Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Editorial

Chronicles of a pandemic: How France coordinated the scientific research response to COVID-19

In December 2019, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) emerged in Wuhan, China and rapidly spread globally, leading to the declaration of pandemic by the World Health Organization (WHO) on March 11, 2020. The first cases of SARS-CoV-2-induced disease, COVID-19 (COrona VIrus Disease-19), imported in the European region, were reported by France on January 24, 2020 [1]. The first clusters emerged in the country as early as February 2020, substantiating active virus circulation. The extremely rapid dissemination of cases led French authorities to impose a national stringent lockdown on March 17, alongside many other countries.

From the early onset of the COVID-19 pandemic, French research institutions were strongly mobilized to accelerate research on the virus and the disease. The REACTing consortium (REsearch and ACTion targeting emerging infectious diseases), coordinated by the French National Institute for Health and Medical Research (Inserm) and assembling members of the French National Alliance for Life Sciences and Health (Aviesan), was solicited to coordinate the early national research response on SARS-CoV-2 by the French Ministry of Higher Education, Research and Innovation (MESRI) and the French Ministry of Solidarity and Health (MSS). In this context, a COVID-19 Scientific Council was promptly set up in January 2020 by REACTing to support authorities on strategic issues of epidemic management. However, REACTing did not have the adequate means or leverages nor the full mandate to fully accomplish the national research coordination task at later stages of the pandemic. In late March 2020 the COVID-19 Analysis, Research and Expertise Committee (CARE) was set up to support REACTing, informing public authorities on scientific, therapeutic, and technological innovations proposed by the scientific community. The REACTing COVID-19 Scientific Council defined French priority research areas, accordingly to research priorities identified by the World Health Organization (WHO) and the Global Research Collaboration for Infectious Disease Preparedness and Response (GLOPID-R) in February 2020 [2]. Hence, monitoring of infected populations and diagnosis, epidemiological modelling, fundamental research, vaccine and therapeutic clinical research, and social sciences were primarily targeted. In February 2020, REACTing COVID-19 Scientific Council awarded seed funding provided by the government to 20 research projects selected according to national priorities, for a total budget of €1 M.

The overall effort of the French research community was thereafter supported by established national funding institutions and programs, such as the French National Research Agency (ANR), the National Research Agency on AIDS and Viral Hepatitis (ANRS), the Hospital Clinical Research Program (PHRC), and private for-profit and non-profit organizations, research institutes and foundations. The ANR, in synergy with MESRI, opened two funding calls in spring 2020, supporting 234 research projects on disease pathophysiology, epidemiology, disease control and prevention, and ethical and social sciences, for a total amount of €32.2 M [3]. The ANR further expanded its commitment by including COVID-19 as a research priority in its 2021 funding plan. The ANRS opened a call for projects dedicated to low- and middle-income countries (LMICs). The *Fondation de France*, the Public Hospitals of Paris (AP–HP) and the *Institut Pasteur* coordinated efforts to support health care workers and hospital first response, and to fund research projects on COVID-19 detection, treatment and prevention through a community-based solidarity initiative “All united against the virus”, launched in March 2020. National and interregional PHRC programs funded the implementation of 58 clinical studies. Overall, nearly 100 research projects on pharmaceutical treatments and more than 300 on non-pharmaceutical interventions were launched within the first six months of the pandemic, facilitated by a pivotal shortening of authorization delays through fast-track procedures. Pharmaceutical treatments tested included several classes of repositioned antivirals, anti-inflammatory drugs to contrast the excessive inflammatory response and anti-coagulants to prevent thrombotic events observed in COVID-19 patients. Projects on non-pharmaceutical interventions ranged from the clinical context, such as characterization of disease progression and biomarkers, and patient management, to epidemiologic and transmission studies, investigation of mental health status of different populations, and diagnostic tool development.

