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# Quality assessment of clinical trial registration with traditional Chinese medicine in WHO registries

Xuan Zhang,[1] Ran Tian,[1] Zhen Yang,[1] Chen Zhao,[1] Liang Yao,[1] Chungtai Lau,[1] Taixiang Wu,[2] Hongcai Shang,[3] Xiaoyang Zhang,[4] Aiping Lu,[1] Zhaoxiang Bian[1]

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For numbered affiliations see end of article.

**Correspondence to**
Professor Zhaoxiang Bian; bianzxiang@gmail.com

## ABSTRACT

**Objective** This study aimed to assess the registration quality of clinical trials (CTs) with traditional Chinese medicine (TCM) in the WHO International Clinical Trials Registry Platform (ICTRP) and identify the common problems if any.

**Methods** The ICTRP database was searched for all TCM CTs that were registered up to 31 December 2017. Registered information of each trial was collected from specific registry involved in ICTRP through hyperlink. The primary analysis was to assess the reporting quality of registered trials with TCM interventions, which is based on the minimum 20 items of WHO Trial Registration Data Set (TRDS, V.1.2.1) plus optional additional three items recommended by ICTRP, and some specific items for TCM information (including TCM intervention, diagnosis, outcome and rationale). Descriptive statistics were additionally used to analyse the baseline characteristics of TCM trial registrations.

**Results** A total of 3339 records in 15 registries were examined. The number of TCM registered trials has increased rapidly after the requirement of mandatory trial registration proposed by International Committee of Medical Journal Editors on 1 July 2005, and the top two registries were Chinese Clinical Trial Registry and ClincialTrials.gov. Of 3339 trials, 61% were prospective registration and 12.8% shared resultant publications. There were 2955 interventional trials but none of them had a 100% reporting rate of the minimum 20 items and additional three items. The reporting quality of these 23 items was not optimal due to 11 of them had a lower reporting rate (<65%). For TCM details, 49.2% lacked information on description of TCM intervention(s), 85.9% did not contain TCM diagnosis criteria, 92.6% did not use TCM outcome(s) and 67.1% lacked information on TCM background and rationale.

**Conclusion** The registration quality of TCM CTs should be improved by prospective registration, full completion of WHO TRDS, full reporting of TCM information and results sharing. Further full set of trial registration items for TCM trials should be developed thus to standardise the content of TCM trial registration.

## Strengths and limitations of this study

- Systematic searches of International Clinical Trials Registry Platform (ICTRP) database for any clinical trials of traditional Chinese medicine (TCM).
- This study included TCM trial registrations up to 31 December 2017, at which time the ICTRP had already been updated to 17 WHO registries.
- All interventions involving any TCM were included for analysis of registration quality.
- The minimum 20 items of WHO Trial Registration Data Set, optional additional three items recommended by ICTRP and some TCM information (including TCM intervention, diagnosis, outcome and rationale) items were applied to assess the registration quality of TCM interventional trials.
- Registered information of each trial was collected from specific registry involved in ICTRP through hyperlink.

## INTRODUCTION

Clinical trial registration (CTR) is considered to be an ethical, scientific and moral responsibility of those performing the trials.[1 2] CTR was first proposed in 1986 to reduce publication bias.[3 4] In 1997, the USA incorporated CTR into the requirement for new drug registration by the Food and Drug Administration and launched the first registry—ClinicalTrials.gov.[5] However, it was not until September 2004 that the International Committee of Medical Journal Editors (ICMJE) introduced the first international policy on trial registration. According to this policy, trials must be registered before enrolment of the first patient. This policy applies to any clinical trial that started recruiting on or after 1 July 2005.[6] During these periods, there were some CTR centres that established and operated, respectively, such as ClinicalTrials.gov (launched in 1997, United States), International Standard Randomized Controlled Trial Number Register (ISRCTN; launched in 2000, UK)[7] and Australian New Zealand Clinical Trials Registry (ANZCTR; launched in 2005, Australia).[8] They are not compatible with each other and easily lead to duplicate registration of the same trial. Therefore, WHO supported the ICMJE statement and,

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further, called for members to '*establish a voluntary platform to link clinical trials registers in order to ensure a single point of access and the unambiguous identification of trials with a view to enhancing access to information by patients, families, patient groups and others*'. In August 2005, the WHO International Clinical Trials Registry Platform (ICTRP) was established, a searchable platform that give access to trial information from various national registry sites, which included three primary registry (ie, ClinicalTrials.gov, ISRCTN and ANZCTR).[9] In May 2007, the WHO Trial Registration Data Set (TRDS) was announced, specifying a minimum of 20 items for trial registration; the ICMJE adopted it as its requirement immediately.[10] In China, the Chinese Clinical Trial Registry (ChiCTR) was authorised by WHO ICTRP as the fourth primary registry in July 2007. This represented a milestone in clinical research in China.[11] Currently, 17 trial registries are involved in the WHO ICTRP.[12]

In October 2008, the Declaration of Helsinki revised their statement to the following: '*Every clinical trial must be registered in a publicly accessible database before recruitment of the first subject, and researchers have a duty to make publicly available the results of their research on human subjects*'.[13] As more and more institutions require registration, and as more and more researchers become aware of the value of registration, the number of CTR is steadily increasing.[14] Unfortunately, the full value of trial registration is not being realised because of untimely registration, unavailable results and inadequate registered information and so on. For example, Viergever *et al* found that approximately 50% of included trials (1131 samples during 2008–2013) were retrospectively registered and omitted description of intervention specifics.[15 16] Scott *et al*[17] identified 181 clinical trials published in the top five psychiatry journals from 2009 to 2013 and found that only 14.4% (26/181) of trials were registered accurately in advance, with no changes in primary outcome measures between registration and implementation of the trial. Prayle *et al*[18] revealed that only 22% (163/738) trials had reported results within 1 year of completion of the trials' registrations in ClincialTrials.gov. Rosati *et al* analysed 20 paediatric RCTs published from July to November 2013 and found major discrepancies between CTR records and the published papers. Specifically, all 20 RCTs selectively reported or failed to report main outcomes, and 11 downgraded or modified primary outcome or upgraded secondary outcomes.[19] In China, Liu *et al* conducted a survey of registration quality of 766 trials sponsored by China in 2008. Using the scale of 20 items of WHO TRDS, they found that only one trial (0.1%, 1/766) met the full score (20). The other trials (765) registered in a total of four primary registries did not meet the full score, with varying results in each registry. The average scores for trials in China in ANZCTR, ChiCTR, ISRCTN and ClinicalTrials.gov are 18.7±0.6 points, 17.9±0.9 points, 16.4±1.4 points and 12±2.3 points, respectively.[20] In November 2012, the document of 'International Standards for Clinical Trial Registries' was published, which provided explanations of the minimum 20 items of TRDS and optional additional three items (ie, lay summary/synopsis, approvals and links to results) for collection at the time of registration.[21] In summary, only complete, accurate and prospective registration can achieve transparency of CTs and, through transparency, quality of CTs improves. Complete registration should include: (1) prospective registration before the start of the trial, (2) sufficient, accurate information with updates or any change in records during the trial, (3) publication of results and (4) sharing of individual participant data after trial completion.[22] These complete and accurate information is the basis of transparency, which is the goal of trial registration.[23]

