Analysis of clinical research publication patterns to characterize the cooperation among China's "double first-class" construction medical universities: based on social network analysis

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Background: The "Double First-Class" refers to world first-class university and first-class academic discipline construction proposed by China government. The "Double First-Class" construction medical universities have made many clinical research achievements, but the analysis and evaluation of research collaboration networks in the field of clinical research are still lacking.

Methods: Clinical research papers by 23 "Double First-Class" construction medical universities in China from 2000 to 2019 indexed in the databases of the China National Knowledge Infrastructure and Web of Science (WoS) databases were collected. Through the social network analysis (SNA) method and Ucinet software, the interuniversity research cooperation networks of domestic and international publications were comparatively analyzed at the overall, individual, and group levels in terms of number of publications, cooperation network matrix, centrality analysis, cohesive subgroup analysis, and core–periphery structure to understand the developmental status of the cooperative network of clinical research publications among China's "Double First-Class" construction medical universities.

Results: The cooperation among China's "Double First-Class" construction universities showed certain regional distribution characteristics, and they showed closer cooperation in publishing papers in international journals than in domestic ones. The overall density of the domestic-journal research collaboration network of the universities was 0.4229, mainly centered on Beijing University of Traditional Chinese Medicine and Shanghai University of Traditional Chinese Medicine. In contrast, the overall density of international-journal research collaboration network was 0.9052, mainly centered on Peking University, Central South University, and Zhengzhou University, with large differences in subgroup density and low integration.

Conclusions: To promote the development of clinical research, it is necessary to improve the construction of the interuniversity clinical research collaboration system, build a national clinical research network with a multilevel structure and sophisticated functions, and expand resource sharing as well as collaborative innovation capacity.

Keywords: "Double First-Class" construction; clinical research; social network analysis (SNA); cohesive subgroup analysis

Introduction

In September 2017, the Ministry of Education of China, in combination with the Ministry of Finance and the National Development and Reform Commission, issued the *Announcement on the lists of the world first-class university and first-class discipline construction universities*, which included 42 world first-class universities and 95 first-class disciplines (hereafter referred to as "Double First-Class") (1). The selection of "Double First-Class" university based on multiple factors including essential science indicators ranking, national economic and social development. The aims of construction of "Double First-Class" university are to strengthen individual faculty departments and comprehensively develop elite Chinese universities into world-class institutions. Among them, the "medicine disciplines" of 21 universities were selected as "Double First-Class" disciplines. In October 2018, the "Double First-Class" Construction Medical University Alliance was formed in Beijing. It is a nonprofit medical higher education and medical collaborative organization established under the guidance of the Department of Degree Management and Postgraduate Education of the Ministry of Education. The first members included nine "Double First-Class" construction universities, i.e., Peking University (the organizing unit), Beijing Union Medical College, Fudan University, Shanghai Jiao Tong University, Zhejiang University, Wuhan University, Huazhong University of Science and Technology, Sun Yat-sen University, and Sichuan University. In December 2019, Central South University and Jilin University were voted to be the governing unit of the Alliance. The "Double First-Class" construction has sounded the charge for Chinese universities to come to the forefront of the world and building the world's top universities and top disciplines.

Clinical research is a scientific activity organized and implemented by multidisciplinary personnel with humans as the main research object. It is a key link that connects basic research and clinical application in order to translate scientific findings to the bedside, and is thus a necessary way for clinical medicine to achieve sustainable development. To strengthen the flow and integration of clinical research, major countries around the world have established interinstitutional and interregional collaborative network systems and research centers to ensure teamwork at different levels and functions (2). China has abundant clinical research resources as well as advantages in doing clinical research. However, China's clinical research still

suffers from unsophisticated university collaborative innovation systems, low resource sharing rates, weak collaborative technological innovation capabilities, and poor overall quality of clinical studies. How to fully integrate domestic and international superior resources, coordinate research, and dissolve bottlenecks restricting the development of clinical medicine through medical research through the construction of "Double First-Class" medical universities is an important question whose answer could help China achieve its national health strategy goals.

The "Double First-Class" construction has been extensively studied. Zhang *et al.* analyzed the key issues in clinical resource integration and clinical discipline construction under the background of "double first-class" construction using Shanghai Jiao Tong University as an example (3). However, the scientific research cooperation networks in the field of clinical research have rarely been analyzed. Social network analysis (SNA) permits accurate quantitative analysis of the relationships through quantitative analytical methods such as mathematical statistics and has been widely favored by scholars in various fields (4). In this study, we investigated the characteristics of published papers and the cooperation between clinical researchers of medical universities involved in the "Double First-Class" construction from the perspective of the overall SNA. We empirically analyzed the connections of the published clinical research papers among 23 "Double First-Class" construction medical universities. We aimed to understand the current status of clinical research in China's "Double First-Class" construction universities, grasp the development and evolution of clinical research in universities, and promote the development of the "Double First-Class" construction practice by focusing on enriching its theoretical basis.

Methods

Research samples and data sources

The data were collected from the China National Knowledge Infrastructure (CNKI) and Web of Science (WoS) databases. CNKI is the largest document database in China, with 15.5 million full-text articles published in approximately 9,000 Chinese and English periodicals in mainland China since 1979, with 1.6 million new articles each year that are divided into nine major areas and 126 thematic literature databases, covering science, engineering, agriculture, medicine and health, literature, history,

Table 1 Geographical distribution of 23 "Double First-Class" construction medical universities in China

Province	Code number	School name
Beijing	1	Beijing University
	2	Peking Union Medical College
	3	China Pharmaceutical University
	4	Beijing University of Chinese Medicine
Shanghai	5	Fudan University
	6	Shanghai Jiao Tong University
	7	Second Military Medical University
	8	Shanghai University of Traditional Chinese Medicine
Guangdong	9	Sun Yat-sen University
	10	Jinan University
	11	Guangzhou University of Chinese Medicine
Zhejiang	12	Zhejiang University
Hubei	13	Wuhan University
	14	Huazhong University of Science and Technology
Sichuan	15	Sichuan University
	16	Chengdu University of Traditional Chinese Medicine
Tianjin	17	Tianjin Medical University
	18	Tianjin University of Traditional Chinese Medicine
Shaanxi	19	Fourth Military Medical University
Hunan	20	Central South University
Jilin	21	Jilin University
Henan	22	Zhengzhou University
Jiangsu	23	Nanjing University of Chinese Medicine

philosophy, economics, politics, law, education, social sciences, electronic technology, and information science. The core collection of the WoS database contains three major citation databases, i.e., Science Citation Index (SCI), Social Sciences Citation Index and Arts & Humanities Citation Index, as well as Conference Proceedings Citation Index-Science and Conference Proceedings Citation Index-

Social Sciences & Humanities, representing an important foreign-language literature database.

