BMJ Open Systematic review of the methodological quality of controlled trials evaluating Chinese herbal medicine in patients with rheumatoid arthritis

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ABSTRACT

Objectives: We appraised the methodological and reporting quality of randomised controlled clinical trials (RCTs) evaluating the efficacy and safety of Chinese herbal medicine (CHM) in patients with rheumatoid arthritis (RA).

Design: For this systematic review, electronic databases were searched from inception until June 2015. The search was limited to humans and non-case report studies, but was not limited by language, year of publication or type of publication. Two independent reviewers selected RCTs, evaluating CHM in RA (herbals and decoctions). Descriptive statistics were used to report on risk of bias and their adherence to reporting standards. Multivariable logistic regression analysis was performed to determine study characteristics associated with high or unclear risk of bias.

Results: Out of 2342 unique citations, we selected 119 RCTs including 18 919 patients: 10 108 patients received CHM alone and 6550 received one of 11 treatment combinations. A high risk of bias was observed across all domains: 21% had a high risk for selection bias (11% from sequence generation and 30% from allocation concealment), 85% for performance bias, 89% for detection bias, 4% for attrition bias and 40% for reporting bias. In multivariable analysis, fewer authors were associated with selection bias (allocation concealment), performance bias and attrition bias, and earlier year of publication and funding source not reported or disclosed were associated with selection bias (sequence generation). Studies published in non-English language were associated with reporting bias. Poor adherence to recommended reporting standards (<60% of the studies not providing sufficient information) was observed in 11 of the 23 sections evaluated.

Limitations: Study quality and data extraction were performed by one reviewer and cross-checked by a second reviewer. Translation to English was performed by one reviewer in 85% of the included studies.

Conclusions: Studies evaluating CHM often fail to meet expected methodological criteria, and high-quality evidence is lacking.

Strengths and limitations of this study

- It is the first study appraising methodological quality and adherence to reporting standards specifically in randomised controlled trials (RCTs) evaluating Chinese herbal medicines in patients with rheumatoid arthritis. No other studies have analysed the characteristics associated with a high risk of bias or poor adherence to reporting standards.
- For methodological quality, we used the risk of bias tool, an instrument endorsed by the Cochrane Collaboration to facilitate improved appraisal of evidence. The tool has shown significant correlations with other appraisal tools.
- For reporting adequacy, we used the Consolidated Standards of Reporting Trials (CONSORT) statement which is a minimum set of recommendations for reporting RCTs. It was developed by a team of international experts and is widely used worldwide and encouraged by the leading journals for the reporting of trials (over 50% of the core medical journals listed in the Abridged Index Medicus on PubMed—eg, BMJ, BMJ Open, New England Journal of Medicine and Journal of the American Medical Association).
- We did not search the Chinese medical databases.
- More than 85% of the studies were evaluated by the translator and cross-checked by another reviewer using the translation from the first reviewer.

INTRODUCTION

Rheumatoid arthritis (RA) is one of the leading causes of disability worldwide, affecting 1% of the world population. According to the Global Burden of Disease 2010 study, years lived with disability from RA increased from 2 566 000 in 1990 to 3 776 000 in 2010.¹ With ageing populations throughout the world, and declines in mortality, the number of people living with RA will increase substantially over coming decades.

Chinese herbal medicines (CHMs) have been used to treat RA for many years, mostly in Asia. The use of CHMs is generally based on experience and is influenced by a holistic concept of health.² In traditional Chinese medicine (TCM), RA belongs to the category of 'bi syndrome'; that is, it is believed to be caused by attacks of wind, cold, dampness or heat, which cause disharmony between bodily systems.³⁻⁴ Patients are classified as having a particular TCM syndrome according to their symptoms and then treated with CHMs to decrease inflammation by restoring the affected system or to ameliorate the side effects of disease-modifying antirheumatic drugs.⁵ TCM guidelines have been developed by the Chinese government for the diagnosis and treatment of these syndromes.⁶⁻⁸

There are numerous CHM preparations for the treatment of RA, including decoctions, whole plants, plant extracts and patented formulas,⁹⁻¹¹ all of which can be given as a single herb or a mixture of herbs.¹² Patented CHMs are often offered as chemical preparations, tablets and capsules with simple and convenient dosing schedules and reduced aftertaste.^{2,12} This has increased the acceptance of CHM in western countries. In 2002, a national survey conducted in the USA reported that almost 20% of adults had used herbal therapies in the past year.¹³ In the UK, a systematic review of 89 surveys on the use of complementary medicine showed that >50% of respondents with a chronic condition reported using this type of medicine during their lifetime.¹⁴ Furthermore, the use rate of herbal therapies in patients with arthritis in US primary care settings has been reported to be as high as 90%.¹⁵

After the introduction of evidence-based medicine in China, several randomised controlled trials (RCT) were conducted to evaluate the efficacy of CHMs for RA.^{10,12,16,17} However, the methodology used to conduct these trials was inconsistent, and the results were conflicting. Quality of reporting is intrinsically linked to the methodological quality of RCTs. Criteria for standardisation facilitate complete and transparent reporting and help to improve critical appraisal and interpretation of an RCT. Since the development of the Consolidated Standards of Reporting Trials (CONSORT) statement in 1996, most high-impact journals have endorsed its use to improve reporting of RCTs.¹⁸ In 2006, the CONSORT extension for reporting herbal medicines was developed, and in 2007, a draft of the extension for reporting TCM was released.¹⁹

To date, no systematic review has explored the study characteristics associated with methodological quality in controlled trials (randomised or not) evaluating the efficacy, effectiveness or safety of CHMs in the treatment of RA. The objectives of our study were to appraise the methodological quality of these studies by ascertaining potential risk of bias, to identify publication factors associated with methodological flaws and to determine the quality of reporting according to CONSORT recommendations.

METHODS

We report our methods and results according to the Preferred Reporting Items for Systematic Review and Meta-Analysis statement.

Information sources

We searched electronic databases (Medline, EMBASE, Cochrane Library and Web of Science) from inception through June 2015 for studies evaluating the use of CHM, including herbals or decoctions (eg, 'tang'), in patients with RA (search terms are listed in online supplementary appendix 1). Our search was restricted to human studies and excluded case reports but was not limited by language, year of publication or type of publication. We also searched the reference lists of potentially relevant citations (controlled trials and reviews, although reviews themselves were later excluded from the analysis) to identify additional studies that were not published or otherwise found. EndNote X6 and DistillerSR were used to manage the records retrieved.

Study selection and eligibility criteria

Two reviewers (XP and PN) independently screened the titles and abstracts of all citations obtained by our searches. They resolved any disagreements through discussion and consensus. When no consensus was reached, a third party acted as an adjudicator (MAL-O). We included any RCT evaluating the efficacy, effectiveness or safety of CHMs in adult patients (age ≥18 years) with RA. All types of CHMs were considered: (1) patented medicines (pharmaceutical preparation or formulations) made from herbs (eg, tablets, liquids, granules, plasters, injections and capsules), (2) herbal decoctions (eg, 'tang') and (3) plants (whole or extracts). Any type of drug and placebo comparison and any follow-up duration were considered for inclusion. We excluded retrieved studies that were published before the year 2000, because the most currently used guidelines for reporting clinical trials (ie, CONSORT statement) were published in 1996, and we conservatively considered 4 years to be enough time for these guidelines to be disseminated and implemented.¹⁸ We also excluded studies published only as abstracts, studies with a non-RA control group and subanalyses of parent studies.

Data collection and outcome measures

One author (XP) extracted the data, which were then cross-checked by another author (MAL-O). A standardised extraction form was used to collect information about the characteristics of the RCTs and their participants, types of interventions, reported outcomes and sources of funding. Our primary outcome measures were the methodological and reporting quality of the RCTs.

Methodological quality in individual studies

The quality of each selected RCT was evaluated independently by two reviewers using the Cochrane risk of bias tool²⁰ for RCTs published in English. RCTs published

in non-English languages were translated and evaluated by one reviewer (XP) and cross-checked by another (MAL-O). In brief, each RCT was evaluated for its potential bias in five domains: selection, performance, detection, attrition and reporting. These domains specifically evaluate how the random sequence was generated, methods of allocation concealment, blinding of participants and personnel, blinding of the outcome assessment, how incomplete outcome data was handled and if there was evidence of selective outcome reporting. Each potential source of bias was graded as low, unclear or high and a justification for each judgement was provided.

Quality of reporting

We examined how closely the RCTs adhered to reporting standards using the CONSORT statement for TCM,²¹ which focuses only on CHM (ie, acupuncture, moxibustion, cupping and massage are not considered). It is a 23-item checklist, and the major recommendations for transparent reporting are (1) title and abstract should reflect the unique aspects of TCM, (2) rationale of formulation selection should be described, (3) diagnostic criteria should be specified for TCM and conventional medicine, (4) detailed information on the treatment and control interventions should be included, (5) the outcome in TCM terms should be included and (6) the ethics approval number and trial registration number should be included.

