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# Impact of the COVID-19 pandemic on clinical research in hospitals: observational study in the first epicenter of the epidemic during the general lockdown in France

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**Abstract. – OBJECTIVE: The COVID-19 epidemic has had a strong impact on the entire healthcare sector in France with priority being given to research for new therapeutic options for COVID-19. Nevertheless, continuity of care for patients suffering from other diseases represents a crucial challenge, and clinical research is no exception in this respect. This study aims to assess the impact of the strict COVID-19 lockdown on non-Covid-19 clinical research in the French University Hospital of Strasbourg.**

**MATERIALS AND METHODS: Clinical research activity (non-Covid-19) from the point of view of pharmacy department was estimated and compared to the pre-lockdown period. The impact of lockdown was assessed through five indicators: site initiation visits, the initiation of experimental therapies in non-Covid-19 patients, the delivery of non-Covid-19 investigational medical products, the number of drug shipments to patients' homes, and the number of monitoring or closure visits.**

**RESULTS: During the study period, the number of site initiation visits decreased by 90%, total inclusions by 72%, and delivery of investigational medical products by 30%. During the lockdown period, 15 treatments were sent to patients' homes. Monitoring activity decreased by 98%.**

**CONCLUSIONS: Although the COVID-19 outbreak has created an incredible momentum in the field of clinical research, research not focused on SaRS-CoV-2 has suffered greatly from this situation. The impact on patients is difficult to estimate but should be further investigated.**

*Key Words:*
Clinical trials, Infectious diseases, Randomized controlled trials.

## Introduction

The emergence of a highly contagious and potentially fatal zoonotic virus – severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) – in late 2019 has been a major challenge for humanity. Following its identification in patients with severe pneumonia in Wuhan Province, China, in November 2019, SARS-CoV2 spread rapidly across the world and now affects most countries. It is the largest pandemic of modern times. As of 1 October 2020, more than 30 million cases have been confirmed worldwide. In addition, human-to-human transmission continues at a sustained rate despite intensified public health measures. As of 1 October 2020, the World Health Organization database has listed more than 2,500 ongoing and completed clinical trials on COVID-19. Research on preventive or curative treatments has monopolized the entire community of clinical research professionals. However, therapeutic options for the management of COVID-19 remain limited. The discovery of new therapeutics remains a strategic challenge at the global level.

Despite the obvious importance of COVID-19 research, it is also important to consider the impact of the epidemic on other areas of clinical research. Indeed, this is the first time that modern clinical research has been confronted with a global pandemic. In France, the occurrence of the first epidemic peak accompanied by the saturation of hospitals led to a strict general lockdown of the population, unique in the history of the country. The European Medicines Agency[1] issued guidelines and proposed several



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changes to ongoing clinical trials and restricted patient visits. It recommended a critical evaluation of feasibility and immediate necessity of starting new clinical trials. Continuity of care and continuation of treatment for patients already included in trials were complicated by travel restrictions, not to mention the risk/benefit ratio of moving at-risk patients to cluster hospitals. The promotion of teleconsultations and the authorization accorded by the French National Agency for Medicines and Health Products Safety[2] to ship experimental treatments to patients' homes allowed certain patients to continue treatment. However, the impact of the pandemic and lockdown on clinical research has been poorly assessed. In French hospitals, pharmacy departments manage investigational medical products (IMPs) for all clinical studies on drugs, giving them a cross-functional view of the entire process and allowing them to easily gain feedback from hospitals about their clinical drug research. The present study evaluates the impact of the Covid-19 pandemic and the strict general lockdown on clinical research in a University Hospital located in one of the epicenters of the SARS-CoV-2 outbreak in France.

## Materials and Methods

This retrospective, single-center, observational study evaluates the changes in clinical research at Strasbourg's University Hospital during the nationwide SARS-CoV-2 lockdown, which lasted from 16 March to 10 May 2020. The analyses compare the clinical trials conducted during the 8 weeks of general lockdown in France with the 8 preceding weeks from 20 January to 15 March 2020.

The pharmacy department is involved in all research projects on drugs or sterile medical devices involving human subjects in the hospital. Data were extracted from the 536 active trials managed using the department's Elips software. All trials were integrated into the analysis. Most of the analyzed studies are phase 2 and 3 (more than 95%) industrial trials (63%). The impact of lockdown was assessed through five indicators: site initiation visits (SIVs) for new non-COVID-19 clinical trials, the delivery of non-COVID-19 IMPs, the initiation of experimental therapies in non-COVID-19 patients, the number of drug shipments to patients' homes, and the number of monitoring or closure visits. IMP delivery was analyzed as a whole and according to medical specialties. The effects of the lockdown and first epidemic peak were verified by measuring a return to balance in the deliveries over the 8-week period following the lockdown.

## Results

### Site Initiation Visits

The number of SIVs decreased sharply between the two study periods from 59 to 6, representing a decrease of 90%.

