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## Schizophrenia trials in China: a survey

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## Abstract

**Introduction:** China's biomedical research activity is increasing and this literature is becoming more accessible online. Our aim was to survey all randomised control schizophrenia trials (RCTs) in one Chinese bibliographic database.

**Methods:** Chinese Academic Journals was electronically searched for RCTs and all relevant citations were also sought on PubMed to ascertain global accessibility.

**Results:** The search identified 3275 records, of which 982 were RCTs relevant to schizophrenia. 71% (699) could be found by using English phrases. All the main body of text of the 982 papers was in Mandarin. On average, these trials involved about 100 people, with interventions and outcome measures familiar to schizophrenia trialists world-wide. Four of the 982 records (<1%) were identified on PubMed.

**Conclusion:** Those undertaking systematic reviews should search the Chinese literature for relevant material. Failing to do this will leave the results of systematic reviews prone to random error, or bias or both.

**Keywords:** Schizophrenia, China, Randomized Controlled Trial.

### Significant outcomes:

An ever-increasing number of schizophrenia trials are originating from China.

The majority of these trials were researching recognizable drug and psychological treatments and using familiar outcome measures.

Less than 1% of these trials were identified on PubMed.

### Limitations:

Multiple publication was difficult to recognize.

Manual searching of the Chinese journals was not preformed.

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## **Introduction**

The People's Republic of China is the most populous country in the world. With over 1.3 billion people (five times the population of the USA, three times that of the EU) (1) and with a life time prevalence of 1%, an estimated 1.3 million people in China suffer from schizophrenia. In China, recently, the total number of hospitals and clinics has expanded to over 300,000 and the number of practising doctors to 1.8 million. Developments such as almost doubling the life expectancy and dramatically lowering the infant mortality rate over the last 30 years, emphasizes the improvement in the country's health care (2). Also, over the last two decades China's economy has strengthened with the Gross Domestic Product (GDP) quadrupling since 1978 (2003 estimate).

It is known that the GDP is one key predictor of national output of schizophrenia trials (3). It seems likely that this expansion in health care and in the economy in China has been paralleled by research effort and output but, for those using English, the Chinese literature has not been easy to access. In the last few years, however, things have changed and more of the Chinese biomedical literature has become accessible. For example, CAJ (Chinese Academic Journals), a bibliographic database indexing the contents of 140 Chinese biomedical journals is now online (4) and can be searched through an English or Chinese interface with full text reports to download.

Previous studies have suggested that literature from less well known sources is not accessible to those searching only mainstream databases (5,6,7,8). For researchers undertaking systematic reviews of the effects of care for people with schizophrenia, failing to include relevant studies can lead to less precise results than would otherwise be possible, and, at worst, biased findings (9).

### **Aim of the study**

To identify and survey all randomized trials in the CAJ relevant to the care of people with schizophrenia.

### **Material and Methods**

The Eastview Online CAJ was accessed initially on their one month free trial offer and though the University of Leeds' subscription thereafter. We searched CAJ in July 2005 (1994-present) in English using the phrase: ((antipsychotic OR antipsychotics OR

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extrapyram, OR psychosis OR psychotic OR schizophrenic OR tardive dyskinesia OR chronic schizophrenia) AND (randomi, OR double-blind, ) in the title or abstract. JX, a Chinese native speaker, translated English terms into traditional Chinese characters and repeated the search using the phrase: ((精神分裂症 OR 抗精神病的 OR 锥体外系 OR 精神病 OR 患精神病的 OR 动作障碍 OR 慢性精神分裂症) AND (随机化 OR 随机选择 OR 双盲 OR 随机)) in title or abstract (see Table 1).

**Table 1: Chinese translation of the English search terms**

精神分裂症	Schizophrenia
抗精神病的	Antipsychotic
锥体外系	Extrapyramidal
精神病	Psychosis
患精神病的	Psychotic
慢性精神分裂症	Chronic schizophrenia
随机化 or 随机选择	Randomization
双盲	Double blind
随机	Randomly
动作障碍	Tardive dyskinesia

Searching the CAJ database involved using the 'advanced search' screen to build search strings with the familiar Boolean operators, and/or/not (i.e. to combine the search terms). This screen, allows use of the 'search in keywords' to collectively scan title, keyword and abstract fields and displays all details of results.