Although simultaneous opening of a multitude of therapeutic clinical research projects by several institutions illustrates the extraordinary mobilization of researchers in the fight against the pandemic, it hampered successful implementation and patient recruitment strategies. The crisis response has been extensive but scattered on various fronts, suffering from an important lack of coordination between funding agencies and between researchers and decision-makers, and from the lack of readiness in the research community to mobilize funding and human resources. The situation assessment documents released in June and July 2020 consequently proposed actions to implement and consolidate a coordinated crisis response in the short and long term. For instance, the Rossignol report [4], commissioned by the MSS and published in June 2020, proposed the implementation of an *ad-hoc* National Steering Committee for Therapeutic Trials and Other

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Research (CAPNET) as a key measure to prioritize and accelerate high-potential clinical research projects. The CAPNET, launched in November 2020, relies on scientific evaluation of research projects by the REACTing COVID-19 Scientific Council to award a National Research Priority label to high-potential proposals in line with national priorities, fostering accelerated regulatory procedures and access to institutional funding. Another key action resulting from evaluations of the French scene was merging REACTing with the ANRS, in January 2021, to form the ANRS|Emerging Infectious Diseases, an autonomous coordination and funding agency within Inserm. The aim was to set the basis for national research coordination and preparedness on emerging infectious diseases, and on existing ones previously managed by the ANRS, by relying on the established infrastructure of the agency and by further fueling it with human resources and financial means.

Although we are convinced that, given its research expertise, France could have implemented a much better response, the actions described above resulted in the implementation of relevant research projects and important achievements, some of which are important for the future. Representative examples are described below (Fig. 1).

As the first COVID-19 outbreak evolved, understanding the viral epidemiology and transmission dynamics became compelling. Several cohorts, population surveys and serologic complementary studies were implemented in France to address this need. As the first COVID-19 patients were hospitalized in February 2020, the CoV-Contact observational cohort was set up to evaluate individual factors associated with COVID-19 development after SARS-CoV-2 exposure, and was coordinated by Inserm in collaboration with the AP–HP and funded by a grant from the European Commission. This study determined early on that health professionals were at high risk of SARS-CoV-2 infection, paving the path to targeted infection control measures [5]. ComCor, a nation-wide survey-based epidemiological study coordinated by *Institut Pasteur* in collaboration with the French National Health Insurance Fund (CNAM), the National Public Health Agency (*Santé publique France*), and the Ipsos Social Research Institute, was launched in October 2020 and counted 160,000 individuals with SARS-CoV-2 infection as of April 2021. ComCor included two branches aiming to describe circumstances of infection of index cases who tested positive for SARS-CoV-2 during implementation of national curfews, and comparing characteristics, behaviors and practices of index cases with those of matched individuals. The study group published two analyses, in December 2020 [6] and March 2021 [7], identifying factors associated with increased or decreased risk of infections, including specific environments and individual behaviors. In February 2021, the ComCor group expanded its studies to vaccination history and vaccine efficacy against variants of concern [8]. In spring 2020, Inserm and the Directorate for Research, Studies, Evaluation and Statistics (DREES) of the Ministry of Solidarity and Health developed a large epidemiological study, EPICOV, based on surveys and serological testing of a representative sample of randomly selected individuals, aiming to define the immunological status of the general population. Analysis of the first 135,000 questionnaires and 12,000 serological samples determined the adult population in metropolitan France that had been exposed to the virus (4.5%) and its socio-demographic characteristics [9].

