

**Review Article**

**A REVIEW OF THE MOST INFLUENTIAL RESEARCH  
PAPERS ON COVID-19: AN EXCERPT WITH COMMENTS  
AND INSIGHTS**

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**Abstract:** For the past two years, COVID-19 has been a global nightmare for human civilization. It genuinely poses a serious threat to public health because of its rapid proliferation. The deadly SARS-COV-2 virus is being researched on a global scale to determine its biology, origin, and potential treatment. Numerous research publications covering various aspects of the COVID-19 issue have already been published as a result of the burgeoning interest in this hot topic. The reputable and well-known search engine SCOPUS is used to compile crucial information. In order to emphasize a thorough and extensive assessment of research output using COVID-19 publications, we looked at 100 research and review papers that received the majority of citations. It discovers a list of keywords that appear more than 14 times. It can be seen that the terms "Human/ Humans," "Coronavirus Disease 2019," "Coronavirus Infection/Coronavirus Infections," "Pneumonia viral," and "Virus pneumonia" held the top five positions. The New England Journal of Medicine is in the first place, having published 15 research papers delineating different features of SARS-CoV-2. In addition to this, a significant number of publications connected to the Covid-19 issue were also published in "The Lancet," "Nature," "JAMA Journal of the American Medical Association," and "Cell." Regarding

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papers published on COVID-19, China is also performing well. The USA and the UK placed second and third, respectively, in terms of the quantity of Covid-related articles published. This work outlines a detailed global research scenario of COVID-19 describing its origin, nature, identification, way of entry in a human cell, symptoms of the infected patients, way of prevention, fatal effects on comorbid and aged patients with the help of correlation between comorbidity and mortality, the effect of on newborn baby and children, the emergence of telemedicine, persistence of the virus on inanimate things, the efficacy of drugs like remdesivir, lopinavir, ritonavir and so on, the progress of vaccine development, usefulness gloves, masks, sanitizer, the advantage of maintaining physical and social distance, infrastructure development. Finally, we conclude by summarizing the main points of the 100 research papers, which will undoubtedly aid in identifying the research gap and future research directions.

**Keywords:** Review, Covid-19, influential publications, human, pandemic, clinical trials.

**MSC:** 90B05.

## 1. INTRODUCTION

Due to the sudden COVID-19 outbreak, people all around the world are in upheaval and struggling for existence. On December 29, 2019, it began in Wuhan Pradesh, China, and as a result of how interconnected the world is, it will eventually encompass the entire planet. Day by day it becomes a challenge to human civilization to keep the normal/usual life of people throughout the world. This terrible illness has had some impact on almost every nation in the world. The COVID-19 virus evolved into a more potent and odder one due to constant and rapid mutation, and scientists are still unable to understand its enigmatic behavior. The fact that millions of people are forced to die without receiving any treatment due to an inadequate supply of oxygen levels, an insufficient of hospital beds, a shortage of doctors, a scarcity of available medications, and other factors is truly appalling. When the virus first emerged, nations such as the United States of America (USA), Italy, France, Brazil, and the United Kingdom (U.K.) were in a state of chaos/turmoil. The deadly virus, called as covid-19, was first identified by WHO in 2019. Because of its crown-like form, this virus is most frequently called a coronavirus. Viruses present a worldwide threat to public health. The majority of the world's nations are being forced to enter lockdown for long time because neither medical professionals nor scientists are aware of a way to stop this lethal virus.

People are instructed or asked to stay inside their homes. Many people died in the first coronavirus outbreak, including many regular citizens as well as medical professionals, law enforcement officers, healthcare workers, and teachers. The entire world was watching this funeral procession. The origin, nature, and traits of the fatal virus, as well as the results of clinical trials, the risk of comorbid patients, the effect on mental health in conjunction with vaccine discovery, and the best course of action for the way of control measure are all being studied by researchers.

Medical, biochemistry, immunology and microbiology, genetics, and molecular biology as well as cross-disciplinary subjects like psychology and neurology are all covered in this study. The majority of the publications are from the department of medicine which is quite natural as it is a worldwide health concern issue, followed by interdisciplinary (11%) and the departments of immunology and microbiology (9%) and biochemistry-genetics & molecular biology (8%) and neuroscience (4%) and psychology

(2%). Immunology consists of more studies because the researchers of entire world are continuously attempting to make a vaccine of Covid-19. People in general, particularly students and youngsters, are greatly impacted by sudden lockdowns.

Bibliometric studies shed light on the research gap and direction in addition to the overall research outcome from different angles. Numerous bibliometric investigations have been conducted on COVID-19 articles. To our understanding/belief, our analysis is the first one to concentrate on the 100 most referenced scientific publications globally. After analyzing 100 research publications, we summarized our bibliometric study in this part. Guan et al. [31] investigated how comorbidities affected the clinical characteristics and prognosis of individuals with Covid-19. They found a strong correlation between the quantity and kind of comorbidities and the severity of the outcomes for covid patients. Acute Respiratory Deficiency Syndrome (ARDS) has a significant role for covid infected patients. Such type of patients has more probability to turn into critical condition and it may sometimes be difficult to make such patients curable. Some researchers have paid keen attention to investigating the risk factors, pathological and clinical findings, and outcomes of the patients associated with ARDS ([92], [88]). Shi et al. [74] investigated how cardiac injury affected Covid patients' mortality and observed that there is a high correlation between these two characteristics. Guo et al. [14] also made the same type of investigation. They assessed the association between cardiovascular disease (CVD) and myocardial injury (MI) of the Covid-infected patients and observed the fatal outcome of the patients. Some researchers have recently become interested in the temporal patterns of viral shedding. He et al. [35] described the temporal pattern of viral shedding and hypothesized that it may begin 5 or 6 days before the onset of symptoms and be at its peak in the throat swab at that time. Existence, persistence, and duration of the coronavirus on inanimate surfaces [45].

Exploring the state of research related to stretch of deadly virus is the prime goal of our study. The 'SCOPUS' search engine revealed a total of 207854 items up to October 14, 2021, while looking for documents that contained "COVID-19" in the title, abstract, or keywords. We restrict the search results to Journal publications and the English language. The search results are then restricted to "article" and "review" types document. We ended up with a total of 143686 documents in this method (122465 articles and 21221 reviews). To emphasize an extensive assessment of research output using COVID-19 publications, we looked at 100 research and review papers for this study that received the majority of citations. With the help of this study, we have attempted to understand what breakthroughs have been invented to combat the mortal virus. The focal research points of this article are summarized in the following questions (i) which countries are leading in Covid-19 research? (ii) which authors have published the most articles (iii)? which authors have obtained a significant number of citations? (iv) How far has global research develop in advancing a drug or vaccine that works effectively? (v) Which institute has reinforced heavily/specifically on Covid-19 research? (vi) what steps could the average person take to prevent infection with the deadly virus? Here, we considered the papers based on the quantity of citations. Naturally, papers released in early 2020 have received more citations than those released more recently. There won't be any medicines or vaccinations on the market during that time. Therefore, covid patients have been exposed to clinical studies of many existing medications. There won't be any medicines or vaccinations on the market during that time. Therefore, the covid patients have been exposed to clinical studies of many existing medications. The following

research questions were highlighted by several researchers (vii) do remdesivir, lopinavir, ritonavir help patients with Covid infections? (viii) whether the virus originated from the animal reservoir. (ix) are patients benefitted from acute Covid-19 infections from convalescent plasma transfusion? (x) How does cytokine storm contribute to the sudden death of COVID-infected patients? (xi) Is there any way to entirely stop the cytokine storm or reduce its intensity? (xii) Is the respiratory failure caused by neuro-invasive potential? (xiii) Is neuro-invasive potential responsible for respiratory failure? (xiv) Is the outbreak under control after contact tracing and isolation? (xv) How many masks and gloves are effective to resist the outbreak? (xvi) what clinical traits are linked to the emergence of ARDS which causes to death when patients are attacked by the virus? (xvii) Does Chest-CT outperform RT-PCR at identifying COVID-19 patients? (xviii) How does the virus weaken the immune systems of infected people, particularly those who have comorbidities like diabetes or breathing problems? (xix) How does the fatal virus bind to human cells? (xx) Has SARS-CoV-2 had a significant impact on pregnant mothers? (xxi) what neurologic symptoms can corona patients-2019 experience? (xxii) What risk factors play major role behind the mortality of critical Covid patients? (xxiii) What are the impacts of lockdown on the mental health of vulnerable groups, and how may social isolation and mental depression be lessened caused by the pandemic situations?

Our bibliometric analysis is extremely relevant given the current state of world upheaval. Some nations are on the verge of the fifth wave of the Coronavirus, while others have already experienced the fourth wave. Research on various facets of the coronavirus is still relevant. More research is essential to solving the riddle of the catastrophe by examining its reasons for sudden arrival, nature, and lethal virus characteristics, as well as the advancement of efficient medications and viral prevention techniques.

## 2. METHODOLOGY AND REVIEW OF LEADING 100 ARTICLES

### 2.1. Detailed Research Methodology

#### 2.1.1. Methodology

- a) Selection of Papers: The initial step involved conducting a comprehensive search of papers/articles based on highest citations using reliable databases 'SCOPUS'.
- b) The search strategy included keywords such as "COVID-19," "SARS-CoV-2," "coronavirus," and related terms to capture a broad spectrum of research articles and reviews. The inclusion criteria encompassed peer-reviewed research papers and reviews related to COVID-19 published within a specified time frame. The selection prioritized articles that received a high number of citations, leading institutes indicating significant impact and influence within the scientific community. The search was not restricted by geographical location, and papers from diverse regions, multiple disciplines and research institutions and covid treatment providing hospitals across the world were considered to ensure a global perspective.

#### 2.1.2. Time frame of the literature search

The literature search encompassed publications from the onset of the COVID-19 pandemic to a specified end date October 14, 2021, ensuring that the selected papers represented a comprehensive and up-to-date view of the evolving research landscape.

### 2.1.3. Limitations in the selection process

It is important to acknowledge potential limitations in the selection process of the papers. We have only considered the publications within the search engine 'SCOPUS'. We hereby reiterate why we have given emphasis on SCOPUS database.

1. Scopus as a Comprehensive Database: The decision to rely solely on Scopus stems from its status as one of the largest and most comprehensive abstract and citation databases. It spans diverse scientific disciplines, ensuring a broad and representative collection of scholarly work.

2. Streamlining the Search Process: Focusing on Scopus serves the purpose of streamlining the search process. Its extensive coverage of journals, conferences, and patents, along with its global scope, simplifies the literature review. This approach aims to maintain a high standard of academic rigor while providing a diverse and manageable dataset for analysis.

3. Managing Scope and Maintaining Rigor: Excluding other databases is a strategic choice to manage the scope effectively and uphold the rigor of the research. In the context of our study on COVID-19, the inclusion of additional databases could introduce a broader array of topics and perspectives, potentially diluting the focus. This decision also mitigates the risks associated with redundancy and inconsistencies that may arise when cross-referencing multiple databases.

4. Overwhelming Volume of Literature on COVID-19: The 'Scopus' search engine revealed a substantial total of 207,854 items related to COVID-19 up to October 14, 2021. To ensure a focused and manageable collection of papers for analysis, specific filters were imposed. This meticulous filtering process aimed to prioritize relevance and quality, contributing to the overall robustness of the study.

5. Balancing Inclusivity and Manageability: Incorporating additional databases, while potentially enriching the dataset, may introduce an overwhelming number of papers, challenging the manageability of the research. The decision to stick to Scopus aligns with the goal of balancing inclusivity and practicality, allowing for an in-depth analysis of the selected literature without compromising the study's coherence.

Expanding the literature search to include other major databases beyond SCOPUS would indeed enhance the robustness and representativeness of the findings. While the current study relied on data obtained from the SCOPUS database, incorporating additional databases such as PubMed, Web of Science, or Google Scholar could provide a more comprehensive view of the research landscape related to COVID-19. But SCOPUS is the most wide and acceptable database. We trust that these points collectively provide a comprehensive overview of the considerations guiding our database selection process.

## 2.2. Review of Leading 100 Articles

Table A1 displays the list of the leading 100 in covid-19 research. In this part, we have delineated the keystone statement of the 100 leading papers. According to the citations' descending order, Table A1 is arranged placing the most cited article in the top position in Table A1 (Appendix). Table A1 summarizes that Huang et al. [43] has gained 18952 citations in a very short time. In order to create their case study, Huang et al. [43] used data from forty (41), 2019 n CoV-infected individuals who were admitted to a hospital in Wuhan, China. The patients' average age was 49. The article, which was

published in Guan et al. [32] collected data from 1099 patients from 552 hospitals in China with different demographics in order to characterize the virus. With a total of 12264 citations quickly, the paper got an impressive number of citations. The importance of the route of transmission, the period of reproduction, the clinical spectrum, and most importantly the formulation of a plan to halt the spread of the virus have all been highlighted by Zhu et al. [101].

