From Skirmishes to Protracted Battles: A Bibliometric Analysis About Human Beings and Coronaviruses From 1991 to 2020

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Abstract

Background: COVID-19 caused unprecedented literature upsurge, and the world has worked together to fight the epidemic.

Methods: We conducted a bibliometric analysis to evaluate the research trends and reveal the core contents, based on publication outputs, geographical distribution, collaborations and hot keywords.

Results: Our analysis revealed the following: (1) The publication outputs obviously increased after SARS and MERS outbreaks, while sharply on rise during COVID-19 outbreak. Compared with SARS and MERS, COVID-19 aroused more dramatic and prolonged upsurge. (2) Compared with SARS and MERS, COVID-19 caused more widespread and powerful influences on countries or territories at short notice. Countries or territories displayed more international collaborations and communications to cope with the epidemics, and COVID-19 remarkably boosted the research advancements. (3) Given the keywords, we identified that multiple optional methods were used to cope with the SARS-CoV-2 infection based on the features of biology and immune responses.

Conclusions: Epidemics extremely accelerated the research boom and evolution.

Background

There are seven known coronaviruses that cause diseases in humans. HCoV-229E, HCoV-NL63, HCoV-OC43, and HCoV-HKU1 lead to mild upper respiratory infections. SARS-CoV, MERS-CoV and SARS-CoV-2 are three human highly pathogenic coronaviruses, which are responsible for the pandemic diseases SARS, MERS and COVID-19 [1].

SARS had been circulating in 32 countries or territories, from November 2002 to August 2003, the cumulative number of infections was 8,422, and the mortality rate reached 10.87%; MERS had been spread to 27 countries from April 2012 to December 2019, and there were 2,496 cases of infections, while the mortality rate was as high as 34.77% [2].

COVID-19 has caused a worldwide pandemic since December 2019, propagating through a surprising speed in a short time. The pattern of the global COVID-19 epidemic has changed dynamically from the first stage of a single epidemic center (China) in January and February of 2020 to the second stage of multiple epidemic centers (Italy, Iran, and South Korea) in March, and the world began experiencing a rapidly increasing number of cases with an estimated 50,000 cases confirmed globally per day at the end of March [3]. By 26 July, 2020, COVID-19 has been reported in 215 countries or territories, and there were 15,785,641 reported cases, with 4.05% mortality [4].

As for the pathogenicity of SARS-CoV, MERS-CoV and SARS-CoV-2, they share certain similarities in terms of their biological, clinical and epidemiological features. But what is more different, according to gene-sequencing, the main differences among them are in open reading frame 1a (ORF1a) and the sequence
of gene spike coding protein-S [5]. The protein-S of SARS-CoV-2 has the largest sequence divergence, and it has 380 amino acid sequence substitutions [6], contributing to its munity. Given clinical features, COVID-19 varied from mild cases to severe cases, while most cases were mild. SARS and MERS tended to be urgent onset and rapidly progress to severe illness respectively [7]. That may suggest COVID-19 was more insidious. From the above-mentioned facts, COVID-19, SARS and MERS have different morbidity and mortality rates. COVID-19 has the highest prevalence but lowest fatality rate, and MERS had the highest fatality rate. As for spreading features, SARS was characterized by superspreading events, and MERS seemed to be less aggressive, while COVID-19 is unique for its indiscriminate transmission among the general public [5]. Based on the unique biological, clinical and epidemiological characteristics, SARS-CoV-2 provoked a protracted battle to humans.

Bibliometrics is an effective tool for evaluating research trends in different science fields. Coronaviruses did not attract worldwide attention until the 2003 SARS epidemic, followed by the 2012 MERS outbreak and recent COVID-19. Given the research booms caused by coronavirus epidemics, we conducted 25,835 publications to reveal the research trends and core contents of coronavirus fields between 1991 and 2020. Our article focused on analyzing the changes of research trends and the characteristics of coronavirus infections, which may provide further guidelines for the present and future studies.