In this study, we used the CNKI database analysis to represent the domestic journal cooperation network of universities and WoS analysis to represent the international journal cooperation network of the universities. Twenty-three "Double First-Class" construction medical colleges were used as the unit of measurement, covering various regions such as Beijing, Shanghai, Guangdong, Zhejiang, and Sichuan (*Table 1*). We used the keywords "clinical research", "observational study", "cohort study", "case-control study", "cross-sectional study", and "randomized controlled trial" to search for collaborative publications of the above-described 23 universities over 20 years (2000–2019), from which 4,042 valid academic documents were obtained after excluding non-academic documents such as conference notices and those with off-topic themes. Similarly, 47,096 valid academic documents were obtained from the core collection of the WoS database.

Statistical analysis

Based on the clinical research publication data of China's 23 "Double First-Class" construction medical universities obtained from the CNKI and WoS databases published from 2000 to 2019, we used Ucinet, NetDraw, SPSS, and other software for bibliometric analysis, overall network analysis, centrality analysis, cohesive subgroup analysis, faction analysis, block model, and core–periphery structure analysis (5) and generated diagrams of scientific research cooperation networks. The indicators are described in detail below.

Network density

Network density in overall network analysis is used to measure the closeness and connectivity of the overall network structure. The greater the network density was, the closer the clinical research publication collaboration among universities was. The calculation formula of network density is as follows:

$$D = \frac{\sum_{i=2}^{n}\sum_{i=2}^{n} d_i(c_i, c_j)}{n \times (n-1)} \qquad [1]$$

where D is the network density; $d_i(c_i, c_j)$ is the university node; $\sum_{i=2}^{n} d_i(c_i, c_j)$ is the connection between university i and university j; and n is the number of university nodes.

Centrality

Centrality is three measurements that reflect the extent to which a node is at the network' center, with three indicators. The first indicator is degree centrality; the greater the node's degree centrality, the stronger its ability to communicate with other nodes in the network, indicating that it has an advantageous position. It is calculated as

$$C_{xd}(i) = \frac{C_{zd}(i)}{n-1} \qquad [2]$$

where $C_{xd}(i)$ is the relative degree centrality of node i; $C_{zd}(i)$ is the number of universities that are directly connected to node i, representing the absolute degree centrality of the node, i.e., the maximum number of universities that may have a relationship with the node.

The second indicator is betweenness centrality; the greater the betweenness centrality, the stronger the influence of the node on other nodes, i.e., the stronger the node's mediating effect. It is calculated as

$$C_{xdi}^{-1} = \frac{\sum_{j=1}^{n} d_{ij}}{n-1} \qquad [3]$$

where C_{xdi}^{-1} is the node's relative closeness centrality and d_{ij} is the shortest distance between node i and node j.

The third indicator is closeness centrality; the greater the closeness centrality of a node, the shorter its path to other nodes, i.e., the more central the position it occupies in the network. It is calculated as

$$C_{DAi} = \frac{2C_{DBi}}{n^2 - 3n + 2} \qquad [4]$$

where C_{DAi} and C_{DBi} are, respectively, the relative betweenness centrality and absolute betweenness centrality of nodes i and j.

Cohesive subgroup, block model, and core–periphery analyses

A cohesive subgroup is a subgroup formed by the combination of certain actors in the network that are close. Faction analysis is a method of cohesive subgroup analysis based on group reciprocity relationships. Through faction analysis, the small groups in which any two members are in two-way communication can be revealed (6). The block model uses the iterative correlation convergence method to partition nodes based on structural information to reveal the relationship between the partitions in the spatial network and the role of each partition in the overall network (7). Core–periphery structure analysis aims to understand which nodes are in a core position and which nodes are in a peripheral position in a social network (8). Their specific calculation formulas and methods are detailed in the literature (9,10).

Results

Bibliometric analysis

In this study, cooperation meant publication of a paper by authors from different universities, as determined from the affiliated institution list of the authors of a publication. The search results show that in the past 20 years, the number of clinical research papers published by China's 23 "Double First-Class" construction medical universities had a rising trend, with a total of 4,042 papers in the CNKI database and a total of 47,096 papers in the WoS database (*Table 2*).

SNA

Overall network matrix

Based on the numbers of papers published by 23 "Double First-Class" construction medical universities indexed in the CNKI and WoS databases in the period from 2000 to 2019, we obtained two 23×23 scientific collaboration network matrices (*Tables 3,4*). In the tables, the number represents the code number of each university (e.g., "1" represents Peking University and "2" Peking Union Medical College). In the 20 years, the numbers of cooperative publications between Peking University and Peking Union Medical College indexed in the CNKI and WoS databases were 0 and 245, respectively. The numbers on the diagonal of the matrix are the total number of papers published by each university (e.g., in 20 years, the total numbers of clinical research papers published by Peking University indexed in the CNKI and WoS databases were 134 and 7,345, respectively).

Analysis of overall network density

To more intuitively show the status and development of clinical research collaboration among the 23 universities, based on the symmetric matrices shown in *Tables 3,4*, we used the NetDraw software to generate the diagrams of the networks (*Figures 1,2*). The 23 colleges and universities are represented as nodes. Any two universities with a cooperative publication are represented as an edge. The number of cooperative publications is the thickness of that edge. As shown in *Figures 1,2*, universities have established

Table 2 Number of annual publications by "Double First-Class" construction medical universities indexed by CNKI and WoS databases

Year	Number of papers indexed in CNKI	Number of papers indexed in WoS	Total
2000	77	65	142
2001	65	122	187
2002	68	144	212
2003	81	222	303
2004	80	359	439
2005	91	402	493
2006	126	477	603
2007	178	708	886
2008	196	904	1,100
2009	233	1,236	1,469
2010	255	1,558	1,813
2011	228	1,891	2,119
2012	280	2,525	2,805
2013	234	3,029	3,263
2014	311	3,739	4,050
2015	311	4,511	4,822
2016	301	4,962	5,263
2017	269	5,603	5,872
2018	303	6,452	6,755
2019	355	8,187	8,542
Total	4,042	47,096	51,138

CNKI, China National Knowledge Infrastructure; WoS, Web of Science.