They also emphasized the ongoing and meticulous observation of the virus's characteristics. Chen et al. [16] investigated the clinical and epidemiological characteristics of 99 patients from Wuhan Jinyintan Hospital and found that the virus had become highly severe in the older males with concomitant conditions. For the purpose of predicting the likelihood of mortality, they also recommend a thorough research or study. Zhou et al. [100] identified 2019n SARS-CoV-2 as the potential causative agent for the current catastrophe in human-life. In this sense, they emphasize further investigation.

Hoffmann et al. [38] conducted a thorough investigation to determine whether the human body contains any cells or hosts with a propensity to draw the SARS CoV-2 virus or whether there are any barriers preventing the virus from entering the body. They discovered that ACE2 speeds up the virus's fast entry into the human body. They also urged that an inhibitor of the cellular series protease TMPRSS2, which is used by SAERS-CoV-2 for S protein priming, be used to prevent the entry of fatal viruses. six-member family cluster's five patients were the subject of an investigation by Chan et al. [13] into the epidemiological, clinical, laboratory, radiographic, and microbiological findings.

They are linked to Wuhan hospital and are affected by unexplained pneumonia. The authors also looked at the influence of family members' person-to-person transmission in hospital and family settings. The pathological findings of Covid-19 patients with acute respiratory distress syndrome were investigated by Xu et al. [92]. They hope that these findings may aid in determining the cause of mortality and provide fresh insights into the etiology of SARS-CoV-2-related pneumonia. Their observations may help physicians treat covid patients more effectively. 5700 individuals who were admitted to hospitals in New York City with the symptom of COVID-19 were studied by Richardson et al. [68] for their features, comorbidities, and outcomes. The paper's credibility is ensured by its citations (3476). Wu et al. [88] studied the clinical features and risk factors of 201 covid confirmed patients admitted to China's Wuhan Jinyintan Hospital for one month (25.12.2.19-26.01.2020). Male patients accounted for 128 of the 201 patients, with the median age of the entire group being 51 years. Patients with a higher age have more hazards and require ICU, according to the researchers. Wang et al. [83] investigated the psychological effects of the pandemic during the early stages. Anxiety, depression, and stress are all psychological effects. They conducted an online survey from the 31st of January to the 2nd of February, 2020, and collected 1210 responses from 191 Chinese cities. Fearing the lethal and unpredictable illness, the majority of responders (84.7%) stayed at home for 20 to 24 hours and did not dare to leave their houses. The patient's previous medical history is kept on file. What symptoms do they have, did they come into touch with infected individuals, and what preventive steps have they done in the recent 14 days? The psychological impact is measured using the Impact of Event Scale-Revised (IES-R) and the Depression, Anxiety, and Stress Scale (DASS-21). The first coronavirus case in the United States was discussed by Holshue et al. [41]. And their findings have been published in the prestigious New England Journal of Medicine.

During the conflict, various medications were put through clinical trials. The virological evaluation of COVID-2019 hospitalized patients was examined by Wölfel et al. [87] of the United Kingdom. The work, which was published in *Nature*, quickly attracted 2685 citations and received attention from the scientific community. Cao et al. [10] observed a trial involving lopinavir-ritonavir treatment in individuals hospitalized with severe conditions. The medications lopinavir and ritonavir are thought to be beneficial in combating the deadly virus.

The work contains a sizable number of citations as well. The deadly coronavirus's effects were so terrible that everyone in the globe eagerly anticipated the prophylactic vaccine. Therefore, the study supporting the lopinavir-ritonavir clinical trials has attracted a lot of interest from researchers.

Mao et al. [57] pointed out the neurologic manifestations. They studied patients admitted between the time period of one month (16th January 2020 to 19th February 2020) at the Huazhong University of Science and Technology in Wuhan of China to reach their conclusion. Gautret et al. [25] assayed whether hydroxychloroquine and azithromycin are effective or not in lowering the viral load in covid infected patients. Based on a short sample, they observed that hydroxy chlorine is helpful in lessening the viral load. The effect of dexamethasone among hospitalized patients infected with the COVID-19 virus was examined by Horby et al. [42]. Among the admitted patients, 2104 patients were treated with dexamethasone, and 4321 were treated with usual care. Ai et al. [2] attempted to establish a link between reverse-transcription polymerase chain reaction (RT-PCR) and chest CT-Scan, as well as comparing the utility of the two methods in diagnosing COVID-19 infection. They looked at 1049 patients in Wuhan, China, with an average age of 51. For diagnosis and quantification of COVID-19 impact, the Chest city scan is found to be more effective and reliable than the RT-PCR assay. Outcomes of clinical trials of two-dose 30 µg vaccine BNT162b2 have been explored by Polack et al. [63] in 'The New England Journal of Medicine' with 2180 citations. The clinical trials consider the different aspects of vaccines like percentage (%) of efficacy, safety measurement, and its impact. They made their experiment on 43548 participants from the United States, and Germany with ages greater or equal to 16 some of which are given double doses of vaccine, and some of which are applied placebo. Lauer et al. [50] delineated the length of the incubation period of COVID-19-infected patients. They considered the time period between 4th January 2020 to 24th February with the demographic area outside of the Hubei province of China. Beigel et al. [5] also submitted a report about the use of the much-discussed drug remdesivir, by considering 1062 patients among which 541 are given remdesivir while the remaining 521 were applied placebo. Lai et al. [49] investigated the post-traumatic disorder of nurses in China by distributing questionnaires to 202 people who had been exposed to the coronavirus sickness in 2019. Lai et al. [48] examined the mean incubation period of the aggressive SARS-CoV-2, patient symptoms and signs, duration of dyspnea, hospitalization, and ARDS in 278 individuals infected in Wuhan, China. Based on the clinical symptoms of the entire patient population, they attempted to evaluate the patients' results and highlight treatment options accordingly. They discovered that 25% of the individuals in question require an Intensive Care Unit (ICU), but just 3.2% required invasive mechanical ventilation. Male and elderly individuals had a higher death rate. To reduce the risk of infection as well as to slow down the aggressiveness of the devastating virus, they stressed the broad guidelines issued by the US Centres for Disease Control and

Prevention USA such as avoiding spitting, the compulsion of wearing masks, avoiding close contact from infected people, maintaining distance, and overall cautiousness of common people as we have little knowledge about the nature of SARS-CoV-2. Wan et al. [82] studied the structure of coronavirus (2019n-CoV) that emerged from the Wuhan province of China based on the prior knowledge of SARS-CoV-2. The symptoms of Covid confirmed patients, epidemiology, route of transmission, pathophysiology, and control measures of the lethal virus were all studied by Rothan et al. [69]. Qin et al. [64] investigated the various characteristics and basic symptoms of the covid 19 patients with an average age of 58 years, as well as the results of various laboratory tests performed on the 452 patients admitted to Tongji Hospital, Central China's most comprehensive medical center. They look at the period from January 10th to February 12th, 2020. Severe patients accounted for 286 of the 452 patients, whereas non-severe patients accounted for 166, and male patients accounted for 235. After studying seriously ill Covid-19 patients having thrombotic complications, Klok et al. [46] suggested applying pharmacological thrombosis prophylaxis among all covid-19 patients admitted to ICU.

The basic structure of SARS-Cov-2 was addressed by Yan et al. [93]. Chen et al. [14] sketched a comprehensive picture during a very short period from December-2019 to 27th December 2020 delineating the detailed characteristics of twenty (21) patients admitted to Tongji hospital, Wuhan city. They also compared immunological and clinical features of severe and moderate cases and analyzed the different aspects of laboratory results observing clinical, radiological, microbiological, and immunological descriptions Ackermann and colleagues [1] conducted a comparative analysis of lung specimens obtained from seven deceased patients, comprising both COVID-19 cases and those afflicted with acute respiratory distress syndrome (ARDS). Their investigation unveiled pronounced endothelial injury and a predominance of angio-centric inflammation within the lungs of individuals affected with the lethal virus. Guo et al. [34] discussed the origin, structure, and mode of transmission of SARS-Cov-2, as well as recent breakthroughs in vaccine and medicine research to treat the fatal virus's severe infection. Chen et al. [15] looked into the clinical characteristics of nine pregnant women from 20th January to 31st January 2020 to examine if there was any evidence of intrauterine vertical transmission. Pregnant women diagnosed with COVID-19 pneumonia were admitted to Wuhan University's Zhongnan Hospital in Wuhan, China. Sohrabi and colleagues [76] conducted a comprehensive review of the 2019 novel coronavirus, emphasizing the pressing need for meticulous surveillance, close scrutiny, and dedicated efforts to unravel the intricacies of this formidable virus. Shi et al. [74] conducted a cohort study of 416 patients hospitalized at Renmin Hospital of Wuhan University in Wuhan, China, between January 20th and February 10th, 2020, to determine how many patients had a cardiac injury as a result of the covid. During the period of January 13th to February 12th, 2020, Chen et al. [17] investigated 799 mild to critical patients to see how COVID-19 affected them. They tracked the outcome of clinical data till February 28th, 2020. The victims are being treated at Tongji Hospital in Wuhan, China. Among the 799 patients, 113 had died, 161 had been rescued, and the remaining 525 were still being treated. The median time of death for the deceased was 16 days after the commencement, and the median age of the deceased was 68 years.

Shi et al. [73] revealed the radiological findings of 81 individuals in Wuhan, China, who were proven to have COVID-19 pneumonia. Patients were admitted to Wuhan Jinyintan Hospital of Tongji Medical College's Union Hospital. CT scans of the lungs are



useful for determining whether or not the lungs of covid infected patients are affected. Even when the patients' lungs are asymptotic, it is sometimes found that their lungs are significantly harmed. As a result, early detection is critical. A total of 31 patients out of 81 had direct contact with the seafood market. Guo et al. [33] analyzed the database of 187 covid patients gathered from seven hospitals in Wuhan, China, to see if there was any myocardial injury or cardiovascular illness as a result of the covid infection. The duration of the patient's database is only one month, from January 23rd to February 23rd, 2020. They emphasized the demographic area, comorbidity among covid infected individuals, and treatment options for such patients. Holmes et al. [40] have expressed keen interest in assessing the multifaceted impact of the pandemic on society, encompassing aspects such as social dynamics and mental health. They underscored the importance of collaborative and interdisciplinary research approaches. In parallel, researchers referenced in [23] investigated into the epidemiological characteristics and transmission patterns among children ranging from one day to eighteen years of age.

They looked at 2135 youngsters, with 1208 boys (about 56.6%) and a median age of 7 years. The majority of the youngsters had no symptoms, mild symptoms, or significant symptoms. The infection incidence among youngsters was high at first, but it steadily decreased. Children's infectivity is thought to be due to either direct contact with COVID-19 patients or living in an epidemic area. The author demanded that they do the first retrospective study of its kind in China, taking into account the epidemiological characteristics and transmission dynamics of COVID-19-infected infants. Only one child out of 2135 died, indicating that the mortality rate among children is low. Children's criticalness appears to be lower than that of adult patients. The authors emphasized the importance of further research into look into the mechanism of the immune system, and clinical manifestations in children. He et al. [35] studied the temporal patterns of viral shedding in 94 confirmed COVID-19 patients. They also proposed an infectiousness model that took into account a separate 77 transmission pair of infectious-infected people who obtained the database from public sources both inside and outside mainland China. The patients, on average, were 47 years old when they were admitted to Guangzhou's Eighth People's Hospital. Sixty-one patients were mildly unwell, but their viral load was extremely high at the time of start. The author discovered that viral shedding began 2-3 days before symptoms appear and that these people were naturally spreading the infection because they were unaware of their infections. As a result, contact tracking/tracing is critical. To prevent the transmission of the disease, special attention should be paid to personal hygiene and preserving social distancing. Tang et al. [77] investigated the efficacy of anticoagulant treatment in patients with disseminated intravascular coagulation problems. Yang et al. [94] contributed a systematic review and meta-analysis to identify the characteristics that influence the occurrence of co-morbidity and its impact on COVID-infected patients. After a review of 108 papers, they screened seven articles to prepare this study. Patients with hypertension, respiratory problems, diabetes, and cardiovascular disease are more at risk than normal patients, according to the researchers. Nicola et al. [59] presented a review paper depicting the global socio-economic scenario due to the sudden advent of the calamitous virus. To [79] designed a cohort study of viral load monitoring by collecting posterior oropharyngeal saliva and observing serum-antibody reactions in 23 covid patients admitted to the Princes Margaret Hospital and Queen Mary Hospital. To avoid intimate contact between patients and health personnel, the authors recommended that saliva samples be collected by the

patients themselves. For statistical analysis of their collected data, they employ SPSS. The authors utilized the Spearman correlation coefficient approach, and  $p$ -values less than 0.05 were considered significant. Despite the fact that their study was approved by the University of Hong Kong's International Review Board and the Hong Kong West Cluster Hospital Authority, the authors claimed that the cohort study may have various flaws, such as a small sample size and a short time span. Wang et al. [84] conducted a study focusing on adult patients infected with the virus, who were admitted to ten hospitals located in the Hubei province of China. These patients received treatment with a controlled dosage of the drug remdesivir. However, despite meticulous observation, the authors did not observe any significant results associated with the widely discussed remdesivir drug.

