Characteristics of registered systematic reviews on traditional Chinese medicine for COVID-19

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Research

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Abstract

**Background:** Characteristics of registered systematic reviews (SRs) on traditional Chinese medicine (TCM) for coronavirus disease 2019 (COVID-19) remain unclear. This study aimed to analyze research collaboration, interventions, and outcomes in registered SRs of TCM associated with COVID-19.

**Methods:** PROSPERO was searched to obtain SRs of TCM related to COVID-19 up to July 1, 2020. VOSviewer 1.6.14 software was used to generate network maps for countries, institutions, and provinces.

**Results:** A total of 80 SRs were included, which were registered by 81 institutions from 6 countries. China (76, 95.00%) was the country with the highest output. 21 provinces in China contributed to the registration of SRs, Sichuan (25, 30.12%), Beijing (13, 15.66%), and Shaanxi (7, 8.43%) were the top three productive provinces. The top three productive institutions were Chengdu University of traditional Chinese medicine (18, 24.66%), Shaanxi University of traditional Chinese medicine (7, 9.59%), and Beijing University of traditional Chinese medicine (6, 8.22%). Collaborations among countries, provinces, and institutions were sparse. Interventions investigated included traditional Chinese medicine, integrated Chinese and Western medicine, acupuncture, and Taijiquan, but the description was brief, and no specific implementation plan was provided. The most frequently used primary outcome was clinical efficiency (45, 56.25%), and the most frequently used secondary outcome was the adverse event (50, 62.5%). The expression of the outcomes was not standardized.

**Conclusions:** Although there were some collaborations between provinces and institutions, cooperation between countries should be further strengthened. The identified deficiencies in interventions and outcomes should be given more attention by future researchers.

1. Introduction

In late December 2019, an outbreak of pneumonia of unknown origin characterized by strong interpersonal transmission. Then scientists found that the Coronavirus Disease 2019 (COVID-19) caused by Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), an enveloped RNA virus. Within three months, the COVID-19 outbreak had already affected six continents, and the WHO upgraded its status from epidemic to pandemic on March 11, 2020. As of August 1, 2020, a total of 17,396,943 cases were reported, including 675,060 deaths.

PROSPERO is an international database of prospectively registered systematic reviews in health and social care, welfare, public health, education, crime, justice, and international development. China's first novel coronavirus pneumonia diagnosis and treatment plan (trial version third) issued on January 23, 2020 was first written into the Chinese medicine treatment plan. Novel coronavirus pneumonia diagnosis and treatment plan (Fourth Edition) issued on January 27, 2020 recommended the Chinese herbs. Medical workers and scientific researchers actively carry out research and have registered numerous Chinese medicine related COVID-19 systematic reviews (SRs). However, no research has focused on the
characteristics of these registered SRs. This study was designed to evaluate the cooperation between institution and the distribution of outcome measures in registered SRs of Chinese medicine related to COVID-19, to provide a reference for future researchers to register and carry out COVID-19 SRs.

2. Materials And Methods

2.1. Data sources

We systematically searched the PROSPERO registration platform (https://www.crd.york.ac.uk/prospero/) to identify all COVID-19 SRs related to TCM. The retrieval time limit is from the establishment of the database to July 1, 2020.

2.2. Inclusion and exclusion criteria

The type of included study was registered SRs on PROSPERO. The study population was patients diagnosed with COVID-19, and there were no restrictions on age, gender, race, and course of disease. Intervention was TCM treatment, including traditional Chinese medicine treatment, integrated Chinese and Western medicine, acupuncture, Taijiquan and so on. We excluded basic science, diagnostic tests, empirical studies, and health services. Duplicate records and record records were also excluded.

2.3. Study selection and data extraction

Two researchers independently reviewed the records and screened out eligible registrations according to the inclusion and exclusion criteria, and then proceeded to a cross-check. Conflicts were settled through discussions with a third reviewer.

We developed a data extraction form using Microsoft Excel 2016 (Microsoft Corp, Redmond, WA, www.microsoft.com) through discussions with the review team. Then, one author extracted data from the included SRs using the pre-defined form and a second reviewer checked the extracted data. The detailed data included: title, author, registration time, start time and expected completion time, whether conducted literature search, names of databases searched, intervention, control, countries, provinces, institutions, primary outcomes, secondary outcomes, software used for data analyses, and other information.