Table 3 Collaborative network matrix of clinical research papers published by 23 "Double First-Class" construction medical universities indexed in CNKI (partial)

University	1	2	3	4	5	21	22	23
1	134	0	0	10	2	0	0	2
2	0	30	0	2	0	0	0	0
3	0	0	52	2	0	0	1	1
4	10	2	2	912	1	0	1	13
5	2	0	0	1	37	0	0	0
21	0	0	0	0	0	20	0	1
22	0	0	1	1	0	0	15	1
23	2	0	1	13	0	0	0	1,218

CNKI, China National Knowledge Infrastructure.

Table 4 Collaborative network matrix of clinical research papers published by 23 "Double First-Class" construction medical universities indexed in WoS (partial)

University	1	2	3	4	5	21	22	23
1	7,345	245	2	42	302	21	22	23
2	245	3,081	2	17	116	126	99	8
3	2	2	19	0	0	37	67	0
4	42	17	0	93	5	0	1	0
5	302	116	0	5	1,812	7	5	4
21	126	37	0	7	94	1,858	62	2
22	99	67	1	5	100	62	2,002	1
23	8	0	0	4	3	2	1	47

WoS, Web of Science.
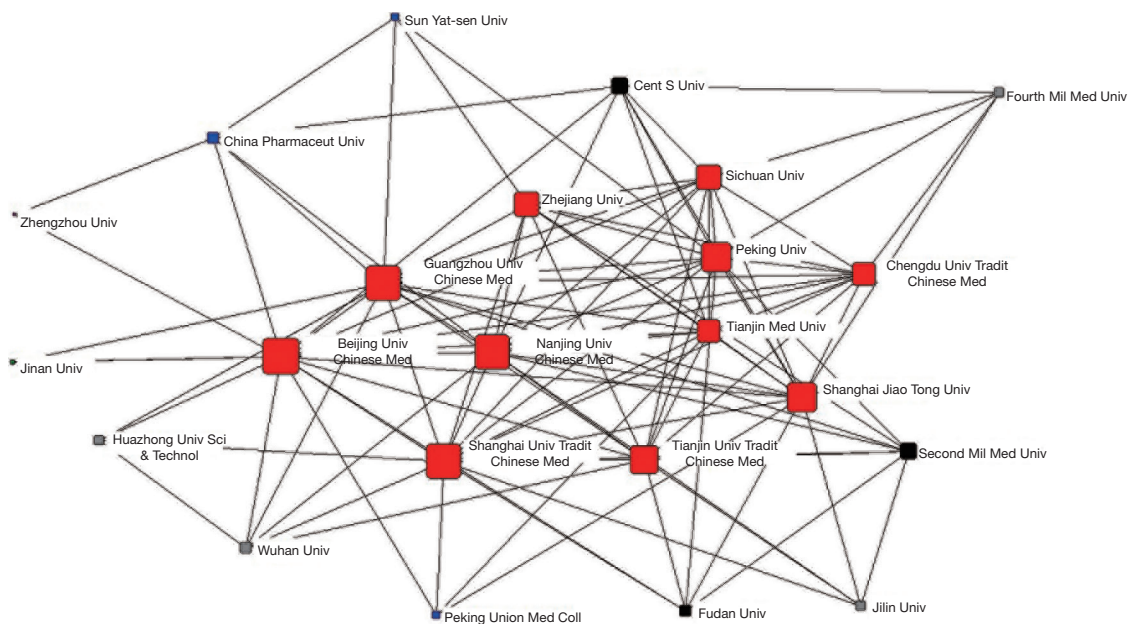
Figure 1 Clinical research publication cooperation network of the 23 "Double First-Class" construction medical universities in CNKI (density =0.4229). CNKI, China National Knowledge Infrastructure.

extensive connections in publishing in domestic and foreign journals, but with great variation in terms of number of cooperative publications. The node weight in *Figure 2* is generally greater than that in *Figure 1*, with little difference between nodes, while the number of edges in *Figure 2* is greater than that in *Figure 1*, with a greater connection strength and a smaller connection difference, indicating that the scientific research cooperation of universities in publishing in foreign journals has been more extensive than that in domestic journals, and it has had a narrower range of difference.

Using Ucinet software, we found that the density of the network model of interuniversity clinical research publication collaboration in CNKI was 0.4229, representing
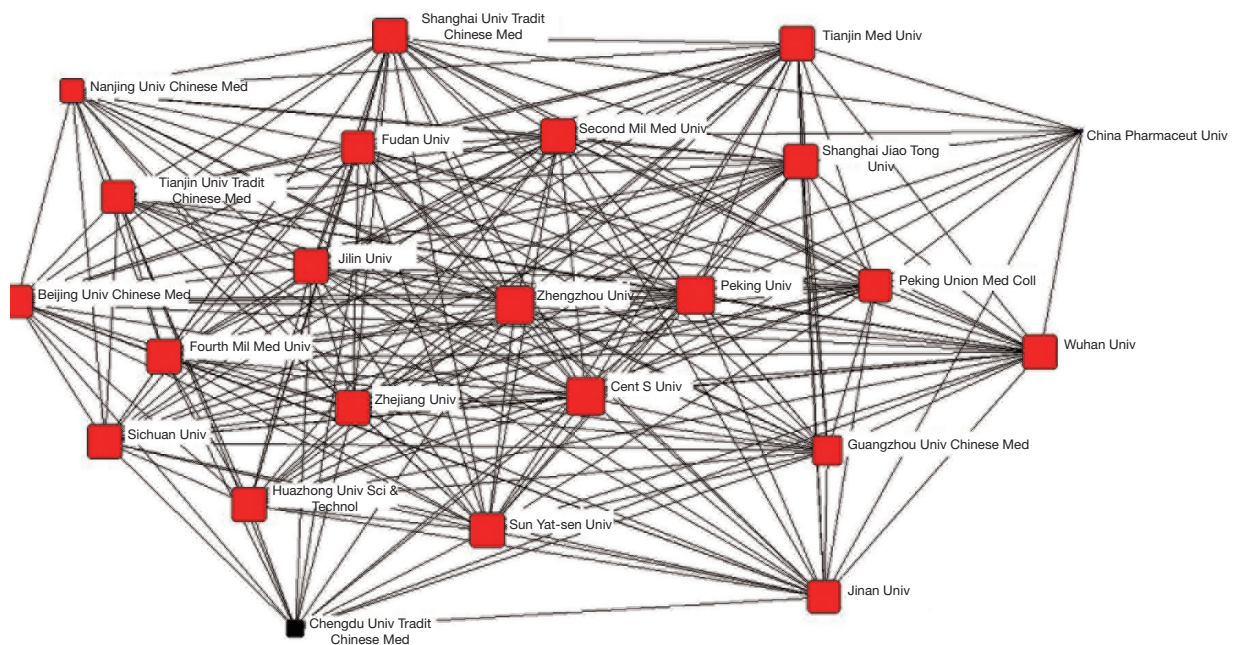
Figure 2 Clinical research publication cooperation network of the 23 "Double First-Class" construction medical universities in WoS (density =0.9052). WoS, Web of Science.