Remuzzi and colleagues [67] attempted to provide an overview of the healthcare landscape in Italy following the outbreak of the pandemic. Their study also emphasized that in the event of the graph's trends persisting, the Italian Government would need to take swift action to bolster healthcare infrastructure to address the challenges posed by such a severe pandemic situation.

Tay et al. [78] analyzed the different mechanisms of SARS-CoV2, and put emphasis on immunopathogenesis. The efficiency and safety of the m-RNA vaccination developed by drug sponsor Moderna were investigated by Baden et al. [3]. Volunteers are assigned to 30240 for two doses of the study, each weighing 100  $\mu$ g. The actual vaccine is given to 50% of the participants (15210), while the placebo is given to the remaining 15210. The volunteers are separated into two groups: one for those over the age of 65, and another for those between the ages of 18 and 65. Critical co-morbid patients are those who are less than 65 years old. The trial period is quite short, running from July 27, 2020, to October 23, 2020. In this context, it's crucial to note that the vaccine's efficacy and safety are also critical. Qiu et al. [65] conducted a comprehensive survey by sending a questionnaire to 52730 people in 36 provinces across China to find out how the unexpected epidemic of COVID-19 affected the Chinese people's mental health. They demanded that it is the first study of such kind to assess the psychological impact. Male respondents accounted for 18599 (35.27 %) of the total 52730 respondents, while female respondents accounted for 34131 (64.73 %). The study was conducted from the 31st of January to the 10th of February, 2020, which corresponds to the early stages of the epidemic. The questionnaire was created using the guidelines provided by the 11th Revision of the International Classification of Diseases, as well as expert comments from psychiatrists. In this study, they used a scale of 0 to 100 to determine the frequency of sadness, anxiety, particular phobias, cognitive change, abnormal behavior, and loss of social function, in addition to demographic variables. A score of 52 indicates a severe psychological problem, whereas a score of 28 to 51 suggests mild to moderate psychological disorder. Finally, the authors offer some suggestions for reducing psychological suffering, particularly among Chinese youth, women, migrant workers, and the elderly. Guan et al. [32] studied the effects of co-morbidity on covid infected individuals. They looked at 1590 patients from 575 hospitals across China between the 11th of December 2019 and the 31st of January 2020, which was the early stage of the Covid-19 outbreak. Only 399 of the 1590 covid confirmed patients were found to have comorbidities such as COPD, diabetes, hypertension, cardiovascular illness, cerebrovascular disease, and so on, with diabetic patients being the most closely followed by patients with hypertension. Clinical research has shown that individuals with two or

more comorbidities become more critical than the other. Grein et al. [29] used the remdesivir drug among the 61 hospitalized confirmed infected patients with an oxygen level of less than or equal to 94 oxygen level and found that this drug may be beneficial to the critically ill. Li et al. [53] investigated the psychological effects of rapid confinement owing to an unanticipated epidemic of the Covid-19 virus among Chinese college students. They took into account a variety of factors such as psychological discomfort, depression, anxiety, and so on. From January to March 2020, the time period was relatively brief. In order to conduct their longitudinal study, they used 555 undergraduate students. Verity et al. [81] created a model to estimate the severity of the deadly coronavirus. To do so, they looked into the reasons why mainland Chinese and international patients died and observed that the average time from onset of symptoms to mortality was 17.8 days, while the average time from onset of symptoms to hospital discharge was 24.7 days. The overall infection mortality ratio for China was 0.66%, as measured by the ratio of the total number of fatalities to the total number of cases. They looked at the data up to the 8th of February, 2020 for China and the 25th of February, 2020 for the rest of the world. In their research, they aimed to address fundamental questions pertaining to COVID-19 confirmed patients, such as the origin of infection, potential travel history, and various key dates including symptom onset, hospitalization, confirmation of infection, recovery, and unfortunately, date of mortality. Gordon and colleagues [26] undertook a chemo-proteomic analysis with the goal of identifying effective drugs for the treatment of COVID-19 patients. They also emphasized the importance of deciphering the underlying mechanism of the virus, with hopes that their study would pave the way for innovative strategies against not only the coronavirus but also other viruses.

To gauge the virus's transmissibility, the positivity rate ( $R_0$ ) served as a crucial metric. Liu et al. [54] estimated the positivity rate for the COVID-19 virus. Their findings revealed that when  $R_0$  exceeds one ( $R_0 > 1$ ), the likelihood of infection increasing is substantial, whereas if  $R_0$  is less than one ( $R_0 < 1$ ), the infection rate tends to decline. According to their estimation, the mean  $R_0$  stood at 3.28 in mid-February 2020, a value notably higher than the estimate provided by the World Health Organization (WHO).

Chen et al. [18] presented a review paper outlining the overall characteristics of CoV as well as the diseases induced by various CoV in humans and animals. They also included a list of significant pathogenic coronaviruses, along with descriptions of their kind, origin, and symptoms. Different types of structural and non-structural proteins have been discussed as well. The transcriptional responses to SARs-CoV-2 were investigated by Blanco-Melo et al. [9]. They concluded that SARS-CoV-2 is distinct from other highly pathogenic coronaviruses like MERS-CoV, SARS-CoV1, HPIV3, IAV, and RSV. Bioanalysis of the genome sequence of coronavirus has been performed by Chen et al. [13]. A complete comparison of characterization between this disastrous virus and other relevant coronaviruses that appeared earlier had been offered by the authors. They also stated that more research is needed to determine the virus's possible origins and the involvement of intermediate animals in the spread of this lethal infection. They hope that their research will point them in the right way in terms of diagnosis, control measures, and immunization. Bikdeli et al. [8] reviewed the pathophysiology, epidemiology, and therapeutic options for Covid-19 positive patients. A Covid-infected patient's life may be

jeopardized by thrombotic illness. The properties of computed tomography in Covid-19 patients were investigated by [27].

Chu and colleagues [20] conducted a comprehensive systematic review and meta-analysis, assembling a dataset from 21 reputable sources endorsed by the World Health Organization (WHO). These data were sourced from 16 different countries spanning six continents. The research involved a meticulous screening process, encompassing both healthcare workers and the general population. Their findings highlighted the observation that close human-to-human contact can significantly accelerate the transmission of the virus. Xu et al. [91] investigated whether tocilizumab and glucocorticoids are effective/useful in the treatment of covid infection. They discovered that no patients had reported any negative side effects. Antibody responses of Covid-19 patients have been studied by Long et al. [55]. They considered 285 patients for inquiry and observed that IgG and IgM antibody titers rise within three (03) weeks after symptom start, and surprisingly aimed that severe/critical patient achieved more titers than non-severe patients. They also looked at 26 seronegative patients at first but were surprised to find that all of them had gained seropositivity. The median time for conversion is roughly 13 days after symptom onset.

Bhatraju et al. [7] contributed a case study of covid infected individuals in the Seattle region of the United States and made some important observations concerning their physical conditions and needs. To compile their case study, they looked at 24 patients from nine Seattle-area hospitals who were admitted between February 24th and March 9th, 2020, and tracked their treatment outcomes through March 23rd, 2020. Only 5 patients were discharged from the hospital after 12 out of 24 (50%) people died. The majority of the patients were above 65 years old. Korber et al. [47] expect that their research will aid in the understanding of the mutagenic nature of spike protein and will be very useful in the creation of vaccines. In their examination of research papers within the realm of social and behavioural science, Bavel et al. [4] delved into critical aspects of pandemic management. They addressed the imperative of threat prevention, the necessity of societal and behavioural adaptations, the enhancement of science communication, effective leadership strategies, and the impact of stress. Their comprehensive analysis also encompassed a review of prior research insights and identified existing gaps. The authors aimed to provide valuable guidance to policymakers, with the ultimate goal of mitigating the potentially catastrophic consequences of COVID-19 through prompt interventions. Emanuel and his team [24], on the other hand, put forth a set of six recommendations aimed at achieving equitable distribution and optimal utilization of scarce medical resources. Their roadmap outlined a path towards equal access to healthcare facilities and opportunities for all. Among their key points, they stressed the need for balanced consideration of all patient types, be they COVID-19 or non-COVID-19 cases. Their recommendations prioritized saving the maximum number of lives and maximizing individual benefits, emphasizing the importance of increased testing and the use of personal protective equipment (PPE). Additionally, they advocated for the provision of intensive care units (ICUs) for critical patients and highlighted the crucial role of unhindered research for the greater societal good. They underscored the importance of prioritizing patients based on scientific evidence rather than adopting a first-come-first-served approach.

Chinazzi et al. [19] use a global metapopulation disease transmission model. According to Hollander et al. [39], telemedicine is an ideal technique to treat patients

during a pandemic. Patients can discuss their requirements with doctors over the phone. Jin et al. [44] attempted to develop a drug design strategy to combat SARS-CoV-2. They tried to explore the antiviral compounds and attempted to characterize the enzymatic activity of those antiviral compounds' by producing a fluorescence resonance energy. Bernheim et al. [6] looked into the relationship between the beginning of symptoms and the first CT scan. For this study, they looked at 121 individuals with an average/mean age of 48 years (ranging from 18 to 80 years) who were seen between January 18th and February 2nd, 2020. The knowledge about T-cell responses to SARS CoV-2 is highlighted by Grifoni et al. [30]. They measured the virus-specific CD 4+ and Cd 8+ T cells to better understand such responses. There are several methods for evaluating such responses. They sought to determine the infected areas of the human body and the existence of corona immunity among the people after analyzing the recovered patients. They discovered that people with robust immunity are better equipped to combat the deadly illness. Immune power is assessed using 21-color flow cytometry and phenotypic markers in the recovered patients. They compared 20 participants who had never been exposed to the virus to 20 recently recovered patients, with median ages of 31 and 44, respectively. Finally, they reinforced and reiterated the vaccine development.

Shereen et al. [72] discussed the emergence, mode of transmission, and nature of the coronavirus. They tried to explore the advancement of vaccine development and therapeutic treatment to handle the calamitous situation. Ou et al. [60] evaluated SARS-CoV-S and SARS-CoV-2S protein stability and found that SARS-CoV-S protein is more stable than SARS-CoV-2S protein. The susceptibility of cell type, route entrance, and protease priming for SARS-Cov-2, as well as many therapeutic development possibilities, were analyzed by them. They checked neutralizing action between SARS and covid patients' convalescent sera and, tested whether SARS-CoV S and SARS-CoV-2S pseudo virions could be neutralized by sera taken from recovered SARS and COVID patients. They collected a sample of sera from one recovered SARS patient and five recovered COVID patients and checked the neutralization ability against transduction on 293/hACE2 cells by SARS-CoV-S and SARS-CoV-2S. Zhao, J. et al [98] attempted to explore antibody responses of COVID-infected patients and examined the seroconversion rate of antibody titer. They looked at 173 COVID patients who were 48 years old on average (ranging between 35-61 years). Total antibodies such as Ab, IgM, and IgG were found in 535 samples from 173 patients. The seroconversion rates were found to be 93%, 82.7 %, and 64.7 %, respectively. Out of 173 patients, 116 have a history of epidemiological travel or residence in Wuhan, China. They expect that their research could mark a new era in the diagnosis of COVID-19 patients, and Governments around the world would be benefitted from their discoveries/observations. Xu et al. [90] investigated the possible routes of 2019 n CoV infection. They discovered that ACE2 expression was high in the tongue, suggesting that the mucosa of the oral cavity is at high risk for CoV infection in 2019. They used single-cell RNA sequencing to investigate and evaluate the expression of ACE2 on the mucosa of the oral cavity. They discovered that the mean expression of ACE2 was higher in the oral tongue (13 tissues) than in other organs. Pfefferbaum et al. [62] investigated the impact of lockdown, quarantine, isolation, and other pandemic-related measures on the mental health of the general public. People have been experiencing emotional devastation. Healthcare employees, in particular, have been subject to emotional strain. There is a dearth of a particular medicine, personal protective equipment shortages, and infrastructure. As a result,

individuals are forced to labor in a high-risk environment. Wiersinga et al. [85] described the disastrous COVID-19 virus's potential causes, symptoms, and diagnosis, among other things. They recommended supportive therapy and prompt hospitalization for critical patients because there is no specific medicine to treat the deadly illness. But they are not able to investigate whether or not a patient can be infected multiple times. They have also tried to observe the efficacy of the drug remdesivir. They infer that the drug is able to shorten the recovery time for non-severe covid-infected patients. A comprehensive review of COVID-19 has been presented by Singhal [75]. In this review paper, the author sheds light on the different features like symptoms of the infected people, and process of treatment, and so on from the perspective of Indian patients. Letko et al. [52] attempted to develop a method for quick screening the lineage of B-beta coronavirus (SARS-CoV& SARS-CoV-2) and examine their ability to cell infection from different species.