As modern medical models evolve, traditional Chinese medicine (TCM) is recognised, more and more, as having profound value because of its demonstrated curative effects.[24 25] TCM's impact worldwide is increasing.[26] There are a variety of TCM interventions, such as Chinese herbal medicines, acupuncture, moxibustion, tuina (massage), cupping, guasha (spooning), Qigong, Tai Chi, and Ba Duan Jin; however, all of them are based on the TCM therapeutic principles and theories.[27] According to WHO, TCM has spread to 183 countries and regions around the world. Among them, 103 member states have given approval to the practice of acupuncture and moxibustion, 29 have enacted special statutes on traditional medicine and 18 have included acupuncture and moxibustion treatment in their medical insurance provisions.[28] The earliest CTR of TCM, sponsored by National Institute of Allergy and Infectious Diseases in USA, was registered in ClinicalTrials.gov (USA) on 2 November 1999.[29] After that, the number of CTR in TCM increased rapidly, even more so after ICMJE required mandatory CTR in 2005. Chen *et al*[30] found that from October 2000 to September 2005, 95 trials were registered; however, from 2005 to 2015, more than 1150 TCM trials were registered in ClinicalTrials.gov. In terms of the reporting quality of CTR in TCM, Gu *et al* assessed the quality of 740 acupuncture CTs, registered in 11 registries, from 1999 to 2012, using the WHO TRDS and special items for acupuncture intervention. The study found that 80% (16/20) of the WHO data set had a higher reported percentage of above 85%, but the information on acupuncture intervention was typically insufficient. Of 740 trials, 89.2% lack of information on the style of acupuncture, 80.8% no details regarding the needles used, 53.5% no information on the treatment regimen and 76.2% no details of other interventions used with acupuncture.[31] A similar study conducted by Liu *et al*,[32] examining 425 CTs with acupuncture and moxibustion registered from 2013 to 2015, found quite similar results. However, there is no study so far to provide the landscape of CTR with various TCM interventions.

This study aimed to assess the overall registration quality of TCM CTs. The objectives were as follows: (1) to summarise the general features of CTR of TCM; (2) to assess the quality of TCM registration with the current standard registration data set; and (3) to conclude whether TCM trial registration as currently practised can



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**Box 1 The Trial Registration Data Set (TRDS) provided in International Standards for Clinical Trial Registries[21]**

**The TRDS, Version 1.2.1:**

The 20-item WHO TRDS outlines the minimum amount of information about a trial that must appear in a register for a given trial to be considered fully registered:

1. Primary registry and trial identifying number.
2. Date of registration in primary registry.
3. Secondary identifying numbers.
4. Source(s) of monetary or material support.
5. Primary sponsor.
6. Secondary sponsor(s).
7. Contact for public queries.
8. Contact for scientific queries.
9. Public title.
10. Scientific title.
11. Countries of recruitment.
12. Health condition(s) or problem(s) studied.
13. Interventions.
14. Key inclusion and exclusion criteria.
15. Study type.
16. Date of first enrollment.
17. Target sample size.
18. Recruitment status.
19. Primary outcome(s).
20. Key secondary outcomes.

**Optional additional items for collection at the time of registration:**

The International Clinical Trials Registry Platform recommends that registries at least consider collecting the following data items

1. Lay summary/synopsis.
2. Approvals.
3. Results links.

provide sufficient information to accurately reflect TCM characteristics. These results will be the basis for setting up registration recommendation data set for CTR with different TCM interventions.

## METHODS

### Data source

The database of the ICTRP (http://apps.who.int/trialsearch/) was searched on 15 January 2018 for all TCM studies that had been registered up to 31 December 2017. There are 17 registries in the ICTRP: ANZCTR, ChiCTR, ClinicalTrials.gov, EU Clinical Trials Register (EU-CTR), ISRCTN, the Netherlands National Trial Register (NTR), Brazilian Clinical Trials Registry (REBEC), Clinical Trials Registry-India (CTRI), Clinical Research Information Service-Republic of Korea (CRIS), Cuban Public Registry of Clinical Trials (RPCEC), German Clinical Trials Register (DRKS), Iranian Registry of Clinical Trials (IRCT), Japan Primary Registries Network (JPRN), Pan African Clinical Trial Registry (PACTR), Sri Lanka Clinical Trials Registry (SLCTR), Thai Clinical Trials Register (TCTR) and Peruvian Clinical Trials Registry (REPEC).

### Patient and public involvement

This study was designed to assess the reporting quality of TCM registered trials. Thus, study does not involve human subjects.

### Search strategy

Standard search, provided by WHO ICTRP (ICTRP Search Portal, http://apps.who.int/trialsearch/), was selected, and the search strategy was developed including 'Chinese medicine OR traditional Chinese medicine OR Chinese materia medica OR Chinese herbal medicine OR acupuncture OR moxibustion OR tuina OR massage OR cupping OR guasha OR Tai Chi OR Ba Duan Jin', without any restrictions.

### Inclusion and exclusion criteria

All TCM CTs registered in ICTRP before 31 December 2017 were eligible for inclusion. For TCM CTs that were registered in more than one registry ('duplicate' registration), only the record with the earliest registration date was included in this study. The scope of TCM CTs included Chinese herbals and compound formulas (decoctions, pills, powders, granules, ointments and so on), Chinese proprietary medicine (pills, tablets, pods, capsules and so on), Chinese medicinal material extraction or injection, acupuncture (electric acupuncture, ear acupuncture, acupoint therapy and so on), moxibustion, tuina (massage), cupping, guasha (spooning), Qigong, Tai Chi and Ba Duan Jin and so on. All CTs belonging to the scope of conventional physical therapy (CPT) or other complementary alternative medicine rather than TCM, such as Swedish/Thai/ice/aroma massage, Korean medicine and so on, which clearly pointed out that the theoretical basis is not Chinese medicine, were excluded. For example, some trials with Japanese/Korean acupuncture were excluded because of clear indication of Japanese/Korean medicine theoretical basis in the registered information.

### Data extraction

Using a predefined data extraction form that collected information for this study, two researchers (XuZ and RT) extracted the data from each trial independently. Disagreements in the data extraction were resolved by Professor ZB. The content of the data extraction forms was mainly composed of two parts: (1) the standard registration data set (included minimum 20 items and optional additional three items) provided in 'International Standards for Clinical Trial Registries' (box 1)[21] and (2) specific TCM information, namely: (1) TCM background and rationale, (2) TCM diagnosis criteria, (3) TCM intervention details and (4) TCM outcome(s). All extracted data were checked and supplemented manually from the specific registries through hyperlink to each record provided in ICTRP.

### Data analyses

The descriptive statistics were conducted first, including: (1) number of CTR of TCM during 1999–2017; (2)



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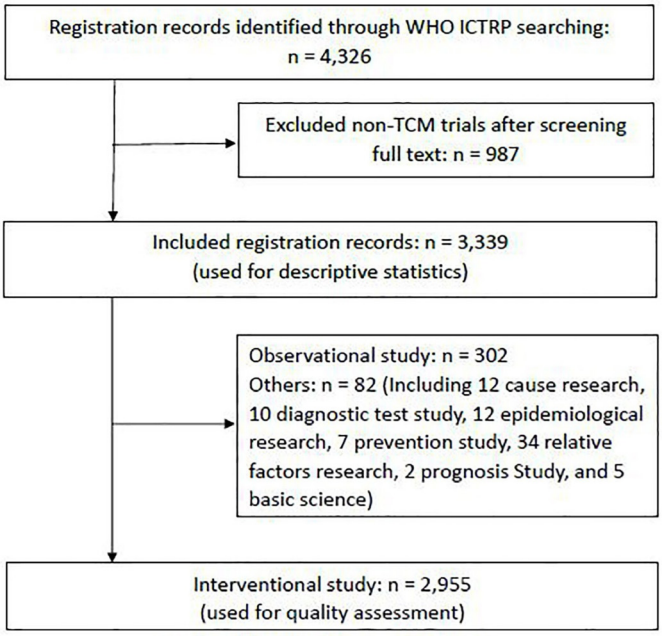


**Figure 1** Flow chart of data search. ICTRP, International Clinical Trials Registry Platform; TCM, traditional Chinese medicine.

distribution of CTR of TCM among 17 registries; (3) increase in number of registries from 1999 to 2017; (4) category of primary sponsor; (5) category of study type; (6) types of TCM interventions involved in the interventional studies; (7) methodology of study design; (8) information of trial recruitment, including target sample size, gender of participants, countries of recruitment and recruitment status; (9) timely registration, prospectively or retrospectively; and (10) resultant publications linked to registry.