2.4. Data management and analysis

We used standardized names to replace different expressions of institutions, interventions, and outcome indicators. After that, the data extraction information table was designed by Microsoft Excel 2016 (Microsoft Corp, Redmond, WA, www.microsoft.com), and the information was extracted. After sorting out the data in a recognizable format, VOSviewer 1.6.14 (Leiden University, Leiden, Netherlands) software was used to generate the cooperation network maps of institutions, countries, and provinces. In the network maps, the size of nodes indicates the frequency of analysis elements, and the color of nodes and lines represents the cooperative relationship or co-occurrence relationship 11-14. The parameters of the
VOSviewer are as follows: counting method (fractional counting), ignoring documents with multiple authors (the maximum number of authors per document is 25).

3. Results

3.1. General characteristics of registered trials

80 registrations were retrieved, all of which met the inclusion criteria. By July 24, 2020, 27 (33.75%) registrations have reached the expected completion time. Among them, 25 (92.59%) are still under study, 1 (3.70%) registration has been published and 1 (3.70%) registration has been completed but not yet published. The number of daily registrations for COVID-19 related to traditional Chinese Medicine fluctuated significantly. The earliest registration date was February 5, 2020. The largest number of registrations (7, 8.75%) was on April 22, 2020. The registration time of included SRs is shown in Figure 1.

Among the 80 included SRs, 1 (1.25%) SR was performed by only one author, 56 (70.00%) SRs had 2-5 participants, 21 (26.25%) SRs had 6-10 participants, and 2 (2.50%) SRs had more than 10 participants. All 80 studies were systematic reviews, including meta-analysis (64, 80.00%), network meta-analysis (8, 10.00%), review of reviews (3, 3.75%), narrative synthesis (3, 3.75%), synthesis of qualified studies (1, 1.25%), individual patient data (IPD) meta-analysis (1, 1.25%). The types of studies included in these SRs are diverse. 3 (3.75%) SRs did not limit the types of included studies. RCTs (77, 96.25%) was the most involved type. The second to the fourth were observational studies (10, 12.50%), case-control studies (7, 8.75%), and quasi randomized studies (4, 5.00%).

Of the 80 SRs, 75 (93.75%) assessed the risk of bias of primary studies included and 5 (6.25%) did not. Cochrane risk of bias (73, 91.25%) was the most widely used bias risk assessment tool, followed by NOS (14, 17.50%), the modified downs and black instrument (2,2.50%), and the Hoy risk of bias tool (1, 1.25%). Data analysis software was reported in 59 (73.75%) SRs. Review manager software (49, 68.06%) was the most frequently used software, the remaining software included STATA (7, 9.72%), R (6, 8.33%), Excel (3, 4.17%), and SPSS (2, 2.78%). 42 (52.50%) SRs were funded and 38 (47.50%) were not. 14 (17.55%) were supported by the National Natural Science Foundation of China, Table 1.

3.2. Database

All SRs reported the retrieved databases. 77 (96.25%) SRs searched English and Chinese databases, and 3 (3.75%) only searched English databases. PubMed/Medline (78,97.5%) was the most frequently used English database and CNKI (77,96.25%) was the most frequently used Chinese database. Wanfang (61,76.25%), CBM (57,71.25%) and the Cochrane library (34,42.5%) were also commonly searched. As for the combination of databases, 75 (93.75%) SRs searched CNKI and PubMed/Medline, 61 (76.25%) SRs retrieved CNKI and Wanfang, and 75 (93.75%) SRs retrieved PubMed/Medline and EMBASE, more details are presented in Table 2.

3.3. Country and Province
Among the included SRs, 76 (95.00%) were completed by only one country, including 72 (94.73%) from China, 1 (1.31%) from Australia, 1 (1.31%) from Singapore, 1 (1.31%) from India and 1 (1.31%) from the UK. 4 (5.00%) SRs were completed by national cooperation, including one (25.00%) by China and Australia, two (50.00%) by China and Northern Ireland, and one (25.00%) by China and the United Kingdom.