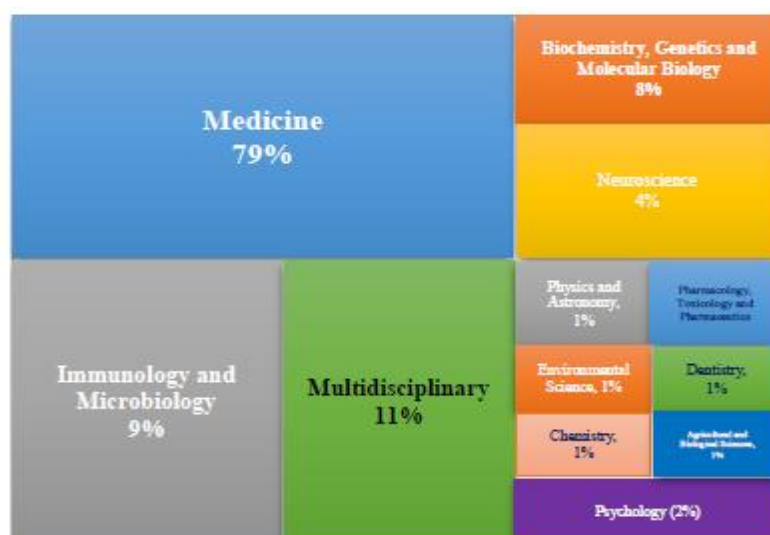
Based on findings from clinical trials, Helms and colleagues [37] have highlighted the potential efficacy of CT pulmonary angiography (CTPA) in aiding severe COVID-19 patients with a high risk of pulmonary embolism (PE). Their research highlights the limitations of relying solely on lung ultrasonography in uncovering the underlying causes of deterioration in COVID-19 patients. Meanwhile, Zhang and his team [97] conducted an in-depth analysis of the x-ray crystal structure of SARs-CoV-2, examining two distinct crystal forms at resolutions of 1.95 and 2.20 Å. Their investigation primarily focused on the main protease (M pro or 3CL pro) responsible for slicing viral polyproteins translated from viral RNA into functional viral proteins. Additionally, they aimed to establish a valuable framework for the discovery of pyridine-containing inhibitors as potential candidates for anti-coronaviral drugs. Pan and colleagues [61] directed their attention to a noteworthy radiological discovery pertaining to changes observed in chest CT scans of COVID-19-infected patients, tracing these changes from the initial diagnosis to the recovery phase. They looked at a total of 21 patients, 6 men, and 15 women, who were hospitalized at Tongji Medical College in China between the 12th of January and the 6th of February, 2020, with severe pneumonia and heavy respiratory troubles. A total of 82 CT scans had been performed on the 21 recovered patients. The average time until discharge was  $17 \pm 4$  days. The evolution of a CT scan of the chest was divided into four windows namely the early stage (0-4 days), progressive stage (5-8 days), peak stage (9-13 days), and absorption stage ( $\geq 14$  days). Lechien et al. [51] conducted an investigation into the condition of hospitalized patients with confirmed COVID-19 infections, specifically examining the prevalence of olfactory and gustatory disorders among this patient population. Their research revealed that these symptoms were frequently observed among European patients. Furthermore, they highlighted the importance of recognizing anosmia or ageusia as crucial symptoms indicative of COVID-19 infection.

A review paper by Ye et al. [95] highlighted the pathophysiology and therapy of cytokine storm in COVID-19-infected individuals. The researchers discovered that cytokine storm is mostly responsible for COVID patients' rapid organ failure. Excessive cytokine release also raises the death rate. IFN-1 or IFN-  $\alpha/\beta$  plays an important part in resisting this deadly virus and strengthening the human immune system. In epithelial cells, IFN-  $\lambda$  activates antiviral genes. Mizumoto et al. [58] developed a statistical model to assess the asymptomatic proportion and infection time among Covid infected people. To calculate the mean incubation period and monitor its fluctuations, they employed time series analysis and sensitivity analysis. According to their calculations, it has been

determined that the asymptomatic fraction of COVID-19 cases stands at approximately 17.9%. Additionally, Rajkumar [66] discussed the significant impact of COVID-19 on the mental health of the general population, citing increased instances of anxiety, depression, and mental stress. The author emphasized the potential for further research to unveil various facets of this issue, particularly among individuals at higher risk due to pre-existing health conditions. A paper by Li et al. [53] focused on the neuro-invasive potential of SARS-CoV-2. They discovered that neuro-invasive potential has a significant influence on respiratory failure and recommended more investigation. They laid emphasis on public awareness in order to combat the deadly illness and provided some advice as well as treatment options. Hellewell et al. [36] presented a stochastic mathematical model to test the efficacy of isolation and contact tracing in preventing the lethal virus from spreading. They used the initial number of cases, the basic reproduction number ( $R_0$ ), the time span from symptom start to isolation, and the number of cases that are not recognized by self-report or contact tracing, i.e., cases under subclinical illness, to develop their transmission model. Docherty et al. [22] reported the clinical characteristics of critical Covid-19 patients admitted to UK hospitals throughout the first wave's expansion in their cohort research. They gathered data on 20133 hospital patients with a median age of 73 years from 208 acute care hospitals in the UK for their observational study. Their investigation lasted only six weeks, from February 6th to April 19th, 2020. It has been discovered that mortality and risk factors are proportional to increasing age, and comorbidities such as people with respiratory problems, liver and kidney problems, and obesity. They anticipate that their observational cohort study may assist the government in anticipating the sudden advent of such a devastating/calamitous virus.

### 3. BIBLIOMETRIC EXPLORATION OF THE LEADING 100 ARTICLES

This section discusses bibliometric outcomes of the most cited 100 articles on Covid-19. Figure 1 shows subject areas of the leading 100 articles.



**Figure 1:** Subject areas of the leading 100 articles on Covid19

It's important to highlight that the percentages in Figure 1 do not sum up to 100%. This discrepancy arises because certain journals may fall under more than one subject area in SCOPUS, leading to the possibility of a single document being counted multiple times. As anticipated, approximately 80% of the top articles are published in journals related to the field of Medicine. Table 1 provides a list of the prominent authors featured in the top 100 COVID-19 research articles.

**Table 1:** Leading authors in the leading 100 covid-19 research articles

Rank	Author	Affiliation	Country	TP	TC
1.	Wei, Y.	Wuhan Jinyintan Hospital (WJH)	China	4	41468
1.	Yu, T.	WJH	China	4	41468
2.	Zhang, L.	WJH	China	4	34012
2.	Xia, J.	WJH	China	4	34012
3.	Cao, B.	China-Japan Friendship Hospital (CJFH)	China	4	34008
3.	Fan, G.	CJFH	China	4	34008
3.	Gu, X.	CJFH	China	4	34008
3.	Xu, J.	CJFH	China	4	34008
3.	Wang, Y.	CJFH	China	4	34008
4.	Xiang, J.	Jin Yin-tan Hospital	China	4	27325
5.	Zhao, J.	Tongji Medical College (TMC)	China	4	20967
6.	Yuen, K.Y.	The University of Hong Kong	Hong Kong	4	19226
7.	Hu, Y.	TMC	China	4	17651
8.	Shan, H.	Sun Yat-sen University	China	4	16132
9.	Li, H.	Chinese Academy of Medical Sciences (CAMS)	China	3	32540
10.	Li, X.	Beijing Ditan Hospital Capital Medical University	China	3	32043
11.	Hu, Y.	TMC	China	3	24286
12.	Guo, L.	CAMS	China	3	22783
13.	Liu, Y.	Wuhan Institute of Virology	China	3	22516
14.	Liu, Z.	CAMS	China	3	15056
14.	Zhang, Y.	CJFH	China	3	15056
14.	Zhou, F.	CJFH	China	3	15056
15.	Zhang, D.	Wuhan Jinyintan Hospital	China	3	14559
16.	Drosten, C.	Universitätsmedizin Berlin	Germany	3	10520
17.	Chan, J.F.W.	The University of Hong Kong	Hong Kong	3	6854
17.	To, K.K.W.	The University of Hong Kong	Hong Kong	3	6854
18.	Jaki, T.	Lancaster University	United Kingdom	3	6556
19.	Horby, P.W.	Nuffield Department of Medicine, Oxford	United Kingdom	3	5168

Twenty-eight (28) authors are included in Table 1 with the last serial number 19. Authors receiving the same number of citations are denoted by the same serial number. It is seen that out of 28 leading authors 23 belong to China, 3 belong to Hongkong which is a part of South China, 2 are included in the United Kingdom (U.K.), and 1 is in Germany. We can infer that China is the pioneer in carrying covid-19 research. Y. Wei, and T. Yusecure first place receiving the same number of citations 41468. Wuhan Jinyintan Hospital takes the leading role in carrying out the research. Clinical trials are abundantly held/organized at Wuhan Jinyintan Hospital. It is to be remembered that COVID-19 is first out broken in the Wuhan province of China. China-Japan Friendship Hospital is also taking an important part in advancing the research. Five authors (B. Cao, G. Fan, X. Gu, J. Xu, and Y. Wang) of China-Japan Friendship Hospital, China received the same number of citations with a value of 34008. Table 2 highlights the leading journals, pioneering Institutions/Hospitals/Medical Colleges, and the names of the country in terms of the number of publications.



**Table 2:** Leading journals, universities, and countries in the leading 100 articles

R	Source	TP	Affiliation	TP	Country	TP
1	New England Journal of Medicine	15	Tongji Medical College	14	China	55
2	Lancet	9	Huazhong University of Science and Technology	13	United States	33
3	Nature	6	University of Oxford	9	United Kingdom	23
4	JAMA Journal of The American Medical Association	5	Icahn School of Medicine at Mount Sinai	7	Germany	10
5	Cell	4	Chinese Academy of Sciences	7	Australia	7
6	Radiology	4	Chinese Academy of Medical Sciences & Peking Union Medical College	7	Canada	6
7	Lancet Infectious Diseases	3	Tsinghua University	6	France	6
8	Science	3	University of Cambridge	6	Italy	6
9	BMJ	2	Wuhan Jinyintan Hospital	5	Netherlands	5
10	Clinical Infectious Diseases	2	The Central Hospital of Wuhan	5	Japan	4
11	International Journal of Antimicrobial Agents	2	The University of Hong Kong	5	Singapore	4
12	International Journal of Surgery	2	University of Washington	5	Spain	4
13	JAMA Cardiology	2	Sun Yat-Sen University	5	Switzerland	4
14	Journal Of Medical Virology	2	Capital Medical University	5	Brazil	3
15	Nature Medicine	2	University of California, San Diego	5	Austria	2
16			Chinese Center for Disease Control and Prevention	5	Belgium	2
17			Renmin Hospital of Wuhan University	5	Denmark	2
18			Zhongnan Hospital of Wuhan University	5	Greece	2
19			Hong Kong	2		
20			India	2		
21			Russian Federation	2		

It is observed that the New England Journal of Medicine ranks first in terms of total publications which amounts to 15 in number. The ‘Lancet’ and ‘Nature’ respectively secure 2nd and 3rd places in the Table 2 publishing 9 and 6 papers. ‘Tongji Medical College’ ranks in the highest position following ‘Huazhong University of Science and Technology’, and ‘University of Oxford’ publishing 14, 13, and 9 papers respectively. Among the educational institutions ‘The University of Oxford’ had a nice performance in performing research regarding the Covid-19 outbreak. The Country ‘China’ has shown outstanding performance in carrying research on Covid-19 publishing 55 papers. The United States and the United Kingdom are placed in the 2nd and 3rd position in the table 2 respectively by publishing 33 and 23 papers. Table 3 presents frequently used keywords in the leading 100 covid-19 research articles.