Materials And Methods

We obtained data sources from the SCIE and SSCI in the Web of Science. The search terms "Coronavirus*", "SARS", "MERS", "2019-nCoV", "COVID-19", "SARS-CoV*", "MERS-CoV", "HCoV-229E", "HCoV-OC43", "HCoV-NL63", "HCoV-HKU1", "Middle East Respiratory Syndrome*" and "Severe Acute Respiratory Syndrome*" were selected as search terms in the titles, abstracts and keywords of journal publications. We searched publications issued from 1900 to June 30, 2020.

Publications originating from England, Scotland, North Ireland, and Wales were considered to be from the United Kingdom (UK), while Hong Kong, Macau and Taiwan were distinguished from mainland China due to differences in their political systems.

We used ArcGIS (10.6) to map the geographical distribution of global publication outputs and reported cases of three emerging human pathogenic coronaviruses. Gephi (0.9.2) was used to visualize core countries or territories in the international collaboration network.

All publications were analyzed with following aspects: (a) characteristics of publication outputs; (b) geographical distribution and international collaboration; (c) hot keywords.

Results

Characteristics of publication outputs
There were 25,835 publications on coronavirus, with 23,058 SCIE publications (89.25%) and 1,111 SSCI publications (4.30%), and 1,666 publications were both in the SCIE and SSCI (6.45%).

The trend of the growth curve of the SCIE publications was identified with that of the total publications on coronavirus from 1991-2020. The SCIE publications increased slowly before the outbreak of SARS in 2003, and there were about 134 SCIE publications per year on average. While the SCIE publications obviously increased after the SARS outbreak, reaching a peak (1,089 publications) in 2004, and rebounded slowly after the outbreak of MERS in 2012, presenting a peak (734) in 2016. Unlike SARS, the peak during MERS outbreak was lower and came later. The SCIE publications increased dramatically after COVID-19 outbreak, with 10,221 SCIE publications in 2020, displaying an unprecedented research upsurge. Moreover, the SSCI publications as well as publications which were both SCIE and SSCI rose slightly from 2003 to 2019, and obviously increased in 2020 (Fig. 1).

Our results indicate that the SCIE publications played a dominant role in the fields of coronavirus. The outbreaks apparently boosted the research interests, however, the three epidemics responses were different, and the research fields became diversified. Compared with SARS and MERS, COVID-19 aroused more dramatic and prolonged upsurge. In May and June of 2020, the volume of literature increased sharply, and mainly distributed in the epidemic areas (such as China, USA, Italy and UK).

**Geographical distribution and international collaboration**

A total of 23,969 publications included the author addresses. We plotted a global geographical distribution map of publication outputs in different stages and the reported cases of SARS, MERS and COVID-19 (Fig. 2).

In 1991-2002, there were 49 countries involved in the coronavirus researches. The United States of America (USA) produced the most publications (802), followed by the United Kingdom (UK) (126), Netherlands (123), Germany (122) and Canada (117), and they were the five most productive countries. The research areas were mainly distributed across the North America, Europe and Japan. There were 83 countries participating in the coronavirus researches in 2003-2011. The publication outputs of China varied from 4 in 1991-2002 to 2,469, ranking the first, followed by USA (1,907), Canada (517), UK (378) and Germany (354). Except for the North America and Europe, the publication outputs of Asian areas (particularly China, Singapore and South Korea) and Australia greatly increased, as these countries suffered from the impact of SARS. According to the WHO situation reports, there were reported cases of SARS in 32 countries or territories from November 2002 to July 2003, while Asian areas (especially China, Singapore and Vietnam) and North America (especially Canada and USA) were infected more severely [8]. In 2012-2019, 113 countries issued related publications. USA ranked the first (1,759), followed by China (1,502). Saudi Arabia varied from 11 publications in 2003-2011 to 432 publications, being the 3rd. Moreover, South Korea also devoted more attention, ranking the 6th (346). Besides the North America, Europe, China and Japan, Middle East (especially Saudi Arabia, Egypt, United Arab Emirates, Iran and Jordan) and South Korea obviously issued more publications. Given the WHO situation reports, MERS has been spread to 27 countries from 2012 to 30 June 2018, while Middle East and South Korea were the
mainly epidemic territories, and Saudi Arabia accounted for 83% of cases [9]. In 2020, 144 countries put into coronavirus researches. USA ranked the first (3,078), followed by China (2,782), Italy (1,518), UK (1,349) and Canada (588). The publication outputs rapidly increased and the research territories became more diverse following the dramatic and persistent impact of the COVID-19 pandemic.