21 provinces from China participated in the registration of 76 SRs. The top six productive provinces are Sichuan (25, 31.25%), Beijing (13, 16.25%), Shaanxi (7, 8.75%), Jilin (5, 6.25%), Jiangsu (4, 5.00%) and Guangdong (4, 5.00%). The 7th to 12th productive provinces are Henan (3, 3.75%), Tianjin (3, 3.75%), Jiangxi (3, 3.75%), Shandong (3, 3.75%), Hebei (2, 2.50%) and Gansu (2, 2.50%). Hainan, Heilongjiang, Hong Kong, Chongqing, Hunan, Liaoning, Shanghai, Taiwan, and Zhejiang registered only 1 (1.25%) SR, Table 3. A social network analysis of provinces revealed that 7 provinces formed a cooperative relationship (Figure 2). However, the collaborations between provinces were sparse.

### 3.4. Institutions

A total of 81 institutions contributed to the registrations of COVID-19 SRs of TCM. These institutions are universities and hospitals. 38 (47.50%) SRs were completed by one institution, 26 (32.50%) by two organizations, 10 (12.50%) by three organizations, 5 (6.25%) by four organizations, and 1 (1.25%) by five organizations. The top six productive institutions are Chengdu University of traditional Chinese medicine (18, 24.66%), Shaanxi University of Traditional Chinese medicine (7, 9.59%), Beijing University of Traditional Chinese medicine (6, 8.22%), Chengdu University of traditional Chinese medicine hospital (5, 6.85%), Guang’anmen Hospital (5, 6.85%) and Changchun University of Traditional Chinese medicine (5, 6.85%), Table 4.

A social network analysis of institutions revealed that 10 institutions formed a cooperative relationship (Figure 3). Beijing Traditional Chinese medicine, located in the network center, had more cooperation with other institutions. There was less cooperation between institutions.

### 3.5. Interventions

78 (97.50%) registrations reported interventions and 2 (2.50%) did not. The reported interventions were classified into TCM (46, 58.97%), acupuncture (8, 10.25%), integrated Chinese and Western medicine (26, 33.33%), and Taijiquan (2, 2.56%). 17 registrations reported the specific names of traditional Chinese medicines used. They were Lianhua Qingwen capsule (6, 35.29%), Shufeng Jiedu capsule (3, 17.65%), Jinhua qinggan granule (2, 11.76%), Reduning injection (2, 11.76%), Xuebijing injection (2, 11.76%), ginseng (1, 5.88%), and Qingfei Paidu decoction (1, 5.88%). The administration methods included oral administration (14, 82.35%) and injection (3, 17.64%). The control measure was placebo or conventional medicine or no treatment (80, 100%).

### 3.6. Outcome measures

#### 3.6.1. Primary outcome measures
All the included SRs used multiple outcome indicators. The primary outcome measures used in each study were related to clinical symptoms, signs, and laboratory tests. The most frequently used primary outcome measure was clinical efficiency (45, 56.25%), followed by the time of clinical improvement time (31, 38.75%), clinical symptoms improvement (31, 38.75%), antipyretic time (29, 36.25%), lung function (26, 32.50%), body temperature (22, 27.50%), mortality (21, 26.25%), rate of viral nucleic acid turning negative (14, 17.50%), time of viral nucleic acid turning negative (12, 15.00%), and incidence of adverse events (12, 15.00%), Table 5.

3.6.2. Secondary outcome measures

Of the 80 included SRs, 65 (81.25%) reported secondary outcome measures. The most frequently used secondary outcome measure was adverse events (50, 62.5%), followed by hospital stay (15, 18.75%), clinical symptoms improvement (15, 18.75%), clinical recovery time (14, 17.50%), fever disappearance time (13, 16.25%), safety measurements (13, 16.25%), TNF-a/IL-6 (13, 16.25%), WBC (11, 13.75%), chest/lung CT (10, 12.50%), and rate of progression to severe (9, 11.25%), Table 6.

4. Discussion

The PROSPERO platform opened COVID-19 retrieval channels and made a reasonable and meticulous classification and management of the literature so that all the documents retrieved were in line with inclusion criteria. As of July 24, 2020, 27 (33.75%) registrations have reached the expected completion time. However, only two registrations were completed on time, and the completion rate was only 7.41%. The shortest study was decided to be completed within 28 days. It can be inferred that the reasons for the low completion rate on time may be that the amount of literature in the early stage is less, it is difficult to obtain enough data, the expected completion time is too short to complete the research, and so on. This shows that in the future research, we should evaluate the feasibility of the study, reasonably plan the research progress, and strive to complete it within the expected registration time.