### Deliveries of Investigational Medical Products

Before lockdown, 612 prescriptions from 18 medical disciplines were dispensed to trial patients. The most represented discipline was oncology with 257 IMP deliveries (43% of all activity). Neurology trials also represented a large proportion with 88 deliveries (15%), with the remainder being split between several disciplines as shown in Figure 1. During the lockdown period, 428 prescriptions were dispensed. The total number of

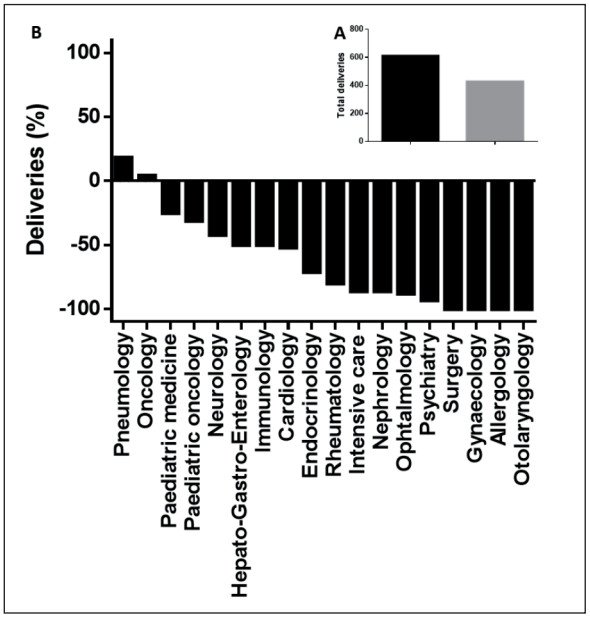


**Figure 1.** Comparison of the number of deliveries of investigational medical products before and during the general population lockdown. Deliveries fell by 30% during this period (**A**). The percentage of investigational medical products delivered during lockdown is relative to the period before lockdown. The decrease in deliveries occurred across all medical disciplines except for oncology and pneumology (**B**).

IMP deliveries thus decreased by 30%. With the exception of oncology and pneumology, where distributions remained stable or increased (+4% and +18%, respectively), all medical specialties were affected with fewer deliveries: IMP deliveries decreased by 25% for pediatric medicine and were totally discontinued for trials in surgery, allergology, otolaryngology, and gynecology. The lower number of IMP deliveries would appear to result from the epidemic peak and lockdown. Indeed, during the 8 weeks following lockdown (11 May to 5 July 2020), the number of distributions was comparable to the period before lockdown (652 deliveries, or a 6.5% increase compared to the pre-lockdown period).

### Initiations of New Treatments

During the 8 weeks of routine activity prior to lockdown, 155 new patients were enrolled in clinical trials and received IMPs as opposed to 44 treatment initiations during the lockdown period, excluding COVID-19 trials. This resulted in a 72% decrease in the number of enrolled patients (Figure 2).

### Home Shipments

During the lockdown period, 15 treatments were sent to patients' homes by the pharmacy to limit their travel to the hospital (no shipments outside of the lockdown period).

### Monitoring and Closure Visits

Monitoring activity decreased by 98%, with the number of monitoring sessions falling from 58 to 2. Two monitoring sessions were conducted remotely by telephone. All closure visits were postponed during lockdown.

## Discussion

The COVID-19 pandemic is affecting clinical research worldwide. In this study, we evaluated the impact of the epidemic on non-COVID-19 clinical trials. Our results are particularly concerning, since they show a clear decrease in non-COVID-19 clinical research activity in our university hospital. During lockdown, the initiation of new clinical trials was severely limited. Our study suggests that the epidemic has significant consequences, not only by limiting clinical research activity but also by preventing patients from enrolling in new studies and continuing initiated treatments. It is well known that in some situations, the lack of patient inclusion in clinical trials may act as a loss of opportunity for patients, particularly in pediatric oncology[3]. It should also be noted that the number of IMP deliveries fell despite the possibility of sending some treatments to patients at home. Unfortunately, this arrangement is not feasible for all clinical trials (e.g., infused therapies with a short shelf life). The only medical specialty in which the number of IMP deliveries remained stable was oncology, which is consistent with the fact that oncology is a medical discipline in which delays and lags in treatment delivery can affect the course of the disease. During lockdown, treatment delivery increased in pneumology, because a previously active study to evaluate the role of corticosteroids in serious lung infections included patients infected with SARS-CoV-2. It is also noteworthy that the decrease in non-COVID-19 clinical research activity was offset by the increased activity related to the COVID-19 pandemic (14 initiations, 132 inclusions, 100 IMP deliveries).