Internationally co-authored publications varied from 0.45% in 1991-2019 to 10.34% in 2020. Collaborations between countries or territories became frequent after SARS and MERS outbreaks, while obviously being closer after COVID-19 outbreak (Fig. 3). In 1991-2019, USA took the central position in the collaboration network. USA collaborated with China and UK more closely, while most countries or territories were more inclined to produce single-country publications. In 2020, we identified that USA, China, UK, Italy, Canada, Australia and Germany took part in more international-collaborative publications. It turned out that countries or territories strikingly put into more intensive collaborations, with more diversity in cooperation and communication (Fig. 4).

Our results reveal some striking findings. Firstly, research areas became more diversified due to the epidemics of SARS, MERS and COVID-19, while COVID-19 caused more widespread and powerful influences on countries or territories at short notice. COVID-19 is a globally substantial threat to public health, with severe economic implications. The COVID-19 pandemic calls for increased research on traceability analysis, transmission, diagnosis methods, epidemiology, treatment, prevention, and containment of the disease [10]. Patients in the early outbreak provided large samples of clinical characteristics and predictive spread of COVID-19. Secondly, countries or territories presented more international collaborations and communications to cope with the epidemics, and COVID-19 remarkably boosted the research advancements. Scientists from different countries worldwide have strengthened their research collaborations and launched joint research projects for the prevention and control of the epidemic.

Hot keywords

There were 11,574 publications with author keywords in 1991-2020. In order to further identify the main research directions and core contents of the coronavirus fields, we classified the author keywords into six categories (Table 1). They were "Epidemiological features", "Biological features", "Immune response features", "Age/sex", "Diseases /Symptoms" and "Diagnosis/Therapy". China, as the early outbreak area, conducted numerous studies on the clinical characteristics and biochemical markers of COVID-19, as well as studied on the routes of transmission, effective control of the spread (for instance, rapid outbreak responses and lockdown), epidemiology, diagnosis, treatment (for instance, traditional Chinese medicine) and vaccine of COVID-19. The focus of countries or territories varied from epidemiology, prevention and control, etiology and antibody to transmission, detection and diagnosis, treatment as well as prognosis followed the global spread of the epidemic.

Discussion
"Epidemiological features" mainly focused on transmitting feature and surveillance. Although SARS-CoV, MERS-CoV and SARS-CoV-2 mainly induce respiratory infections, the pathways and affecting factors of transmission will be of great significance in prevention and control of epidemic. SARS-CoV and MERS-CoV transmitted with two routes (respiratory droplets and close contact) [5]. Although the primary mode of transmission of SARS-CoV-2 is also via respiratory droplets and contact routes, fomite and aerosol transferring is possible; the fecal oral route may be also a route of transmission [11]. Moreover, the transmission route has been reported even in the cases of asymptomatic patients in many countries and territories [11-13], and this route becomes key point of prevent and control. It has suggested that cold chain transmission is also a potential route through long-distance marine products, which may explain the epemics of Beijing, Qingdao and Dalian in China. It may also provide a reminder to the traceability of the outbreak of Huanan seafood market in Wuhan. The traceability is currently uncertain, and becomes complex and confusing. In addition, vertical transmission may be a pathway [1], and WHO has also indicated the risks of women transmitting COVID-19 to their babies during breastfeeding [14]. Environmental factors (ambient temperature and humidity) have also been studied to understand the COVID-19 transmissions [15]. It turns out that the transmission of SARS-CoV-2 is complicated and diverse. As for preventive measures, face mask, hand hygiene, social distance and ventilation are effective routine methods [16, 17].