In Table 3, we have included 60 keywords from the 100 most cited papers which appear more than 14 times. There is a subtle difference between the words ‘Human’, and ‘Humans’ which appear 98, and 88 times and secure 1st and 3rd places respectively. Similarly, the words ‘Coronavirus Infection’, and ‘Coronavirus Infections’ are very close to each other. Among the countries, only the country ‘China’ is included in the table 3. Figure 2 presents density visualization of keywords based on their occurrences in the top cited research works. We use the VoS viewer software to prepare the graph base on the dataset downloaded from SCOPUS.



#### 4.1. Disciplines/Subject Areas

One hundred research papers have been categorized into different disciplines such as (i) Medicine (ii) Multi-Disciplinary (iii) Immunology & Microbiology (iv) Biochemistry, Genetics, Molecular Biology (v) Neuroscience (vi) Others.

##### 4.1.1. Medicine

Since Covid-19 is a global health threat issue, most of the papers considered here belong to the medicine category. Researchers are continuously trying to uncover the mystery of the epidemiological, clinical, laboratory, and radiological characteristics of the calamitous virus [43, 82, 97, 101] and doctors, scientists, researchers are rendering their full and heartiest effort to reveal the risk factors, treatment with different types of drugs, standard care, outcomes of the different types of Covid infected patients ([8, 15, 17, 23, 32, 33, 35, 55, 73, 74, 77, 79, 91, 99]. He et al. [35] gathered detailed information on Covid-infected patients like pre-symptomatic transmission, the onset of symptoms, the profile of infections, and so on, and assesses the viral shedding of the patients. They concluded that contact tracing is very important in capturing potential transmission events in the pre-symptomatic stage. According to Tang et al. [77] analysis, patients with elevated D-dimers or SIC scores may benefit more from anticoagulation medication than patients who were chosen at random. The presence of thrombotic illness may exacerbate the critical situation of Covid-19 patients. Therefore, the highest level of care is also required for non-Covid patients having a thrombotic illness. Bikdeli et al. [8] made an effort to clarify the pathophysiology, epidemiology, management, and results of Covid-19 patients who required anti-thrombosis medication and had venous or arterial thrombosis. Zhou et al. [99] delineated the risk factors for mortality as well as the viral shedding of the covid infected patients. Patients have several and so many problems. Most of the patients have comorbidities namely respiratory trouble, diabetes, ARDS, respiratory trouble, and so on. So, it is very difficult to provide treatment for such patients as it is a new virus and the characteristics of the virus are completely unknown to the scientists, doctors, and researchers. Hoffmann and their colleagues [38] focused that the host protein ACE2 and TMPRSS2 influencing the entry of SARS-CoV-2. Gordon et al. [26] highlighted the interaction between SARS-CoV-2 proteins and human proteins which includes several multiple biological processes, including protein trafficking, translation, transcription and regulation of ubiquitination, and so on. Klok et al. [46] investigated thrombotic complications among severe Covid patients who were treated in ICU facilities in three hospitals in the Netherlands. For proper diagnosis, they suggested that an imaging test is essential, and in addition to that, they also proposed to strictly apply pharmacological thrombosis prophylaxis to all critical Covid patients.

##### 4.1.2. Multi-disciplinary

Sudden confinement has had a profound psychological influence on the general populace, particularly on youngsters, students at various levels, women, patients with coexisting conditions, physically frail individuals, and others. The unexpected advent of the coronavirus has had a significant negative impact on mental health. In order to protect the psychological welfare of the community, it is important to examine mental health across demographic groups and genders. Some researchers ([83], [40], [53], [62], and [66]) reinforced to survey the mental health and outcome of the psychological influence on the people/children due to unanticipated lockdown.

The psychological problem of Chinese people during the pandemic was examined by Qiu et al. [65]. By providing participants with a questionnaire, they made an effort to gauge psychological disorders including unwarranted panic, anxiety, and depression. Finally, they recommended some policies to deal with the problem during the tumultuous period.

#### 4.1.3. Immunology & Microbiology

To expedite the development of vaccines using a standard protocol, Polack, F.P. et al [63] initiated phase-I clinical studies of the RNA vaccine BNT162b2 in the USA and Germany. They had 43448 volunteers total, of whom 21720 received two 30 g doses of the vaccination spaced 21 days interval, and 21728 received a placebo. It was noted that respondents who administered the BNT162b2 vaccine had higher antibody titers than those who received the placebo. They assessed the efficacy and the safety measure as well. The entire method, including data collecting, data analysis, data interpretation, manuscript writing, conclusions, and so forth, was handled by the Pfizer company. The entire clinical trial was funded by BioNTech. The epidemiological, clinical, laboratory, radiographic, and microbiological results of the five patients with unexplained pneumonia in a family cluster were highlighted by Chan et al. [13]. This novel coronavirus's linkage to a potential animal source was proposed by the phylogenetic analysis.

The pathophysiology of SARS-CoV-2 infection is outlined by Tay et al. [78] in their article. They also explain how the virus interacts with our body's immune system and how this affects the disease's progression. In Table 1, the authors also include a list of vaccines undergoing current clinical trials. Zhou et al. [99] visualized the entire genome sequencing and witnessed the first spread of human respiratory secretions onto human airway epithelial cells using a transmission electron microscope. They came to the conclusion that additional research was necessary to identify unidentified respiratory infections.

#### 4.1.4. Biochemistry, Genetics, Molecular Biology

The epidemiological, clinical, laboratory, radiographic, and microbiological results of the five patients with unexplained pneumonia in a family cluster were highlighted by Chan et al. [13]. This novel coronavirus's linkage to a potential animal source was proposed by the phylogenetic analysis. The genome structure and traits of Covid-19 confirmed patients related to the other patients were compared by Chan et al. [12].

#### 4.1.5. Neuroscience

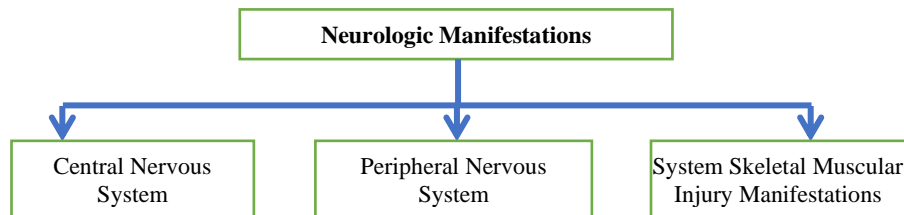
Neurologic manifestations of Covid-19 infected patients are studied by Mao et al. [57]. 214 hospitalized patients are taken into consideration to perform their case study. The period is from January 2020 to February 2020. Neurologic manifestations can be categorized into three categories (Figure 3):

(i) Dizziness, headaches, altered awareness, acute cerebrovascular illness, ataxia, and seizures are all signs of the central nervous system.

(ii) Affected senses of taste, smell, vision, and nerve pain are examples of peripheral nervous system manifestations.

(iii) Manifestations of skeletal muscular injuries include pain, edema, ecchymosis, weakness, decrease of muscle ability and so on

Li et al. [53] highlighted the neuro-invasive potential of SARS-CoV-2. They summarized that neuro-invasive potential has a significant role in respiratory failure. They opined that more exploration is needed in this matter.



**Figure 3:** Category of neurological manifestation

#### 4.1.6. Others

Bhatraju et al. [7] examined information on patients who were admitted to hospitals in the Seattle area and found that the majority of patients died from hypoxemic respiratory failure. The incubation period has been noticed by Lauer et al. [50]. They also highlighted the patients' potential exposure, symptom onset, and fever onset, and recommended prompt hospitalization.

#### 4.2. Types of Articles/Research, Number of Respondents, Male -Female Ratio, Median Age of the Infected Patients

With the sudden emergence and quick spread of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that originated in the Chinese city of Wuhan, there is a new public health disaster that is posing a threat to the entire world. It is frequently referred to as a new coronavirus because it first surfaced in 2019. The virus appears to have started in zoonotic animals like bats or other unidentified animals in the seafood market of Wuhan, and then spread quickly to humans through person-to-person contact due to the fast global connectivity of different countries. As a result, the COVID-19 pandemic is a serious global health emergency that has spread to practically every country in the world. Emergent research has taken on all around the world to learn more about the features and nature of the deadly virus. Different studies have uncovered several mysteries regarding the virus's nature and effects. Researchers have discovered clinical, radiological, and laboratory results of individuals with Covid-19, and some of them have noted the impact on psychological and mental health brought on by unexpected confinement, lockdown, and isolation, among other things. Researchers have conducted a variety of studies, including reviews, surveys, case studies, and retrospective studies, on various nations to observe the consequences. Research papers published during the initial wave of the coronavirus were taken into consideration because we have largely considered the 100 most referenced publications in this article. The classification table includes information on the number of responders, the male-to-female ratio, the median age of the covid-infected patients, and the types of the research study.

### 4.3. Epidemiological and/or Clinical Investigation

Some researchers are interested to look into the origin, structure, nature, and characteristics of the coronavirus and some of them tried to find the symptom, onset, incubation period, clinical characteristics, pathological findings, effects on comorbid patients, and so on. Therefore, characteristics may be separated into two categories (i) Characteristics or nature of the virus (ii) Characteristics of the covid-infected patients.

#### 4.3.1. Investigation of the Nature or Characteristics of Corona Virus

Research works like ([31], [72], [82], [34], [76], [18]) examined the corona virus's origin, structure, nature, transmission, spectrum, and clinical characteristics and so on. Through the case study Holshue et al. [41] emphasized the first confirmed case of Covid-19 in the United States, outlining/eliciting his symptoms, history of travel and contact, clinical features, and the time of viral shedding. Certainly, these findings will help the American administration in identifying the sick promptly and isolating them to stop rapid transmission. Using X-ray, the structural dynamics of unliganded SARs-CoV-2 M pro had been characterized by Zhang et al. [97]. They also attempted to identify the inhibitor of  $\alpha$  -ketoamide. Guo et al. [34] reviewed the most recent studies on the epidemiology, etiology, and clinical features of COVID-19 and talked about the available therapies and technological developments to stop the spread of the novel coronavirus that is causing the epidemic.

#### 4.3.2. Investigation of the nature or characteristics or nature of Covid confirmed patients

Different researchers have looked into several relevant sectors, suggesting that the Covid-19 problem has had a considerable impact. To start, numerous researchers have looked into the clinical characteristics, pathological findings, epidemiological investigations, symptoms, symptom onset, and manifestations of pneumonia in covid-infected patients ([43], [99], [101], [16]). A cluster of family members' epidemiological, clinical, laboratory, radiographic, and microbiological findings was examined by Chan et al. [13] in 2020. Chen et al. [15] made an effort to look at the clinical traits of pregnant women who had the Covid infection and looked at the likelihood of intrauterine vertical transfer of the Covid-19 infection. They found that the clinical features of Covid-19-positive pregnant and non-pregnant women are not significantly different. To et al. [79] analyzed the serial viral load, antibody kinetics, and viral genome of the patients with Covid-19 belonging to Hong Kong and observed that such patients have more viral load than the patients infected with other SARS-CoV. Lechien et al. [51] noted the occurrence of gustatory and olfactory impairment in European patients with Covid-19. These characteristics are thought to be common among Covid-infected people in Europe who can be recognized by anosmia or ageusia. Feminine patients tend to experience more olfactory and gustatory dysfunctions than male patients. The authors concluded that sudden/unexpected anosmia or ageusia should be taken seriously as a sign of Covid. For nine pregnant women with laboratory-confirmed Covid-19 pneumonia, Chen et al. [15] retrospectively evaluated the clinical notes, laboratory results, and chest computed tomography scans. However, they were unable to identify any distinct and unique causes among the nine pregnant women who had Covid-19 pneumonia. A thorough analysis of the epidemiological traits and transmission dynamics of 2135 pediatric patients under the age of 18 years, confirmed with Covid-19, was presented by [23]. They noted that children are in a low-risk stage in terms of severity, mortality, and other factors.

#### 4.4. Vaccine Development

Outcomes of clinical trials of two-dose 30 µg vaccine BNT162b2 have been explored by Polack et al. [63]. The clinical trials consider the different aspects of vaccines like percentage (%) of efficacy, safety measurement, and its impact. They made their experiment on 43548 participants from the United States, and Germany with ages greater or equal to 16 some of which are given double doses of vaccine, and some of which is applied a placebo. The vaccine is based on RNA which only needs information about the virus's genetic sequence. Extracting the trials, it is elicited that this vaccine may be able to provide 95% resistance against SARS-CoV-2.

In 2020, Baden et al. [3] highlighted mRNA-1273, describing the efficacy and safety of the vaccination. This vaccine is an m-RNA-based lipid nanoparticle vaccination. There were 30420 participants participating in the clinical trials of the vaccine at 99 centers around the United States. It demonstrated greater than 94% efficacy, giving critically ill covid patients very good results.