Summary measures and synthesis of results

Descriptive statistics were used to report RCT and participant characteristics, as well as the methodological quality of the RCTs. Risk of bias assessment was summarised per domain. Bivariate analysis was used to compare RCT characteristics according to the risk of bias judgement. Univariate and multivariable logistic regressions were performed to determine the factors associated with high or unclear risk of bias in the five domains in RCTs. We combined the unclear and high risk of bias categories for the analyses. Evidence suggests that the magnitude of treatment effects may be similar in studies appraised as having high or unclear risk of bias, but not for studies assessed as low risk of bias.²² The variables tested as predictors were year of publication, sample size, number of authors, publication language (English or non-English), reporting or disclosing of funding (yes or no) and setting (academic or non-academic). Variables with a univariate $p < 0.15$ were initially included in a multivariable logistic regression model and reduced using the stepwise selection method. Associations were described using ORs and their associated 95% CIs. We categorised each CONSORT TCM checklist item as reported or not reported.^{21 23} We then summarised our findings in five sections: title/abstract, introduction, methods, results and discussion. Subgroup analyses were performed to compare rates of potential bias (low risk or unclear/high risk, unclear vs high risk) and adherence to

reporting guidelines according to (1) publication before or after the Cochrane risk of bias tool was released and (2) publication before or after the CONSORT statement for TCM was released. SAS V.9.3 (SAS Institute, Cary, North Carolina, USA) was used to carry out the computations for all analyses. Apart from the univariate analysis, $p < 0.05$ was considered statistically significant.

RESULTS

RCT selection

Out of 2342 unique citations, 232 full-text articles were retrieved to assess for eligibility. Of those, 119 RCTs were included^{5 24–141} evaluating 18 919 patients. Figure 1 shows the number of studies screened, assessed for eligibility and included in the review, with reasons for exclusion at each stage.

Characteristics of the included studies

Table 1 shows the aggregated characteristics of the included RCTs, and online supplementary table S1 shows the characteristics of the individual studies. Two-thirds of the RCTs were published before the CONSORT statement for TCM and herbal interventions were published (2000–2007). One RCT was conducted in the USA, one in Korea and the rest in China. Most were single-centre studies and were not indexed in the Web of Knowledge database but were indexed in the China National Knowledge Infrastructure database (CNKI).

Outcomes reported varied across RCTs. More than half of the RCTs assessed efficacy (eg, disease activity score

Figure 1 Flow chart of included studies. Abbreviations: RA, rheumatoid arthritis; CHM, Chinese herbal medicine.

Table 1 Summary of characteristics of the randomised controlled trials (RCTs) included in our analysis (n=119)

RCT characteristic	No. of RCTs (%)*
Duration	
<6 months	93 (78)
>6 months	23 (19)
Not reported	3 (3)
Year	
2000–2007 (before CONSORT TCM) ^{19 23 142}	80 (67)
2008–2014	39 (33)
Language	
English	18 (15)
Chinese	101 (85)
Country	
China	117 (98)
Korea	1 (1)
USA	1 (1)
Scope	
Single centre	108 (91)
Multicentre	11 (9)
Impact factor 2013	
Web of Science (score range from 0.59 to 2.711)	13 (11)
Web of Science (score range from 7.871 to 16.104)	4 (3)
Indexed in CNKI (score range from 0.031 to 1.068)	101 (85)
Not indexed†	1 (1)
Outcomes‡	
Disease activity score	15 (13)
ACR 20/30	28 (24)
Tender joint count	72 (61)
Swollen joint count	78 (66)
Health assessment questionnaire	19 (16)
Pain	53 (45)
Morning stiffness	66 (55)
Laboratory outcomes (ESR, CRP, RF or anti-CCP)	91 (76)
Radiographic outcomes	3 (3)
Discontinuations	51 (43)
Adverse events§	76 (64)
Funding	27 (23)
CHM preparation (main intervention)	
Plant or extract (one herb)	3 (3)
Decoction alone	15 (13)
Decoction+patented	2 (2)
Individualised (not following guidelines or with modifications)	52 (44)
Patented	43 (36)
Patented+individualised	4 (3)
Most common CHM (>1 study)	
<i>Tripterygium wilfordii</i> / <i>Tripterygium polyglycosides</i> (alone or combined)	15 (13)
<i>Juanbi</i> decoction/mixture or <i>yishen juanbi</i> capsule (including those with changes or combined)	11 (9)
<i>Feng shi</i> decoction/granules/wine/injection (including those with changes or combined)	10 (8)

Continued

Table 1 Continued

RCT characteristic	No. of RCTs (%)*
Total glucosides of peony	6 (5)
<i>Xinfeng</i> capsule	4 (3)
<i>Zhengqing fengtongning</i> (alone or combined)	4 (3)
<i>Bi Qi</i> capsule	3 (3)
<i>Lugua</i> polypeptide injection	3 (3)
<i>Guizhi shaoyao zhimu</i> decoction	3 (3)
<i>Tongbi</i> (tablets or decoction)	3 (3)
<i>Xiatianwu</i>	3 (3)
<i>Bizhongxiao</i>	2 (2)
<i>Sanbi</i> decoction	2 (2)
<i>Shi re bi</i> granule/mixture	2 (2)
<i>Siwu wuteng</i> decoction	2 (2)
Unspecified (including decoctions without a name)	11 (9)

*Percentages have been rounded.

†Not indexed in Web of Science or CNKI.

‡RCTs can report on one or more outcomes.

§Including either clinical safety or laboratory parameters (alanine transaminase, aspartate transaminase, creatinine, white cell count, platelet count or haemoglobin).

ACR 20/30, American College of Rheumatology criteria for improvement at 20% or 30%; anti-CCP, anticyclic citrullinated peptide antibodies; CHM, Chinese herbal medicine; CNKI, China National Knowledge Infrastructure database; CONSORT TCM, Consolidated Standards of Reporting Trials statement for traditional Chinese medicine (including herbal interventions); CRP, C reactive protein; ESR, erythrocyte sedimentation rate; RCT, randomised controlled trial; RF, rheumatoid factor.

either 28¹⁴³ or 44;¹⁴⁴ 20%, 30%, 50% or 70% improvement, according to American College of Rheumatology criteria,¹⁴⁵ in tender or swollen joint counts, physician global assessment or grip strength; or good to moderate improvement according to European League Against Rheumatism criteria,¹⁴⁶ laboratory outcomes (eg, erythrocyte sedimentation rate, C reactive protein, rheumatoid factor or anticyclic citrullinated peptides) or adverse events. However, <56% of RCTs reported on patient-reported outcomes (eg, pain, patient global assessment, health assessment questionnaire or morning stiffness), and only 3% reported radiographic outcomes (eg, Sharp score, erosion, joint narrowing, marked radiographic progression or no progression). Thirty-one RCTs (26%) reported improvement of symptoms but did not provide additional details on the type of symptoms or how these symptoms were assessed.

Characteristics of the participants and interventions

Most participants included in the RCTs met the 1987 American College of Rheumatology (ACR) diagnostic criteria for RA.¹⁴⁷ One RCT included only patients meeting the 2010 ACR classification criteria¹⁴⁸ and in another, patients with RCT included met either the 1987 or 2010 criteria. In addition, 52.5% of the participants met the criteria for one or more of the traditional TCM 'pathological factors' or syndromes (ie, *feng*

(wind), *shi* (damp), *tan* (phlegm), *re* (heat) and *qi* or *yin* deficiency). The most common pathological factors reported are listed in table 2. A total of 10 108 patients received a single CHM and 6550 received one of 11 treatment combinations. Of those receiving combination treatment, 5061 patients received combinations that included CHMs (with disease-modifying antirheumatic drugs, non-steroidal anti-inflammatory drugs, steroids or antibiotics). More than half of the CHMs were individualised preparations targeting pain relief and improvement in joint function. In the control groups, 1402 patients received disease-modifying antirheumatic drugs alone, (ie, methotrexate, leflunomide, sulfasalazine or etanercept), 644 received non-steroidal anti-inflammatory drugs alone and 165 received an inert placebo. In 35 studies, patients were described as having active disease, and two RCTs included patients with refractory disease, one included patients with early RA, three included patients at intermediate stages of RA and one included patients with RA and anaemia. Discontinuation rates were not reported in 68 RCTs, but in those that reported discontinuation rates, they ranged from 0% to 55%.

Quality assessment

Online supplementary figure S1 summarises the results across RCTs. A high or unclear risk of bias was observed across all domains. When evaluating selection bias, we found that 29% of the RCTs did not report sufficient detail to evaluate methods of random sequence generation or in 31% allocation concealment (judged unclear). In addition, 21% were judged to have high risk for selection bias (11% from sequence generation, 30% from allocation concealment). Risk of performance bias (not blinding participants or personnel) was judged to be high in 85% of the RCTs, and detection bias (blinding of assessment of primary outcome) was judged to be high in 89% of the RCTs. More than two-thirds of the RCTs did not provide sufficient detail to judge the risk for attrition bias and lacked data on withdrawal rates, power calculation and how missing data was handled. From the remaining RCTs providing details to evaluate attrition bias, 4% were judged to be of high risk. Risk of reporting bias was high in 40% of the RCTs, and 86% of the RCTs did not report the source of funding or included a disclosure statement.