China’s first COVID-19 diagnosis and treatment plan (trial version third) issued on January 23, 2020 was first written into the Chinese medicine treatment plan. Novel coronavirus pneumonia diagnosis and treatment plan (Fourth Edition) issued on January 27, 2020 recommended the Chinese herb, Huo Xiang Zheng Qi capsule, Jinhua Qinggan Granule, Lianhua Qingwen capsule, Shu Feng Jiedu Capsule, and Feng Feng Tong Sheng pill. The first registration was on February 5, 2020, and the second was on March 20, 2020. Registration was concentrated in April when the outbreak had spread worldwide. At the same time, as of April 30, 2020, the global cumulative number of cases exceeded 3.13 million. The registered concentration months are associated with the severity of the epidemic worldwide. With the expansion and severity of the epidemic, scholars began to pay more attention to this aspect of research, making SRs to produce high-quality evidence to support clinical practice.

More representative data and more advanced data can be obtained by searching the Chinese and English databases of 77 (96.25%) studies. Only English databases were searched for the 3 (3.75%) registrations. Each study did not use a single database. The most commonly used database combination is CNKI
combined with PubMed/MEDLINE (75,93.75%) and PubMed/MEDLINE combined with EMBASE (75,93.75%).

A total of 6 countries have registered COVID-19 SRs of traditional Chinese medicine, of which 76 (95.00%) SRs were undertaken by China. Only 4 (5.00%) studies were conducted by cooperation between countries. A total of 21 provinces in China have registered COVID-19 SRs of TCM, of which 7 (33.33%) have formed cooperative relations. A total of 81 institutions involved in the included SRs, but only 10 (12.35%) institutions had collaborations. Sichuan Province participated in 25 SRs, Chengdu University of traditional Chinese medicine participated in 18 (31.25%) SRs, and the Chengdu University of traditional Chinese medicine hospital participated in 5 (6.25%) studies. Beijing has 13 (16.25%) SRs with the second largest number of registrations, including 6 (7.5%) from Beijing University of traditional Chinese medicine and 5 (6.25%) from Guang'anmen Hospital. In the social network of provinces, Beijing is in the central position and has more cooperative relations. In the social network of the institutions, Beijing University of traditional Chinese medicine is at the center and has cooperative relations with eight institutions. In general, there is little cooperation among provinces and institutions. Therefore, researchers in the future should strengthen more comprehensive research and carry out extensive cooperation between provinces and institutions.

The main clinical manifestations of COVID-19 are fever, dry cough, and fatigue. Laboratory examination can be found in the early detection of normal or reduced peripheral WBC, most patients with C-reactive protein and erythrocyte sedimentation rate increased. Novel coronavirus nucleic acids can be detected in specimens of nasopharyngeal swabs and other samples by RT-PCR or NGS10.

The description of intervention measures is very brief. Most of the registrations did not indicate the TCM treatment methods used. Only 17 (21.25%) registrations gave the specific drug names. The primary outcome measure used most in the included literature was clinical effective rate (45, 56.25%), followed by clinical improvement time (31, 38.75%) and clinical symptoms improvement (31, 38.75%). The most frequently used secondary outcome measure was adverse events, which was used by 62.5% of the included literatures. Compared with the primary outcome measures of the top 20, the secondary outcome measures of the top 20 increased adverse events, safety measurements, WBC, quality of life, mechanical ventilation, blood gas analysis, blood routine, and canceled clinical efficiency, lung function, the incidence of adverse events, serum cytokine levels, nucleic acid detection, cure rate, and oxygenation index. In the top 20 primary outcome measures, clinical symptoms, laboratory tests, and signs were associated. The secondary outcome measures focused more on the quality of life, safety measures, and adverse drug events. TCM symptom score was used in both indicators, and the frequency of use was relatively low (main outcome index, 2.15%, secondary outcome index, 3.17%). This index can be considered to improve the characteristics of traditional Chinese medicine in future research. The description of primary and secondary outcome indicators in the inclusion registry was not coherent.