"Biological features" were associated with the pathogenicity of coronaviruses. The latest studies find spike protein on SARS-CoV-2 surface binds its receptor, angiotensin-converting enzyme 2 (ACE2) to enter the host cells, while the host transmembrane protease serine 2 (TMPRSS2) is essential for viral entry [18]. Notably, the binding affinity of SARS-CoV-2 for ACE2 is 10-20-fold higher than SARS-CoV [6], contributing to its munity. ACE2 expression and Renin-angiotensin system (RAS) are abnormal in hypertension and obesity, while TMPRSS2 is over-expressed when exposed to androgens, indicating these factors are involved in the pathogenic features of SARS-CoV-2 [19]. The members of RAS, abnormal levels of pro-inflammatory angiotensin II and anti-inflammatory angiotensin 1-7 may reflect the severity of COVID-19 [19]. ACE2 and TMPRSS2 expression may modulate the infectivity of SARS-CoV-2, becoming a promising target for the early therapies of patients with COVID-19.

"Immune response features" included multiple immune related factors, while immune cells (particularly T lymphocyte, Macrophage and B lymphocyte) and cytokines (interferons, interleukins, chemokine, TNF and C-reactive protein) accounted for large portions. Cytokine storm was the focus during COVID-19 outbreak. Immune responses play essential roles in the interactions between coronavirus infections and the host, while the cytokine storm has direct correlations with the pathogenesis and disease severity. The signs indicate over-elevated inflammatory factors are associated with the deterioration of patients with SARS and MERS, and there is growing evidence that cytokine storms may lead to the pathogenesis of patients with COVID-19, causing the rapid worsening [20].

Clinical feature, diagnosis and therapy were the concerns of clinical practice. "Age/Sex" mainly included children, pregnant woman and older adult. Older adults tend to suffer from infections due to a weakened immunity [1]. Pregnant women and children are special groups during COVID-19 outbreak. They are
facing difficulties of the surveillance and diagnosis. Pregnant women are more susceptible to infectious diseases due to the immune suppression, moreover, the clinical symptoms of pregnant women are atypical in comparison with the non-pregnant adults. Compared with adults, fewer children are infected with SARS-CoV-2, while their CT imaging presents the non-specific abnormalities (pure ground-glass opacity or consolidation) unlike the adults [21]. There involved diverse systemic manifestations in "Diseases/Symptoms", possibly due to the wide distribution of receptors and systemic inflammations (cytokine storm). The receptor of SARS-CoV-2 and SARS-CoV, ACE2 is widely distributed in organs (oral, nasal mucosa, nasopharynx, lung, stomach, small intestine, colon, skin, lymph nodes, thymus, bone marrow, spleen, liver, kidney, and brain), and the receptor of MERS-CoV, DPP4 (CD26) is expressed on kidney, small intestine, liver, prostate epithelial cells and activated leukocytes, suggesting that the range of their tissue tropism were broader [7]. The nonspecific symptoms and manifestations of COVID-19 may cause difficulties of diagnosis and management. Based on clinical and epidemiological analyses, older age, male and preexisting comorbidity were identified as important risk factors for the development of severe or lethal disease in COVID-19, which were similar to SARS and MERS [22-24]. The five most common comorbidities were hypertension, diabetes, cardiovascular disease, chronic obstructive pulmonary disease and tumor, while higher D-dimer, higher neutrophil/lymphocyte ratio, higher level of C-reactive protein, lymphopenia, thrombocytopenia and obesity were the independent risk factors of death in COVID-19 patients [25-27]. According to epidemiology and large scale data, diabetes has been identified as an important risk factor for mortality and rates of progression to acute respiratory distress syndrome (ARDS) in hospitalized patients with COVID-19 [28, 29]. The mortality of comorbid diabetes reached 7.3%, with 2.3% higher than those of non-diabetic patients [30]. Diabetic patients with poor levels of blood glucose tended to have higher death risk and adverse prognosis among COVID-19 patients in hospital, due to preexisting comorbidities or complications and the roles of cytokine storms [29].