RCT determinants associated with high risk of bias

Characteristics observed in RCTs according to risk of bias are shown in online supplementary table S2. In the univariate analysis, earlier year of publication, fewer authors, funding source not reported or disclosed, publication in a language other than English, authors from non-academic settings and no power calculation reported were associated with high or unclear risk of bias in various domains (table 3). After adjustment for covariates, the following associations remained in the multivariable analysis: (1) earlier year of publication and funding source not reported or disclosed were

Table 2 Characteristics of the participants in the 119 randomised controlled trials included in our analysis (n=18 919, ranging from 30 to 3789 patients per trial)

Characteristic	No. of patients (%)
Weighted mean age $\pm$ weighted SD	43.5 $\pm$ 12.0 years
Female	13 697 (72.4)
Eligibility criteria	
ACR RA alone	8994 (47.5)
ACR RA+1 TCM syndrome*	3040 (16.1)
ACR RA+2 TCM syndromes*	332 (1.8)
ACR RA+ $\geq$ 3 TCM syndromes*	1072 (5.7)
ACR RA+unspecified number TCM syndromes*	300 (1.6)
ACR RA+TCM syndrome (not guideline driven)	5181 (27.4)
Median disease duration (range)	5.4 years (0.04–28 years)
Interventions	
CHM alone	10 108 (53.4)
CHM+DMARDs	1595 (8.4)
CHM+DMARDs+NSAIDs	511 (2.7)
CHM+DMARDs+steroids+NSAIDs	79 (0.4)
CHM+steroids	501 (2.6)
CHM+steroids+NSAIDs	200 (1.1)
CHM+NSAIDs	2101 (11.1)
CHM+NSAIDs+antibiotic	74 (0.4)
DMARDs alone	1402 (7.4)
DMARDs+steroids	78 (0.4)
DMARDs+steroids+NSAIDs	363 (1.9)
DMARDs+NSAIDs	992 (5.2)
NSAIDs+antibiotic	56 (0.3)
NSAIDs alone	644 (3.4)
Antibiotic†	50 (0.3)
Placebo alone	165 (0.9)
Previous WM treatment‡	8518 (45.0)
Most common patterns reported§	
Dampness-heat blockage	1023 (10.3)
Dampness-cold and <i>qi</i> deficiency-blood stasis	557 (5.6)
Heat-cold complex	512 (5.2)
Dampness-cold blockage	300 (3.0)
Dampness-heat and <i>qi</i> deficiency-blood stasis	269 (2.7)
<i>Qi</i> deficiency and blood stasis	226 (2.3)
<i>Yin</i> deficiency	178 (1.8)

*Chinese medical syndrome following governmental guidelines.

†Penicillin.

‡Only 49 studies reported data.

§Percentages are based on the 46 studies in which eligibility criteria included diagnosis with at least 1 TCM syndrome (n=9925).

ACR RA, American College of Rheumatology classification criteria for rheumatoid arthritis; CHM, Chinese herbal medicine; DMARDs, disease-modifying antirheumatic drugs; NSAIDs, non-steroidal anti-inflammatory drugs; TCM syndrome, traditional Chinese medicine syndrome; WM, western medicine.

associated with high or unclear risk of selection bias (sequence generation); (2) fewer authors were associated with high or unclear risk of selection bias (allocation concealment), performance bias and attrition bias and (3) publication in a language other than English

Table 3 Characteristics of randomised controlled trials (RCTs) included in our study (n=119) associated with high or unclear risk of bias

	Year of publication	Sample size	Number of authors	Language		Funding source disclosed		Affiliation*		Power calculation included†	
				English	Chinese	Yes	No	University	Federal/ state	Yes	No
Selection bias (sequence generation)											
Univariate OR (95% CI)	0.79 (0.70 to 0.88)	0.99 (0.99 to 1.0)	0.85 (0.75 to 0.96)	REF	2.6 (0.94 to 7.2)	REF	7.7 (3.0 to 19.8)	REF	1.6 (0.74 to 3.6)	REF	2.2 (0.13 to 36.7)
p Value	0.0001	0.3	0.01		0.07		<0.0001		0.2		0.6
Multivariable OR (95% CI)	0.83 (0.73 to 0.94)					REF	5.0 (1.8 to 13.8)				
p Value	0.003						0.002				
Selection bias (allocation concealment)											
Univariate OR (95% CI)	0.90 (0.77 to 1.1)	0.99 (0.99 to 1.0)	0.85 (0.75 to 0.96)	REF	7.4 (1.9 to 29.0)	REF	4.0 (1.1 to 14.9)	REF	1.1 (0.29 to 4.2)	REF	11.4 (0.66 to 197.6)
p Value	0.2	0.1	0.01		0.004		0.04		0.9		0.09
Multivariable OR (95% CI)			0.85 (0.75 to 0.96)								
p Value			0.01								
Performance bias											
Univariate OR (95% CI)	0.87 (0.75 to 1.0)	0.99 (0.99 to 1.0)	0.83 (0.73 to 0.95)	REF	7.9 (2.1 to 28.5)	REF	4.1 (1.2 to 14.0)	REF	1.2 (0.36 to 4.0)	REF	51.2 (1.2 to 2224.3)
p Value	0.08	0.2	0.007		0.002		0.02		0.8		0.04
Multivariable OR (95% CI)			0.83 (0.73 to 0.95)								
p Value			0.007								
Attrition bias											
Univariate OR (95% CI)	0.83 (0.74 to 0.93)	1.0 (0.99 to 1.0)	0.68 (0.56 to 0.82)	REF	2.7 (0.96 to 7.7)	REF	3.1 (1.2 to 7.6)	REF	1.5 (0.66 to 3.5)	REF	15.0 (0.36 to 633.8)
p Value	0.002	0.7	0.0001		0.06		0.02		0.3		0.2
Multivariable OR (95% CI)			0.68 (0.56 to 0.82)								
p Value			0.0001								
Reporting bias											
Univariate OR (95% CI)	0.91 (0.83 to 1.0)	0.99 (0.99 to 1.0)	0.86 (0.76 to 0.98)	REF	4.9 (1.5 to 16.0)	REF	3.5 (1.4 to 8.9)	REF	2.7 (1.3 to 5.8)	REF	5.8 (0.14 to 243.8)
p Value	0.06	0.3	0.03		0.008		0.008		0.01		0.4
Multivariable OR (95% CI)				REF	4.1 (1.2 to 13.6)	REF	3.0 (1.1 to 7.7)				
p Value					0.02		0.03				

*Two RCTs written by authors affiliated with the State and a University were considered part of the University for this analysis.

†Logistic regression analysis for detection bias was not performed owing to the small number of RCTs that included power calculation (n=2).

and funding source not reported or disclosed was associated with high or unclear risk of reporting bias. Logistic regression analysis could not be performed for detection bias owing to the small number of RCTs in the low risk-of-bias group ($n=2$).

Adherence to CONSORT standards for TCM

Rates of adherence to CONSORT standards for TCM are shown in table 4. Most of the RCTs (98%) stated the objective adequately. However, most RCTs (94%) did not include the recommended information (specification of interventions, name of disease and study design) in the title or abstract. In the introduction sections, more than half (61%) did not provide the three names of the compound formulation (Chinese, Latin and English) as recommended by the WHO. The methods sections of most RCTs were poorly reported (table 4). Most RCTs (ranging from 85% to 98%) failed to describe in enough detail the interventions, type of study design, calculation of sample size or methods of randomisation and blinding. In the results sections, many RCTs (78%) did not indicate how participants moved through the study over time or provide a flow diagram as

recommended, and 93% of RCTs did not include intention-to-treat analysis. The discussion sections were compromised in 8–83% of the RCTs owing to a lack of general interpretation of the results and conflict of interest information.

Additional analyses

When comparing the risk of bias from the 90 RCTs published before the Cochrane risk of bias tool was released in 2008 (year of publication 2000–2008) with that of the 29 RCTs published later, we observed improvement in RCTs published after 2008 in the following domains: selection bias (22% compared with 59%, $p=0.0004$), attrition bias (18% compared with 52%, $p=0.0005$) and reporting bias (41% compared with 66%, $p=0.02$). When comparing adherence to reporting guidelines from the 80 RCTs published before the CONSORT-TCM statement was released in 2007 (publication date 2000–2007) with that of the 39 RCTs published later, we observed improvement in RCTs published after 2007 in most of the items except in reporting sufficient details about the objectives of the study, design, power calculation and methods to avoid bias (data not shown). We also evaluated determinants associated with high risk of bias, compared with unclear risk of bias. In most domains there were no differences. We observed differences in allocation concealment, but the characteristics associated with high risk of bias were the same as those observed with the main comparison high/unclear versus low risk of bias. There were some characteristics not observed in the main comparison associated with detection bias (see online supplementary table S3).