The quality assessment of TCM CTRs was conducted based on a total of 23 items; the explanatory text of each item is presented in the document 'International Standards for Clinical Trial Registries'. Specifically, this 'International Standards for Clinical Trial Registries' was designated for intervention studies. Thus, all non-interventional studies (ie, observational studies) were excluded for quality assessment. For easy assessment, the 23 items were divided into two parts: (1) simple items (ie, items 1–12, 16–18 and 22) and (2) complex items (ie, items 13–15, 19–21 and 23), which contained multiple subitems that needed to be evaluated individually. For example, item 15 (study type) was composed of six subitems: type of study, randomised method, allocation concealment mechanism, masking method, assignment and phase. Additional item 23 (results links) was composed of two subitems: resultant publication links and change history. Because there might be some changes during the process of a trial, providing information about the change history in a timely manner is also important in publications. Therefore, such items were divided into different subitems for evaluation. In addition, according to TCM characteristics, the following information about TCM background and rationale, TCM diagnosis criteria, TCM intervention and TCM outcome were included for assessment. The details are as follows: (1) description of TCM intervention, (2)TCM diagnosis criteria and its basis, (3) TCM-related outcome and (4) TCM background and rationale. Each simple item or subitem of complex items was assessed as '1' score if fully reported or '0' score if incompletely reported or absent. The detailed scoring methods of each item are presented in online supplementary 1 S1. In order to increase the accuracy of scoring, the predefined scoring rules were tested on 30 random records among 17 registries first, and then subsequently applied to all records. After the scoring rules were determined, two researchers (XuZ and RT) assessed the trials independently, and the results were double checked and any problems or ambiguous were resolved by discussion with Professor ZB.

All data were collected and recorded in Microsoft Office Excel (V.2016). Categorical data are presented as number (n) and per cent (%).

## RESULTS

The initial search identified 4326 records. Nine hundred and eighty-seven trials were excluded due to non-TCM study. A total of 3339 TCM registration trials were included for characteristic descriptive analysis, including 2955 interventional studies and 384 non-intervention studies (figure 1). An ID list of all included records is provided in online Supplementary 2 S2.

### Descriptive analysis of included studies

#### Distribution of years and registries

A total of 3339 TCM trials were registered during the period of 1999–2017. The number of registrations increased from 3 in 1999 to 755 in 2017, a dramatic increase. From 1 January 1999 to 1 July 2005, the total number of registered TCM trials was 83. After the mandatory trial registration requirement proposed by ICMJE in 1 July 2005, the total number of registered TCM trials was increased steadily. However, in the recent 3 years (from 2015 to 2017), the number of registered TCM trials grew rapidly, which accounted for 51% (1701/3339) of all TCM registered trials (figure 2).

TCM trials were found in 15 registries sorted in descending order of number of trials registered for 1999–2017 as follows: ChiCTR (1480), ClinicalTrials.gov (1094), IRCT (175), ISRCTN (146), CRIS (129), ANZCTR (120), JPRN (89), REBEC (33), DRKS (27), TCTR (16), CTRI (12), EU-CTR (6), NTR (5), PACTR (5) and SLCTR (2). No TCM registration records were found in RPCEC and REPEC. The number of ChiCTR (ie, China) and ClinicalTrials.gov (ie, USA) altogether accounted for 77.1% (2574/3339) of all TCM trials in the world (figure 3). The first centre that registered TCM trials is ClinicalTrials.gov starting from 1999, followed by ISRCTN (ie, UK) and ANZCTR (ie, Australian and New Zealand), which were the three primary registries in the early time. In 2007,



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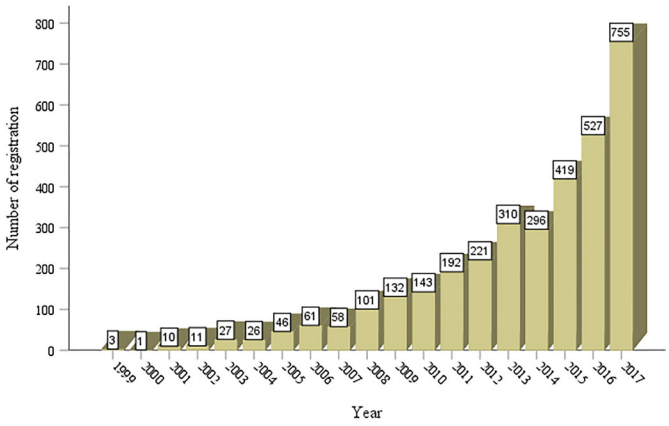


**Figure 2** Number of registration of TCM clinical trials from 1999 to 2017. TCM, traditional Chinese medicine.

ChiCTR was authorised by ICTRP as the fourth primary registry and an increasing number of TCM trials was registered in ChiCTR. Since 2012, ChiCTR has had, and continues to have, the largest number of TCM trial in the world (figure 4).

### Category of sponsor institution, study type and intervention type

The common primary sponsors were hospitals (51.4%, 1716/3339) and universities (33.6%, 1122/3339). Interventional study (88.5%, 2955/3339), as a major type of study, included a variety of TCM interventions, in which acupuncture contributed the largest proportion (50.2%, 1484/2955), followed by Chinese herbal medicines (30.1%, 889/2955). In addition, a small proportion of

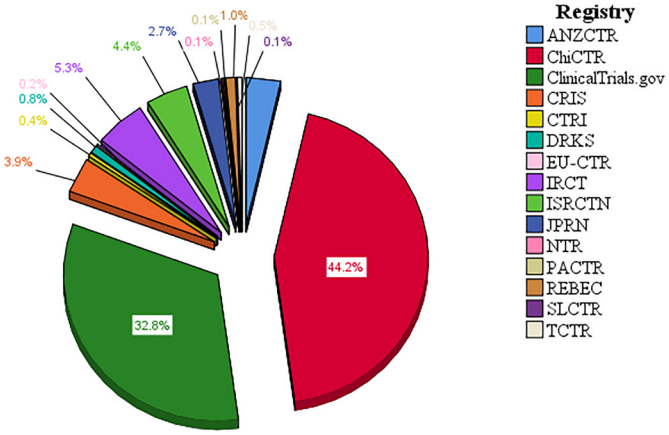


**Figure 3** Distribution of TCM clinical trials registration among 15 registries during 1999–2017. ANZCTR, Australian New Zealand Clinical Trials Registry; ChiCTR, Chinese Clinical Trial Registry; CRIS, Clinical Research Information Service-Republic of Korea; CTRI, Clinical Trials Registry-India; DRKS, German Clinical Trials Register; EU-CTR, EU Clinical Trials Register; IRCT, Iranian Registry of Clinical Trials; ISRCTN, International Standard Randomized Controlled Trial Number Register; JPRN, Japan Primary Registries Network; NTR, Netherlands National Trial Register; PACTR, Pan African Clinical Trial Registry; REBEC, Brazilian Clinical Trials Registry; SLCTR, Sri Lanka Clinical Trials Registry; TCM, traditional Chinese medicine; TCTR, Thai Clinical Trials Register.

