was added to the review.

INDEX TERMS

Medical Subject Headings (MeSH)

*Moxibustion; Antineoplastic Agents [adverse effects]; Leukopenia [etiology] [*therapy]; Nausea [etiology] [*therapy]; Neoplasms [blood] [*drug therapy] [*radiotherapy]; Platelet Count; Publication Bias; Quality of Life; Radiotherapy [adverse effects]; Randomized Controlled Trials as Topic; Vomiting [etiology] [*therapy]

MeSH check words

Humans