DISCUSSION

Our results indicate that serious methodology and reporting flaws still exist in clinical trials evaluating the effect of CHM in RA. We found that the potential for selection bias was high; two-thirds of the RCTs in our analysis lacked sufficient detail on how the random sequence was generated. Similarly, most RCTs were not blinded (eg, for participants, personnel or outcome assessment), thus increasing the potential for performance and detection bias. Risk of attrition bias was high or unclear in more than two-third of the RCTs. Reporting bias was also judged to be high or unclear in half of the included RCTs owing to a lack of study protocol and/or reporting less than the minimum number of outcome measures recommended to be included in RA clinical trials.¹⁴⁹ Furthermore, we found that RCTs that were older, had fewer authors, did not report or disclose funding, were published in a language other than English or were written by authors from non-academic settings, were likely to have a high or unclear risk of bias methodology in at least one of the evaluated domains.

We also found that adherence to reporting standards remains a concern. Title and abstract, introduction and methods were even more problematic. Owing to these

Table 4 Percentage of randomised controlled trials in our analysis ($n=119$) not adherent to reporting standards provided in the Consolidated Standards of Reporting Trials (CONSORT) statement for traditional Chinese medicine

CONSORT item	CONSORT item no.	No. (%)
Title and abstract	1	112 (94)
Introduction		
Background	2	73 (61)
Objectives	3	2 (2)
Methods		
Participants	4	45 (38)
Interventions	5	101 (85)
Outcomes	6	15 (13)
Type of study design	7	117 (98)
Sample size	8	117 (98)
Randomisation		
Sequence generation	9	72 (61)
Allocation concealment	10	109 (92)
Implementation	11	111 (93)
Blinding (blinding)	12	107 (90)
Statistical methods	13	48 (40)
Results		
Participant flow	14	93 (78)
Recruitment	15	33 (28)
Baseline data	16	31 (26)
Numbers analysed	17	111 (93)
Outcomes and estimation	18	11 (9)
Ancillary analyses	19	23 (19)
Adverse events	20	40 (34)
Discussion		
Interpretation	21	9 (8)
Generalisability	22	14 (12)
Overall evidence	23	99 (83)

weaknesses, readers are not provided with clear and transparent information on the interventions or methods to assess bias in selecting, blinding and evaluating participants. Other areas of concern were lack of appropriate general interpretation of the results in the context of current evidence and incomplete descriptions of conflicts of interest.

It is important to differentiate between the two main concepts reported in this review: methodological quality and quality of reporting. One of the main components of evidence-based medicine is the use of available literature to improve decision-making. Stronger inferences can be drawn from studies in which measures have been taken before, during and after the intervention to prevent random and systematic bias. Although RCTs are ranked high in the hierarchy of evidence, not all RCTs share the same quality, which can lead to biased results. Quality of reporting is a separate concern. A lack of complete and transparent reporting of the processes and findings of an RCT is commonly linked to methodological flaws. Poor reporting leaves out critical information needed to judge study safeguards against bias.

A few systematic reviews evaluating the efficacy of CHM and reporting on the methodological quality of the studies have shown similar results. However, none of these studies evaluated CHMs exclusively (ie, excluding other TCM) in patients with RA. Nonetheless, a review evaluating the characteristics of 89 studies published between 2000 and 2003 and indexed in the CNKI reported a lack of unified diagnostic and evaluating standards.¹⁵⁰ Another review evaluating 20 RCTs published between 2000 and 2010 showed that methodological quality according to the Jadad scale was generally low, with an average quality score of 1.2 out of 5.¹⁵¹ Contrastingly, a Cochrane review evaluating herbal medicines in general (including three CHMs) showed that the quality of the studies has improved since 2000, but the risk of bias across different domains was variable.¹⁵² Furthermore, an overview of 31 reviews published between 1999 and 2009 evaluating several TCM approaches (including CHMs) for multiple diseases showed that methodological quality improved over the years, although many issues remained, specifically a high risk of selection (inadequate randomisation methods), attrition (small sample sizes and high withdrawal rates) and reporting (selective reporting of outcomes) biases.¹⁵³

To the best of our knowledge, the current study is the first appraising methodological quality and adherence to reporting standards specifically in RCTs evaluating CHM in patients with RA. No other studies have analysed the characteristics associated with a high risk of bias or poor adherence to reporting standards. For methodological quality, we used the risk of bias tool, an instrument endorsed by the Cochrane Collaboration to facilitate improved appraisal of evidence. The tool has shown significant correlations with other appraisal tools.^{154 155} For example, the risk of bias tool was shown to accurately identify trials that may have overestimated treatment

effects. Studies shown to have a high or unclear risk of bias according to the risk of bias tool have larger effect estimates than studies shown to have a low risk of bias.²²

Our study has certain limitations. First, as with any systematic review, it was constrained by the available data. For example, a protocol or trial registration was not found for most of the RCTs included in our review. This is concerning because the validity of the conclusion of an RCT is largely based on adherence to prespecified methods (including outcomes of interest). Trial registration could improve transparency and help identify gaps in knowledge, prevent unnecessary duplication in clinical trials and improve adherence to international quality standards.¹⁵⁶ Second, we included studies with substantial variation in characteristics (eg, RA diagnosis, TCM syndromes and CHM descriptions). However, this allowed us to evaluate a larger number of RCTs. Third, we did not search the CNKI, Chinese Medical Current Contents (CMCC) and Wanfang Data databases, which could have increased the number of publications included in this review, because they are not widely available outside Asia, and we felt that there was no clear reason to consider that the quality of these studies would have been better.¹⁵⁷ Finally, independent quality assessment for non-English language articles could not be performed. Only one reviewer could translate Chinese articles; therefore, more than 85% of the studies were evaluated by the translator and cross-checked by another reviewer using the translation from the first reviewer.

In summary, our results indicate that trials of CHM for the treatment of RA often fail to meet expected methodological criteria, and high-quality evidence is lacking. Because clinical trials are just below systematic reviews in the hierarchy of evidence and are used to endorse recommendations by health organisations, more attention is needed to improve the methodological robustness of these studies. Future clinical trials evaluating CHMs in RA should be designed, conducted and reported according to current specifications and principles.

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Contributors MES-A had full access to all of the data in the study and takes responsibility for the integrity and the accuracy of the data analysis. MES-A and MAL-O conceptualised and designed the study. GP and Geng were responsible for the search strategy. XP, Nayak and MAL-O were responsible for selection of

the studies. XP, MAL-O contributed in quality appraisal and data extraction. JS, XP, MAL-O and MES-A analysed and interpreted the data. XP, MAL-O, JS and MES-A drafted the manuscript. XP, MAL-O, JS, GP and MES-A critically revised the manuscript for important intellectual content. MES-A provided administrative, technical or material support and supervised the study.