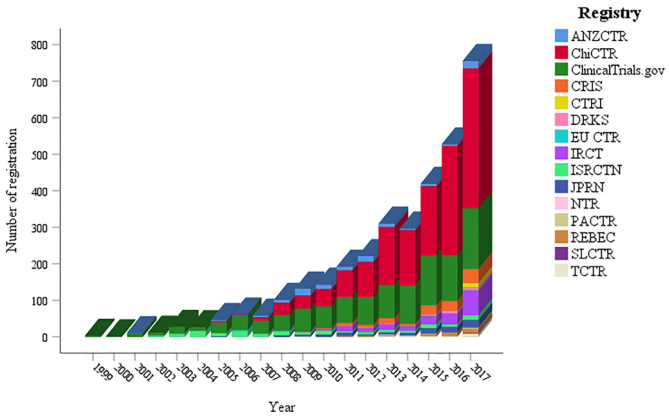


**Figure 4** Number of registration of TCM clinical trials in each registry, each year. ANZCTR, Australian New Zealand Clinical Trials Registry; ChiCTR, Chinese Clinical Trial Registry; CRIS, Clinical Research Information Service-Republic of Korea; CTRI, Clinical Trials Registry-India; DRKS, German Clinical Trials Register; EU-CTR, EU Clinical Trials Register; IRCT, Iranian Registry of Clinical Trials; ISRCTN, International Standard Randomized Controlled Trial Number Register; JPRN, Japan Primary Registries Network; NTR, Netherlands National Trial Register; PACTR, Pan African Clinical Trial Registry; REBEC, Brazilian Clinical Trials Registry; SLCTR, Sri Lanka Clinical Trials Registry; TCM, traditional Chinese medicine; TCTR, Thai Clinical Trials Register.

trials had more than one intervention (3.1%, 93/2955). The relevant data are presented in table 1.

### Characteristics of trial design and recruitment

The common design was randomised (84.0%, 2805/3339) parallel (72.5%, 2422/3339) study. The blinding (29.2%, 973/3339), such as single/double/triple blind, was commonly applied rather than open label (13.4%, 447/3339) design, but more than half (57.5%, 1919/3339) did not report blinding information. The purpose of treatment (53.3%, 1781/3339) was reported in a majority, but 36.7% (1225/3339) did not report trial purpose. Single centre (88.9%, 2970/3339) was the main choice for TCM trials. The sample size varied between 0 and 100 (55.6%, 1855/3339) and 101–500 (36.9%, 1231/3339); relatively few (6.4%, 213/3339) used large samples (>500). The gender of participants was mainly both male and female (81.9%, 2735/3339). The main country of recruitment was the Chinese Mainland (57.4%, 1918/3339), following by the USA (9.2%, 308/3339). For recruitment status, completed and uncompleted trials accounted for 44.1% (1473/3339) and 55.9% (1866/3339), respectively. More detailed information is presented in table 2.

### Prospective and retrospective registration

Thirty-nine per cent (1301/3339) of all included trials were retrospective registrations, distributed in 14 registries. Among these 14 registries, 57.1% (8/14) showed a high percentage (>40%) of retrospective registration. More detailed information is shown in table 3.



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**Table 1** Descriptive information of sponsor, study and intervention type

| Category | Number of records | Percentage of records (%) |
|---|---|---|
| **Primary sponsor*** | | |
| Hospital | 1716 | 51.4 |
| University | 1122 | 33.6 |
| Research institute | 344 | 10.3 |
| Government | 86 | 2.6 |
| Individual | 48 | 1.4 |
| Industry | 17 | 0.5 |
| Not reported | 6 | 0.2 |
| **Type of study†** | | |
| Interventional study | 2955 | 88.5 |
| Observational study | 302 | 9.0 |
| Others‡ | 82 | 2.5 |
| **Intervention type§** | | |
| Acupuncture | 1484 | 50.2 |
| Chinese herbal medicines¶ | 889 | 30.1 |
| Tuina/massage | 174 | 5.9 |
| Moxibustion | 93 | 3.1 |
| Acupoint therapy** | 82 | 2.8 |
| Cupping | 55 | 1.9 |
| Qigong (Tai Chi, Baduanjin, Wuqinxi and so on) | 51 | 1.7 |
| Others†† | 14 | 0.5 |
| Guasha (spooning) | 1 | 0.0 |
| Multiple interventions‡‡ | 93 | 3.1 |
| Not specified§§ | 19 | 0.6 |

*Primary sponsor refers to the individual, organisation, group or other legal entity that takes responsibility for initiating, managing and/or financing a study. The primary sponsor is responsible for ensuring that the trial is properly registered. The primary sponsor may or may not be the main funder.
†The response options of type of study usually interventional or observational, as recommended in International standards for CTR.
‡ChiCTR alone offered other options for type of study, such as cause research (12), diagnostic test study (10), epidemiological research (12), prevention study (7), relative factors research (34), prognosis study (2) and basic science (5).
§Only interventional studies (n=2955) were used for the category of intervention type.
¶Chinese herbal medicines include Chinese medicinal substances (also referred to as Chinese materia medica, represented by single herb), and their formulas are usually formed with more than two herbs (ie, self-designed formulas or patent proprietary formulas).[55]
**Acupoint therapy included acupressure, acupoint injection, catgut embedment in acupoint and acupoint application (ie, Sanfu Tie and Sanjiu Tie).
††Others consisted of diet therapy of TCM, TCM health/psychological education, TCM five elements music therapy and so on.
‡‡Multiple interventions refer to combination of TCM therapies. For example, acupuncture and moxibustion, acupuncture and cupping, massage and cupping, Chinese herbal medicine plus any TCM external treatment and so on.
§§Some general name of interventions (such as TCM therapy based on syndrome differentiation, TCM treatment, TCM therapy and so on) were classified as 'not specified' when intervention specifics were not provided clearly.
CTR, clinical trial registration; TCM, traditional Chinese medicine.

**Table 2** General information of trial design and recruitment

| Category | Specifics | Number of records | Percentage of records (%) |
|---|---|---|---|
| **Study design** | | | |
| Assignment | Single arm | 296 | 8.9 |
| | Parallel | 2422 | 72.5 |
| | Crossover | 122 | 3.7 |
| | Factorial | 42 | 1.3 |
| | Not reported | 457 | 13.7 |
| Method of allocation | Randomised | 2805 | 84.0 |
| | Quasirandomised | 27 | 0.8 |
| | Non-randomised | 220 | 6.6 |
| | Not reported | 287 | 8.6 |
| Masking | Single blind | 446 | 13.4 |
| | Double blind | 470 | 14.1 |
| | Triple blind | 57 | 1.7 |
| | Open label | 447 | 13.4 |
| | Not reported | 1919 | 57.5 |
| Purpose | Treatment | 1781 | 53.3 |
| | Prevention | 81 | 2.4 |
| | Supportive care | 148 | 4.4 |
| | Basic science | 64 | 1.9 |
| | Health services research | 8 | 0.2 |
| | Diagnosis | 22 | 0.7 |
| | Educational/counselling/training | 10 | 0.3 |
| | Not reported | 1225 | 36.7 |
| Trial participating centre | Multicentre | 369 | 11.1 |
| | Single centre | 2970 | 88.9 |
| **Participate sample** | | | |
| Target size | 0–100 | 1855 | 55.6 |
| | 101–500 | 1231 | 36.9 |
| | >500 | 213 | 6.4 |
| | Not reported | 40 | 1.2 |
| Gender | Male | 107 | 3.2 |
| | Female | 474 | 14.2 |
| | Both | 2735 | 81.9 |
| | Not reported | 23 | 0.7 |
| **Countries of recruitment*** | China mainland | 1918 | 57.4 |
| | USA | 308 | 9.2 |
| | Korea | 191 | 5.7 |
| | Iran | 181 | 5.4 |
| | Japan | 93 | 2.8 |
| | Taiwan | 88 | 2.6 |

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Table 2 Continued

| Category | Specifics | Number of records | Percentage of records (%) |
|---|---|---|---|
| | Australia | 82 | 2.5 |
| | German | 70 | 2.1 |
| | Brazil | 67 | 2.0 |
| | UK | 65 | 1.9 |
| | Hong Kong | 39 | 1.2 |
| **Recruiting status** | | | |
| | Completed | 1473 | 44.1 |
| | Recruiting | 1166 | 34.9 |
| | Not yet recruiting | 650 | 19.5 |
| | Stopped/terminated or suspending | 50 | 1.5 |

*Total descriptive information in this category is presented in online supplementary 3 S3. Countries with <1.0% proportion were not listed in the table 2.