In parallel with such epidemiological studies, interdisciplinary research on public health urged to be accelerated, notably promoting the cooperation between epidemiology and social sciences to understand the social dimensions of infection risks and the effects of containment measures on physical and mental health. To this aim, the SAPRIS study, a nation-wide survey coordinated by Inserm and *Santé publique France*, was launched in April 2020 involving 200,000 participants from four pre-existing national general population cohorts. The main questions focused on COVID-19 symptoms, consultations for other pathologies, perception of risk, and effects of preventive measures on daily life, among others. These data were integrated with serological testing of participants to evaluate national seroprevalence and its correlation with socio-demographic factors. EpiCov and SAPRIS data were further exploited by the COVIDSM study, sponsored by Inserm in April 2021, and aimed at evaluating the impact of the health crisis on the population's mental health. Lastly, several mathematical modelling studies have been implemented since the early days of the pandemic, exploiting data such as disease prevalence, infection rates, or mobile phone data tracking population behaviors [10,11]. This approach allowed, among others, to characterize and anticipate the impact of public health interventions, from lockdown and school closure to mass screening and vaccination strategies, on disease control or epidemic rebounds [12,13]. The public health studies described so far, along with many others promptly implemented, helped define control and mitigation strategies. Hence, recommendations were issued by national public health authorities to contain infections while preserving individual health.

While public health notions were developed, research on the natural history of the disease was crucially important to manage COVID-19 patients. A representative instance is the prompt establishment of the French-Covid national cohort of COVID-19 patients admitted to hospital general wards or intensive care units. French-Covid, coordinated by Inserm, exploited clinical, virological, immunological, genetic, serologic, and transcriptomic patient data to better understand clinical manifestations of the disease, particularly in its severe forms. Studies based on the French-Covid cohort allowed to estimate viral dynamics, evolution of patient's clinical status, and mortality of the disease. Moreover, several independent studies relied on data issued from the French-Covid cohort. These helped characterizing genetic and immunologic factors associated with severe COVID-19 presentations (notably linked to type I interferon defects), evaluating the impact of treatments such as corticosteroids or hypertensive drugs on progression of the disease, or identifying disease biomarkers [14,15]. To characterize milder COVID-19 forms not requiring hospitalization, support was provided by COVIDOM, an on-line platform for distance monitoring of patients with a suspected or diagnosed SARS-CoV-2 infection, developed by the AP-HP and Nouveal e-santé. Based on COVIDOM data, a study issued by a collaboration between the AP-HP, Inserm and French universities followed disease progression of 43,000 COVID-19 outpatients, describing clinical worsening as rare [16]. More recently, Covid-A was set up, a prospective observational study to evaluate clinical and virological evolution of symptomatic outpatients older than 8 years with a suspected SARS-CoV-2 infection who referred to a general practitioner or pediatrician.

As the natural history of the disease was unraveled over time, evidence showed that COVID-19 can induce long-term consequences on the patient's physical and mental health, a condition defined as post-acute COVID-19 syndrome (PACS). To study PACS, French-Covid followed the clinical situation of cohort patients after hospital discharge, demonstrating that after 3 to 6 months, 60% of a group of 1,137 patients had at least one persisting symptom [17]. Among several other studies on PACS, the COPER and DisCOVID projects were funded by MERSI and the MSS. The first aimed to characterize persisting symptoms after resolution of a SARS-CoV-2 infection, while the latter, sponsored by the AP-HP, evaluated disability levels and profiles in the mid- and long-term after COVID-19-related hospitalization. Complementarily, researchers from Paris University, AP-HP and Inserm, in the context of the ComPaRe cohort, developed the first scientific tool to measure in a standardized manner the long-term symptoms and impact of COVID-19 [18].

Another national priority in COVID-19 research concerned therapeutics, and France developed research from bench to bedside