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REFERENCES

- Cross M, Smith E, Hoy D, *et al.* The global burden of rheumatoid arthritis: estimates from the global burden of disease 2010 study. *Ann Rheum Dis* 2014;73:1316–22.
- Zhang C, Jiang M, Lu AP. Evidence-based Chinese medicine for rheumatoid arthritis. *J Tradit Chin Med* 2011;31:152–7.
- Li S. Advances in TCM symptomatology of rheumatoid arthritis. *J Tradit Chin Med* 2002;22:137–42.
- Tsang IK, Huang SH, Koehler BE. Traditional Chinese medicine: an opportunity for discovery. *J Rheumatol* 2010;37:1989–90.
- He YT, Ou AH, Yang XB, *et al.* Traditional Chinese medicine versus western medicine as used in China in the management of rheumatoid arthritis: a randomized, single-blind, 24-week study. *Rheumatol Int* 2014;34:1647–55.
- Wang ZM, Bai RX. Integrated medical diagnosis and treatment criteria for four rheumatoid diseases. *Zhong Xi Yi Jie He Za Zhi* 1989;9:52–3.
- Zheng XY. *Guideline of clinical research into new Chinese drugs*. Vol. 116. Beijing: China Medical Sci-tech Press, 2002.
- State Administration of Chinese Medicine. *Criteria of diagnosis and therapeutic effect of diseases and syndromes in traditional Chinese medicine*. Vol. 7. Nanjing University Press, 1994:29–30.
- Canter PH, Lee HS, Ernst E. A systematic review of randomised clinical trials of Tripterygium wilfordii for rheumatoid arthritis. *Phytomedicine* 2006;13:371–7.
- Zhang C, Jiang M, Lu AP. Chinese herbal medicines versus disease modifying antirheumatic drugs for management of rheumatoid arthritis: a systematic review. *Eur J Integr Med* 2011;3: E219–31.
- Zhang P, Li J, Han Y, *et al.* Traditional Chinese medicine in the treatment of rheumatoid arthritis: a general review. *Rheumatol Int* 2010;30:713–18.
- Zhang C, Jiang M, Guo H, *et al.* Chapter 7—Chinese herbal medicines for rheumatoid arthritis. In: Lie-Fen S, Allan SYL, eds. *Advances in botanical research*. Academic Press, 2012:273–313.
- Manheimer E, Wieland S, Kimbrough E, *et al.* Evidence from the Cochrane Collaboration for Traditional Chinese Medicine therapies. *J Altern Complem Med* 2009;15:1001–14.
- Posadzki P, Watson LK, Alotaibi A, *et al.* Prevalence of use of complementary and alternative medicine (CAM) by patients/consumers in the UK: systematic review of surveys. *Clin Med (Lond)* 2013;13:126–31.
- Herman CJ, Allen P, Hunt WC, *et al.* Use of complementary therapies among primary care clinic patients with arthritis. *Prev Chronic Dis* 2004;1:A12.
- Chen ZF, Zhang JH. Traditional Chinese herbs for precancerous lesion of esophagus: a meta analysis. *Traditi Chin Med Res* 1999;12:22–3.
- Ma B, Guo J, Qi G, *et al.* Epidemiology, quality and reporting characteristics of systematic reviews of traditional Chinese medicine interventions published in Chinese journals. *PLoS ONE* 2011;6:e20185.
- Begg C, Cho M, Eastwood S, *et al.* Improving the quality of reporting of randomized controlled trials. The CONSORT statement. *JAMA* 1996;276:637–9.
- Gagnier JJ, Boon H, Rochon P, *et al.* Reporting randomized, controlled trials of herbal interventions: an elaborated CONSORT statement. *Ann Intern Med* 2006;144:364–7.
- Higgins JPT, Green S, eds. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0*. The Cochrane Collaboration, 2011. www.handbook.cochrane.org
- Bian Z, Liu B, Moher D, *et al.* Consolidated standards of reporting trials (CONSORT) for traditional Chinese medicine: current situation and future development. *Front Med* 2011;5:171–7.
- Hartling L, Ospina M, Liang Y, *et al.* Risk of bias versus quality assessment of randomised controlled trials: cross sectional study. *BMJ* 2009;339:b4012.
- Fei YT, Liu JP. [Herbal CONSORT statement and standardization of reporting traditional Chinese drug trials]. *Zhongguo Zhong Yao Za Zhi* 2008;33:89–94.
- Chen L, Qi H, Jiang D, *et al.* The new use of an ancient remedy: a double-blinded randomized study on the treatment of rheumatoid arthritis. *Am J Chin Med* 2013;41:263–80.
- Chen Z, Li XP, Li ZJ, *et al.* Reduced hepatotoxicity by total glucosides of paeony in combination treatment with leflunomide and methotrexate for patients with active rheumatoid arthritis. *Int Immunopharmacol* 2013;15:474–7.
- Chen ZW, Sun J, Li YM, *et al.* [Efficacy of Shenshi Qianghuo Dihuang Decoction in rheumatoid arthritis: a randomized controlled trial]. *Zhong Xi Yi Jie He Xue Bao* 2010;8:35–9.
- Du JH, Dong BD. [Comparative study on clinical efficacy of using methotrexate singly or combined with total glucosides of Paeony in treating rheumatoid arthritis]. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2005;25:540–2.
- Fan D-H, Xia B. [Observation on therapeutic effect of heat needle combined with herb iontophoresis and western medicine on rheumatoid arthritis]. *Zhongguo zhenjiu* 2007;27:731–4.
- Goldbach-Mansky R, Wilson M, Fleischmann R, *et al.* Comparison of Tripterygium wilfordii Hook F versus sulfasalazine in the treatment of rheumatoid arthritis: a randomized trial. *Ann Intern Med* 2009;151:229–40, W49–51.
- He Y, Lu A, Lu C, *et al.* Symptom combinations assessed in traditional Chinese medicine and its predictive role in ACR20 efficacy response in rheumatoid arthritis. *Am J Chin Med* 2008;36:675–83.
- Ji H, Yao S, Luo Q, *et al.* TCM treatment of rheumatoid arthritis by supplementing the kidney and invigorating the blood circulation. *J Tradit Chin Med* 2002;22:252–5.
- Jiang Q, Zhou XY, Wang L, *et al.* A one-year evaluation of radiographic progression in patients with rheumatoid arthritis treated by Qingre Huoxue Decoction (). *Chin J Integr Med* 2012;18:256–61.
- Jiao J, Jiang Q. [External application of compound Tripterygium wilfordii decreased the activity of rheumatoid arthritis]. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2012;32:1470–2, 76.
- Jie HY, Wu QF, Ding ZX. [Clinical study of Biqi Capsule combined with methotrexate for treatment of rheumatoid arthritis]. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2012;32:195–8.
- Kang XZ, Wu QF, Wang KH. [Efficacy of integrative medicine for the treatment of rheumatoid arthritis and its effect on glucocorticoid receptor expression]. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2010;30:1261–4.
- Li EK, Tam LS, Wong CK, *et al.* Safety and efficacy of Ganoderma lucidum (lingzhi) and San Miao San supplementation in patients with rheumatoid arthritis: a double-blind, randomized, placebo-controlled pilot trial. *Arthritis Rheum* 2007;57:1143–50.
- Li YN, Zhao YS, Li X. [Study on abnormality and regulation of T-lymphocyte subsets in peripheral blood of rheumatoid arthritis patients]. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2002;22: 359–61.
- Li YS, Tong PJ, Ma HZ. [Toxicity attenuation and efficacy potentiation effect of liquorice on treatment of rheumatoid arthritis