We then downloaded records, managed them within a MS Access database and removed duplicates. Records were manually scanned for randomized control trials or controlled clinical trials (studies likely to have been randomized but in which description of allocation is unclear) relevant to the care of people with schizophrenia by CK, PR and AC, who all worked independently. This selection was reliable (kappa 0.98). Then CK, PR and AC working together, extracted data on the content and quality of the schizophrenia trials. WW and JX, Chinese native speakers, repeated this for studies only in Mandarin. Finally, MEDLINE (PubMed) database was examined, in order to ascertain how many records of these schizophrenia trials from CAJ were disseminated in PubMed.

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## Results

The search identified 3275 records. After checking for duplicates and relevance we found a total of 982 records that reported randomized studies relevant to schizophrenia. Of these, 29% (283) were identified by solely the Mandarin phrases but 71% (699) could be found by using English phrases (Figure 1). Twenty seven percent of records were solely in Mandarin. An English record predicted an English abstract in the full text of the paper, but all the main body of text of the 982 papers was in Mandarin. Using data from the Cochrane Schizophrenia Group's comprehensive register of trials (10) we calculated the proportions of all schizophrenia trials that originate from China in recent years (Figure 2.).

The average number of people in these Chinese schizophrenia trials was about 100 (mean 98.6, SD 96.2, range 11-1471, median 78, mode 60). The most common drug interventions under evaluation were clozapine (28%), risperidone (24%), chlorpromazine (14%), quetiapine (7%) and haloperidol (5%), but, over the last 4 years, 45% of schizophrenia trials in CAJ involved psychological interventions. The most common outcome scales used in all these trials were familiar to researchers world-wide (BPRS - 38%, TESS - 36%, PANSS - 25%, SANS - 20%, SAPS - 8%, SDSS - 6%).

PubMed, the service of the US National Library of Medicine, includes over 16 million citations from MEDLINE and other life science journals. MEDLINE, the largest component of PubMed, covers over 4,800 journals from more than 70 different countries (11). We found only four out of 982 reports (<1%) of these Chinese schizophrenia trials in PubMed.

## Discussion

CAJ is only one of an increasing number of substantial Chinese biomedical literature databases (12) and, even within it, our search was limited. It is feasible that the improved China National Knowledge Infrastructure (CNKI) format for CAJ would be yet more productive. We also could have experienced some double counting because of not recognizing multiple publication. We have not manually searched any Chinese medical journals listed in CAJ to ascertain what proportion of trials our electronic search

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identified. It is also possible we have not identified some schizophrenia trials from China published in Western journals.

Nevertheless, this study suggests that an ever-increasing number of randomized trials relevant to people with schizophrenia originate from China. About one quarter of the world's population of people with schizophrenia is Chinese. This study suggests that, in the last few years, at least the same proportion of all reports of randomized trials relevant to this group can be readily identified in the Chinese literature.

Our survey could not go beyond identifying studies that seemed to be randomized trials. We know of work suggesting how Chinese studies may use methodological descriptions such as 'randomized' liberally (13,14).

Even if this is so, and a higher than average proportion of what we have identified is not of good quality, it is currently difficult to ascertain which of the hundreds of studies are indeed of value. We argue, all should be considered by those undertaking systemic reviews. In addition, if this scientific activity in China reflects that seen in the plastics and electronic industry, a period of variable quality will be followed by systematic improvements and then dominance of the field (15).

These Chinese trials are, on average, larger than their counterparts from other countries (16). Several investigate interventions not commonly evaluated elsewhere, such as traditional Chinese medicines (17) and Morita therapy (18) and highlight effects of potentially valuable treatments not known to the rest of the world. However, by far the majority of the studies we identified were evaluating recognizable drug and psychological treatments and measuring outcomes in familiar ways.

Systematic reviews are now important influences on practice, being an integral part of guidelines (19). If the results of randomized trials originating from the People's Republic of China do not fundamentally differ from trials from other parts of the world, omitting them from systematic reviews may result in losing opportunities to identify real evidence of benefit or harm (Type II errors) (9). If, however, the results of trials from China are different from those more familiar to the rest of the world, reviews using only more

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accessible studies could be biased and misleading (Type I errors) (9). At present all we can be sure of is that this large body of evidence is relevant and should be considered.

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## **Declaration of Interest**

None.

All statistical analysis was performed at the University of Leeds.

## **Author's Contributions**

AC: helped create the data set, analyse results, format and write the paper.

CA: thought of the study, helped create the data set, analyse results, format and write the paper.

JR: searching, downloading and extracting data, cross checking and formatting data.

JW: searching, downloading.

JX: extracting data in Mandarin.

WW: extracting data in Mandarin.