#### 4.5. Intermediator

Researchers looked into the possibility of an areological agent spreading the infection. Chan et al. [12] concluded from their analysis of the 2019 n-entire CoV's genome that it is a novel lineage B-beta coronavirus that is closely connected to coronaviruses that originated in bats and shed information on the evolutionary history of the emerging coronavirus. Zhou et al. [100] investigated the possibility of an aetiological agent causing the current epidemic; however, they were skeptical of the existence of any causal links between a bacterium and the illness. They suggested that additional research is necessary in this case.

#### 4.6. T-cell Responses

The basic information of CD4+ and CD8+ T cell responses is very useful for vaccine development. The fundamental understanding of CD4+ and Cd8+ T-cell responses to the virus was stressed by [30], since the creation of a vaccine requires this knowledge immediately. Twenty adult patients who had recently recovered from Covid-19 were taken into consideration, and it was hoped that these recovered patients would produce significant Cd4+ T-cell responses against SARS-CoV-2.

Chen et al. [14] considered two categories of 21 patients: severe and moderate. Following several clinical observations, they identified that SARS-CoV-2 primarily affects T-lymphocytes, primarily CD4+ and CD8+ T-cells, leading to a decrease in both their numbers as well as their ability to produce IFN. These remarkable insights marked a significant turning point in the evolution of immunization. They insisted that it be the first initial investigation that outlines the history of the emergence of immunizations.

#### 4.7. Treatment of Plasma Transfusion

Some researchers have looked into the effectiveness of convalescent plasma transfer. According to Shen et al. [71], antibodies obtained through plasma transfusion may be crucial in the treatment of patients with covid infection. Zhao et al. [98] tried to examine the antibody responses like Ab, IBM, and IgG against SARS-CoV-2 by analyzing blood samples of covid confirmed patients. It has a significant diagnostic value like the RNA test.

Within three (3) weeks after the beginning of symptoms, Long et al. [55] studied the antibody responses of SARS-CoV-2 confirmed patients. They noticed that seroconversion for IgG and IgM both happened concurrently or in order. Ag, Ibm, and IgG tests for total antibodies against SARS-CoV-2 Clinical analysis of samples from 535 patients by Zhao et al. [98] revealed that serological testing is crucial for the diagnosis and treatment of Covid confirmed patients.

#### **4.8. Cytokine Storm**

Cytokine storm plays a major role for the covid infected patients. The antiviral transcriptional responses of SARS-CoV-2 and other respiratory viruses were compared by Blanco-Melo et al. [9]. They concluded that SARs-CoV-2 infection results in modest levels of IFN-I and IFN-III and moderate ISG responses. They also concluded that COVID-19's defining and motivating characteristics are diminished innate antiviral defenses along with overactive inflammatory cytokines. Ye et al. [95] studied pathophysiology and management of cytokine storm, a major contributor to ARDS, which results in physiological decline or death.

To determine whether SARS-transcriptional CoV-2's responses have a distinctive footprint from those of other respiratory viruses, Blanco-Melo et al. [9] compared the transcriptional responses to SARS-CoV-2 with those of other pathogenic respiratory viruses. They noticed greater IL-6 and elevated cytokine levels despite the presence of low-level type-I and type-III.

#### **4.9. Role of Angiotensin Converting Enzyme 2 (ACE2)**

ACE2 plays a vital role in accessing SARS-COV-2 in human cells. It is a cellular receptor for SARS-CoV-2 and has a strong affinity for this coronavirus disease-causing virus. Many scientists are expressing an interest in defining the characteristics of the protein ACE2. Hoffmann et al. [38] looked at how SARS-CoV-2 entered human cells through ACE2, and TMPRSS2 and how to prevent it. Yan et al. [93] had previously described the human ACE2's microscopic structures.

Coronavirus entry into human cells is a multi-step process involving a number of unique domains in the spike that mediate the virus's attachment to the cell surface, engagement with the receptor, the activity of the protease, and membrane fusion. Letko et al. [52] looked examined the activity of the recently discovered B beta coronavirus SARS-CoV-2 in human cells and the significance of ACE2 in this process. Additionally, they looked for the virus' entry barrier into human cells. human angiotensin-converting enzyme 2 (hACE2) has been identified as the SARs-CoV-2 receptor by numerous researchers ([60], [52]). Furthermore, Ou et al. [60] discovered that the fatal virus enters 293/hACE2 cells through the endocytosis pathway. They also discovered that the RBD region has significant immunological entropies and that the CoV- S protein is one of the key elements determining the virus's pathogenicity. Additionally, they also checked the cross-neutralization processes between SARS-CoV-2 and convalescent sera. Host protein processing is a key obstacle to viral entrance, as demonstrated by Letko et al. [52]. Wan et al. [82] noticed that 2019 n CoV used ACE2 as its receptor. Moreover, several critical residues in the 2019nCoV receptor binding motif (RBM) like Gln 493 facilitates favorable interaction with human ACE2. According to a phylogenetic study, the 2019nCoV virus originated in bats. Insights from the authors' research could be helpful in the fight against the worldwide public health catastrophe.



#### **4.10. Effect of Remdesivir/ lopinavir/ Ritonavir/ Oseltamivir/ Tocilizumab/ Methylprednisolone**

The clinical studies of remdesivir/lopinavir/ritonavir/dexamethasone in patients with Covid-19 confirmation were also highlighted by researchers ([10], [5], [84], and [29]), and examined the efficacy of azithromycin and hydroxychloroquine in treating covid-19 ([25], [42]). Cao et al. [10] had taken into account a total of 199 Covid patients who were treated with either lopinavir-ritonavir twice a day or were given under standard treatment, but it is seen that there is no benefit for the patients treated with ritonavir/lopinavir than the standard care whereas Gautret et al. [25] investigated 20 patients who were treated with hydroxychloroquine added with azithromycin and assessed the viral load of those patients and it has been observed that these two medicines have a good effect in reducing the viral load of the patients. Xu et al. [91] recommended that the medicine 'tocilizumab' may be beneficial for the treatment of Covid-19 infected patients. From the clinical trials, they inferred it may reduce the mortality rate for critical patients.

During the onset of the covid period, it was assumed that remdesivir might work well for covid-19 infected patients as it was very effective against the previous coronavirus. Wang et al. [84] observed the outcome of the Covid-19 confirmed patients admitted to the 10 hospitals in Wuhan city and treated with the remdesivir but they did not see any significant improvement in the remdesivir applied patients. Horby et al. [42] found that the appropriate use of DEXA methanose significantly lowers the mortality rate for both types of Covid-19 patients who are in a critical condition and are treated with invasive mechanical ventilation or oxygen support, as well as for patients who are treated without oxygen support. Beigel and colleagues [5] presented a report regarding the utilization of the extensively discussed drug, Remdesivir. In their study, Beigel et al. [5] examined a cohort of 1062 patients, with 541 of them receiving Remdesivir while the remaining 521 were administered a placebo. Their findings indicated that patients who received Remdesivir experienced a faster recovery compared to those treated with a placebo. Additionally, the drug demonstrated effectiveness in reducing respiratory tract infections.

#### **4.11. CT Scan of Chest in Diagnosis of Covid Patients**

According to Pan et al. [61], analyzing a CT scan of the lungs is crucial for diagnosing patients who may have COVID. Shi et al. [73] performed a descriptive analysis of individuals with confirmed Covid-19 whose lungs had undergone CT scans. The CT results of 121 Chinese patients with confirmed COVID were described by Bernheim et al. [6].

#### **4.12. Use of Masks/Ace Shields /Gloves, Isolation, Contact Tracing**

The main goal of the researchers following the fast spread of the devastating virus was to figure out how to stop or lessen the intensity of the deadly outbreak. Transmission from person to person may be prevented by physical separation and isolation. Additionally, face shields, gloves, and masks are powerful weapons to fend off the transmission. Chu et al. [20], as well as Bavel et al. [4] explored how to determine the ideal physical distance and the effectiveness of face shields, masks, and eye protection to resist viral transmission. A mathematical model was developed by Hellewell et al. [36] to evaluate the advantages of isolation and contact tracing for epidemic control. Chinazzi et al. [19] measures the impact of travel restrictions on the spread of the fatal virus.

## 5. LARGER FRAMEWORK OF OUR FINDINGS

In this study, we have made our best effort to review the 100 most cited research papers related to COVID-19 whose sudden appearance has muddled the normal life of the entire world. These papers belong to different areas like medicine, Biochemistry, Genetics, Immunology, Microbiology, Neuroscience, Psychology, Multi-disciplinary, and so on. It is seen that the lion's share of those research papers belongs to the medical group. It is quite natural because researchers and scientists across the globe are very much involved in finding a way to the survival of the common people from the devastating and fatal virus. They at first tried to comprehend the nature of the virus and then discharged their earnest effort in finding the vaccine/medicine. These studies divulge/disclose the following outcomes. The journal 'New England Journal of Medicine' holds the first place in terms of the total number of publications (15). After going through the careful reading of the leading 100 papers we see that both the authors Y. Weiland T. Yu of Wuhan Jinyintan Hospital of China have put a remarkable contribution to performing the research related to COVID-19. Both of them published the same number of papers (4) as well as received the same number of citations (41468). Table 1 infers that Wuhan Jinyintan Hospital of China has shown a nice performance in researching different aspects of COVID-19. From the table of leading authors (Table 1) it is observed that almost all the researchers (except 3 in number) belong to China and from China 55 papers have been published within a such short period. Table 2 discloses that 'Tongji Medical College' took first place in terms of the total number of publications. The extract of the 100 leading papers can be summarized as follows:

### 5.1. Origin of the Fatal Virus

The origin of the fatal virus is still in mystery. It is assumed that the calamitous virus may be originated from an intermediate host because, in the early stage, it is observed that patients infected with COVID have a travel history to the seafood market of Wuhan [73]. In this context, it is to be remembered that Wuhan province of China has experienced the first outbreak of the devastating virus.

### 5.2. Mediator

Researchers have emphasized the critical importance of conducting thorough research to investigate both natural and intermediate hosts [89] in the context of the virus's origins. Some hypotheses put forth by researchers suggest that while bats may have served as the original host, certain intermediary animal species may have played a role in facilitating the transmission of the virus to humans [56].

### 5.3. Nature of the Virus

To understand the nature of the virus, tracking spike protein amino acid polymorphisms across different geographic regions is very important. It is seen that D614 was initially detected among the first human infected in Wuhan, G614 rapidly evolved into a more powerful form, eventually displacing D614 [47]. It is a unique lineage B beta coronavirus closely linked to bat SARS coronavirus, with 89 % similarity to bat-borne SARS-CoV. The Covid-19 virus is 82% identical to human SARS-CoV B J01 2003 and human SARS-CoV Tor2 [13]. It is also concluded that SARS-CoV-2 differs from other pathogenic corona and respiratory viruses like MERS-CoV, SARS CoV-1, HPIV3, IAV,

and RSV [9]. It is an RNA virus with a (+) ve strand. There exists a significant structural resemblance between the viruses SARS-CoV (81%) and BatCovRaTG13 (96 %) [93]. It is noticed that Covid-19 is comparable to previous beta coronaviruses [69]. Different aspects of neurologic manifestations are yet to be explored [57] to know the nature of the virus.

#### **5.4. Symptoms of Patients**

The lung infection of these individuals progressed to a serious condition 10 days after the onset of symptoms, but after 14 days, a crazy-paving pattern indicating a decrease in severity was detected [61]. It is noticed that nucleotide-positive and viral-protein sero-conversion exists in all covid confirmed patients [100]. RNA sequencing is very important to determine viral load [9].

#### **5.5. How does it Enter into Human body/cell**

The virus enters the human cell through the receptor hACE-2 by endocytosis as it has a strong affinity with human receptor ACE-2 [56], and may be severe in humans due to its mutant nature [82]. Researchers inferred that all CoVs encode a surface glycoprotein spike that binds the host cell receptor (ACE-2), and facilitates viral entry [52]. For beta coronavirus, a single region of the spike protein known as the receptor-binding domain (RBD) mediates the interaction with the host cell receptor. ACE2 facilitates viral entry into the human cell. The coupling of receptor binding and protease processing are explored by the researchers [52]. It is known that ACE-2 is high in the tongue, so mucosa of the oral cavity is at high risk. The influence of the Renin-Angiotensin-Aldosterone system (RAAS) on ACE2 is examined by some researchers. It is seen that patients are badly harmed if RAAS inhibitors are abruptly withdrawn [80].