a low-density network. This indicates that there have been relatively few clinical research collaborations among the 23 universities in domestic journals, so there is much room for improvement. The density of the network model of interuniversity clinical research publication collaboration in WoS was high, at 0.9052, and without any isolated node, indicating that collaborations among the universities in clinical research publications in international journals are strong, with closer connections.

Cohesive subgroup analysis
Faction analysis
Based on the imported cooccurrence matrix, we conducted a faction analysis on the components and found that the optimal fitness of the four-category cohesive subgroup calculated using Ucinet software was 146. Therefore, the number of factions in the group structure was set to four, and the numbers of subgroup components in the CNKI and WoS databases are shown in *Table 5*. Among them, the largest subgroup from the CNKI database was the third subgroup, which was composed of universities in the first-tier cities such as Beijing University of Traditional Chinese Medicine, Shanghai University of Traditional Chinese Medicine, Guangzhou University of Traditional Chinese Medicine, Peking University, Shanghai Jiao Tong

University, Fudan University, and Sichuan University, with a density of 0.81. The densities of subgroups 1, 2, and 4 were 0.21, 0.33, and 0.35, respectively. The largest subgroup from the WoS database was the third subgroup, which was composed of Peking University, Peking Union Medical College, Beijing University of Traditional Chinese Medicine, Fudan University, Shanghai Jiao Tong University, Second Military Medical University, Sun Yat-sen University, and Jinan University, with a density of 0.98. The densities of subgroups 1, 2, and 4 were 0.85, 0.75, and 0.50, respectively.

Block model analysis
The convergence of iterated correlations (CONCOR) method of Ucinet software was used for cluster analysis, in which the maximum segmentation depth was set to 2 (*Tables 6,7, Figures 3,4*). In *Tables 6,7*, the number on the diagonal represents the density of each subgroup, and the other numbers represent the mutual influence between the subgroups. As shown in *Table 6*, as gathered from the CNKI database, subgroups 1 and 2 had a greater influence on other subgroups, and the intersubgroup density was low, showing that the cooperation was not very close. However, *Figure 3* shows that members of eight subgroups had a more uniform distribution. As shown in *Table 7*, in the data from the WoS database, subgroup 2 had a higher density, having

Table 5 Faction analysis of clinical research publications of 23 "Double First-Class" construction medical universities

Subgroup	CNKI database	WoS database
Subgroup 1	Peking Union Medical College, Huazhong University of Science and Technology, Wuhan University	Nanjing University of Chinese Medicine
Subgroup 2	China Pharmaceutical University, Sun Yat-sen University, Zhengzhou University	Chengdu University of Traditional Chinese Medicine
Subgroup 3	Beijing University of Traditional Chinese Medicine, Chengdu University of Traditional Chinese Medicine, Shanghai University of Traditional Chinese Medicine, Peking University, Tianjin University of Traditional Chinese Medicine, Nanjing University of Traditional Chinese Medicine, Guangzhou University of Traditional Chinese Medicine, Tianjin Medical University, Sichuan University, Shanghai Jiao Tong University, Central South University, Zhejiang University, Fourth Military Medical University	Peking University, Peking Union Medical College, Beijing University of Chinese Medicine, Fudan University, Shanghai Jiao Tong University, Second Military Medical University, Sun Yat-sen University, Jinan University, Guangzhou University of Chinese Medicine, Zhejiang University, Wuhan University, Huazhong University of Science and Technology, Sichuan University, Tianjin Medical University, Shanghai University of Traditional Chinese Medicine, Tianjin University of Traditional Chinese Medicine, Fourth Military Medical University, Central South University, Jilin University, Zhengzhou University
Subgroup 4	Fudan University, Second Military Medical University, Jilin University, Jinan University	China Pharmaceutical University

CNKI, China National Knowledge Infrastructure; WoS, Web of Science.

Table 6 Cohesive subgroup density of clinical research publications by the 23 "Double First-Class" construction medical universities indexed in CNKI

Subgroup	1	2	3	4	5	6	7	8
1	1.000	1.000	0.533	0.500	0.667	0.250	0.000	0.000
2	1.000	0.400	0.560	0.400	0.600	0.400	0.100	0.400
3	0.533	0.560	0.800	0.600	1.000	0.000	0.300	0.000
4	0.500	0.400	0.600	1.000	0.500	0.000	0.500	0.500
5	0.667	0.600	1.000	0.500	1.000	1.000	0.000	0.000
6	0.250	0.400	0.000	0.000	1.000	0.167	0.250	0.250
7	0.000	0.100	0.300	0.500	1.000	0.250	0.000	0.000
8	0.000	0.400	0.000	0.500	0.000	0.250	0.000	0.000

CNKI, China National Knowledge Infrastructure.