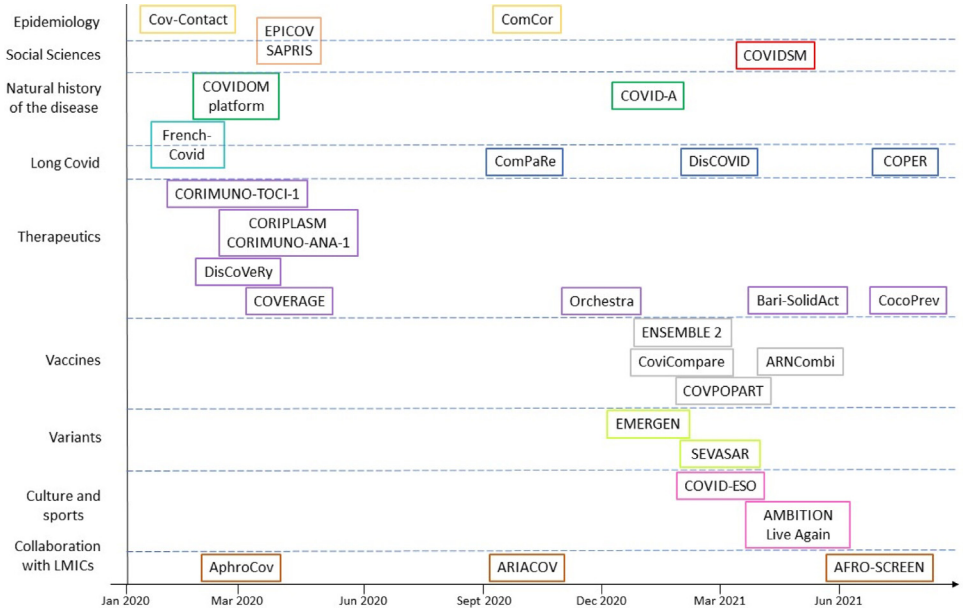

Fig. 1. Schematic representation of the described projects implemented in France in response to the COVID-19 crisis. Projects are categorized by subjects according to a color code and distributed along a timeline based on their launching date.

focusing on both new and repositioned therapeutic candidates. On an international scale, France coordinated the European clinical trial DisCoVeRy, sponsored and coordinated by Inserm. Add-on trial of the WHO clinical trial Solidarity, DisCoVeRy is a multicenter, adaptive, randomized trial of safety and efficacy of four repositioned drugs against COVID-19 in hospitalized patients, launched in March 2020. It contributed to demonstrate the inefficacy of remdesivir, lopinavir/ritonavir combination, lopinavir/ritonavir combined with interferon-β-1a, and hydroxychloroquine on improving patient clinical status [19,20]. Subsequently, Inserm is now coordinating the new European Research and Preparedness Network for Pandemics and Emerging Infectious Diseases, EU-Response. This structure includes Solid-Act, a platform for adaptative trials that is currently evaluating the efficacy and tolerance of the anti-inflammatory baricitinib for management of severe COVID-19 patients (Bari-SolidAct study), and DisCoVeRy that is testing AstraZeneca's AZD7442 monoclonal antibody combination since in April 2021. EU-Response will coordinate with RECOVER (Rapid European COVID-19 Emergency Response research), an EU-funded project aiming to undertake clinical research in primary and hospital care, epidemiological and biological investigations, and modelling studies to fill knowledge gaps on SARS-CoV-2 infectivity and transmission. Besides, France will participate in the European project Orchestra, which aims to establish an international network of cohorts for the conduct of retrospective and prospective studies on prevention and treatment of COVID-19, and to be better prepared for future pandemics.

At a national level, an outstanding number of clinical trials were implemented in France aiming both at managing the clinical progression of mild and severe forms of the disease, and at identifying antiviral molecules active against SARS-CoV-2. In hospitalized populations, the CORIMUNO-19 platform, sponsored by the AP-HP, implemented various therapeutic studies such as CORIPLASM, for convalescent plasma testing, CORIMMUNO-ANA-1 for anakinra, and CORIMUNO-TOCI-1 for tocilizumab. Although these studies did not show efficacy of anakinra in COVID-19 patients with pneumonia [21], they were among the first demonstrating a potential efficacy of tocilizumab in limiting worsening of clinical conditions in patients with moderate to severe COVID-19 [22]. Of note, an effort was also made to promote clinical trials in outpatients. For instance, COVERAGE, sponsored by Bordeaux hospital, tested therapies such as the anti-hypertensive telmisartan or inhaled glucocorticoid ciclesonide for clinical management of mild disease. Targeted populations were COVID-19 outpatients aged over 60, or over 50 at risk of developing severe disease. Furthermore, in March 2021 the French National Drug Safety Agency (ANSM) granted a cohort temporary authorization of use (ATU) to antiviral monoclonal antibody cocktails (mAb) as early treatment for patients at high risk of developing severe COVID-19. Their use is regulated by strict conditions developed jointly by the ANSM, the National Reference Center for Respiratory Viruses, and the ANRS|Emerging Infectious Diseases. More precisely, the ANSM authorized two mAb dual therapies, casirivimab/imdevimab co-developed by Regeneron Pharmaceutical and Roche, and bamlanivimab/etesevimab by Eli Lilly. The CocoPrev cohort was therefore established by the ANRS|Emerging Infectious Diseases to evaluate the effects of these two mAb cocktails on COVID-19 outpatients and their impact on variant emergence.