CK, SB, CP, JB, MM, KK, PV: downloading and extracting data, cross checking and formatting data, helped create the data set and analyse results.

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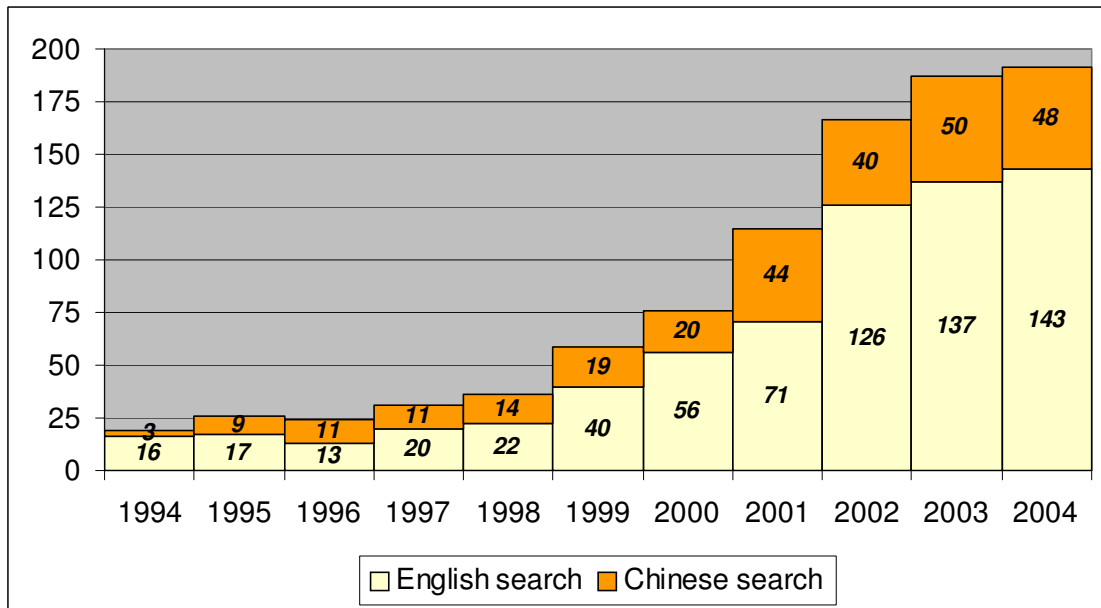
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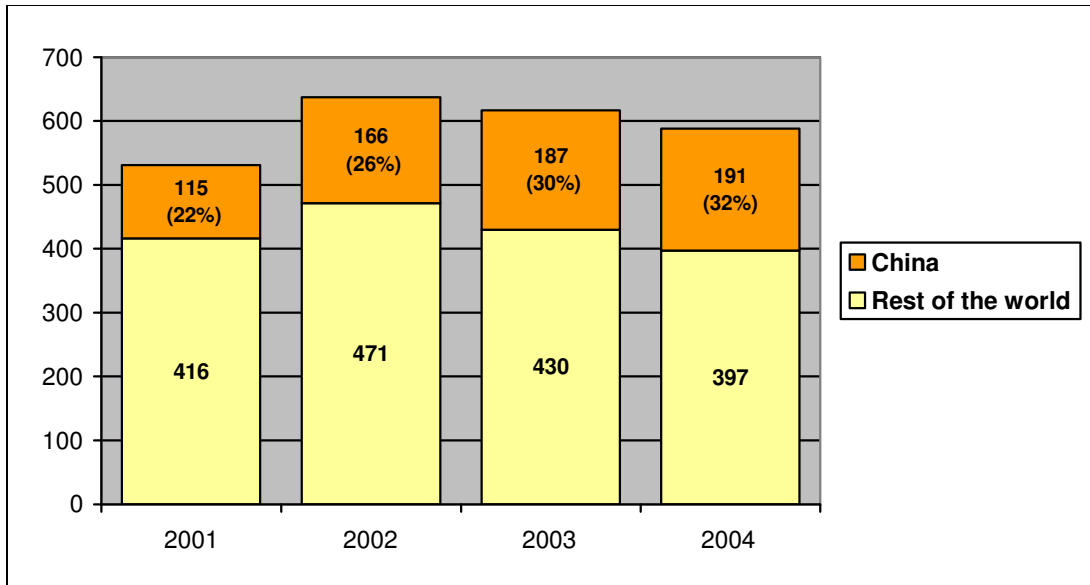
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**Figure 1: Number of schizophrenia trials in CAJ per year**



**Figure 2: Number of reports of schizophrenia trials worldwide**



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