It has been confirmed that swab test (PCR nucleic acid determination) and chest CT scan play important roles in detection and diagnosis of coronavirus infections [1]. CT scan has great value in screening and detecting patients with COVID-19 pneumonia, especially in the highly suspicious, asymptomatic cases with negative nucleic acid testing [13]. With regard to therapies, vaccine, antibody, traditional Chinese medicine and targeted drugs are four therapeutic methods. Safe and effective vaccines are currently in clinical trial stage [31]. High-risk groups (for example, medical workers) and high-risk groups (for example, children, pregnant women, older adults and people with preexisting diseases) will be given priority for vaccination. Early signs are that plasma with SARS-CoV-2 antibodies from recovered patients can reduce the mortality in SARS-CoV-2 patients [11]. There are certain emerging therapies to cope with the infections. Hydroxychloroquine, Chloroquine, Lopinavir/ritonavir and Remdesivir have antiviral activity that can control SARS-CoV-2 in-vitro [32]; moreover, Viral entry inhibitors, ACE2 modulators (angiotensin receptor blockers) and TMPRSS2 inhibitors (camostat mesylate) are promising clinical drugs, and it has suggested that Shuanghuanglian oral liquid and Lianhuaqingwen are effective for certain patients with COVID-19 in China [18, 33, 34]. Given the high level of cytokines in the host, the immunosuppressive drugs targeting the interleukin-6 (IL-6) receptor, tocilizumab are reported to treat COVID-19-related cytokine storms [35], and the application of blood purification technology (plasma exchange,
blood/plasma filtration, adsorption, perfusion and continuous renal replacement therapy) is helpful to the removal of cytokines and may be beneficial to improve the clinical outcome of critically ill patients [20].

**Conclusion**

Our study provides further understandings for the research progress and direction of global coronavirus fields. We summarize six categories of features of coronavirus infections, and analyze the implications, revealing the epidemiological and biological properties, clinical features and currently therapeutic methods. These effective experience in preventing, controlling, cutting off transmission routes and treating can be regarded as significant guidelines for the epidemics of other countries and territories.

**Declarations**

Ethics approval and consent to participate: Not applicable.

Consent for publication: Not applicable.

Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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Tables

Table 1 The classification of core keywords in 1991-2020

(4) Circulatory systemEncephalitis* (4) Circulatory systemEncephalitis*
### (a) Epidemiological features

|                       | TP |
|-----------------------|----|
| Transmission          | 325|
| Aerosol*              | 71 |
| Droplet*              | 26 |
| Temperature*          | 20 |
| Humidity*             | 13 |
| Temperature sensitivity | 4 |
| Temperature-sensitive mutant | 3 |
| Respiratory infection | 248|
| Prevention/Control    | 146|
| Isolation*            | 104|
| Quarantine*           | 95 |
| Face mask*            | 88 |
| Ventilation*          | 54 |
| Hand hygiene          | 30 |
| Lockdown*             | 29 |
| Mortality*            | 157|
| Risk factor*          | 62 |
| Morbidity             | 19 |
| Clinical feature*     | 104|
| Clinical symptom*     | 56 |
| Complication*         | 51 |
| Prognosis*            | 36 |