- with Tripterygium wilfordii]. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2006;26:1117–19.
39. Liang Q, Tang T, Zhang H. [Clinical investigation of effects of bizhongxiao decoction (BZX) on rheumatoid arthritis on active phase]. *Hunan Yi Ke Da Xue Xue Bao* 2000;25:449–52.
 40. Lin CS, Yang XY, Dai L. [Multi-center clinical study on therapeutic effect of kunxian capsule on rheumatoid arthritis]. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2011;31:769–74.
 41. Liu DF, Guo MY, Zhang J. [Treatment of active rheumatoid arthritis by sanhuang yilong decoction]. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2008;28:743–6.
 42. Liu J, Li H, Chen X. [Effects of traditional Chinese medicine for invigorating spleen to resolve dampness and dredging collaterals on patients with rheumatoid arthritis and anemia]. *Zhong Xi Yi Jie He Xue Bao* 2006;4:348–54.
 43. Liu W, Liu XY, Liu B. [Clinical observation on treatment of rheumatoid arthritis with zhengqing fengtongning retard tablets: a report of 60 cases]. *Zhong Xi Yi Jie He Xue Bao* 2006;4:201–2.
 44. Liu W, Liu XY, Wang Y. [Effect of Chinese herbs in enhancing prednisone for treatment of refractory rheumatoid arthritis]. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2007;27:742–4.
 45. Liu W, Zhang L, Xu Z. [Clinical observation on treatment of rheumatoid arthritis with biqi capsule]. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2006;26:157–9.
 46. Liu XD, Zhang JL, Ye LH. [Effects of wenhua juanbi recipe on TNF-alpha and IL-1beta in peripheral blood of rheumatoid arthritis patients]. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2009;29:787–90.
 47. Lu SJ, Shao J, Li XR. [Clinical observation on treatment of rheumatoid arthritis by combined therapy with methotrexate, sulfasalazine and Chinese herbal medicine]. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2002;22:571–3.
 48. Shen HB, Bai YJ, Huo ZJ, et al. Assessment of clinical effect of therapy combining disease with syndrome on rheumatoid arthritis. *J Tradit Chin Med* 2011;31:39–43.
 49. Shen Y, Qu Q, Wang D. Clinical observation on treatment of rheumatoid arthritis with fengshi xianan in 53 cases. *J Tradit Chin Med* 2003;23:21–6.
 50. Song YW, Lee EY, Koh E-M, et al. Assessment of comparative pain relief and tolerability of SKI306X compared with celecoxib in patients with rheumatoid arthritis: a 6-week, multicenter, randomized, double-blind, double-dummy, phase III, noninferiority clinical trial. *Clin Ther* 2007;29:862–73.
 51. Tao X, Younger J, Fan FZ, et al. Benefit of an extract of Tripterygium Wilfordii Hook F in patients with rheumatoid arthritis: a double-blind, placebo-controlled study. *Arthritis Rheum* 2002;46:1735–43.
 52. Wang JM, Tao QW, Zhang YZ, et al. [Treating rheumatoid arthritis patients of Shen deficiency and cold invading syndrome by bushen quhan zhiwang decoction combined methotrexate: an evaluation of clinical efficacy and safety]. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2013;33:614–18.
 53. Wu YJ, Lao ZY, Zhang ZL. [Clinical observation on small doses Tripterygium wilfordii polyglycoside combined with methotrexate in treating rheumatoid arthritis]. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2001;21:895–6.
 54. Yang W, Ouyang J, Zhu K, et al. TCM treatment for 40 cases of rheumatoid arthritis with channel blockage due to yin deficiency. *J Tradit Chin Med* 2003;23:172–4.
 55. Yu JP, Zhang YZ, Li XY. [Effect of strengthening Pi and activating blood circulation therapy on serum levels of adrenocorticotrophic hormone and vascular endothelial growth factor in rheumatoid arthritis patients]. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2007;27:593–5.
 56. Yu SY, Yu ZA. [Clinical observation of compound xiatianwu tablets in treatment of 120 cases with active rheumatoid arthritis]. *Zhongguo Zhong Yao Za Zhi* 2013;38:899–901.
 57. Yu WY, Shen SW, Yang ZH. A clinical study of Suogudan granule in the treatment of rheumatoid arthritis. *Chin J Integr Med* 2005;11:255–9.
 58. Zhang JH, Wang JP, Wang HJ. [Clinical study on effect of total panax notoginseng saponins on immune related inner environment imbalance in rheumatoid arthritis patients]. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2007;27:589–92.
 59. Zhao SS, Wang J. [Short-term clinical observation on compound Xiatianwu combined with methotrexate in treating rheumatoid arthritis]. *Zhongguo Zhong Yao Za Zhi* 2012;37:3664–6.
 60. Zhao YX, Liu Y. [Clinical observation on effects of leflunomide and total glucosides of paeony on rheumatoid arthritis]. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2006;26:355–7.
 61. Zhou CY, Pan Z, Ma F, et al. [Controlled clinical trials of external using of Cheezheng Qingpeng ointment on relieving analgesia and swelling for the treatment of rheumatoid arthritis]. *Zhongguo Gu Shang* 2009;22:917–19.
 62. Zhou CY, Tang JY, Fang DY. [Clinical study on active rheumatoid arthritis treated with simiao xiaobi decoction]. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2010;30:275–9.
 63. Zhou DQ, Liu DX. [Juanbi mixture in treating 100 cases of rheumatoid arthritis patients]. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2002;22:386–7.
 64. Zhou H, Zhong Y. [Clinical observation on liang's anti-rheumatism and rheumatoid granule in rheumatoid arthritis in the active stage]. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2006;26:248–50.
 65. Zhou X, Zhou Z, Jin M, et al. Intermediate and late rheumatoid arthritis treated by tonifying the kidney, resolving phlegm and removing blood stasis. *J Tradit Chin Med* 2000;20:87–92.
 66. Zhou X, Zhou Z, Jin M, et al. Clinical study of qingluo tongbi granules in treating 63 patients with rheumatoid arthritis of the type of yin-deficiency and heat in collaterals. *J Tradit Chin Med* 2004;24:83–7.
 67. Zhang GX, Zhang YM, Cao SY. Ameliorating effect of external therapy of Chinese herb on joint function of patients with rheumatoid arthritis. *Chinese Journal of Clinical Rehabilitation* 2006;10:24–6.
 68. Zuo C, Chen YT, Wang ZM. [Clinical efficacy of Corydalis composite combined with methotrexate in treating rheumatoid arthritis]. *Zhongguo Zhong xi yi jie he za zhi Zhongguo Zhongxiyi jiehe zazhi=Chinese journal of integrated traditional and Western medicine / Zhongguo Zhong xi yi jie he xue hui, Zhongguo Zhong yi yan jiu yuan zhu ban* 2009;29:1023–5.
 69. Sun SM, Min SP, Luo SP, et al. Clinical study on effect of Tongyong Tongfeng Decoction combined with methotrexate on pain and swelling after rheumatoid arthritis. *Chinese Journal of Clinical Rehabilitation* 2002;6:148–9.
 70. Li HR, Zhang X, Ding J, et al. Curative effect of Yishen Juanbi Capsule combined with fumigation therapy by Chinese materia medica on rheumatoid arthritis. *Chinese Traditional and Herbal Drugs* 2013;44:335–7.
 71. Hang WP, Li J, Xu J, et al. Double-blind randomized placebo controlled trial (phase II) on the efficacy and safety of Ranjiangduoqi capsule in the treatment of patients with active rheumatoid arthritis (Retention of Cold-damp in the collaterals). *Chinese Journal of Evidence-Based Medicine* 2005;5:286–90+322.
 72. Xun XQ, Xiong XG, Chen J, et al. Effects of heat-clearing and detoxicating (bizhongxiao decoction) on bone erosion of rheumatoid arthritis: compared with combination of methotrexate and sulfasalazine therapy. *Journal of Clinical Rehabilitative Tissue Engineering Research* 2010;14:7696–9.
 73. Ding F, Zhang Y, Chang Y. Effects of Sanwushaoxie decoction on IL-18, TNF-alpha, IL-4 and IL-10 in patients with rheumatoid arthritis. *Zhongguo Zhongyao Zazhi* 2010;35:790–3.
 74. Tang SJ, Yue YS, Zhao WH. 53 cases of rheumatoid arthritis treated with quartet therapy. *Journal of Anhui Traditional Chinese Medical College* 2002. <http://onlinelibrary.wiley.com/doi/cochrane/central/articles/811/CN-00716811/frame.html>
 75. Tu SH, Hu YH. [Assessment on life quality of patients with rheumatoid arthritis and efficacy of tripterygium wilfordii hook]. *Journal of Traditional Chinese Medicine University of Hunan [Hu Nan Zhong Yi Xue Yuan Xue Bao]* 2006. <http://onlinelibrary.wiley.com/doi/cochrane/central/articles/193/CN-00976193/frame.html>
 76. Guo JB, Xue G, Zhang LF, et al. [Clinical observation of treating rheumatoid arthritis using compound tripterygium wilfordii wine]. *Hebei Journal of Traditional Chinese Medicine [He Bei Zhong Yi]* 2003. <http://onlinelibrary.wiley.com/doi/cochrane/central/articles/302/CN-00975302/frame.html>
 77. Chen ZH. [Clinical observation of Yishen Zhuanggu Tongbi Decoction in the treatment of rheumatoid arthritis]. *Journal of Guangzhou University of Traditional Chinese Medicine [Guang Zhou Zhong Yi Yao da Xue Xue Bao]* 2005. <http://onlinelibrary.wiley.com/doi/cochrane/central/articles/005/CN-00976005/frame.html>
 78. Guan BS. [Clinical observation on the effect of acupuncture combined with Chinese medicine for rheumatoid arthritis]. *Chinese Journal of Gerontology [Zhong Guo Lao Nian Xue za Zhi]* 2005. <http://onlinelibrary.wiley.com/doi/cochrane/central/articles/015/CN-00976015/frame.html>
 79. Ma HY, Huo YL, Ma XS. [Clinical observation on the effect of acupuncture combined with Chinese medicine for rheumatoid arthritis]. *Clinical Journal of Traditional Chinese Medicine [Zhong Yi Yao Lin Chuang za Zhi]* 2008. <http://onlinelibrary.wiley.com/doi/cochrane/central/articles/783/CN-00976783/frame.html>
 80. Hu YM. [Clinical observation on the effect of Chinese medicine combined with anus suppository for rheumatoid arthritis in 74 cases]. *Zhejiang Clinical Medical Journal [Zhe Jiang Lin Chuang Yi*