### Sharing results in the CTR System

Among the 3339 included trials, 428 (12.8%) linked their resultant publications to the trial registration system; of these, 300 (70.1%) were completed trials. There were seven registries (47% of 15 registries) that provided link to resultant publications, while eight registries (43% of 15 registries), including ChiCTR, had no links to resultant publications. Of all registries, ClinicalTrials.gov had a higher proportion (72.9%, 312/428) in resultant publications sharing. More detailed information is shown in table 4.

## Quality assessment of CTR with TCM as intervention

### Targeted CTR records from different registries

As noted in Methods above, the total number of eligible trials with TCM interventions was 2955. The majority (75%) of eligible trials came from ChiCTR (41%, 1200/2955) and ClinicaTrials.gov (34%, 1013/2955); the remaining 25% came from the other 13 registries (ie, ANZCTR, CRIS, DRKS, IRCT, ISRCTN, JPRN and so on). In other words, most of TCM trial registrations are being done in China and the USA.

### Simple items

The total reporting rate of these 16 items varied from 39.9% to 100%. Information on the primary registry and trial identifying number, date of registration in the primary registry, public title and recruitment status was present in all trials. Most trials (>90%) mentioned the following items: primary sponsor, contact for public queries, contact for scientific queries, scientific title, countries of recruitment, health condition(s) or problem(s) studied, date of first enrolment and target sample size. More than half of trials provided items of source(s) of monetary or material support and approvals. Less than half of trials provided information of secondary identifying numbers and secondary sponsor(s).

However, in terms of the lowest reporting items, there were some differences between different groups. In ChiCTR, 8.8% of trials reported item of secondary identifying numbers. In ClinicalTrials.gov, no trial provided information on source(s) of monetary or material support and approvals. In other registries, 19.1% of trials provided information of secondary sponsor(s) (table 5).

Table 3 Descriptive information of registration status

| Category | Number of records | Percentage of records (%) |
|---|---|---|
| **Registration status*** | | |
| Prospective registration | 2038 | 61.0 |
| Retrospective registration | 1301 | 39.0 |
| **Distribution of retrospective registration†** | | |
| ANZCTR | 34 | 28.3 |
| ChiCTR | 490 | 33.1 |
| ClinicalTrials.gov | 429 | 39.2 |
| CRIS | 71 | 55.0 |
| EU-CTR | 1 | 16.7 |
| DRKS | 14 | 51.9 |
| IRCT | 103 | 58.9 |
| ISRCTN | 85 | 58.2 |
| JPRN | 40 | 44.9 |
| NTR | 1 | 20.0 |
| PACTR | 3 | 60.0 |
| REBEC | 19 | 57.6 |
| TCTR | 7 | 43.8 |
| CTRI | 4 | 33.3 |

*Prospective is when (by ICTRP standards) the date of the 'date of registration' field is prior to the date of the 'date of first enrolment' field. Otherwise is considered retrospective.
†Fourteen included registries (except SLCTR) have TCM trials with retrospective registration. To calculate the proportion of retrospective registration in each registry, the percentage of records was based on the total number of every registry itself, and the trial number of each registry is presented in figure 2. Take ChiCTR for example, 33.1%=490/1480 (TCM trials with retrospective registration in ChiCTR/all TCM trials in ChiCTR).
ANZCTR, Australian New Zealand Clinical Trials Registry; ChiCTR, Chinese Clinical Trial Registry; CRIS, Clinical Research Information Service-Republic of Korea; CTRI, Clinical Trials Registry-India; DRKS, German Clinical Trials Register; EU-CTR, EU Clinical Trials Register; ICTRP, International Clinical Trials Registry Platform; IRCT, Iranian Registry of Clinical Trials; ISRCTN, International Standard Randomized Controlled Trial Number Register; JPRN, Japan Primary Registries Network; NTR, Netherlands National Trial Register; PACTR, Pan African Clinical Trial Registry; REBEC, Brazilian Clinical Trials Registry; SLCTR, Sri Lanka Clinical Trials Registry; TCM, traditional Chinese medicine; TCTR, Thai Clinical Trials Register.

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Table 4 Descriptive information of registered trials with publications links

| Category | Number of records | Percentage of records (%) |
|---|---|---|
| **All trials** | | |
| Linked publications | 428 | 12.8 |
| Unlinked publications | 2911 | 87.2 |
| **Trials linked to publications** | | |
| Completed trials* | 300 | 70.1 |
| Uncompleted trials | 128 | 29.9 |
| **Registries with links to publications†** | | |
| ClinicalTrials.gov | 312 | 72.9 |
| ISRCTN | 67 | 15.7 |
| ANZCTR | 18 | 4.2 |
| DRKS | 12 | 2.8 |
| CRIS | 10 | 2.3 |
| JPRN | 8 | 1.9 |
| NTR | 1 | 0.2 |

*'Completed' is refers to the recruitment status, not the completion date of a trial. The number of trials that completed the recruitment of participants was 300.
†Eight registries, namely ChiCTR, EU-CTR, IRCT, PACTR, REBEC, CTRI, SLCTR and TCTR, have no links to publications or resulting data and, therefore, are not listed in the table.
ANZCTR, Australian New Zealand Clinical Trials Registry; ChiCTR, Chinese Clinical Trial Registry; CRIS, Clinical Research Information Service-Republic of Korea; CTRI, Clinical Trials Registry-India; DRKS, German Clinical Trials Register; EU-CTR, EU Clinical Trials Register; IRCT, Iranian Registry of Clinical Trials; ISRCTN, International Standard Randomized Controlled Trial Number Register; JPRN, Japan Primary Registries Network; NTR, Netherlands National Trial Register; PACTR, Pan African Clinical Trial Registry; REBEC, Brazilian Clinical Trials Registry; SLCTR, Sri Lanka Clinical Trials Registry; TCTR, Thai Clinical Trials Register.

## Complex items

The total reporting rate of these seven items presented in a descending order as: interventions (62.9%), study type (61.9%), lay summary or synopsis (61.6%), key inclusion and exclusion criteria (52.8%), primary outcome(s) and key secondary outcomes (45.1%), and results links (14.1). The detailed TCM information were also assessed, including: (1) details of TCM intervention(s) (50.8%), (2) TCM diagnosis criteria (14.1%) and basis (10.1%), (3) TCM-related outcome (7.4%) and (4) TCM background and rationale (32.9%). Specific analyses are as follows (table 6).

### *Item 13: interventions*

Detailed descriptions of TCM intervention(s) were reported in 1500 (50.8%) trials. Although most provided basic information of dosage form, dosage, frequency and duration, information on details of TCM, such as the ingredients in compound formulas, the technique details of moxibustion, cupping or other non-pharmacy therapies and so on, were seriously inadequate or totally absent. For example, in ChiCTR, only 83 (6.9%) trials provided detailed information for TCM intervention(s), 93.1% did not report ingredients and its dosage in Chinese herbal medicine formulas (ie, for drug interventions) or did not report operating methods for non-drug intervention(s), even some did not provide any description except the name(s) of intervention(s).