### (b) Biological features

|                       | TP |
|-----------------------|----|
|                       | TP |
|                       | TP |
| Clinical feature*     | 104|
| Clinical symptom*     | 56 |
| Complication*         | 51 |
| Prognosis*            | 36 |
| ORF                  |      |
|---------------------|------|
| Spike glycoprotein  | 405  |
| Spike gene          | 79   |
| Nucleocapsid glycoprotein | 196 |
| Nucleocapsid gene   | 26   |
| Membrane glycoprotein | 73  |
| Membrane gene       | 14   |
| Envelope glycoprotein | 47  |
| Nsp                 | 106  |
| 3C-Like protease    | 161  |
| Papain-like protease| 48   |
| Helicase            | 25   |
| TP                  |      |
| ACE2*               | 249  |
| Receptor-binding domain | 60 |
| DPP4                | 35   |
| TMPRSS2*            | 29   |
| SARS unique domain  | 7    |
| TP                  |      |
| Protease            | 54   |
| Accessory protein   | 41   |
| Peptide             | 29   |
| Cysteine protease   | 15   |
| Serine protease*    | 5    |
| Type II transmembrane serine protease | 2 |
| ADAM-17             | 1    |
| TP                  |      |
| Renin-angiotensin system* | 35 |
| Angiotensin         | 20   |
| (c) Immune response features |
|-------------------------------|
|                             |
| Angiotensin II*              | 19 |
| TP                           |    |
| T lymphocyte                 | 125|
| Macrophage                   | 40 |
| B lymphocyte                 | 34 |
| NK cell                      | 13 |
| TP                           |    |
| Immunity                     | 121|
| Immune response              | 76 |
| Innate immune response       | 72 |
| Mucosal immunity             | 24 |
| Cellular immune response     | 13 |
| Antibody dependent enhancement| 17 |
| Humoral immunity             | 8  |
| TP                           |    |
| Interferon                   | 117|
| Type I interferon            | 41 |
| Type III interferon          | 27 |
| Type II interferon           | 22 |
| Interferon signaling pathway | 12 |
| Interferon-stiumulated gene  | 9  |
| Type I and II interferon     | 3  |
| TP                           |    |
| Cytokine                     | 95 |
| Inflammation*                | 88 |
| Cytokine storm*              | 69 |
| Chemokine                    | 36 |
| Inflammatory cytokine response* | 32 |
| Interleukin | TNF | NF-kappa B |
|------------|-----|------------|
| 18         | 14  | 21         |
| Interleukin-6* | TP |            |
| 43         |     |            |
| Interleukin-1* |   |            |
| 8          |     |            |
| Interleukin-8 |   |            |
| 7          |     |            |
| Interleukin-10 |   |            |
| 7          |     |            |
| Interleukin-2 |   |            |
| 5          |     |            |
| Interleukin-4 |   |            |
| 3          |     |            |

**Age/Sex**

| Age group      | TP |
|----------------|----|
| Children*      | 133|
| Pregnant woman*| 92 |
| Older adult*   | 58 |
| Newborn*       | 24 |
| Infant         | 15 |
| Adult          | 14 |
| Female         | 7  |
| Male           | 3  |

**Diseases /Symptoms**

| Disease                     | TP  |
|-----------------------------|-----|
| Pneumonia*                  | 332 |
| ARDS*                       | 161 |
| Respiratory disease         | 49  |
| Respiratory failure*        | 39  |
| Lung injury                 | 30  |
| Asthma                      | 26  |
| Tuberculosis                | 19  |

**Respiratory system**

| Disease            | TP  |
|--------------------|-----|
| Pneumonia*         | 332 |
| ARDS*              | 161 |
| Respiratory disease| 49  |
| Respiratory failure*| 39  |
| Lung injury        | 30  |
| Asthma             | 26  |
| Tuberculosis       | 19  |
| (2) Digestive system          | COPD* | 15 |
|-------------------------------|-------|----|
|                               | Pulmonary embolism* | 14 |
|                               | Pulmonary complication* | 2 |
|                               | Diarrhea | 91 |
|                               | Enteritis | 33 |
|                               | Gastroenteritis | 15 |
|                               | Inflammatory bowel disease | 9 |
|                               | Liver injury* | 9 |
|                               | Liver function | 3 |
|                               | Liver failure | 2 |
|                               | Liver disease | 2 |