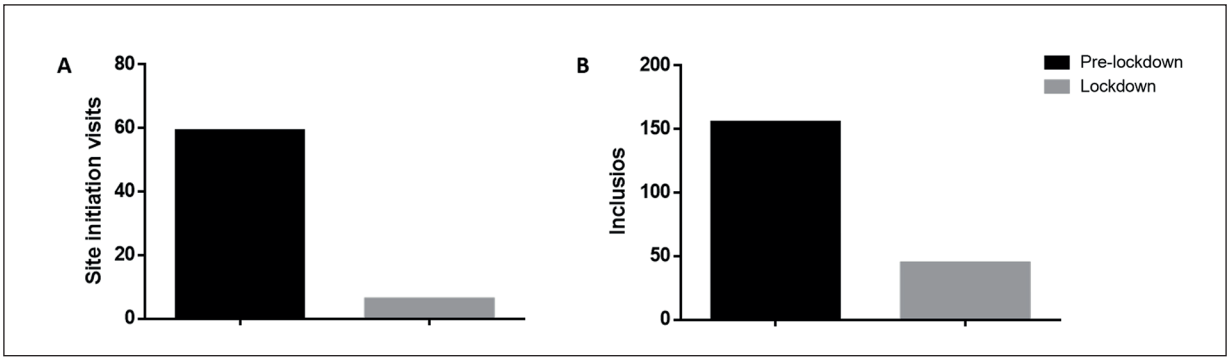


**Figure 2.** Comparison of the number of site initiation visits (**A**) and initiations of new treatments (**B**) before and during the general population lockdown. During the study period, the number of site initiation visits decreased by 90% and the number of inclusions by 72%.

The reference activity was defined as the 8-week period immediately preceding lockdown. A longer period of comparison that included the previous year could have been considered. However, the active trials and investigators would have differed, thus significantly biasing the analysis. While the number of initiations and closures may vary throughout the year (e.g., depending on school holidays), this is generally not the case for treatment deliveries. The period chosen for the comparison included 2 weeks of school holidays, which could have minimized the observed differences.

In addition, it may be interesting to collect data on trial discontinuations, deviations, or changes in the study design, which aimed to compensate for the epidemic context. Some authors have already described how the epidemic is affecting research and study design. Nevertheless, this is the first study to assess the impact of the epidemic on the global research activity of hospitals. Bian and Lin[4] recently described that 10% fewer full-length non-COVID-19 studies have been published in major medical journals since 31 January 2020. This includes clinical studies with a control group and randomized controlled trials. Further, Gaudino et al[5] assessed the effect of the COVID-19 pandemic on active non-COVID-19 trials, reporting that the number of discontinued trials increased significantly over the first few months of the pandemic. Most of the trials that stopped during the COVID-19 pandemic received non-governmental funding (95.4%). During the pandemic, the cumulative proportion of trials stopped by country ranged from 1% to 17%, which is weakly correlated to the number of COVID-19 cases adjusted to the national population[5].

Recently, members of the UK Trial Managers' Network reported the main problems encountered in the management of non-COVID-19 trials and proposed solutions to the issues of recruitment and consent, delivery, data collection, and restarting of trials. Nevertheless, the literature published to date is very limited on the impact of the epidemic on non-COVID-19 trials. Many active trials continue to face difficulties, which may be related to the stopping of inclusions, difficulties in communicating with patients, treatment delivery, data collection, or specific patient populations. The management of clinical trials in elderly or immunocompromised patients, for example, is particularly complicated[6-8]. This backlog of non-COVID-19 research, especially in rare diseases or specialties such as oncology, will have significant ramifications that need to be explored and anticipated in the future. Several protocols have been or are in the process of being amended to specify the procedure to be followed in epidemic situations. However, these amendments often focus on formalizing the possibility of shipping treatments, authorizing teleconsultations, or allowing non-centralized biological acts. A general reflection on the difficulties encountered and the quality of the data collected is essential in order to optimize the management of trials in a pandemic situation. New lockdowns in the context of the COVID-19 pandemic cannot be excluded. Similarly, the emergence of new epidemics caused by viruses with different characteristics should also be considered.

## Conclusions

While clinical research has not failed during the first epidemic peak of COVID-19, the general lockdown had a strong impact on the initiation of new studies, the inclusion of patients in ongoing clinical trials, and the continuation of experimental treatments. Faced with the prolongation of the COVID-19 epidemic throughout the world, a global reflection on the management of non-COVID-19 clinical trials should be initiated in order to avoid loss-of-chance for patients who suffer from other pathologies and could benefit from clinical research.

### Conflict of Interest

The Authors declare that they have no conflict of interests.

### Declaration Statements

The authors received no financial or material support for the research. The data reproduced in this retrospective observational study are in accordance with the ethical standards of our institution. No ethical approval is required.

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### Authors' Contribution

GB, TM, EAD and BG designed this study. TM, GB and FB collected data. TM, GB, ANS, FB and AH did the anal-

ysis. GB, TM, ANS, BM, EAD and LM wrote the draft of the manuscript. BM, LM, EAD and BG reviewed and gave critical comments on the manuscript draft. All authors reviewed, wrote, and approved the final version. The corresponding author, GB had ultimate responsibility for the decision to submit for publication.

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