We conducted a comprehensive analysis of the Chinese medicine related COVID-19 SRs registered in PROSPERO using the bibliometric analysis method and presented collaborations of provinces and institutions.
institutions by using visual network maps. However, this study also has some limitations. Due to the lack of registered research, the cooperation between countries and institutions is not close enough to reflect the future cooperation trend. Although we have standardized some institutions, interventions, and outcomes in different ways, there may still be bias.

5. Conclusions

Many COVID-19 SRs of TCM have been registered, but the completion rate was low. China was the country with the largest number of registrations, Sichuan was the province with the largest output, and Chengdu University of traditional Chinese medicine was the institution with the largest output. Collaborations between countries, provinces, and institutions were not close enough. More comprehensive and extensive collaborations between different provinces and different regions should be further strengthened to strengthen communication, share information, and obtain more representative experimental results. More attention should be paid to the deficiency of interventions and outcome measures, and the standardization of results should be strengthened.

Abbreviations

COVID-19: Corona virus disease 2019; TCM: Traditional Chinese Medicine; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; SR: Systematic review.

Declarations

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Author contributions
RNL, YG, JHZ and JHT planned and designed the study. RNL, YG, RNZ, DRX, YZ and MZ participated in the literature search and data collection. RNL, YG, and JHZ analyzed the data. RNL and YG drafted the manuscript. RNL, YG, JHZ and JHT revised the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials
The data will be made available upon request.

Ethics approval and consent to participate
Not applicable.
Consent for publication

Not applicable.

Conflict of interest
The authors declare that they have no competing interests.

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Tables

Table 1. Characteristics of registered COVID-19 SRs of traditional Chinese Medicine
| Items                                      | N   | Percentage |
|-------------------------------------------|-----|------------|
| Registration month                        |     |            |
| February                                  | 1   | 1.25%      |
| March                                     | 15  | 18.75%     |
| April                                     | 43  | 53.75%     |
| May                                       | 16  | 20.00%     |
| June                                      | 5   | 6.25%      |
| Publication                               |     |            |
| Review Ongoing                            | 78  | 97.50%     |
| Review Completed published                | 1   | 1.25%      |
| Review Completed not published            | 1   | 1.25%      |
| Report deviation risk assessment          |     |            |
| Yes                                       | 75  | 93.75%     |
| No                                        | 5   | 6.25%      |
| Bias risk assessment method               |     |            |
| Cochrane risk of bias                     | 73  | 91.25%     |
| NOS                                       | 14  | 17.50%     |
| modified Downs and Black instrument       | 2   | 2.50%      |
| The Hoy Risk of Bias Tool                 | 1   | 1.25%      |
| Report analysis software                  |     |            |
| Yes                                       | 59  | 73.75%     |
| No                                        | 21  | 26.25%     |
| Data analysis software                    |     |            |
| Review Manager software                   | 49  | 61.25%     |
| STATA                                     | 7   | 8.75%      |
| GeMTCO                                    | 1   | 1.25%      |
| ADDIS                                     | 1   | 1.25%      |
| SPSS                                      | 2   | 2.50%      |
| Type of Systematic Evaluation       | Count | Percentage |
|------------------------------------|-------|------------|
| Pairwise meta-analysis             | 64    | 80.00%     |
| Review of reviews                  | 3     | 3.75%      |
| Network meta-analysis              | 8     | 10.00%     |
| Narrative synthesis                | 3     | 3.75%      |
| Synthesis of qualitative studies   | 1     | 1.25%      |
| Individual patient data meta-analysis | 1   | 1.25%      |

| Type of Included Studies           | Count | Percentage |
|------------------------------------|-------|------------|
| RCT                                | 77    | 96.25%     |
| Case-control study                 | 7     | 8.75%      |
| Observational study                | 10    | 12.50%     |
| Quasi randomized study             | 4     | 5.00%      |
| Quasi RCT                          | 3     | 3.75%      |
| Prospective controlled trial       | 3     | 3.75%      |
| Quasi experimental study           | 2     | 2.50%      |

| Funding                            | Count | Percentage |
|------------------------------------|-------|------------|
| None                               | 38    | 47.50%     |
| Yes                                | 42    | 52.50%     |