#### **5.6. Vaccine Development**

After several trials, the researchers concluded that the RNA-based vaccine can give 95% resistance against SARS-CoV-2. The vaccine is based on RNA which only needs information about the virus's genetic sequence. Extracting the trials, it is elicited that RNA-based vaccine is able to provide 95% resistance against SARS-CoV-2. It is observed that COVID-19 patients' serum could successfully kill SARS-CoV-2S but not SARS-CoV-S pseudo virions. These findings might open up new avenues for medication and vaccine development [60].

#### **5.7. Usefulness of the Drugs Remdesivir, lopinavir and so on**

There is a controversy about the researcher about the usefulness of the drug remdesivir. Some researchers concluded that drugs like lopinavir, ritonavir, and remdesivir have a positive effect on the covid infected patients [29]. Remdesivir can rise the oxygen level of critically ill covid infected patients. Remdesivir and chloroquine work well for the quick recovery of infected patients [48]. Some of the researchers found that heparin users had a decreased 28-day mortality than non-users [35]. Xu et al. [91] found that if tocilizumab and glucocorticoids are used correctly, they may be beneficial for people with moderate or severe covid. Azithromycin in conjunction with hydroxychloroquine is more effective to lessen the severity of the covid infected patients Gautret et al. [25]. Methylprednisolone has a positive effect in lessening the mortality rate of covid infected patients [88]. It is observed that patients who received remdesivir recovered faster than those who are treated with a placebo. The drug is also helpful in

reducing respiratory tract infections [5]. A prophylactic dose of heparin for critically ill corona patients admitted to ICU acts very well [46]. Some researchers concluded that the above-mentioned much-discussed drugs have no significant positive effect on the treatment of the covid infected patients ([70], [10]).

### 5.8. Treatment

Anti-thrombotic medications in the treatment of Covid contaminated individuals, careful therapeutic use of anti-thrombotic medications should be kept in mind [8]. These researchers pointed out the consequences of thrombotic disease and offered helpful anti-thrombotic treatment recommendations. The use of chloroquine, ulihastatin, oxidized phospholipids (OxPL), stem cell therapy, and plasma therapy have been recommended by some researchers for urgent treatment of covid infected patients [95]. It is observed that dexamethasone is effective to lower the mortality rate of patients supported by invasive mechanical ventilation [42]. Long et al. [55] believed that serological tests could aid in the diagnosis of questionable cases. Pneumonia was a prevalent condition among all patients, regardless of the severity of their chest injuries, necessitating treatment, including ICU care for some. Interestingly, an unexpected observation emerged: patients in the ICU exhibited more favorable plasma level outcomes compared to those who did not require intensive care.

Convalescent plasma therapy may be beneficial to covid infected patients Shen et al. [71]. Surprisingly noticed by [28], people inhabitants in the Lombardy region of Italy covid have a high mortality rate and need urgent need of ICU, and Invasive Mechanical Ventilation (IMV). Some researchers recommended a variety of treatments, including chloroquine, ulihastatin, oxidized phospholipids (OxPL), stem cell therapy, and a blood purifying process [95].

### 5.9. Antibody

Some researchers concluded that N, E, and some other proteins have the ability to boost an infected person's immune system [34]. The antibody Ab is the first discovered antibody, followed by IgM and IgG [98].

### 5.10. Correlation between Comorbidity and Mortality

Mortality and risk factors are proportional to old age, obesity, pre-existing comorbidity of patients like ARDS, cardiovascular disease, hypertension, diabetes, respiratory diseases, liver and kidney problem, cancers, and so on ([17], [86], [32], [22]). These patients are at high risk because radiological abnormalities emerged suddenly for such types of patients, and thus, they should be careful from infection by the virus. It is noticed that there exists a strong link between myocardial infection and covid infection [33]. Such patients require immediate post-covid therapy. It is hypothesized that the flu vaccine could lessen the severity of co-morbid patients Yang et al. [94]. It is also noticed that the salivary viral load is highest in the first week after the onset of symptoms. Then it rapidly degrades. It has also been discovered that the viral load is larger in the elderly [79].

### 5.11. Factors Behind the Severity (Cytokine storm, declination of T-cell)

It is seen that the basic symptoms of the covid infection are common, such as fever, shortness of breath, expectoration, weariness, and dry cough [64]. They made a significant discovery about T-cells. The condition of the patients tends to deteriorate as

the number of T-cells declines. Therefore, an increase in T-cells may take an effective role to prevent the crisis of critical patients [78]. Cytokine storm plays a major role in the rapid multi-organ failure of the covid infected patients as it decreases the T-lymphocytes especially CD4+ and Cd8+ of the patients ([30], [14]). To achieve success against the calamitous virus it is urgent to stop the cytokine storm or to reduce the release of cytokine as much as possible by adopting various approaches [95].

#### **5.12. Identification**

RTPCR tests and radiographic investigations namely CT scans play a significant role in identifying the covid infected patients [2]. It is also noted that a CT scan of the lungs could enlighten different stages of illness [6]. Computed tomography provides a clear image depicting the condition of the lung of a covid infected person [27]. CTPA is extremely useful to explore the unknown and peculiar characteristics/symptoms of the virus [37].

#### **5.13. Impact on Other Sectors**

Some researchers also investigated pre and post covid impact in diverse fields like education, the production of goods, the food sector, the economic sector, and so on [59]. The social, mental, and environmental impacts are also measured by some researchers [40].

#### **5.14. Effect of Covid on Common People, New Born Baby and Children**

Patients with cardiac damage have permanently adverse radiological consequences such as higher creatinine levels, increased c-reactive protein, excessive multiple mottling, and so on, compared to patients without cardiac injury [74]. Some researchers showed that Sars-Cov-2 does not affect the newborn baby. When it comes to giving birth to a new baby, there are no significant distinctions between covid and non-covid pregnant women. There was also no indication of vertical transmission, and no covid infections were found in the newborn baby [15]. Scientists have yet to solve the mystery of why children are less vulnerable. Lack of bronchial tissue in children is the key cause for their lower susceptibility than adults. The lower binding affinity of ACE2 among youngsters might be the cause. Furthermore, it is concluded by some researchers have that children's immune systems are still developing, and their antibody levels may significantly be boosted [23].

#### **5.15. Psychological and Mental Effect among the People**

Psychological counseling is needed to help nurses cope with their trauma [49]. Rajkumar, R. P. [66] noticed adverse effects on the mental health of the common people like anxiety, depression, insomnia, distress, and mental stress.

#### **5.16. Role of Inanimate Things as a Carrier**

It has been determined that inanimate objects like metal, glass, or plastics can harbour the coronavirus and that they can do so for up to nine days. It has also been established that chemical agent like ethanol, sodium hypochlorite, and hydrogen peroxide can kill most of the virus within one minute of contact up to a certain percentage [45].

#### **5.17. Encouraging the Telemedicine**

Telemedicine is suggested for the treatment of covid patients to meet the scarcity of doctors and to avoid close contact with some researchers. It is seen in subsequent time

that telemedicine plays a very effective role in the treatment of covid patients throughout the entire globe [39].

#### **5.18. Prevention is better than cure**

It is believed that since there is no vaccine or treatment at the initial stage, so early identification, isolation, reporting, and epidemiological information were critical in preventing and controlling the lethal illness [18]. It is suggested that the three main ways to prevention from the spread of SARS-CoV-2 [20].

- (i) on maintaining a gap between each other of at least one meter,
- (ii) the most effective usage of masks, specifically N-95, surgical, and 12–16 layers of cotton masks,
- (iii) the usage of face shields, goggles, and other eye- and nose-protective devices.

The researchers also noted that N-95 masks prove to be more effective for healthcare workers when compared to surgical masks. Additionally, they suggested that both the general public and healthcare workers may utilize N-95 masks, as well as surgical or cotton masks for added protection.

Researchers have observed that implementing international travel restrictions can effectively decelerate the spread of the novel coronavirus [19]. However, they also found that early detection, frequent handwashing, self-isolation, and household quarantine prove to be more beneficial strategies compared to travel limitations in preventing the rapid transmission of the deadly virus. Notably, isolation has been identified as a successful measure in controlling the outbreak [69].

#### **5.19. Infrastructure Development**

It has been observed that patients admitted with hypoxemic respiratory failure needed mechanical ventilation, and that vasopressor medication is particularly helpful for patients admitted with hypotension, so infrastructure improvement for ICU care and ventilatory support is urgent for the critical covid infected [7]. The proper length of lockdown and an adequate supply of basic healthcare commodities are recommended by Li et al. [53].

### **6. A CRITICAL APPRAISAL OF THE STUDIES, DISCUSSING POTENTIAL BIASES, THE STRENGTH OF EVIDENCE, AND THE CONSISTENCY OF FINDINGS ACROSS DIFFERENT STUDIES**

The critical appraisal of the studies is very important for evaluating the potential biases, strength of evidence, and consistency of findings across different studies. The document provides insights into the top 100 research papers on COVID-19, shedding light on various aspects of the pandemic. However, it's important to consider potential biases in the selection of these papers, as the criteria for inclusion and exclusion may impact the representation of the overall interpretation of COVID-19 research. Here, we prepare the bibliometric study based on most cited papers available in SCOPUS. The others search engine like web of science is not considered.

Furthermore, the strength of the evidence presented in our study should be critically/carefully evaluated. This includes assessing the nature/characteristics of corona virus, the clinical investigation, characteristics of covid confirmed patients or examine the efficacy of medicines like remdesivir/lopinavir/ritonavir/oseltamivir/tocilizumab/

methylprednisolone, vaccine development, possibility of an areological agent or mediator, basic information of CD4+ and CD8+ T cell responses, possible treatments, role of ACE2, correlation between comorbidity and mortality and so on, statistical analyses, and the quality of the data. Given the urgency of addressing the COVID-19 pandemic, a large number of studies have been conducted rapidly to resolve the acute situation under time constraints, potentially impacting the robustness of the evidence.

The consistency of findings across different studies should be examined. While the top 100 research papers may have made significant contributions to the understanding of COVID-19, it's important to assess whether their findings align with those of other studies in the field.

## **7. PRACTICAL IMPLICATIONS FOR HEALTHCARE PROVIDERS, POLICYMAKERS, AND PUBLIC HEALTH OFFICIALS, AND OFFER CLEAR POLICY RECOMMENDATIONS**

### **i) Healthcare Providers: -**

It is important to pay special emphasis to the healthcare providers as they discharged their duties ignoring their life risk. Therefore, emphasis must be given on the importance of ongoing monitoring and care for COVID-19 survivors to address potential long-term health complications. Mental health support for the healthcare workers affected by the pandemic should also be prioritized.

### **ii) Policymakers: -**

Implement targeted public health campaigns to address vaccine hesitancy and promote widespread vaccination, particularly among underserved communities. Intense programme should be organized to monitor the long-term health effects of COVID-19 and develop comprehensive support programs for survivors. Address social determinants of health through policies that support economic recovery, affordable housing, and access to education and healthcare. Overall awareness for preventive measures among the people should be grown up and it is possible only by the continuous and intense campaigning.

### **iii) Public Health Officials: -**

Strengthen surveillance systems to monitor and respond to emerging variants of SARS-CoV-2, informing public health measures and vaccination strategies.

### **Clear Policy Recommendations:**

a) Continuous monitoring the long-term health outcomes of COVID-19 survivors, informing targeted interventions and support programs.

b). Implement strategies to address vaccine hesitancy, including community engagement, culturally sensitive messaging, and accessible vaccination sites.

c) Prioritize mental health support in healthcare systems, integrating mental health services into primary care and providing resources for healthcare workers' well-being.

d) Pay attention to keep normal supply of essential goods for the survival of the common people.

e) Foster international collaboration and information sharing to strengthen global pandemic preparedness and response efforts. By implementing these practical implications and policy recommendations, healthcare providers, policymakers, and public health officials can work collaboratively to address the immediate and long-term

impacts of COVID-19, promote health equity, and enhance global resilience to future public health challenges.

## **8. RESEARCH GAPS AND SUGGESTS SPECIFIC AREAS FOR FUTURE INVESTIGATION**

There are some research gaps which are mentioned below. We also try to give some suggestions to mitigate the gaps in future.

### **i) Health Disparities and Vulnerable Populations:**

While existing research has highlighted the impact of COVID-19 on various demographic groups, there is a need for further investigation into the specific health disparities experienced by vulnerable populations, including racial and ethnic minorities, low-income communities, and individuals, comorbid patients with underlying health conditions. Future studies should aim to elucidate the underlying factors contributing to these disparities and explore targeted interventions to mitigate the impacts.