Table 7 Cohesive subgroup density of clinical research publications by the 23 "Double First-Class" construction medical universities indexed in WoS*

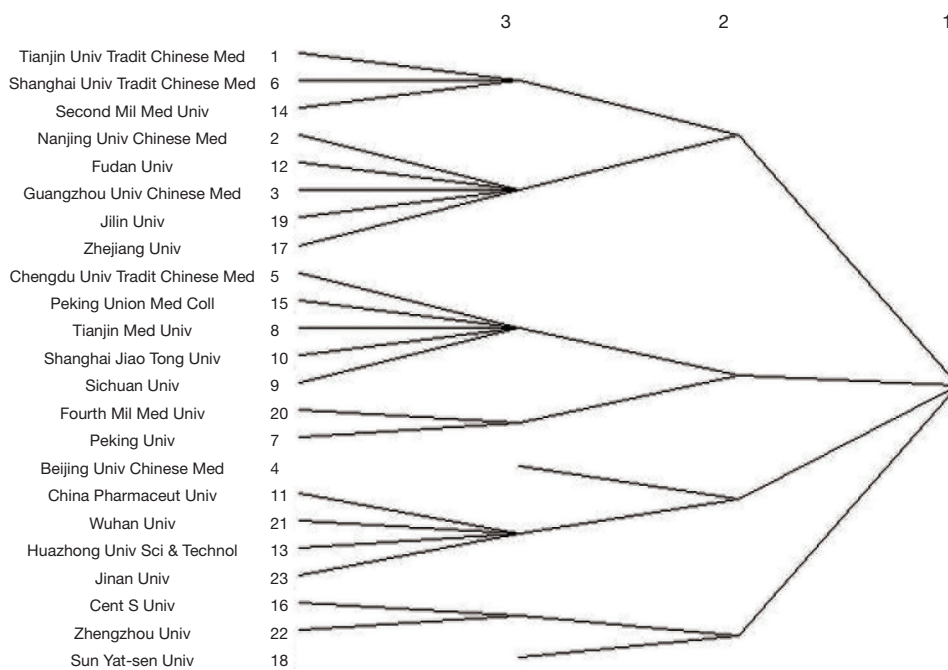| Subgroup	1	2	3	4	5	6
1	0.000	4.929	1.500	3.000	0.000	0.250
2	4.929	96.648	15.786	8.500	1.286	67.946
3	1.500	15.786	10.000	0.500	0.500	5.750
4	3.000	8.500	0.500	0.000	0.000	4.000
5	0.000	1.286	0.500	0.000	0.000	0.500
6	0.250	67.946	5.750	4.000	0.500	46.167

WoS, Web of Science.

Figure 3 Faction analysis result of clinical research publications by the 23 "Double First-Class" construction medical universities indexed in CNKI. CNKI, China National Knowledge Infrastructure.
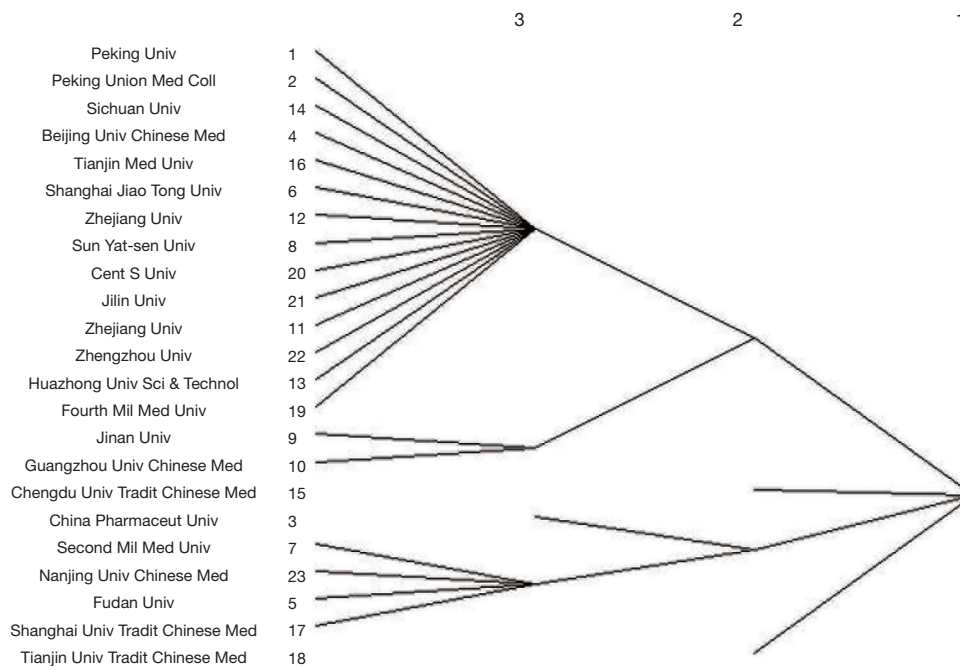

Figure 4 Clinical research publications by the 23 "Double First-Class" construction medical universities indexed in WoS. WoS, Web of Science.

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not only close cooperation among universities within the subgroup and a high degree of integration but also a greater influence on other subgroups.

Network centrality analysis

Using Ucinet software, we calculated the degree centrality values of the "Double First-Class" construction medical universities networks. The degree centrality of the network using the CNKI data was 36.57%, and that from the WoS data was 19.39%. The "Double First-Class" construction medical universities influenced each other's degree centrality when cooperatively publishing papers indexed in the CNKI database, i.e., most universities had a relatively balanced influence on the publication of papers by other universities. However, regarding the papers indexed by the WoS database, the degree centrality was low, suggesting that the network is not dominated by one or some central nodes. There was a low convergence tendency, i.e., the collaborations among the 23 universities were mainly concentrated in several universities.

We calculated three indicators of centrality for each of the 23 universities in the cooperation networks (*Tables 8,9*). Overall, 23 universities showed different forms of centrality in the clinical research collaboration network in publishing papers indexed by the CNKI and WoS databases.

Centrality analysis mainly uses three indicators. (I) Degree centrality. For papers from the CNKI database, the degree centrality of Beijing University of Traditional Chinese Medicine was 17, indicating that it was directly connected to 17 nodes and was at the core of the network. At the same time, Shanghai University of Traditional Chinese Medicine, Guangzhou University of Traditional Chinese Medicine, and Nanjing University of Traditional Chinese Medicine also had high degree centrality, indicating that these nodes were also at the center of the network and have a strong connections to other nodes. When we used papers from the WoS database, Peking University, Central South University, Zhengzhou University, and Sichuan University showed higher degree centrality, while Tianjin University of Traditional Chinese Medicine, Guangzhou University of Traditional Chinese Medicine, and Nanjing University of Traditional Chinese Medicine ranked 19th, 20th and 21st, respectively, in terms of degree centrality. Papers from the CNKI and WoS databases showed completely different distribution patterns in terms of degree centrality. (II) Betweenness centrality.