| (3) Tumor                      | Tumor* | 9 |
|--------------------------------|--------|---|
|                                | Cancer* | 85 |
|                                | Head and neck cancer* | 26 |
|                                | Lung cancer* | 15 |
|                                | Breast cancer* | 12 |
|                                | Colorectal cancer* | 4 |
|                                | Bladder cancer* | 4 |
|                                | Prostate cancer | 3 |
|                                | Ovarian cancer | 3 |
|                                | Oral cancer | 3 |
|                                | Cervical cancer | 3 |
| Kidney cancer | 3 |
| Thyroid cancer | 2 |
| Skin cancer | 2 |
| Penile cancer | 2 |
| Pediatric cancer | 2 |
| Gynaecological cancer | 2 |
| Colon cancer | 2 |

| (4) Psychological illness | TP |
|----------------------------|----|
| Mental health* | 80 |
| Anxiety* | 56 |
| Depression* | 49 |
| Stress* | 38 |
| Fear* | 23 |

| (5) Endocrine and metabolism | TP |
|-------------------------------|----|
| Diabetes* | 67 |
| Obesity* | 16 |
| Hyperglycemia | 4 |

| (6) Nervous system | TP |
|--------------------|----|
| Demyelination | 49 |
| CNS | 46 |
| Anosmia* | 33 |
| Stroke* | 28 |
| 26 |
| Smell disorder* | 17 |
| Neurological complication* | 7 |
| Taste disorder* | 6 |
| (7) Circulatory system | TP |
|------------------------|----|
| Cardiovascular disease*| 40 |
| Hypertension*          | 29 |
| Heart failure*         | 23 |
| Myocarditis*           | 14 |
| Cardiac injury*        | 12 |
| Coronary Heart Disease | 1  |

| (8) Urinary system     | TP |
|------------------------|----|
| Kidney failure         | 15 |
| Kidney injury*         | 12 |
| Kidney disease*        |  4 |
| Renal complication     |  1 |

| (6) Tumor              |
|------------------------|

| (f) Diagnosis/Therapy  | TP |
|------------------------|----|
| Diagnosis              | 176|
| rRT-PCR                | 445|
| Chest CT scan*         | 147|
| Genomic sequence analysis| 143|
| ELISA                  |  88|
| X-ray Computed*        |  33|
| (2) Laboratory testing                      |       |
|---------------------------------------------|-------|
| Swab test*                                  | 22    |
| TP                                          |       |
| Thrombosis*                                 | 32    |
| Lymphopenia*                                | 23    |
| D-dimers*                                   | 15    |
| C-reactive protein*                         | 11    |
| Thrombocytopenia*                           | 11    |
| Neutrophil                                  | 9     |
| Neutrophil/lymphocyte ratio*                | 6     |