Table 2. Reporting information of literature search
| Category                          | Characteristic      | N  | Percentage |
|----------------------------------|---------------------|----|------------|
| Language of databases searched   | English             | 3  | 3.75%      |
|                                  | English-Chinese     | 77 | 96.25%     |
| Reported search strategy         | Yes                 | 80 | 100.00%    |
| Name of database                 | PubMed/Medline      | 78 | 97.50%     |
|                                  | CNKI                | 77 | 96.25%     |
|                                  | EMBASE              | 77 | 96.25%     |
|                                  | Wanfang             | 61 | 76.25%     |
|                                  | VIP                 | 9  | 11.25%     |
|                                  | CBM                 | 57 | 71.25%     |
|                                  | Cochrane Library    | 34 | 42.50%     |
|                                  | Web of Science      | 29 | 36.25%     |
|                                  | CENTRAL             | 16 | 20.00%     |
|                                  | Ovid                | 10 | 12.50%     |
|                                  | AMED                | 7  | 8.75%      |
|                                  | Chinese Clinical Trial Registry | 6 | 7.50%     |
|                                  | WHO Trials          | 3  | 3.75%      |
|                                  | Physiotherapy Evidence Database | 1 | 1.25%    |
| Combination of database          | CNKIPubMed/Medline  | 75 | 93.75%     |
|                                  | CNKIWanfang         | 61 | 76.25%     |
|                                  | CNKIVIP             | 59 | 73.75%     |
|                                  | PubMed/MedlineCBM   | 53 | 66.25%     |
|                                  | PubMed/MedlineEMBASE| 75 | 93.75%     |
|                                  | CNKIPubMed/MedlineEMBASE | 72 | 90.00%   |
|                                  | CNKIVIP             | 49 | 61.25%     |
|                                  | PubMed/MedlineEMBASECBM | 44 | 55.00%   |

Table 3. Provinces contributed to the registration of COVID-19 SRs of traditional Chinese Medicine [N (%)]
| Rank | Province    | N(%)   | Rank | Province    | N(%)   |
|------|-------------|--------|------|-------------|--------|
| 1    | Sichuan     | 25(31.25%) | 12   | Gansu       | 2(2.50%) |
| 2    | Beijing     | 13(16.25%) | 13   | Hainan      | 1(1.25%) |
| 3    | Shaanxi     | 7(8.75%)  | 14   | Heilongjiang| 1(1.25%) |
| 4    | Jilin       | 5(6.25%)  | 15   | Hong Kong   | 1(1.25%) |
| 5    | Jiangsu     | 4(5.00%)  | 16   | Chongqing   | 1(1.25%) |
| 6    | Guangdong   | 4(5.00%)  | 17   | Hunan       | 1(1.25%) |
| 7    | Henan       | 3(3.75%)  | 18   | Liaoning    | 1(1.25%) |
| 8    | Tianjin     | 3(3.75%)  | 19   | Shanghai    | 1(1.25%) |
| 9    | Jiangxi     | 3(3.75%)  | 20   | Taiwan      | 1(1.25%) |
| 10   | Shandong    | 3(3.75%)  | 21   | Zhejiang    | 1(1.25%) |
| 11   | Hebei       | 2(2.50%)  |      |             |        |

Table 4. Institutions contributed to the registration of COVID-19 SRs of traditional Chinese Medicine (>1) [N (%)]
| Rank | Institution                                                      | N(%) |
|------|------------------------------------------------------------------|------|
| 1    | Chengdu University of Traditional Chinese Medicine               | 18(24.66%) |
| 2    | Shaanxi University of Traditional Chinese Medicine               | 7(9.59%)  |
| 3    | Beijing University of Traditional Chinese Medicine               | 6(8.22%)  |
| 4    | Hospital of Chengdu University of Traditional Chinese Medicine  | 5(6.85%)  |
| 5    | Guang'anmen hospital                                            | 5(6.85%)  |
| 6    | Changchun University of Traditional Chinese Medicine            | 5(6.85%)  |
| 7    | Nanjing University of Traditional Chinese Medicine              | 4(5.48%)  |
| 8    | Shandong University of Traditional Chinese Medicine             | 3(4.11%)  |
| 9    | Shaanxi Academy of Traditional Chinese Medicine                 | 3(4.11%)  |
| 10   | Jiangxi University of Traditional Chinese Medicine              | 3(4.11%)  |
| 11   | Guangzhou University of Traditional Chinese Medicine            | 2(2.74%)  |
| 12   | Tianjin University of Traditional Chinese Medicine              | 2(2.74%)  |
| 13   | Central hospital of Xiangtan City                               | 2(2.74%)  |
| 14   | Central South University                                       | 2(2.74%)  |
| 15   | People's Hospital of Lixia District                             | 2(2.74%)  |
| 16   | Hunan University of Traditional Chinese Medicine                | 2(2.74%)  |