### *Item 14: key inclusion and exclusion criteria*

Most (>95%) trials provided information regarding the inclusion and exclusion of age, sex and western medicine diagnosis of participants. By contrast, very few (417 or 14.1%) trials used TCM diagnoses of condition(s) studied, including the name of 'TCM disease' or 'TCM syndrome/zheng'. Even fewer (42 or 10.1%) provided the specific basis of TCM diagnosis criteria.

### *Item 15: study type*

The type of study was reported in most (>90%) trials, except those registered in IRCT, and most (>99%) reported assignment information. Information as to whether the interventions were randomised or not was reported in 1779 (60.2%) trials, and for randomised trials, only 741 (25.1%) trials mentioned the allocation concealment mechanism. Complete information of masking method, including whether masking used and, if so, who is masked, was reported in 1686 (57.1%) trials. In addition, 1040 (35.2%) trials reported the trial phase.

### *Items 19 and 20: primary outcome(s) and key secondary outcomes*

A total of 2919 (98.8%) trials provided the primary outcome(s) and 2227 (75.4%) reported key secondary outcomes. For these outcomes, the average reporting rates of measurement and timepoint(s) were 32.4% and 49.8%, respectively. Especially in ChiCTR, information on measurement and timepoint(s) were seldom reported (<9%). For TCM trial characteristics, 220 (7.4%) trials used TCM-related outcome(s), and 442 (15.0%) trials reported adverse event outcome(s).

### *Additional item 21: lay summary or synopsis*

Most (>96%) reported purpose of trials, and 55.6% provided a short description of included participants, interventions and outcome(s). In terms of study hypothesis or background, 972 (32.9%) trials provided information on TCM background and rationale; of these 972, only 88 were registered in ChiCTR.

### *Additional item 23: results links*

Only 224 (7.6%) interventional trials linked the resulting publications to registration platform; of these, 170 were registered in ClinicalTrials.gov. In addition, 610 (20.6%) trials provided information of any change in records; of these 571 were also registered in ClinicalTrials.gov.



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Table 5 Quality assessment of registration information on simple items (n [%])*

| No. | Simple items (n=16) | Total (n=2955) | ChiCTR (n=1200) | ClinicalTrials.gov (n=1013) | Other registries (n=742) |
|---|---|---|---|---|---|
| 1 | Primary registry and trial identifying number | 2955 (100) | 1200 (100) | 1013 (100) | 742 (100) |
| 2 | Date of registration in primary registry | 2955 (100) | 1200 (100) | 1013 (100) | 742 (100) |
| 3 | Secondary identifying numbers | 1469 (49.7) | 106 (8.8) | 1013 (100) | 350 (47.2) |
| 4 | Source(s) of monetary or material support | 1885 (63.8) | 1153 (96.1) | 0 (0) | 732 (98.7) |
| 5 | Primary sponsor | 2950 (99.8) | 1199 (99.9) | 1011 (99.8) | 740 (99.7) |
| 6 | Secondary sponsor(s) | 1179 (39.9) | 722 (60.2) | 315 (31.1) | 142 (19.1) |
| 7 | Contact for public queries | 2726 (92.3) | 1200 (100) | 896 (88.5) | 630 (84.9) |
| 8 | Contact for scientific queries | 2695 (91.2) | 1200 (100) | 758 (74.8) | 737 (99.3) |
| 9 | Public title | 2955 (100) | 1200 (100) | 1013 (100) | 742 (100) |
| 10 | Scientific title | 2928 (99.1) | 1200 (100) | 1004 (99.1) | 724 (97.6) |
| 11 | Countries of recruitment | 2871 (97.2) | 1197 (99.8) | 932 (92.0) | 742 (100) |
| 12 | Health condition(s) or problem(s) studied | 2950 (99.8) | 1200 (100) | 1013 (100) | 737 (99.3) |
| 16 | Date of first enrollment | 2954 (99.9) | 1199 (99.9) | 1013 (100) | 742 (100) |
| 17 | Target sample size | 2950 (99.8) | 1200 (100) | 1012 (99.9) | 738 (99.5) |
| 18 | Recruitment status | 2955 (100) | 1200 (100) | 1013 (100) | 742 (100) |
| 22† | Approvals | 1612 (54.6) | 1157 (96.4) | 0 (0) | 455 (61.3) |
| Total items | Average report percentage (%) | 86.7 | 91.3 | 80.3 | 87.9 |

*The total number of eligible trials with TCM interventions was 2955. Of them, 1200 trials were registered in ChiCTR and 1013 came from ClinicaTrials.gov. For purposes of calculation and comparison, we treated the other 13 registries (ie, ANZCTR, CRIS, DRKS, IRCT, ISRCTN, JPRN, etc.) as a single group. There included three groups of: (1) ChiCTR (1200 trials), (2) ClinicaTrials.gov (1013 trials) and (3) other registries (742 trials).
†Additional item 22.
ANZCTR, Australian New Zealand Clinical Trials Registry; ChiCTR, Chinese Clinical Trial Registry; CRIS, Clinical Research Information Service-Republic of Korea; DRKS, German Clinical Trials Register; IRCT, Iranian Registry of Clinical Trials; ISRCTN, International Standard Randomized Controlled Trial Number Register; JPRN, Japan Primary Registries Network.

## DISCUSSION

### Current situation of CTR of TCM

In this study, we retrieved all registered trials of TCM from the WHO ICTRP during 1999–2017 and assessed the overall quality to identify possible deficiencies and problems in CTR of TCM. Our results indicate that the number of TCM trial registrations has increased rapidly since 1 July 2005, the year mandatory trial registration was proposed, especially in the recent 3 years (2015–2017) when 51% of all 3339 TCM trials registered in the past 19 years were recorded. The number of registries with TCM trials has also increased, now up to 15 all over the world. The largest number of TCM trials has been registered with the Chinese registry, ChiCTR, while the second biggest centre was the US registry, ClinicalTrials.gov. A percentage of 88.5 of all TCM registered trials were interventional studies, and the major interventions were acupuncture and Chinese herbal medicines. The most common design for TCM trials has been randomised, parallel trials at a single trial centre and enrolled participants typically number <100 subjects.

In this study, we found several problems in CTR of TCM. First, retrospective registration. Timely registration means prospective registration, that is, registering the trial before it begins. Prospective registration can avoid redundancy in studies, help patients learn about trials in which they might participate and ensure that trials are not registered based on their results.[33] Unfortunately, of 3339 registered TCM trials, 39% were retrospective, distributed in 14 of the 15 registries. This appears to be a problem in all registries, and one that prevents registration from achieving its full potential in advancing TCM clinical research.

Second, failure to link publications to registration. We found that only 12.8% of TCM trials linked their resulting publications to the registry system. It is irresponsible not to make the results available to the public after trial registration,[34 35] even there might exist some differences between the published results and registration information.[36 37] In addition, there might be some changes during the process of a trial. If the registered data were not up-to-date or change history was not provided during the trial, it is more difficult to figure out the consistency between published results and its previous registered information. Thus, when publications are linked to registration information, the public and other researchers can clearly relate original intention with changes made and results obtained.

