AN Analysis of COVID-19 Clinical Research Based on Trials & Publications in 2020

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Abstract. The global pandemic of COVID-19 has brought huge public health challenges to the world. To meet the challenge, researchers worldwide have carried out a series of clinical studies. This article aims to analyze the progress of COVID-19, and explore the development and main research directions in 2020. The clinical trials focus on the design of the trial plan, which can be registered on the platform after the design is completed. The purpose of clinical publications is to publish trial results, focusing on in vitro tests, drug screening and so on. Based on these characteristics, this paper analyzes both clinical publications and clinical trials, and explores the development of global clinical research in 2020 from countries, intervention methods and trial designs. The experimental results show that the United States and China have published the most publications and carried out the most clinical trials. The maximum intervention methods in clinical trials & publications are focused on the drugs.

1. Introduction
In early December 2019, unexplained cases of pneumonia were reported that have since been reported in large numbers in most countries[1]. On January 30, 2020, the World Health Organization declared the spread of this disease as a Public Health Emergency of International Concern[2] and later named the disease novel coronavirus disease 2019[3] (COVID-19). The COVID-19 pandemic has had a global impact[4]. According to data released by Johns Hopkins University[5], as of December 31, 2020, there were over 83 million cases of SARS-CoV-2 infection with more than 1,818,116 deaths worldwide[6]. The rapid spread of the epidemic has also caused a surge in the number of related literature and clinical trials. There have been some publications on scientometric research. Haghani and Bliemer analyzed the co-occurrence of key terms, bibliographic coupling, and citation relations of journals and collaborations between countries on SARS, MERS and 2019-nCOV literature[7]. Chinese researchers analyzed 107 clinical trials registered in China up to February 14[8], this article was used only descriptive statistics without evaluating data quality. In addition, more than half of the articles belong to secondary articles (perspectives and syntheses of the available knowledge), which indicated that a large amount of literature is not directly related to clinical research[9].
This article analyzes the clinical publications and clinical trial data of COVID-19, to provide an overview of clinical research on COVID-19 and a reference for future clinical studies.

2. Data And Methods
We carried out a quantitative study using statistical approaches. We downloaded the data of registered clinical trials and publications on COVID-19 from the WHO website and the WoS core collection in 2020, respectively. We divided all interventions into five categories: traditional Chinese medicine, chemical agents and drugs, vaccines, yoga and others, by matching a keyword list. Then we analyzed clinical trials and publications related to these interventions using a variety of statistical methods. We also analyzed these data at the country level.

The search query of publications is TS = ("covid-19" OR "sars-cov-2" OR "2019-ncov" OR "novel coronavirus" OR "new corona virus" OR "coronavirus disease 2019" OR "severe acute respiratory syndrome coronavirus 2") AND (therapy OR "clinical trial" OR drug OR vaccine). At the same time, the search document types are limited to Article, Letter and Proceedings Paper, and the time is 2020.

On January 1, 2021, 5475 clinical publications were downloaded. After removing the duplicates according to the AB and TI fields, there are 5445 articles left. After non-clinical data screening, 3450 articles remain. On the same day, the global online registration of clinical trial data was downloaded on the WHO website (update on 16 December 2020), with a total of 7431 records. Excluding canceled trials (44), non-interventional trials (3561), trials with the wrong registration time (81), data with the same public title and scientific title (10), non-COVID-19 clinical trials (1277), remaining 2458 articles.

3. Result
3.1. Overall status of clinical trials and publications
The overall situation of the publications and trial is shown in figure 1. It can be seen that the growth rate of the number of infections increased in February and March, and then began to decline. There is also a slight increase in July and October-November. The number of publications mainly showed an upward trend before September, and the number of trials rose sharply in April, after which the number began to decrease. It can be seen that trials and publications, especially trials, have a similar trend to the growth rate of the number of infected people in the early stage, and show a certain lag.

After the outbreak, the number of publications published in February was less than that in January, because some journals only published one issue per year. In this case, no matter what months of this year’s publications are, they will be counted as the first issue of 2020 (that is, published in January), so there are more publications in January than in February.
3.2. Status of clinical trials and publications in various countries

We analyze the status of clinical trials and publications in various countries, and the analysis results are shown in figure 2 and figure 3. It can be seen that the number of publications published in the United States is the largest (998, 28.93%), and the number of trial registrations is the second (398, 16.19%). China has the largest number of trial registrations (408, 16.60%), and the number of publications ranks second (681, 19.74%). In addition, Italy (363, 10.52%), India (327, 9.48%) and the United Kingdom (321, 9.30%) have the largest number of publications; India (348, 14.16%), Spain (181, 7.38%) and France (123, 5.00%) has the largest number of trials.