Nevertheless, as no decisive therapy for COVID-19 or related complications exists yet, the need for a COVID-19 vaccine has been compelling. An unprecedented effort on vaccine research and development allowed approval of the first COVID-19 vaccines via emergency use authorization within 11 months from viral sequence publication. To date, 19 COVID-19 vaccines based on different technologies including mRNA platforms, adenoviral vectors or inactivated SARS-CoV-2 virus are approved or authorized for emergency use across the world. The WHO further counts 292 new vaccines in the pipeline, 108 of which in clinical phases.

To promptly develop a COVID-19 vaccine, France relied on major pharmaceutical companies: Sanofi Pasteur, Valneva, and Merck who collaborated with *Institut Pasteur*. Sanofi Pasteur leading vaccine candidate is an adjuvanted recombinant subunit vaccine, developed in collaboration with American authorities. Technical issues related to antigen concentration [23] led to delays in its clinical development, postponing expected authorization to end of 2021. Valneva is currently carrying out a phase III clinical trial of their inactivated adjuvanted vaccine with financial support of the United Kingdom, aiming at authorization by the British regulatory authorities by fall 2021. Merck and *Institut Pasteur* interrupted their research in January 2021 due to unconclusive results in phase I

trial [24]. France further contributed to COVID-19 vaccine research efforts by supporting second-generation candidate development. Three high potential academic projects led by the Vaccine Research Institute (VRI), the *Institut Pasteur* of Lille, and the CEA-LETI/Inserm, respectively, received MESRI funding to accelerate their development. Moreover, the NANO-SARS-CoV-2 project, led by Tours University, was awarded an ANR grant for vaccine preclinical development, and evolution to human clinical trials is expected for 2022. The vaccine candidate from *Institut Pasteur*–TheraVectys Common Lab has recently shown to provide sterilizing protection in animal models [25], opening the path to clinical development. Lastly, BPI France has supported two vaccine candidates primarily targeting T cell immunity, developed by French biotech companies OSIVAX and OSE, respectively.

Today, French vaccine clinical research relies on the COVIREIVAC platform, established in April 2020 and based on the pre-existing vaccine research network I-REIVAC, coordinated by Inserm and funded by the MSS ad MESRI. To date, COVIREIVAC includes 37 clinical investigation centers, a network of 11 immunology laboratories and counts over 40,000 volunteers for trials. COVIREIVAC hosts ENSEMBLE 2, a phase III clinical trial sponsored by Janssen to assess safety and efficacy of a two-dose regimen of their vaccine Ad26.CoV2.S. Three major academic studies are also hosted by COVIREIVAC: ARNCombi, CoviCompare and COV-POPART. ARNCombi compares immunological efficacy of the homologous two-dose standard vaccine regimen with the same mRNA vaccine with that of an heterologous regimen combining two different mRNA vaccines. CoviCompare program evaluates immunogenicity of different COVID-19 vaccines in the over 65 population compared to young adults. A phase II trial series, CoviCompare is currently testing mRNA vaccines and will soon include other available vaccine platforms, aiming to tailor their use to the population type by investigating optimal efficacy. The national vaccination cohort COV-POPART [26] aims to evaluate immune response induced by COVID-19 vaccines in immunodeficient or immunosuppressed populations, and to identify and characterize vaccine failures and the role of SARS-CoV-2 viral variants on them.

