

Investigation for quality of claimed “randomised controlled trials” published in China



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Background

- **A number of so-called randomised controlled trials (RCTs) have been published rapidly in China**
- **A systematic review had found that some countries include China publish unusually high proportions of positive results**

Vickers A, Goval N, Harland R, Rees R. Do certain countries produce only positive results? A systematic review of controlled trials. Controlled Clin Trials, 1998;19(2):159-66.
- **Publication bias was considered a possible reason**



Objective

- **Our objective of this study is to investigate the quality of RCTs published in Chinese journals**
- **To interpret the reasons why a high rate of positive results exists in these trials**
- **We hypothesized that the reasons of high rate of positive results resulted from**
 - **overestimate of treatment effects due to inadequate randomisation approaches and**
 - **did not conceal the random sequence of allocation in studies claimed “random allocation”**



Methods

- 21 investigators were trained in relevant knowledge before conducting the investigation
- We designed a special question processing to interview the authors

Processing of telephone interview for authors.doc



Methods

Inclusion criteria

- **Type of studies**
 - **We only included claimed ‘randomised controlled trials’ written by Chinese authors and published in Chinese journals**
 - **Any article claimed “randomised controlled trial”, “randomly allocated patients into two groups” was considered eligible**



Methods

Types of diseases

- **We selected some commonly encountered diseases include**
 - **respiratory tract infections, heart failure, hypertension, peptic ulcer, nephrotic syndrome, iron deficiency anemia, prostatic hyperplasia, psoriasis, esophageal cancer, pregnancy induced hypertension, angina pectoris, ovary cancer, Cardiomyopathy, icterohepatitis**



Methods

- **We searched in electronic database China National Knowledge Infrastructure (CNKI) from 1994 to June, 2005.**



Methods

- **The first author of claimed RCT at first been selected to interview by telephone; If the first author is unavailable, another author of the article was selected, depends on who could be contacted.**



Randomisation criteria

- Allocation sequence was generated from random number table, or calculator or computer random-number generator was considered eligible.
- Coin tossing or draw straws to decide which group the participant will be allocated to were considered ineligible randomisation approach due to unable to ensure free from influence of the inclination of participant for allocation and the participants will know the treatment allocation schedule very easy.



Randomisation criteria

- **If coin tossing or draw straws were performed independent from study population in order to generate random allocation sequence, it would be considered adequate randomisation.**
- **Methods for allocating participants according to date of birth, the number of their hospital records, the date at which they were invited to participate in the study depended on odd or even were considered inadequate and the studies used these methods to allocate study population were not considered as true RCTs.**



Judgement for the author's honest

- If the author deemed the wrong method of randomisation they used was correct, the author would be judged hasn't knowledge of randomisation
- If the author claimed that he/she known well about the method of randomisation they used was wrong or cannot control the allocation according to random sequence generated exactly, the author would be judged to label RCT incorrect intentionally



Data analysis

- Outcomes were computed about the percentage of real RCTs over the claimed RCTs
- The results were stratified by
 - hospitals level
 - test remedies with traditional Chinese Medicine (TCM) and Western medicine (WM)
 - purposes of the trials with the aim of new drug test or not;
 - funding sources with government and other official organisation supported projects.



Data analysis

- **Outcomes include percentage of**
 - **real randomised controlled trials**
 - **multiple versions of published papers**
 - **authors fail to contact**
 - **authors refuse to answer our question**
 - **number of authors incorrectly claimed non-RCT as RCT due to absence the knowledge of RCT and**
 - **intentionally claim non-RCT as RCT though they do not absence the relative knowledge.**



Quality control for investigation

- Investigators were trained before conducting telephone interview. The contents of training include
 - randomisation approach
 - design and conducting of randomised controlled trials
 - critical appraisal for clinical trials' quality
 - communication skills



Quality control for investigation

- The interview results were recorded in a special designed form which include
 - publication information
 - randomisation approach
 - the author interviewed knew or not know the randomisation approach
 - concealment for random sequence
 - support source



Findings

- **Initial search yielded 37,313 papers by search strategy. After full-text examination we identified 3035 claimed RCTs from the search results.**



Findings

Of the total 3,035 claimed RCTs

- **83 (2.7%) were published with more than two versions in different journals**
- **735 (24.9%) authors couldn't be connected for interview**
- **84 (2.8%) authors refused to answer question**
- **In the rest of claimed RCTs, only 207 studies were identified as real RCTs (6.8%, 95%CI 5.9 to 7.7)**
 - **103 (7.3%, 95%CI 5.9 to 8.7) were in TCM field**
 - **104 (6.4%, 95%CI 5.2 to 7.6) in WM field**



Stratified analysis according to the hospital levels

- Medical universities or colleges affiliated hospitals published 713 claimed RCTs (23.4%). Of them
- 30 (4.2%) have more than two versions
 - 162 (23.8%) authors failed to contacting
 - 18 (2.6%) authors refused to answer question
 - 128 studies in the rest were identified as real RCTs (18.7%, 95%CI 15.7 to 21.5)
 - all of new drug development trials were identified as real RCTs (100%, 35/35)
 - 51.6% (32/62)(95%CI 39.2 to 64.1) government and other official organisation supported projects were identified as real RCTs



Stratified analysis according to the hospital levels

- Authors of level 3 hospitals or medical institutes published 495 claimed RCTs (16.3%). Of them,
- 27 (5.5%) have more than two versions
 - 103 (22.0%) original authors could not be contacting by phone
 - 13 (2.8%) refuse to response our inquiry
 - 55 studies were identified as real RCTs (11.8%, 95%CI 8.8 to 14.7)
 - percentages of real RCTs in clinical test for new drug was 100% (10/10)
 - in government and other sources supported projects was 56.3% (9/16)(95%CI 32 to 81.0)



Stratified analysis according to the hospital levels

Authors of class 2 and lower level hospitals published 1,884 claimed RCTs and contributed to 62.1% of total publications

- **26 studies (1.4%) have more than two versions**
- **470 authors could not be contacted for interviewing**
- **53 (2.9%) authors did not cooperate with us**
- **only 24 studies were identified as real RCTs (1.3%, 95%CI 0.8 to 1.8)**
- **Only 1 new drug clinical test and 1 official support study took place, they were all real RCTs**



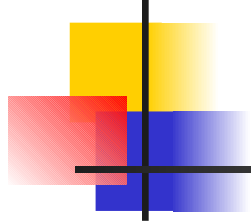
How many authors don't know randomisation exactly

- 115 authors (5.1%, 95%CI 4.2 to 6.0) knew about randomisation methods but they claimed their non-RCTs as RCTs.
- 1913 authors (85.6%, 95%CI 84.1 to 87.1) did not fully understand randomisation but they incorrectly claimed their non-RCT or pseudo-RCT as RCT
- We cannot judge whether the authors who were failed to contact or who refused to answer our question known the randomisation approach or not.
- **G:\Dublin\Table 1.doc**



Discussion

- **Selection bias should be considered as the most important reason of high rate of positive results of Chinese trials rather than publication bias**
- **It is insufficient to include Chinese RCTs in systematic review or meta-analysis just depended on what the original author claimed in published paper**
- **Carefully consider whether the claimed RCT is true or not is necessary**



*Thank you for
your attention!*



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