Third, inadequate reporting. More than half of the minimum 20 items and optional additional three items were not adequately reported, especially in some key information of participants, intervention, comparison



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Table 6 Quality assessment of registration information on complex items (n [%])

| No. | Complex items (n=7) | Specifics | Total (n=2955) | ChiCTR (n=1200) | ClinicalTrials.gov (n=1013) | Other registries (n=742) |
|---|---|---|---|---|---|---|
| 13 | Interventions | 13.1 Name | 2865 (97.0) | 1111 (92.6) | 1013(100) | 741 (99.9) |
| | | 13.2 TCM description* | 1500 (50.8) | 83 (6.9) | 911 (89.9) | 506 (68.2) |
| | | 13.3 More interventions | 1019 (34.5) | 436 (36.3) | 526 (51.9) | 57 (7.7) |
| | | 13.4 Controlled interventions | 2048 (69.3) | 508 (42.3) | 878 (86.7) | 662 (89.2) |
| | | Total average | 1859 (62.9) | 535 (44.6) | 832 (82.1) | 492 (66.3) |
| 14 | Key inclusion | 14.1 Age | 2839 (96.1) | 1133 (94.4) | 1013(100) | 693 (93.4) |
| | and exclusion | 14.2 Sex | 2934 (99.3) | 1185 (98.8) | 1013(100) | 736 (99.2) |
| | Criteria | 14.3 Conventional medicine clinical diagnosis | 2941 (99.5) | 1199 (99.9) | 1010 (99.7) | 732 (98.7) |
| | | 14.4 Have healthy volunteers | 185 (6.3) | 19 (1.6) | 131 (12.9) | 35 (4.7) |
| | | 14.5 Adopted TCM diagnosis† | 417 (14.1) | 363 (30.3) | 49 (4.8) | 5 (0.7) |
| | | 14.6 TCM diagnosis with clearly criteria‡ | 42 (10.1) | 29 (8.0) | 11 (22.4) | 2 (40.0) |
| | | Total average | 1560 (52.8) | 655 (54.6) | 538 (53.1) | 367 (49.5) |
| 15 | Study type | 15.1 Type of study | 2796 (94.6) | 1200(100) | 1013(100) | 583 (78.6) |
| | | 15.2 Randomised/non-randomised | 1779 (60.2) | 1155 (96.3) | 312 (30.8) | 312 (42.0) |
| | | 15.3 Allocation concealment mechanism | 741 (25.1) | 323 (26.9) | 117 (11.5) | 301 (40.6) |
| | | 15.4 Masking methods/open label | 1686 (57.1) | 251 (20.9) | 982 (96.9) | 453 (61.1) |
| | | 15.5 Assignment (single arm, parallel and so on) | 2929 (99.1) | 1199 (99.9) | 1013 (100) | 717 (96.6) |
| | | 15.6 Phase (if applicable) | 1040 (35.2) | 537 (44.8) | 354 (34.9) | 149 (20.1) |
| | | Total average | 1829 (61.9) | 778 (64.8) | 632 (62.4) | 419 (56.5) |
| 19 | Primary | 19.1 Name | 2919 (98.8) | 1197 (99.8) | 987 (97.4) | 735 (99.1) |
| | Outcome(s) | 19.2 Measurement | 1157 (39.2) | 53 (4.4) | 740 (73.1) | 364 (49.1) |
| | | 19.3 Time point(s) | 1538 (53.6) | 105 (8.8) | 973 (96.1) | 505 (68.1) |
| 20 | Key secondary | 20.1 Name | 2227 (75.4) | 748 (62.3) | 856 (84.5) | 623 (84.0) |
| | Outcomes | 20.2 Measurement | 760 (25.7) | 43 (3.6) | 475 (46.9) | 242 (32.6) |
| | | 20.3 Time point(s) | 1359 (46.0) | 69 (5.8) | 850 (83.9) | 440 (59.3) |
| 19/20 | Outcome(s)§ | 19/20.1 Include TCM-related outcome(s)¶ | 220 (7.4) | 110 (9.2) | 105 (10.4) | 5 (0.7) |
| | | 19/20.2 Included adverse event outcome(s)** | 442 (15.0) | 174 (14.5) | 150 (14.8) | 118 (15.9) |
| | | Total average | 1333 (45.1) | 312 (26.0) | 642 (63.4) | 379 (51.1) |
| 21†† | Lay summary | 21.1 Primary purpose | 2844 (96.2) | 1200 (100) | 1013 (100) | 631 (85.0) |
| | or synopsis | 21.2 Study hypothesis/ background (with TCM theories)‡‡ | 972 (32.9) | 88 (7.3) | 647 (63.9) | 237 (31.9) |
| | | 21.3 Description of PIO | 1644 (55.6) | 223 (18.6) | 791 (78.1) | 630 (84.9) |
| | | Total average | 1820 (61.6) | 504 (42.0) | 817 (80.7) | 499 (67.3) |
| 23†† | Results links | 23.1 Results publications, websites and so on | 224 (7.6) | 0 (0) | 170 (16.8) | 54 (7.3) |
| | | 23.2 Change history | 610 (20.6) | 0 (0) | 571 (56.4) | 39 (5.3) |
| | | Total average | 418 (14.1) | 0 (0) | 371 (36.6) | 47 (6.3) |

Continued



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Table 6 Continued

| No. | Complex items (n=7) | Specifics | Total (n=2955) | ChiCTR (n=1200) | ClinicalTrials.gov (n=1013) | Other registries (n=742) |
|---|---|---|---|---|---|---|
| Total items | Average report percentage (%) | | 50.4 | 38.6 | 63.1 | 49.5 |

*In item 13, the description of TCM intervention details was added as a subitem (ie, 13.2), which reflected TCM characteristic in the requirement of intervention item. Except the requirements of TRDS in this item, such as dosage form, dosage, frequency and duration and so on, the more detailed information of TCM specifics were added as criteria to be assessed. For example, the ingredients in compound formula could be reported in trials with TCM herbal medicines, and the basic technique details could be reported in trials with TCM non-pharmacy therapies, such as acupuncture and moxibustion, cupping, guasha and so on.
†In item 14, whether TCM diagnosis criteria, for disease or 'zheng', was adopted was added as a subitem (ie, 14.5).
‡The percentage figure in brackets = (trials with clear basis of TCM diagnostic criteria/trials with TCM diagnostic criteria) × 100%.
§19/20 outcome(s) included 19 (primary outcomes) and 20 (key secondary outcomes).
¶In items of outcome(s), TCM-specific outcomes was added as a subitem (ie, 19/20.1).
**Adverse event(s) were listed in the outcome(s) column as a subitem (ie,19/20.2), because there were many trials with purposes of efficacy and safety of TCM interventions.
††Additional items 21 and 23.
‡‡In this subitem, the assessment criterion was whether it included TCM rationale/background content, no matter how much.
ChiCTR, Chinese Clinical Trial Registry; PIO means participants, interventions and outcomes; TCM, traditional Chinese medicine; TRDS, Trial Registration Data Set.

and outcomes. Although it is generally believed that the completeness of these items might be related to the establishment time of the registry,[38] such as the registries established after the announcement time of the WHO TRDS would have better completeness in item formats than those established prior to that time,[39] this was not discovered in this study. ChiCTR with the largest number of registered TCM trials, is a good example. WHO TRDS was announced in May 2007, and ChiCTR was established soon after. However, more than half of data items were scored by a lower reporting rate (<45%). In comparison, ClinicalTrials.gov, the second biggest registry with TCM trials, was established prior to May 2007 and had slight increase or reduction of some items compared with WHO TRDS.[40] However, the completeness of data items in ClinicalTrials.gov was better than ChiCTR because only five items were scored by a lower reporting rate (<45%).