As SARS-CoV-2 and the COVID-19 pandemic evolve, research is developing accordingly. Noteworthily, as new and highly transmissible viral variants emerged, the EMERGEN consortium was set up in January 2021 by the ANRS|Emerging Infectious Diseases and *Santé publique France* to implement genomic surveillance of SARS-CoV-2 variants, and in the long-term of other emerging pathogens. It also aims to promote related research projects, such as biological studies in animal models, clinical studies, mathematical modelling studies or wastewater screenings. In the clinical setting, SEVASAR was launched in March 2021 to evaluate whether the Alpha variant, first identified in the United Kingdom, is associated to specific or more severe clinical manifestations.

In addition, as the pandemic is progressively controlled and societies seek to safely going back to normality, research responds with projects to monitor and control viral spread during cultural and sporting events. For instance, projects have been implemented to study SARS-CoV-2 transmission in the context of a live concert (AMBITION Live Again, sponsored by the AP-HP), or of a sporting event (COVID ESO for participant athletes, sponsored by Lyon Hospital).

Finally, the French global research strategy to fight SARS-CoV-2 also prioritized collaborations with LMICs. Nearly 100 funded projects were identified covering a wide range of research areas from public health to fundamental and clinical research and to social sciences. A relevant example is the implementation in 2021 of AFROSCREEN, coordinated by the ANRS|Emerging infectious diseases, in partnership with the French National Research Institute for Sustainable Development (IRD) and the Pasteur Network, and funded by the French Agency for Development (AFD). The objective of this project, implemented in 13 African partner countries, is to build laboratory capacity to improve the detection of SARS-CoV-2 variants, allowing their adequate control in the short-term, and overall genomic surveillance on emerging and re-emerging infectious diseases in the long-term. AFROSCREEN generated projects such as AphroCoV, launched by REACTing in March 2020, and ARI-ACOV and REPAIR, commenced in October 2020 by the IRD and Institut Pasteur, respectively. These projects aimed at strengthening laboratory human and technical resources for early diagnostic and appropriate patient care of COVID-19 cases, and reinforcing quantitative and qualitative data collection mechanisms, in African partner countries.

The projects described so far represent a non-exhaustive list of clinical research efforts in response to the COVID-19 crisis. However, the atlas of implemented research projects of all scientific disciplines is much broader. To assess how French research contributed to tackling the SARS-CoV-2 pandemic, we performed a cross-sectional study of articles published on COVID-19 as of June 2021 through a bibliometric analysis. The research targeted all articles and letters on the Web of Science platform containing SARS-CoV-2, COVID-19 or equivalent terms, and was further filtered by country of author affiliation. This research retrieved 97,348 articles on SARS-CoV-2 and COVID-19, regardless of their country of publication. For reference, a total of 3,501,266 publications, all topics and countries included, were counted in the same timeframe. Regarding the proportion of SARS-CoV-2 or COVID-19-related publications per country, if we only consider the number of publications regardless of the real-world impact of trials, France ranked tenth (3.9%) preceded by the United States of America (26.6%), China (13%), Italy (10%), England (9%), India (6.5%), Spain (5%), Germany (4.7%), Canada (4.2%), and Australia (4%) (Table 1). Of note, the contribution of French research to global scientific research during the COVID-19 crisis compares to that of non-pandemic times (3.8%), representing a steady commitment of the scientific community. Among SARS-CoV-2 or COVID-19-related articles, 3,847 report a French affiliation of the authors. When considering high-impact journals that fall in the first quartile of all journals based on their impact factor, France ranks second, following the Netherlands. Of the 3,847 articles mentioning a French affiliation, 3,175 are registered as of June 20, 2021, in Incites, a citation-based research analytic tool. Among them, 34.8% are categorized within the top 10% and 11.4% within the top 1% of most-cited publications. Lastly, French authors co-affiliated with international partners, such as the Unites States of America (17% of publications), Italy (14%), or England (13%). Concerning research topics based on keywords and journal of publication, clinical subjects such as infectious diseases, general medicine, and critical care medicine occur as predominant, while fundamental research subjects are seemingly less developed. This is evident particularly when comparing to countries such as Germany, the Unites States of America, or the United Kingdom. However, a modest shift towards fundamental topics, namely immunology and microbiology, as well as towards public health and environmental subjects, was recently observed in France.