- Xue] 2007. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/391/CN-00976391/frame.html>
81. Li WJ, Liu P. [Clinical observation on the effect of Chinese medicine for rheumatoid arthritis]. *Chinese Journal of Traditional Medical Traumatology & Orthopedics [zhong Guo Zhong Yi Gu Shang]* 2003. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/316/CN-00975316/frame.html>
 82. Liu YH, Ren XR, Zhang QX, *et al.* [Clinical observation on the effect of Chinese medicine, physical therapy and exercises for rheumatoid arthritis in 50 cases]. *Modern Rehabilitation [xian Dai Kang Fu]* 2000. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/089/CN-00975089/frame.html>
 83. Wang ZQ. [Clinical observation on the effect of external and internal use of Chinese medicine for rheumatoid arthritis]. *Hubei Journal of Chinese Medicine [hu Bei Zhong Yi za Zhi]* 2001. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/090/CN-00975090/frame.html>
 84. Xiao M. [Clinical observation on the effect of Fengshi Tincture for rheumatoid arthritis in 48 cases]. *Journal of Baotou Medical College [bao Tou Yi Xue Yuan Xue Bao]* 2008. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/778/CN-00976778/frame.html>
 85. Zou YJ. [Clinical observation on the effect of Guizhi Shaoyao Zhimu Decoction for rheumatoid arthritis in 30 cases]. *Journal of Emergency in Traditional Chinese Medicine [zhong Guo Zhong Yi Ji Zheng]* 2007. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/372/CN-00976372/frame.html>
 86. Wang SM, Wang X, Gong Q. [Clinical observation on the effect of integrated Chinese and western medicine for rheumatoid arthritis in 40 cases]. *Journal of Sichuan of Traditional Chinese Medicine [si Chuan Zhong Yi]* 2006. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/208/CN-00976208/frame.html>
 87. Ma YB, Li DM, Zhang HD. [Clinical observation on the effect of self-developed Fengshiling Wine for rheumatoid arthritis]. *Chinese Journal of Convalescent Medicine [zhong Guo Liao Yang Yi Xue]* 2002. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/093/CN-00975093/frame.html>
 88. Wu CL. [Clinical observation on the effect of Siwu Wuteng Decoction combined with methylamine pterin for rheumatoid arthritis in 46 cases]. *Jiangxi Journal of Traditional Chinese Medicine* 2004. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/789/CN-00975789/frame.html>
 89. Jiang GL, Liu DJ, Wang FG, *et al.* [Clinical observation on the effect of Tongbi Pills combined with Wutou Capsules for rheumatoid arthritis]. *Acta Chinese Medicine and Pharmacology [Zhong Yi Yao Xue Bao]* 2000. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/076/CN-00975076/frame.html>
 90. Liang YM. [Clinical observation on the effect of Yishen Huoxue Juanbi Decoction for rheumatoid arthritis in 36 cases]. *Yunnan Journal of Traditional Chinese Medicine and Materia Medica [yun Nan Zhong Yi Zhong Yao za Zhi]* 2000. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/095/CN-00975095/frame.html>
 91. Tao JZ. [Clinical observation on the effect of Zhufeng Tougou Huoluo Pell combined with Zhufeng Tougou Huoluo Powder for rheumatoid arthritis in 70 cases]. *Chinese Community Doctors [zhong Guo She Qu Yi Shi]* 2002. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/092/CN-00975092/frame.html>
 92. Lv MH, Zhang YQ. [Clinical observation on the long term effect of Juanbi Decoction combined with Huangqi injection for rheumatoid arthritis]. *Anhui Clinical Journal of Traditional Chinese Medicine [an Hui Zhong Yi Lin Chuang za Zhi]* 2000. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/063/CN-00975063/frame.html>
 93. Zhang GH. [Clinical research on the effect of Shirebi Compound for rheumatoid arthritis]. *Hubei Journal of Traditional Chinese Medicine [hu Bei Zhong Yi za Zhi]* 2005. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/998/CN-00975998/frame.html>
 94. Chen X, Li H. [Clinical research on the effect of Zhengqing Fengtongning for rheumatoid arthritis]. *Journal of Anhui Traditional Chinese Medicine College [an Hui Zhong Yi Xue Yuan Xue Bao]* 2005. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/018/CN-00976018/frame.html>
 95. Xiao F, Wu FJ. [Clinical study of Bi Qi Capsule for rheumatoid arthritis]. *Journal of Liaoning University of Traditional Chinese Medicine [liao Ning Zhong Yi Yao da Xue Xue Bao]* 2008. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/748/CN-00976748/frame.html>
 96. Huang GD, Li JB, Huang YH, *et al.* [The clinical study on sinomenine for 100 patients with rheumatoid arthritis]. *Journal of Emergency in Traditional Chinese Medicine [zhong Guo Zhong Yi Ji Zheng]* 2007. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/380/CN-00976380/frame.html>
 97. Fan CP, Chen Q, Qi WL. [Comparison of Zhengqing Fengtongning and tripterygium glycosides for rheumatoid arthritis]. *China Pharmaceuticals [zhong Guo Yao Ye]* 2000. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/096/CN-00975096/frame.html>
 98. Zhen HX, Liu W, Zhang L. [Curative effect of combined Chinese medicines on rheumatoid arthritis with damp-heat blocking collaterals]. *Tianjin Journal of Traditional Chinese Medicine [tian Jin Zhong Yi Yao]* 2006. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/207/CN-00976207/frame.html>
 99. Ji YL, Wan WW, Chen Y, *et al.* [Curative effect of external application of Chinese medicine on active rheumatoid arthritis]. *Journal of Nursing Science [hu Li Xue za Zhi]* 2008. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/785/CN-00976785/frame.html>
 100. Xu DS, Tong LM, Qin DH, *et al.* [Effect of Wudang Zhufeng Shengshi Liquor as fumigation bath for ESR, CRP and RF in rheumatoid arthritis]. *Hubei Journal of Traditional Chinese Medicine [hu Bei Zhong Yi za Zhi]* 2005. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/011/CN-00976011/frame.html>
 101. Wang Y, Wu Q, Wei JX, *et al.* [Experience of total glucosides of paeony, Methotrexate and Tripterygium wilfordii (Tripterygium Wilfordii Hook) for rheumatoid arthritis in 150 cases]. *Journal of Zhengzhou University (medical Sciences) [zhen Zhou da Xue Xue Bao (yi Xue Ban)]* 2006. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/186/CN-00976186/frame.html>
 102. Liu L. [The internal and external use of Feng Shi Ning Decoction for rheumatoid arthritis in 32 cases]. *Shaanxi Journal of Traditional Chinese Medicine [shan Xi Zhong Yi]* 2007. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/370/CN-00976370/frame.html>
 103. He JF, Liang YY. [Observation of rheumatoid arthritis treated by integration of traditional Chinese medicine and western medicine]. *Hebei Journal of Traditional Chinese Medicine [he Bei Zhong Yi]* 2001. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/088/CN-00975088/frame.html>
 104. Liu XY, Liu JH, Liu LN, *et al.* [Observation of rheumatoid arthritis treated by a traditional Chinese medicine method of removing blood stasis and invigorating for deficiency]. *Hebei Journal of Traditional Chinese Medicine [he Bei Zhong Yi]* 2003. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/299/CN-00975299/frame.html>
 105. Huang N, Huang CJ, Huang XF. [Observation of Rheumatoid arthritis treated by Sanbi decoction]. *Hebei Journal of Traditional Chinese Medicine [he Bei Zhong Yi]* 2002. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/073/CN-00975073/frame.html>
 106. Li B, Li Y. [Treatment of early rheumatoid arthritis with Chinese medicine combined with acupuncture in 46 cases]. *Shandong Medical Journal [shan Dong Yi Yao]* 2001. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/091/CN-00975091/frame.html>
 107. Li JC, Zhao DR. [Treatment of refractory rheumatoid arthritis with integrated Chinese and western medicine in 86 cases]. *Journal of Sichuan of Traditional Chinese Medicine [si Chuan Zhong Yi]* 2003. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/319/CN-00975319/frame.html>
 108. Xin XF, Chen Y. [Treatment of rheumatoid arthritis in old age with integrated Chinese and western medicine]. *Zhejiang Journal of Integrated Traditional Chinese and Western Medicine [zhe Jiang Zhong Xi Yi Jie He za Zhi]* 2005. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/007/CN-00976007/frame.html>
 109. Leng YL, Li Y, Chen XN, *et al.* [Treatment of rheumatoid arthritis with acupoint thread implanting combined with Chinese medicine in 48 cases]. *Lishizhen Medicine and Materia Medica Research [shi Zhen Guo Yi Guo Yao]* 2000. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/082/CN-00975082/frame.html>
 110. Wang YG, Song JY, Zhao T. [Treatment of rheumatoid arthritis with Chinese medicine combined with multi-function inotophoresis in 108 cases]. *China Science and Technology Information [zhong Guo Ke Ji Xin Xue]* 2005. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/009/CN-00976009/frame.html>
 111. Zeng YH, Huang RQ. Treatment of rheumatoid arthritis with Feng Shi Ning Injection in 42 cases. *Chinese Journal of Information on TCM* 2006. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/980/CN-00796980/frame.html>
 112. Ji FR, Zhao XL. [Treatment of rheumatoid arthritis with Guizhi Shaoyao Zhimu Decoction in 45 cases]. *Chinese Community Doctors [zhong Guo She Qu Yi Shi]* 2007. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/371/CN-00976371/frame.html>
 113. Cai JW, Hong BF. [Treatment of rheumatoid arthritis with Guizhi Shaoyao Zhimu Decoction in 50 cases]. *Gansu Journal of Traditional Chinese Medicine* 2006. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/190/CN-00976190/frame.html>