### **ii) Long-Term Health Outcomes:**

As the pandemic continues to unfold, there is a growing need to understand the long-term health outcomes of COVID-19 survivors. Research should focus on the potential long-term effects on respiratory function, cardiovascular health, mental well-being, and other aspects of survivors' health. Additionally, investigating the post-acute sequelae of SARS-CoV-2 infection, and developing strategies for managing and treating these conditions is crucial.

### **iii) Mental Health and Psychosocial Impacts:**

The psychological impact of the pandemic, including increased rates of anxiety, depression, and stress, especially the impact on children warrants further investigation. The impacts of very long lockdown on children, lower class people, students, comorbid patients are yet to explore. Future studies should explore the long-term mental health implications of the pandemic, particularly among frontline healthcare workers, children and adolescents, and individuals with pre-existing mental health conditions. Additionally, research should focus on identifying effective interventions and support systems to address these mental health challenges.

### **iv) Vaccine Development and Distribution:**

While significant progress has been made in vaccine development, ongoing research is needed to address vaccine hesitancy, optimize vaccine distribution strategies, and assess the long-term efficacy and safety of COVID-19 vaccines. Furthermore, investigating the potential need for booster doses and the impact of emerging variants on vaccine effectiveness is critical for informing public health policies.

### **v) Socioeconomic and policy implications:**

Understanding the broader socioeconomic and psychological impacts of the pandemic, including its effects on employment, education, and social welfare, requires interdisciplinary research. Future investigations should focus on evaluating the effectiveness of policy responses, assessing the economic recovery process, and identifying strategies to build more resilient and equitable societies in the post-pandemic era.



vi) Uninterrupted logistics of daily needs of the people:

There was a lack of proper supply chain management in uniform distributions of essential goods during the period of lockdown due to the Covid-19. Therefore, emphasis should be given to determine the optimal strategy in keeping normal supply of essential goods if such pandemic situation further arises in future.

vii) Global health preparedness and response as a preventive measure:

Research should address the lessons learned from the COVID-19 pandemic and identify opportunities to strengthen global health preparedness and response mechanisms. The Government of each country of the world should develop their healthcare infrastructure to prove the basic treatment of the common people. International collaborations are essential for the coordination in future public health emergencies/crisis. By systematically identifying these research gaps and suggesting specific areas for future investigation, the scientific community can prioritize critical areas of inquiry and contribute to a more comprehensive understanding of the multifaceted impacts of COVID-19.

## 9. CONCLUSION

This review analysis of COVID-19 highlighting the one hundred most influential papers in covid-19 research has been framed with great care. Here, we have tried to sketch a detailed scenario of the global research progress of COVID-19 delineating its origin, nature, identification, way of entry in a human cell, symptoms of the infected patients, way of prevention, fatal effects on comorbid and aged patients with the help of correlation between comorbidity and mortality, the effect of on newborn baby and children, the emergence of telemedicine, persistence of the virus on inanimate things, the efficacy of drugs like remdesivir, lopinavir, ritonavir and so on, the progress of vaccine development, usefulness gloves, masks, sanitizer, the advantage of maintaining physical and social distance, infrastructure development, and so on. Thus, through this study, we are aware of the progress of the current status of the Covid-19 related research. After careful study, we observe that J Wei and T Yu of China affiliated with Wuhan Jinyintan Hospital has received the highest number of citations. Both of them received 41468 citations publishing 4 papers in each. 'New England Journal of Medicine' has published 15 papers followed by 'The Lancet', 'Nature' and 'The Journal of American Medical Association (JAMA)'. From this, we can infer that researchers are highly eager to publish their valuable work in these pioneering world-famous journals. These journals are working hard to bring the essence of Covid related research around the world as soon as feasible. China is in the leading position followed by the USA, and the UK. The keyword 'Human' appears the greatest number of times amounting to 98 in number and the highest number of papers belong to the field of medicine which is quite natural.

There arise some convergent and divergent opinions regarding the use of different drugs/ medicines for the treatment of COVID-19 patients. There are convergencies in the opinions of Beigel et al. [5], Gautret et al. [25], Horby et al. [42], Xu et al. [91] regarding the effectiveness of different drugs like remdesivir, lopinavir, ritonavir, hydroxychloroquine. They conclude that the above drugs may be beneficial to reduce the viral load of covid patients and lowers the fatality rate of the serious patients. In contrast, Cao et al. [10], Wang et al. [84] opined that these drugs have no effect at all in the treatment of Covid infected patients.

We have also provided a classification table to realize the outcome of our study at a glance.

Last, but not least we hope that our study will add some salt to the discussion of the covid related research in the near future, some of which may be as follows:

(i) The real cause behind the sudden appearance of coronavirus is still unknown. Thus, extensive researches are necessary regarding the exploration of the cause.

(ii) Is there any permanent effect of the infected people in subsequent time which is very important as the affected people are still suffering from many diseases, and are feeling a dearth of immune/resistance power of their body.

(iii) Interdisciplinary research is to be encouraged as the prolonged lockdown impacted all other fields like education, environment, socio-economic conditions of the people, share market, change of human development index, and so on.

(iv) Does COVID-19 research employ artificial intelligence (AI)?

(v) What impact does the current scenario have on the logistics of supply chain across various sectors?

This study has a notable limitation. It relied on data obtained from the Scopus database, and the findings are inherently dependent on the content and accuracy of that particular database.

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## APPENDIX

Table A1. Classification of the leading 100 covid-19 research articles

Sl. No	Publication	Citations	Subject					Epidemiological, Pathological &/or Clinical investigation	Review	Survey/Case study	No of respondents /patients	Male	Female	Development	Intermediate Vaccine	Role of ACE2	Cytokine	Plasma transfusion	T-cell Responses	Use of masks/face shields/gloves, isolation, contact tracing etc
			Medicine	Immunology & microbiology (psychological/mental Effect)	Neuroscience	Biochemistry, Genetics, Molecular Biology	Others	Patients (symptoms, Characteristics)	Virus Origin, nature characteristics)											
1	Huang et al. [43]	18952	✓					✓		✓	41	30	11							
2	Guan et al. [31]	12372				✓			✓		1099	58.1%	41.9%		✓					
3	Zhou et al. [99]	10907	✓					✓		✓	191				✓					
4	Zhu et al. [101]	10410	✓			✓		✓							✓					
5	Chen et al. [16]	8928	✓					✓		✓	99	67	32		✓					
6	Zhou et al. [100]	8072	✓												✓	✓				
7	Hoffmann et al. [38]	6711	✓												✓		✓			
8	Lu et al. [56]	4943				✓			✓	✓	9				✓	✓	✓			
9	Chan et al. [13]	4106	✓	✓				✓			5									✓
10	Xu et al. [92]	3962						✓												✓
11	Wu et al. [89]	3866							✓		1	1	0		✓					
12	Richardson et al. [68]	3501	✓					✓		✓	5700	3437	2263							
13	Wu et al. [88]	3451	✓					✓			201									
14	Wang et al. [83]	3030		✓						✓	1210									
15	Holshue et al. [41]	2883							✓	✓										✓
16	Wölfel et al. [87]	2719	✓					✓			09									
17	Cao et al. [10]	2681	✓																	
18	Mao et al. [57]	2677				✓				✓	214	87	127							
19	Gautret et al. [25]	2672	✓																	
20	Horby et al. [42]	2407		✓							6425		36%							
21	Ai et al. [2]	2358					✓				1049	467	547							
22	Grasselli et al. [28]	2253	✓								3988	3188	800							
23	Polack et al. [63]	2247		✓							43448				✓					
24	Lauer et al. [50]	2223					✓			✓										
25	Beigel et al. [5]	2218	✓								1062									
26	Lai et al. [49]	2215		✓							1257	293	964							
27	Lai et al. [48]	2170	✓								278									✓
28	Wan et al. [82]	1968	✓						✓						✓					✓
29	Rothan and Byrareddy [69]	1930							✓	✓					✓					✓
30	Qin et al. [64]	1874	✓					✓		✓	452	235	217							
31	Klok et al. [46]	1867	✓								184									
32	Yan et al. [93]	1852					✓									✓				
33	Chen et al. [14]	1830		✓					✓		21	17	4		✓					
34	Ackermann et al. [1]	1824																		
35	Guo et al. [34]	1772	✓						✓	✓					✓	✓				
36	Chen et al. [15]	1763	✓					✓		✓	9									
37	Sohrabi et al. [76]	1752					✓		✓	✓										✓
38	Shi et al. [74]	1749	✓					✓			416	205	211							
39	Chen et al. [17]	1739		✓	✓			✓		✓	799									
40	Shi et al. [73]	1698	✓					✓			81	42	39		✓					
41	Guo et al. [33]	1647	✓							✓	187									
42	Holmes et al. [40]	1637		✓						✓	2198									
43	Zhang et al. [96]	1627						✓			140	50.7%	49.3%			✓				
44	Dong et al. [23]	1604				✓		✓			2135				✓					
45	He et al. [35]	1598	✓								94	47	47							✓
46	Tang et al. [77]	1577	✓								449	268	181							
47	Yang et al. [94]	1535					✓				1576									
48	Nicola et al. [59]	1531		✓						✓										
49	Kampf et al. [45]	1512								✓										✓
50	To et al. [79]	1505	✓					✓			23									
51	Wang et al. [84]	1468	✓								237									
52	Remuzzi and Remuzzi [67]	1452					✓													
53	Tay et al. [78]	1403		✓					✓	✓					✓					

Sl. No	Publication	Citations	Subject	Epidemiological, Pathological &/or Clinical investigation	Review	Survey/Case study	No of respondents /patients	Male	Female	Development	Intermediator Vaccine	Role of ACE2	Plasma transfusion	T-cell Responses	Use of masks/glove, shield,gloves, isolation, contact tracing etc.								
																Medicine	Multi Disciplinary (psychological/mental Effect)	Immunology & microbiology	Biochemistry, Genetics, Molecular Biology	Neuroscience	Others	Patients (symptoms, Characteristics)	Virus (Origin, nature, characteristics)
54	Baden et al. [3]	1392		✓			30240 volunteers			✓													
55	Qiu et al. [65]	1372		✓		✓	52730	18599	34131														
56	Guan et al. [32]	1365	✓				1590	904	686														
57	Williamson et al. [86]	1358				✓																	
58	Grein et al. [29]	1350					61																
59	Cao et al. [11]	1318		✓		✓																	
60	Verity et al. [81]	1309			✓																		
61	Gordon et al. [26]	1300	✓									✓											
62	Liu et al. [54]	1298	✓									✓											
63	Chen, Liu and Guo [18]	1279				✓																	
64	Blanco-Melo et al. [9]	1274	✓									✓											
65	Shen et al. [71]	1260				✓	05	03	02														
66	Chan et al. [12]	1243		✓						✓	✓												
67	Bikdeli et al. [8]	1237				✓									✓								
68	Sanders et al. [70]	1237	✓			✓																	
69	Chung et al. [21]	1234	✓				21	13	8														
70	Chu et al. [20]	1194				✓	172 studies								✓								
71	Xu et al. [91]	1190	✓			✓	21																
72	Long et al. [55]	1186	✓			✓	285																
73	Bhatraju et al. [7]	1185			✓		24																
74	Korber et al. [47]	1184	✓			✓				✓													
75	Bavel et al. [4]	1181		✓											✓								
76	Emanuel et al. [24]	1174			✓																		
77	Chinazzi et al. [19]	1173			✓																		
78	Hollander and Carr [39]	1168																					
79	Jin et al. [44]	1164																					
80	Bernheim et al. [6]	1161																					
81	Grifoni et al. [30]	1155		✓		✓	121	61	60														
82	Shereen et al. [72]	1153				✓	20	9	11	✓	✓				✓								
83	Ou et al. [60]	1150		✓		✓																	
84	Zhao et al. [98]	1130	✓			✓	173		51.4%	✓													
85	Xu et al. [90]	1118			✓																		
86	Pfefferbaum and North [62]	1113		✓																			
87	Wiersinga et al. [85]	1111			✓	✓					✓				✓								
88	Singhal [75]	1105		✓		✓	99				✓				✓								
89	Letko et al. [52]	1095		✓								✓											
90	Helms et al. [37]	1094				✓	150	122	28														
91	Zhang et al. [97]	1090	✓			✓																	
92	Pan et al. [61]	1080			✓	✓	21	6	15						✓								
93	Lechien et al. [51]	1076	✓			✓	417	154	263														
94	Ye et al. [95]	1072				✓				✓	✓												
95	Vaduganathan et al. [80]	1063			✓	✓																	
96	Mizumoto et al. [58]	1058		✓			634	321	313						✓								
97	Rajkumar [66]	1057				✓	28 articles																
98	Li et al. [53]	1041			✓	✓																	
99	Hellewell et al. [36]	1023			✓										✓								
100	Docherty et al. [22]	1019			✓		20133																