Fourth, insufficient or absence of information on TCM characteristics. Among the 2955 registered trials, 49.2% lacked specific descriptions of TCM intervention(s) and 67.1% did not give related TCM theories in the contents of background and rationale of the study. The selection of different TCM interventions and their technical methods treat different disease are based on TCM theories. Thus, it is better to include intervention details and the TCM theoretical basis in the registration information of TCM trials, which can reflect the unique characteristics of TCM theory, principles, methods and treatments. Although available reporting standards of TCM studies recommended the combined use of western medicine and TCM syndrome/zheng factors in the diagnostic criteria and outcome(s),[41 42] most TCM trial registrations did not include TCM diagnostic criteria (85.9%) and even more did not use TCM outcome(s) (92.6%). If a TCM CT does not consider TCM syndrome differentiation ('zheng') or use TCM 'zheng'-related outcome(s), participants may not be properly treated and/or the efficacy of TCM intervention(s) may not be evaluated properly.[43] Therefore, although ensuring the completeness of WHO TRDS is the first step in assessing the quality of a registered trial, the current TCM trial registration still cannot fulfil the purposes of CTR owing to insufficient information on TCM details.

## Improvement measures and suggestions

The primary purposes of CTR are to improve transparency of data, reduce bias and avoid repeating research.[44] Fulfilling these purposes is considered to be the ethical responsibility of the scientific community.[45] To achieve these purposes, prospective registration with complete details of protocol, updates of changes, summary results and links to resulting publications are necessary for each clinical trial.[46 47] Unfortunately, as shown by the above statistics, some deficiencies in the registration quality of TCM trials mean failure to achieve the benefits of CTR. This unsatisfactory quality made trial registration only aimed to obtain a registration ID number,[48] which is required as a precondition to publish results in journals with high-impact factors.[49] Based on the current situation of CTR of TCM, some improvements are needed.

On one hand, it is necessary to practice the requirements of ICMJE and WHO ICTRP, especially in terms of prospective registration, full completion of TRDS and results sharing. This could be achieved by concerted efforts from journal editors, registries and researchers and is already being done. In July 2017, ICMJE issued



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the following data sharing statement: '*As of July 1, 2018, manuscripts submitted to ICMJE journals that report the results of clinical trials must contain a data sharing statement. Clinical trials that begin enrolling participants on or after January 1, 2019, must include a data sharing plan in the trial's registration. If the data sharing plan changes after registration this should be reflected in the statement submitted and published with the manuscript, and updated in the registry record*'.[50] Similarly, for the WHO registry network, in November 2017, four new items (ie, ethics review, completion date, summary results and IPD sharing statement) have been added to the WHO TRDS such that its updated version 1.3 now contains 24 items.[51] Before version 1.3, there were three previous versions (including versions 1.1, 1.2 and 1.2.1), which always included 20 items as the minimum amount of trial information that must appear in a register in order for a given trial to be considered fully registered. In the explanatory document of 'International Standards for Clinical Trial Registries', published in November 2012, optional additional three items were provided as ICTRP recommended data items. Thus, in this study, the minimum requirement of 20 items and additional three items were together adopted to assess the reporting quality of TCM trials registered before 1 January 2018. Compared with the previous TRDS version, this new list of 24 items especially emphasises the sharing of results and individual participant data. Meanwhile, a new version of the document 'International Standards for Clinical Trial Registries' is being drafted and will be published in 2018, and the ICTRP and the primary registries will be working to implement those changes by the end of 2019.[52] Consequently, starting from January 2018, complete trial registration will mean full completion of the updated 24 items of the WHO TRDS. In addition, some scholars suggested that the requirements of CTR in each country could be legislated to develop a mandatory system because legislation appears to be the most efficient and effective way to enforce triallists compliance with registration rules.[53]

On the other hand, information on the details of TCM characteristics were seriously insufficient. The main reason for this phenomenon is that TCM-specific items were not included in the WHO data set such that registries then lacked these requirements for TCM trials.[54] In other words, researchers were not asked to report these TCM-related items so they did not. The details of TCM registration items including TCM theory, diagnostic criteria, interventions and outcomes are distinctly different from those of Western medical interventional trials, and thus cannot be adequately captured by items designed or written for typical western CTs. Therefore, a series of standard registration recommendation data items for TCM key information in CTs are necessary to be developed as an extension version of WHO TRDS. This extension should include several special requirements for different types of TCM interventions, reference to Consolidated Standards of Reporting Trials extension for Chinese herbal medicine formulas 2017,[55] Revised Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA)[56] and The Standards for Reporting Interventions in Clinical Trials of Moxibustion (STRICTOM),[57] which reflected the unique characteristics in CTs of Chinese herbal medicines, acupuncture and moxibustion, respectively. We understand that some detailed requirements set of TCM interventions in the extension may not be easy to meet at this stage. It is expected to practice critically starting from the phase of trial registration for researchers, which is beneficial to the improvement of trial quality.[58] It maybe better to establish a TCM partner registry, which could collect the TCM extension of the TRDS and advise researchers to register their TCM trials with complete information. In August 2016, the Acupuncture-Moxibustion Clinical Trial Registry, a partner registry of the ChiCTR, was established.[59] Such a registry accepts CTR with acupuncture-moxibustion interventions and manages the trials' registration quality.[60] However, the registration quality of these acupuncture-moxibustion interventional trials were still difficult to improve because of the lack of standard registration recommendation data items for TCM interventional trials.

### Limitations

Our study has some limitations. First, this study included TCM registered trials up to 31 December 2017, at which time the WHO ICTRP had already been updated to 17 registries. There is chance that some TCM trials registered in other regions, which had not yet been included in ICTRP and have not been included in our study. Second, our study mainly focused on registering information from different registries instead of acquiring study protocols, which might influence the results due to incomplete information. Third, some TCM trials were conducted without being registered. This means that our results are not necessarily accurate; this situation could be worse than what we have observed in terms of prospective registration.

## CONCLUSION

The goal of CTR of TCM is to help the international recognition in TCM modernisation, and then, bring TCM into mainstream medicine. Specifically, the purposes of any registry are to make clinical study data available to the public and the research community; to reduce bias; and to prevent repetition in studies done, thereby ensuring efficient, objective, accurate transfer of information and progress in healthcare. The registration quality of CTs with TCM has been disappointing due to retrospective registration, unavailable links to resulting publications and inadequate reporting of WHO TRDS and TCM characteristics. The former three deficiencies are general problems in CTR, which can be improved by enforcing the existing policies (eg, the requirements of the ICMJE and the WHO ICTRP). More importantly, further measures are needed to solve the insufficient reporting of TCM information. This could be achieved by extending the WHO TRDS to include several additional



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items related to TCM specifics. It is extremely vital to develop a standard reporting recommendation of CTR of TCM, including items of TCM intervention(s), diagnosis criteria, outcome(s) and background theory that are based on the unique characteristics of TCM theory, principles, formulas and Chinese herbal medicines or other TCM treatments.

**Author affiliations**
[1]Chinese Clinical Trial Registry (Hong Kong), Hong Kong Chinese Medicine Clinical Study Centre, School of Chinese Medicine, Hong Kong Baptist University, Hong Kong, China
[2]Chinese Cochrane Centre, West China Hospital, Sichuan University, China Trial Registration Center, Chengdu, China
[3]Key Laboratory for Internal Chinese Medicine of Ministry of Education and Beijing, Dongzhimen Hospital, Beijing University of Chinese Medicine, Beijing, China
[4]Peking Union Medical College Hospital, China Academy of Medical Sciences, Beijing, China

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**Data sharing statement** The data used for this study can be freely downloaded from ICTRP search portal at http://apps.who.int/trialsearch/ and from the websites of some of the 17 individual registries. Some data of quality assessment in this study is available from the corresponding author on receiving a reasonable request.

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