114. Wu JR, Meng LH. [Treatment of rheumatoid arthritis with integrated Chinese and western medicine in 56 cases]. *Practical Clinical Journal of Integrated Traditional Chinese and Western Medicine*[*shi Yong Zhong Xi Yi Jie He Lin Chuang*] 2004. <http://onlinelibrary.wiley.com/doi/cochrane/central/articles/797/CN-00975797/frame.html>
115. Guo SX. [Treatment of rheumatoid arthritis with modified Baihu Guizhi Tang in 120 cases]. *Modern Journal of Integrated Traditional Chinese and Western Medicine* [*xian Dai Zhong Xi Yi Jie He za Zhi*] 2003. <http://onlinelibrary.wiley.com/doi/cochrane/central/articles/297/CN-00975297/frame.html>
116. Li F, Pang XF. [Treatment of rheumatoid arthritis with Sanbi Decoction in 30 cases]. *Shaanxi Journal of Traditional Chinese Medicine* [*shan Xi Zhong Yi*] 2008. <http://onlinelibrary.wiley.com/doi/cochrane/central/articles/770/CN-00976770/frame.html>
117. Chen YL. [Treatment of rheumatoid arthritis with self-developed Huangqi Shudi Jisheng Decoction in 140 cases]. *Shaanxi Journal of Traditional Chinese Medicine* [*shan Xi Zhong Yi*] 2007. <http://onlinelibrary.wiley.com/doi/cochrane/central/articles/395/CN-00976395/frame.html>
118. Li GJ, Bai CY, Wang B, et al. [Treatment of rheumatoid arthritis with self-developed Juanbi Decoction combined with MTX in 24 cases]. *Chinese Journal of Integrated Traditional and Western Medicine* [*zhong Guo Zhong Xi Yi Jie He za Zhi*] 2003. <http://onlinelibrary.wiley.com/doi/cochrane/central/articles/317/CN-00975317/frame.html>
119. Du YK, Wang JW, Huang SQ. [Treatment of rheumatoid arthritis with self-developed Sancang Juanbi Decoction in 40 cases]. *Modern Traditional Chinese Medicine*[*xian Dai Zhong Yi Yao*] 2003. <http://onlinelibrary.wiley.com/doi/cochrane/central/articles/318/CN-00975318/frame.html>
120. Xu C-H. [Treatment of rheumatoid arthritis with warm needling and Juanbi decoction: A report of 35 cases]. *Journal of Anhui Traditional Chinese Medical College* [*An Hui Zhong Yi Xue Yuan Xue Bao*] 2004. <http://onlinelibrary.wiley.com/doi/cochrane/central/articles/583/CN-00676583/frame.html>
121. Shi B. [Treatment of rheumatoid arthritis with Wutou Decoction in 64 cases]. *Chinese Community Doctors* [*zhong Guo She Qu Yi Shi*] 2007. <http://onlinelibrary.wiley.com/doi/cochrane/central/articles/386/CN-00976386/frame.html>
122. Hui CL, Li FP. [Treatment of rheumatoid arthritis with Yanghe Decoction combined with tripterygium glycosides in 60 cases]. *Shaanxi Journal of Traditional Chinese Medicine* [*shan Xi Zhong Yi*] 2008. <http://onlinelibrary.wiley.com/doi/cochrane/central/articles/780/CN-00976780/frame.html>
123. Meng QL, Guo HQ, Zhao YQ. [Treatment of rheumatoid arthritis with Yishen Juanbi Decoction combined with MTX in 40 cases]. *Traditional Chinese Medicine Research* [*zhong Yi Yan Jiu*] 2006. <http://onlinelibrary.wiley.com/doi/cochrane/central/articles/205/CN-00976205/frame.html>
124. Wang W. [Xianteng Fengshi Decoction in treating rheumatoid arthritis]. *Journal of Henan University of Chinese Medicine*[*he Nan Zhong Yi Xue Yuan Xue Bao*] 2004. <http://onlinelibrary.wiley.com/doi/cochrane/central/articles/794/CN-00975794/frame.html>
125. Huang CB, Liu J, Chen X, et al. [Treatment of rheumatoid arthritis by xinfeng capsule: an efficacy observation]. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2013;33:1599–602.
126. Kou QA, Li L, Yao JY, et al. [Treatment of rheumatoid arthritis arthralgia by xiaoyan zhitong paste: a clinical observation]. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2013;33:1320–2, 27.
127. Liu J, Cao Y, Huang C, et al. Use of xinfeng capsule to treat abarticular pathologic changes in patients with rheumatoid arthritis. *J Tradit Chin Med* 2014;34:532–8.
128. Wang Z, Tao XJ. [Treatment of rheumatoid arthritis by Yangxue Tongluo Recipe combined with immunosuppressive agents: a clinical observation]. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2014;34:276–8.
129. Guo SY, Lin LJ, Chu H, et al. [Efficacy of Lugua polypeptide injection on active rheumatoid arthritis]. *Zhongguo Gu Shang* 2008;21:610–12.
130. Tao Q, Xu Y, Jin D, et al. Clinical effect and safety of Lugua Polypeptide injection in the treatment of rheumatoid arthritis. *Journal of Clinical Orthopaedics* 2011;14:336–8.
131. Zhu Y, Lin W, Yang F, et al. Lugua Polypeptide injection in the treatment of rheumatoid arthritis. *Journal of Clinical Orthopaedics* 2011;14:334–6.
132. Zheng LH, Kang XZ, Wang KH, et al. Clinical research of the syndrome differentiation treatment of TCM in combination with stage-based treatment of western medicine on patients with rheumatoid arthritis. *JETCM* 2009;18:1256–8.
133. Liu J, Liu X, Han M. Treatment of 20 cases of rheumatoid arthritis in active stage with Xinfeng capsule. *Journal of Anhui Traditional Chinese Medical College* 2003;22:12–16.
134. Sun S, Zhou C, Fan B. Clinical study on Bisuqing Mixture for rheumatoid arthritis in active stage. *Shandong J Tradit Chin Med* 2003;2003:9.
135. Cui Z, Bian R, Chen Z, et al. Clinical observation of Bitong decoction treating 54 cases of rheumatoid arthritis. *Journal of Sichuan of Traditional Chinese Medicine*[*si Chuan Zhong Yi*] 2004;22:39–40.
136. Liu J, Wang C, Liu S. Clinical research of YiShenJuanBi capsules in the treatment of rheumatoid arthritis. *Chinese J Trad Med Traum & Orthop* 2008;16:24–6.
137. Ao X, Chen C, Zen H, et al. Synergistic action of fuming—washing therapy with Qingbixifang on rheumatoid arthritis with heat retention. *Journal of Guangzhou University of Traditional Chinese Medicine* [*guang Zhou Zhong Yi Yao da Xue Xue Bao*] 2005;22:436–9.
138. Wu Y, Lao Z, Zhang Z. Clinical observation on small doses tripterygium wilfordii polyglycoside combined with methotrexate in treating rheumatoid arthritis. *Chinese Journal of Integrated Traditional and Western Medicine* [*zhong Guo Zhong Xi Yi Jie He za Zhi*] 2001;21:895.
139. Wang D. Clinical observation on combine with total Glucosides of Peony in treating 32 cases rheumatoid arthritis. *Shaanxi Journal of Traditional Chinese Medicine* [*shan Xi Zhong Yi*] 2007;28:421–2.
140. He D, Shen J, Zhang Z, et al. "Shi Re Bi Granule" for rheumatoid arthritis in 46 cases. *Shanghai Journal of Traditional Chinese Medicine* 2002;36:14–15.
141. Lv QW, Zhang W, Shi Q, et al. Comparison of Tripterygium wilfordii Hook F with methotrexate in the treatment of active rheumatoid arthritis (TRIFRA): a randomised, controlled clinical trial. *Ann Rheum Dis* 2014.
142. Tai-xiang W, You-ping L, Zhao-xiang B, et al. Consolidated Standards for Reporting Trials of Traditional Chinese Medicine (CONSORT for TCM). *Chinese Journal of Evidence-Based Medicine* 2007;8:601–5.
143. Prevoo ML, van 't Hof MA, Kuper HH, et al. Modified disease activity scores that include twenty-eight-joint counts. Development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. *Arthritis Rheum* 1995;38:44–8.
144. van der Heijde DM, van 't Hof M, van Riel PL, et al. Development of a disease activity score based on judgment in clinical practice by rheumatologists. *J Rheumatol* 1993;20:579–81.
145. Felson DT, Anderson JJ, Boers M, et al. American College of Rheumatology. Preliminary definition of improvement in rheumatoid arthritis. *Arthritis Rheum* 1995;38:727–35.
146. van Gestel AM, Prevoo ML, van 't Hof MA, et al. Development and validation of the European League Against Rheumatism response criteria for rheumatoid arthritis. Comparison with the preliminary American College of Rheumatology and the World Health Organization/International League Against Rheumatism Criteria. *Arthritis Rheum* 1996;39:34–40.
147. Arnett FC, Edworthy SM, Bloch DA, et al. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. *Arthritis Rheum* 1988;31:315–24.
148. Aletaha D, Neogi T, Silman AJ, et al. 2010 rheumatoid arthritis classification criteria: an American College of Rheumatology/ European League Against Rheumatism collaborative initiative. *Ann Rheum Dis* 2010;69:1580–8.
149. Bykerk VP, Lie E, Bartlett SJ, et al. Establishing a core domain set to measure rheumatoid arthritis flares: report of the OMERACT 11 RA flare Workshop. *J Rheumatol* 2014;41:799–809.
150. Kim YW, Zhang MQ. Characteristics of traditional Chinese medicine in treating rheumatoid arthritis: a retrospective analysis. *Chinese Journal of Clinical Rehabilitation* 2005;9:152–5.
151. Zhang C, Jiang M, Lu A. Chinese herbal medicines versus disease modifying antirheumatic drugs for management of rheumatoid arthritis: a systematic review. *Eur J Integr Med* 2011;3:e219–31.
152. Cameron M, Gagnier JJ, Chrusaski S. Herbal therapy for treating rheumatoid arthritis. *Cochrane Database Syst Rev* 2011;(2):CD002948.
153. Jiang M, Yang J, Zhang C, et al. Clinical studies with traditional Chinese medicine in the past decade and future research and development. *Planta Med* 2010;76:2048–64.
154. Jadad AR, Moore RA, Carroll D, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Control Clin Trials* 1996;17:1–12.
155. Schulz KF, Chalmers I, Hayes RJ, et al. Empirical evidence of bias. Dimensions of methodological quality associated with estimates of treatment effects in controlled trials. *JAMA* 1995;273:408–12.
156. Califf RM, Zarin DA, Kramer JM, et al. Characteristics of clinical trials registered in ClinicalTrials.gov, 2007–2010. *JAMA* 2012;307:1838–47.
157. Wu XY, Tang JL, Mao C, et al. Systematic reviews and meta-analyses of traditional Chinese medicine must search Chinese databases to reduce language bias. *Evid Based Complement Alternat Med* 2013;2013:812179.