For papers from the CNKI database, the betweenness centrality of each university showed a strong geographic regionality. Beijing, Guangzhou, Nanjing, Shanghai, and other provinces and cities were on the top in terms of this indicator, indicating that these universities are in the center of the paper-publishing cooperation network and control the planning and execution of clinical research published by other universities. However, universities in Zhengzhou, Jilin, Shaanxi, and other provinces showed a betweenness centrality <1, indicating that they have little influence and control on other universities in the regional paper publishing cooperation network. For papers from the WoS database, Peking University, Central South University, Zhengzhou University, and Shanghai University of Traditional Chinese Medicine were on the top in betweenness centrality, while Nanjing University of Traditional Chinese Medicine, Tianjin University of Traditional Chinese Medicine, and Chengdu University of Traditional Chinese Medicine were on the bottom, showing a similar pattern of distribution of clinical research in traditional Chinese medicine (TCM) and comprehensive universities to their pattern of degree centrality. (3) Closeness centrality. The closeness centrality of each university in the clinical research paper cooperation network was uniformly low. Among the universities, Zhengzhou University was most independent in terms of the CNKI database, while China Pharmaceutical University was most independent in terms of the WoS database.

Analysis of core–periphery structure

We also analyzed the constructed continuous core-periphery model. As shown in *Table 10*, the correlation coefficients of core-periphery models on the data from the CNKI and WoS databases were 0.771 and 0.742, respectively, indicating good model fits. As shown in *Table 11*, Tianjin University of Traditional Chinese Medicine, Nanjing University of Traditional Chinese Medicine, Guangzhou University of Traditional Chinese Medicine, and Beijing University of Traditional Chinese Medicine had core positions when considering the CNKI database, while Zhengzhou University and Jinan University were peripheral. In the data from the WoS database, Peking University, Peking Union Medical College, Fudan University, and Shanghai Jiao Tong University had core positions, while Central South University, Jilin University, Zhengzhou University, and Nanjing University of Traditional Chinese Medicine were at peripheral positions.

Table 8 Centrality ranking of the 23 "Double First-Class" construction medical universities in the clinical research paper cooperation network as indexed in the CNKI database

Ranking	School name	Degree centrality	School name	Betweenness centrality	School name	Closeness centrality
1	Beijing University of Chinese Medicine	17.000	Beijing University of Chinese Medicine	39.125	Beijing University of Chinese Medicine	27.000
2	Shanghai University of Traditional Chinese Medicine	16.000	Guangzhou University of Chinese Medicine	20.109	Shanghai University of Traditional Chinese Medicine	28.000
3	Guangzhou University of Chinese Medicine	16.000	Nanjing University of Chinese Medicine	18.185	Guangzhou University of Chinese Medicine	28.000
4	Nanjing University of Chinese Medicine	16.000	Shanghai University of Traditional Chinese Medicine	15.938	Nanjing University of Chinese Medicine	28.000
5	Shanghai Jiao Tong University	14.000	Peking University	13.161	Shanghai Jiao Tong University	30.000
6	Peking University	14.000	Shanghai Jiao Tong University	12.996	Peking University	30.000
7	Tianjin University of Traditional Chinese Medicine	13.000	Zhejiang University	6.921	Tianjin University of Traditional Chinese Medicine	31.000
8	Zhejiang University	12.000	Tianjin University of Traditional Chinese Medicine	6.582	Sichuan University	32.000
9	Sichuan University	12.000	China Pharmaceutical University	4.727	Tianjin Medical University	33.000
10	Tianjin Medical University	11.000	Sichuan University	3.808	Chengdu University of Traditional Chinese Medicine	33.000
11	Chengdu University of Traditional Chinese Medicine	11.000	Central South University	3.330	Zhejiang University	33.000
12	Central South University	8.000	Tianjin Medical University	3.302	Central South University	36.000
13	Second Military Medical University	8.000	Chengdu University of Traditional Chinese Medicine	2.956	Second Military Medical University	37.000
14	Fudan University	6.000	Second Military Medical University	1.571	Fudan University	38.000
15	Wuhan University	6.000	Sun Yat-sen University	0.610	China Pharmaceutical University	38.000
16	China Pharmaceutical University	6.000	Fudan University	0.525	Wuhan University	39.000
17	Huazhong University of Science and Technology	5.000	Wuhan University	0.400	Huazhong University of Science and Technology	40.000

Table 8 (*continued*)

Table 8 (*continued*)

Ranking	School name	Degree centrality	School name	Betweenness centrality	School name	Closeness centrality
18	Fourth Military Medical University	5.000	Huazhong University of Science and Technology	0.377	Peking Union Medical College	41.000
19	Jilin University	5.000	Jilin University	0.234	Jilin University	41.000
20	Sun Yat-sen University	4.000	Fourth Military Medical University	0.143	Sun Yat-sen University	42.000
21	Peking Union Medical College	4.000	Peking Union Medical College	0.000	Jinan University	42.000
22	Jinan University	3.000	Zhengzhou University	0.000	Fourth Military Medical University	43.000
23	Zhengzhou University	2.000	Jinan University	0.000	Zhengzhou University	46.000

CNKI, China National Knowledge Infrastructure.

This is essentially consistent with the result of the centrality analysis. In addition, the node connection density of the core area and that of the peripheral area in the case of the CNKI database were 0.972 and 0.143, respectively, while the node connection density between the core area and the peripheral area was only 0.468. The node connection densities of the core area and the peripheral area in the case of the WoS database were 0.991 and 0.896, respectively, and that between the core area and the peripheral area was 1.000. These results indicate that with the data from the CNKI database, connections between the peripheral areas and those between the peripheral and core area nodes were weak and differed significantly from those between core nodes, while in the case of the WoS database, nodes had a closer relationship.

Discussion

In the context of the "Double First-Class" construction, the number of papers published by Chinese universities in important international and domestic journals has increased rapidly, and the quality of the publications has improved significantly, showing a significantly greater international influence. At the same time, with the in-depth implementation of the innovation-driven development strategy in the field of health and medicine, relying on its huge numbers of patients and clinical data, China's development of clinical research is at a stage of great opportunities as well as great challenges (11).

In this study, we comparatively analyzed the medical research cooperation among China's universities and its network structure and found that the scientific research cooperation among 23 medical universities in publishing papers in foreign journals is more extensive than that in domestic journals, with more uniform development and little difference between the universities, which is consistent with the results of Zhao *et al.* regarding the scientific research cooperation network of 42 "Double First-Class" construction universities (12). In recent years, China's clinical research has made great progress, but no high-quality, systematic clinical research system has been established, and academic achievements with global influence are still lacking. Luan *et al.* showed that small, single-center, and purely positive results are the mainstream works published in China's domestic medical journals, which are plagued by issues such as poor research standardization, lack of method specifications, and low quality of reports, leading to low conversion rates of domestic clinical research papers (13).