![Figure 2. the number of publications in each country](image1)

![Figure 3. the number of trials in each country](image2)

![Figure 4. Monthly publications of the top 10 countries.](image3)

![Figure 5. Monthly trials of the top 10 countries.](image4)

We select the top 10 countries in the total number of publications and trials, and analyze the monthly publication/registration, as shown in figure 4 and figure 5. It can be seen that July and September is the peak period of publications published in various countries. From January to April, the number of publications published in China was significantly higher than that of other countries. April was the peak period of trial registration in European and American countries, after which the number of trial registrations in various countries began to decrease. The registration peak for the Indian trial was in June, after which India has been the main force of trial registration. The peak of China's trial registration was in February, which is related to the earliest outbreak in China.

3.3. Intervention method analysis

As mentioned earlier, the intervention measures are divided into five categories and the results are shown in figure 6. It can be seen that there are the most publications and trials on drugs, 1743 (50.52%) and 1437 (58.46%) respectively. The main intervention methods in the publications are chemical agents and drugs, and vaccines (1465, 42.46%), and the main intervention methods in the trials are chemical agents and drugs, and others (580, 23.60%). There are relatively few studies on traditional Chinese medicine,
including 92 publications (2.67%) and 142 trials (5.78%). The number of vaccine publications and trials is quite different, which is related to the limited types of vaccine trials and the possibility of interference information in the abstracts of the publications, resulting in an increase in the number of publications.

![Figure 6. The intervention methods of publications and trials.]

Figure 6. The intervention methods of publications and trials.

We analyzing the publication/registration of the main countries of intervention methods, and the results are shown in figure 7 and figure 8. It can be seen that the publications of various countries mainly focus on drugs and vaccines, and the main research country of traditional Chinese medicine is China. Also, the trials are mainly focused on drugs. The leading research countries of others are China and the United States, trials related to traditional Chinese medicine are mainly registered by China, and trials related to yoga are mainly registered by India.

3.4. Trial statistics analysis
Finally, we analyzed the statistical characteristics of the clinical trials carried out so far and drew a thermal diagram (figure 9). 8.8% of clinical trials are in the preclinical phase, and most of them are conducted in China (144/164). Clinical trials conducted in countries other than China are mainly concentrated in phase 2 and phase 3, while phase 4 trials (73/308) in China are relatively the most. 45.8% of clinical trials are recruiting patients, and 50.6% of clinical trials in Spain have been authorized.
Figure 9. Heat map of trial statistics

In all clinical trials, the median of target size was 120 (IQR 50 – 329.5). The medians for China and India are small, at 100 (IQR 49.5-200) and 105 (IQR 60-300) respectively. In the EU, 105 trials had a population size of exceeded 1000 of which 18 were exceeded 10000. This is related to the promotion of pan-European cooperation by the European Union and the prioritization of large-sample clinical trials. Almost all clinical trials (99.3%) involve both male and female, and more than 90% of clinical trials cover people aged 15-69. However, more than half (50.2%) of trials in EU did not specify the age group covered.

In China, only 18.1% of trials were randomized and controlled, compared to 89.4% in France and exceed 60% in other countries. 70.9% (61/86) of clinical trials in Italy are not blinded, which is higher than in other countries. However, 66.2% of the trials in China did not indicate whether the blind method was used. In the United States, 31.3% of the trials adopt triple blinded or more method. In addition to participants and care providers as in the double-blind trials, investigators and outcome assessors were blinded to group assignment, thereby minimizing bias.

4. Conclusion
The outbreak of the COVID-19 has brought immeasurable losses to the world. The analysis of clinical publications and trials can help researchers to grasp the research directions and hot spots as soon as possible. In general, both the number of clinical publications and the number of clinical trials have a similar trend to the growth rate of the number of patients infected with COVID-19 and shows a certain lag, which is more obvious in the early stages of clinical trials. The research situation is also related to the local development of the epidemic. Most of the early studies were conducted in China, and by the time the pandemic reached the global level, a large number of trials were being conducted in Europe and the United States.

Both the United States and China have the largest number of clinical publications and clinical trials. More than half of the clinical trials involve chemical agents and drugs. The clinical cooperation between Europe and the United States is very close. The main publishing organizations for clinical publications are universities or government agencies. Some countries have registered more clinical trials, but there
are fewer publications with research results. At the same time, the design of some clinical trials has problems such as fewer subjects, no blinding, no randomized control and so on. Even if the results of such trials are published, it is difficult to prove the effectiveness of the method. Style and spacing

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