Table 5. The top 20 primary outcome measures in terms of frequency [N (%)]
| Rank | Primary outcome measures                  | N(%)       | Rank | Primary outcome measures                  | N(%)       |
|------|------------------------------------------|------------|------|------------------------------------------|------------|
| 1    | Clinical efficiency                      | 45(56.25%) | 11   | Hospital stay                            | 12(15.00%) |
| 2    | Clinical improvement time                | 31(38.75%) | 12   | Rate of progression to severe            | 12(15.00%) |
| 3    | Clinical symptoms improvement            | 31(38.75%) | 13   | Serum cytokine levels                    | 12(15.00%) |
| 4    | Antipyretic time                         | 29(36.25%) | 14   | Chest/lung CT                            | 11(13.75%) |
| 5    | Lung function                            | 26(32.50%) | 15   | Nucleic acid detection                   | 8(10.00%)  |
| 6    | Body temperature                         | 22(27.50%) | 16   | C-reactive protein                       | 8(10.00%)  |
| 7    | Mortality                                | 21(26.25%) | 17   | Cure rate                                | 7(8.75%)   |
| 8    | Rate of viral nucleic acid turning negative | 14(17.50%) | 18   | TCM symptom score                       | 7(8.75%)   |
| 9    | Time of viral nucleic acid turning negative | 12(15.00%) | 19   | TNF-a/IL-6                               | 3(3.75%)   |
| 10   | Incidence of adverse events              | 12(15.00%) | 20   | Oxygenation index                        | 3(3.75%)   |

Table 6. The top 20 secondary outcome measures in terms of frequency [N (%)]
| Rank | Secondary outcome measures                  | N(%)  | Rank | Secondary outcome measures                  | N(%)  |
|------|--------------------------------------------|-------|------|--------------------------------------------|-------|
| 1    | Adverse events                             | 50(62.50%) | 11   | C-reactive protein                         | 9(11.25%)     |
| 2    | Hospital stay                              | 15(18.75%) | 12   | Quality of life                            | 9(11.25%)     |
| 3    | Clinical symptoms improvement              | 15(18.75%) | 13   | TCM symptom score                         | 7(8.75%)     |
| 4    | Clinical recovery time                     | 14(17.50%) | 14   | Body temperature                           | 6(7.50%)      |
| 5    | Fever disappearance time                   | 13(16.25%) | 15   | Mortality                                  | 6(7.50%)      |
| 6    | Safety measurements                        | 13(16.25%) | 16   | Mechanical ventilation                     | 6(7.50%)      |
| 7    | TNF-a/IL-6                                 | 13(16.25%) | 17   | Blood routine                              | 6(7.50%)      |
| 8    | WBC                                        | 11(13.75%) | 18   | Time of viral nucleic acid turning negative | 3(3.75%)      |
| 9    | Chest/lung CT                              | 10(12.50%) | 19   | Rate of viral nucleic acid turning negative | 3(3.75%)      |
| 10   | Rate of progression to severe              | 9(11.25%)  | 20   | Blood gas analysis                         | 3(3.75%)      |

**Figures**
Figure 1

Registration time of COVID-19 SRs related to traditional Chinese Medicine
Figure 2
The social network analysis of provinces

University of Southampton
Third affiliated hospital of Beijing University
Gulou Hospital affiliated to Capital Medical School
Beijing University of Traditional Chinese Medicine
Heilongjiang University of Traditional Chinese Medicine
China Academy of Chinese Medical Sciences
Beijing Hospital of Traditional Chinese Medicine

Figure 3
The social network analysis of institutions