In the domestic-journal scientific research cooperation network, the faction with Tianjin University of Traditional Chinese Medicine and Nanjing University of Traditional Chinese Medicine as the core and the fraction with Peking Union Medical College and Central South University as the core are the most abundant, and they are evenly distributed, with loose connections to each other. However, the quality of clinical research papers published in domestic journals has not been highly evaluated and widely

Table 9 Centrality ranking of the 23 "Double First-Class" construction medical universities in the clinical research paper cooperation network, as indexed in WoS* database

Ranking	School name	Degree centrality	School name	Betweenness centrality	School name	Closeness centrality
1	Peking University	22.000	Peking University	2.055	Peking University	22.000
2	Central South University	22.000	Central South University	2.055	Central South University	22.000
3	Zhengzhou University	22.000	Zhengzhou University	2.055	Zhengzhou University	22.000
4	Sichuan University	21.000	Shanghai University of Traditional Chinese Medicine	1.943	Sichuan University	23.000
5	Tianjin Medical University	21.000	Wuhan University	1.655	Tianjin Medical University	23.000
6	Huazhong University of Science and Technology	21.000	Jinan University	1.605	Huazhong University of Science and Technology	23.000
7	Second Military Medical University	21.000	Second Military Medical University	1.478	Second Military Medical University	23.000
8	Sun Yat-sen University	21.000	Tianjin Medical University	1.478	Sun Yat-sen University	23.000
9	Fourth Military Medical University	21.000	Shanghai Jiao Tong University	1.478	Fourth Military Medical University	23.000
10	Jilin University	21.000	Peking Union Medical College	1.155	Jilin University	23.000
11	Shanghai Jiao Tong University	21.000	Sichuan University	0.746	Shanghai Jiao Tong University	23.000
12	Wuhan University	21.000	Sun Yat-sen University	0.746	Wuhan University	23.000
13	Shanghai University of Traditional Chinese Medicine	21.000	Fourth Military Medical University	0.746	Shanghai University of Traditional Chinese Medicine	23.000
14	Zhejiang University	21.000	Zhejiang University	0.746	Zhejiang University	23.000
15	Peking Union Medical College	20.000	Huazhong University of Science and Technology	0.746	Peking Union Medical College	24.000
16	Beijing University of Chinese Medicine	20.000	Jilin University	0.746	Beijing University of Chinese Medicine	24.000
17	Jinan University	20.000	Beijing University of Chinese Medicine	0.640	Jinan University	24.000
18	Fudan University	20.000	Guangzhou University of Chinese Medicine	0.640	Fudan University	24.000
19	Tianjin University of Traditional Chinese Medicine	20.000	Tianjin University of Traditional Chinese Medicine	0.640	Tianjin University of Traditional Chinese Medicine	24.000
20	Guangzhou University of Chinese Medicine	19.000	Fudan University	0.335	Guangzhou University of Chinese Medicine	25.000
21	Nanjing University of Chinese Medicine	17.000	Chengdu University of Traditional Chinese Medicine	0.155	Nanjing University of Chinese Medicine	27.000
22	Chengdu University of Traditional Chinese Medicine	15.000	Nanjing University of Chinese Medicine	0.105	Chengdu University of Traditional Chinese Medicine	29.000
23	China Pharmaceutical University	10.000	China Pharmaceutical University	0.050	China Pharmaceutical University	34.000

WoS, Web of Science.

Table 10 Measurement of the centrality of clinical research paper collaboration of the 23 "Double First-Class" construction medical universities

Province	School name	Degree of centrality (CNKI)	Degree of centrality (WoS)
Beijing	Peking University	0.278	0.225
	Peking Union Medical College	0.092	0.208
	China Pharmaceutical University	0.097	0.103
	Beijing University of Chinese Medicine	0.297	0.209
Shanghai	Fudan University	0.132	0.212
	Shanghai Jiao Tong University	0.272	0.217
	Second Military Medical University	0.164	0.217
	Shanghai University of Traditional Chinese Medicine	0.313	0.214
Guangdong	Sun Yat-sen University	0.076	0.220
	Jinan University	0.075	0.205
	Guangzhou University of Chinese Medicine	0.304	0.198
Zhejiang	Zhejiang University	0.247	0.220
Hubei	Wuhan University	0.132	0.216
	Huazhong University of Science and Technology	0.106	0.220
Sichuan	Sichuan University	0.266	0.220
	Chengdu University of Traditional Chinese Medicine	0.251	0.157
Tianjin	Tianjin Medical University	0.240	0.217
	Tianjin University of Traditional Chinese Medicine	0.267	0.209
Shaanxi	Fourth Military Medical University	0.100	0.220
Hunan	Central South University	0.155	0.225
Jilin	Jilin University	0.109	0.220
Henan	Zhengzhou University	0.032	0.225
Jiangsu	Nanjing University of Chinese Medicine	0.313	0.180

CNKI, China National Knowledge Infrastructure; WoS, Web of Science.

praised (14). There are even research results indicating that the quality of the papers and academic influence of clinical research in China are still lower than those in European and American countries (13). In the international-journal scientific research cooperation network, the main faction is centered on Peking University, Peking Union Medical College, and Beijing University of Traditional Chinese Medicine and composed of most of the universities, with a high density, with close collaborations between universities within the faction and a high degree of integration as well as a greater influence on other subgroups. Similar to the results of the faction analysis, the centrality of each of the universities also shows a strong geographical regionality, which is consistent with the geographical distribution of China's 50 national medical research centers and 244 provincial medical research centers (15). Based on the CNKI search result regarding the number of coauthored papers published by 26 universities of the "211 Project" and the "Province-ministry Joint Construction Project" in the Beijing–Tianjin–Hebei region over 10 years, Li concluded that geographical aggregation is a major factor affecting the strength of scientific research cooperation (16). To promote collaborative innovation among universities, in addition to spontaneous organization among universities, the geological locations of universities and the similarity of research fields should be considered. Large cities with faster and better development in relevant fields can quickly obtain various types of research funds and do higher-level scientific research, while it is more difficult for areas with slower development to obtain this support, not to mention the low strength of the support. Therefore, it is recommended that the national and provincial governments set up joint clinical research funds for areas with slow technological development to promote collaborative, innovative research

Table 11 Core–periphery structure of clinical research paper collaboration of the 23 "Double First-Class" construction medical universities