| (3) Clinical therapy                        |       |
|---------------------------------------------|-------|
| Therapy*                                    | 260   |
| Vaccine                                     | 357   |
| Vaccination                                 | 45    |
| DNA vaccine                                 | 32    |
| Subunit vaccine                             | 22    |
| Recombinant vaccine                         | 14    |
| Peptide vaccine                             | 10    |
| Inactivated vaccine                         | 9     |
| Influenza vaccine                           | 9     |
| Antibody                                    | 168   |
| Monoclonal antibody                         | 83    |
| Neutralizing antibody                       | 78    |
| Immunoglobulin                              | 14    |
| Immunoglobulin G                            | 35    |
| Immunoglobulin M*                           | 12    |
| Immunoglobulin A                            | 12    |
| Intravenous immunoglobulin*                 | 9     |
| Immunoglobulin Y                            | 7     |
| Term                                      | TP |
|-------------------------------------------|----|
| Antiviral therapy                         | 154|
| Hydroxychloroquine*                       | 61 |
| Chloroquine*                              | 49 |
| Corticosteroid                            | 48 |
| Traditional Chinese Medicine*             | 45 |
| Lopinavir/ritonavir*                      | 37 |
| Tocilizumab*                              | 35 |
| Remdesivir*                               | 31 |
| Antiviral drug                            | 26 |
| Camostat*                                 | 2  |
| Shuanghuangliang oral liquid*             | 1  |
| Lianhuaqingwen*                           | 1  |
| Inhibitor                                 | 74 |
| Protease inhibitor                        | 35 |
| Viral entry inhibitor                     | 11 |
| renin-angiotensin system blockers*        | 10 |
| ACE2 inhibitor*                           | 9  |
| Fusion inhibitor                          | 6  |
| 3C-Like protease inhibitor                | 5  |
| Peptide inhibitor                         | 4  |
| Interleukin-6 inhibitor*                  | 3  |
| Papain-like protease inhibitor            | 2  |
| Imunosuppression*                         | 51 |
| Immunomodulation*                         | 31 |
| Immunotherapy*                            | 29 |
| Immunohistochemistry                      | 36 |
| Term                                | TP |
|-------------------------------------|----|
| Mesenchymal stem cells therapy*     | 27 |
| Immunosuppressant*                  | 14 |
| Kidney transplantation*             | 30 |
| Liver transplantation*              | 13 |
| Heart transplantation               | 5  |
| Lung transplantation                | 3  |
| Hemodialysis*                       | 25 |
| Telemmedicine*                      | 141|

ACE2 angiotensin-converting enzyme 2, DPP4 dipeptidyl peptidase-4, TMPRSS2 transmembrane protease serine 2, SARS severe acute respiratory syndrome, ORF open reading frame, Nsp non-structural protein, ADAM-17 a disintegrin and metalloproteinase 17, NK cell Nature Killer cell, NF-kappa B nuclear factor kappa-light-china-enhancer of activated B cells, TNF tumor necrosis factor, ARDS acute respiratory distress syndrome, COPD chronic obstructive pulmonary disease, CNS central nervous system, rRT-PCR real-time reverse transcriptase-polymerase chain reaction, ELISA enzyme-linked immunosorbent assay

TP total publications, * author keywords mainly presented in 2020

Figures
Figure 1

Global research outputs of Science Citation Index Expanded (SCIE) and Social Science Citation Index (SSCI) and publications on coronavirus in 1991-2020
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Global research outputs of Science Citation Index Expanded (SCIE) and Social Science Citation Index (SSCI) and publications on coronavirus in 1991-2020.
Figure 2

Distribution changes of global publication outputs in the coronavirus fields and the reported cases during three human coronaviruses outbreaks. (a) Publication outputs of countries in 1991-2002. (b) Publication outputs of countries in 2003-2011 and the distributions of world reported cases during SARS outbreak. (c) Publication outputs of countries in 2012-2019 and the distributions of world reported cases during MERS outbreak. (d) Publication outputs of countries in 2020 and the distributions of world reported cases during COVID-19 outbreak. Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.
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Distribution changes of global publication outputs in the coronavirus fields and the reported cases during three human coronaviruses outbreaks. (a) Publication outputs of countries in 1991-2002. (b) Publication outputs of countries in 2003-2011 and the distributions of world reported cases during SARS outbreak. (c) Publication outputs of countries in 2012-2019 and the distributions of world reported cases during MERS outbreak. (d) Publication outputs of countries in 2020 and the distributions of world reported cases during COVID-19 outbreak. Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.
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Figure 3

International-collaborative and independent publications in coronavirus researches IP independent publications, ICP international-collaborative publications, ICPP the percentage of international-collaborative publications
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Figure 4

Collaboration network of the productive countries or territories (a) international collaboration in 1991-2019. (b) international collaboration in 2020
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Figure 4

Collaboration network of the productive countries or territories (a) international collaboration in 1991-2019. (b) international collaboration in 2020