This bibliometric analysis, although reflecting the state of the art at a given moment and evolving over time, shows that the French scientific community maintained a constant participation in research during the international COVID-19 crisis, sustaining a steady research level of publication and being ranked among the top two countries for publication in high impact factor journals.

To conclude, the unprecedented COVID-19 crisis required an unparalleled collaborative multi-disciplinary effort, which France responded to. The COVID-19 pandemic challenged us as nations and as scientific communities, but valuable lessons on coordinated efforts and targeted research funding have been learnt on the way, which will change scientific research for years to come. However, it must be remarked that many of the described crucial

Table 1

Rank	Country	Web of Science Documents	Times Cited	Category Normalized Citation Impact	% Documents in Top 1%	% International Collaborations
1	USA	21,097	213,142	5.2	10.3	34
2	China	9262	276,277	9.7	14.2	31
3	Italy	7653	73,184	5.1	10.6	33
4	England	7426	80,407	5.5	10.2	53
5	Spain	4013	29,214	4.4	8.7	36
6	Germany	3658	47,963	5.6	9.8	51
7	Australia	3233	32,912	5.3	9.8	58
8	France	3175	42,360	6.4	11.4	46
9	Netherlands	1495	26,210	8.3	14.2	67

Bibliometric indicators of publications on SARS-CoV-2/COVID-19 having at least one author with a French affiliation and indexed in Web of Science analysis tool InCite as of June 20, 2021, in comparison to countries for which data were analyzed in our bibliometric analysis. If considering all countries, France ranks 10th as India and Canada would rank 5th and 8th, respectively (data not analyzed). Category Normalized Citation Impact: number of citations received by a publication, compared to the average citation rate received by worldwide publications in the same category, published in the same year and of the same type (article, letter, etc.). Documents in Top 1%: publications over the 1% threshold after ranking all articles on SARS-CoV-2/COVID-19 listed in Web of Science by year, type of document, subject, and by citation rate in descending order.

responses and actions relied on existing networks and research platforms that, fueled by sudden funding, allowed an otherwise unattainable response. A crucial take-home message from the last 18 months must be that proper development of research infrastructure, organized management of financial means and coordination of a common response of scientists, health professionals, regulating agencies and political actors must be the cornerstone in times of preparedness as much as it has been in times of crisis.

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the 1964 Helsinki declaration and its later amendments.

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Contribution of authors

Erica Telford, Guillaume Mellon, and Inmaculada Ortega-Perez conceived and designed the study, drafted the manuscript, and critically revised and reviewed the work. Boris Lacarra conceived and designed the study, and critically revised and reviewed the manuscript. Elisabeth Adjadj performed bibliometric data analysis for the work, and critically revised the manuscript. Claire Madelaine and Eric D'Ortenzio critically revised and reviewed the manuscript. Yazdan Yazdanpanah conceived and designed the study, and critically revised and reviewed the manuscript for final approval.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Disclosure of interest

YY has been a board member receiving consultancy fees from ABBVIE, BMS, Gilead, MSD, J&J, Pfizer, and ViiV Healthcare, however, all these activities have been stopped in the past 4 years. The other authors declare that they have no competing interest.

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