Area	CNKI database	WoS database
Core	Tianjin University of Traditional Chinese Medicine, Nanjing University of Traditional Chinese Medicine, Guangzhou University of Traditional Chinese Medicine, Beijing University of Traditional Chinese Medicine, Chengdu University of Traditional Chinese Medicine, Shanghai University of Traditional Chinese Medicine, Peking University, Sichuan University, Shanghai Jiao Tong University	Peking University, Peking Union Medical College, Fudan University, Shanghai Jiao Tong University, Sun Yat-sen University, Zhejiang University, Huazhong University of Science and Technology, Sichuan University
Periphery	Tianjin Medical University, China Pharmaceutical University, Fudan University, Huazhong University of Science and Technology, Second Military Medical University, Peking Union Medical College, Central South University, Zhejiang University, Sun Yat-sen University, Jilin University, Fourth Military Medical University, Wuhan University, Zhengzhou University, Jinan University	China Pharmaceutical University, Beijing University of Traditional Chinese Medicine, Second Military Medical University, Jinan University, Guangzhou University of Traditional Chinese Medicine, Wuhan University, Chengdu University of Traditional Chinese Medicine, Tianjin Medical University, Shanghai University of Traditional Chinese Medicine, Tianjin University of Traditional Chinese Medicine, Fourth Military Medical University, Central South University, Jilin University, Zhengzhou University, Nanjing University of Traditional Chinese Medicine

CNKI, China National Knowledge Infrastructure; WoS, Web of Science.

in these regions by their leading universities.

In the field of clinical research, the studied universities have published 4,024 papers in domestic journals but 47,096 papers in foreign journals in the past 20 years, a large difference. In the domestic-journal scientific research cooperation network, TCM universities, i.e., Beijing University of Traditional Chinese Medicine, Shanghai University of Traditional Chinese Medicine, and Guangzhou University of Traditional Chinese Medicine, are at the center of the network. In stark contrast, the international-journal scientific research cooperation network has Peking University, Central South University, Zhengzhou University, and Sichuan University on the top in terms of degree centrality, with few publications in Chinese periodicals and a tendency to publish in international journals, while Tianjin University of Traditional Chinese Medicine, Guangzhou University of Traditional Chinese Medicine, and Nanjing University of Traditional Chinese Medicine are at the bottom, demonstrating the gap between TCM universities and other comprehensive universities in publications at home and abroad.

Clinical research is a major feature of TCM treatment. After decades of development, TCM treatment has spread to more than 180 countries and regions, laying a solid foundation for the understanding and use of TCM in countries all over the world. In 2019, Xi Jinping gave important instructions on the work of TCM, emphasizing that it is necessary to follow the law of development of TCM, inherit its essence, keep up with innovations, accelerate the modernization and industrialization of TCM, adhere to the equal emphasis on TCM and Western medicine, and promote mutual complement and coordination of TCM and Western medicine, and the high-quality development of TCM cause and industry, as well as the introduction of TCM to the world, so that the unique advantages and functions of TCM in disease prevention and treatment can be taken advantage of (17). In this regard, how to significantly increase the international community's recognition of TCM and give full play to the supporting and leading role of technological innovation in TCM are issues that need to be focused on in the clinical research done by TCM universities. At the same time, the Ministry of Science and Technology and the Ministry of Education formally issued a notice on *Several Measures to Eliminate the Bad 'Publication-only' Orientation in Scientific and Technological Achievement Evaluation (for Trial Implementation)* and *Opinions on Regulating the Use of SCI Paper-related Indices in Higher-Education Institutions and Establishing a Correct Evaluation Orientation*, to rid universities of the mindset of "SCI first" and "paper-only" when evaluating researchers and encourage scientific investigators to publish more high-quality papers and publish them in domestic journals with international influence (18). The core leading role of top universities in publishing scientific results in high-level Chinese journals needs to be further strengthened.

Through the core–periphery analysis, we found that

in the domestic-journal scientific research cooperation network, the connection between nodes of peripheral areas and that between nodes of core and peripheral areas are very weak, and there is a gap between the two. In contrast, in the foreign-journal scientific research cooperation network, the relationship between the nodes is stronger, suggesting that most high-quality domestic resources are still in the hands of some top universities. The construction of first-class universities is not a single advance but aims to lead the improvement of other universities through the efforts of first-class universities. A truly first-class university must be able to play a leading role in the development of the country's scientific and technological construction (19). Universities in the core regions should also take the initiative in constructing first-class disciplines, strive to become leaders and main forces in clinical research, make full use of their own advantages and resources, coordinate the development of peripheral universities, participate in and promote clinical research, and make greater contributions to national social and economic development. Given China's scattered and uneven development of medical resources and centralized technology management system, relevant departments such as science and technology management departments, health management departments, and education management departments should establish a mechanism and system for collaborative innovation in clinical research. How to focus on the major needs of disease prevention, diagnosis, and treatment, organize the construction of collaborative innovation networks, build public service platforms, strengthen the construction of research platforms for key common technologies oriented toward clinical application, and make further explorations and advances in promoting clinical research, collaborative innovation, talent training, and service promotion, etc., will be important challenges in the construction of "Double First-Class" medical universities in China. Our results demonstrated that the cooperation between "Double First-Class" universities was less organized and quite heterogeneous. The cooperation pattern restricts the development of scientific research to some extent. In order to enhance the collaboration and improve the quality of clinical research, it is necessary to improve scientific system and to build comprehensive supporting mechanism.

Cooperation in clinical research can take many forms. In this study, we examined the scientific research cooperation between universities only from the perspective of paper publication. Many other aspects, such as cooperation between universities in a certain field and joint projects, should be addressed future studies. Whether it is a TCM university or a comprehensive university, China still needs to strengthen the top-down design of the clinical research field to promote the combination and translation of clinical and basic research and the cross-integration of interdisciplinary teams, so the results of medical research can reap benefits to society. With the continuous advancement of technology, the continuous improvement of systems and mechanisms, big data in biomedicine and clinical medicine should be fully used to promote the rapid development of clinical research in China. The "Double First-Class" university should focus on building effective scientific research team, promoting scientific cooperation and encouraging innovation to improve the quality of clinical research. Performing clinical research on the basis of strengthening the collaboration among "Double First-Class" construction universities will surely open up a new world of clinical research in China and help realize the Healthy China strategy as soon as possible.

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Footnote

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-22-516/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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