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# Thrombosis Update

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## Surviving and thriving in thrombosis research during a global pandemic: Experiences of a vascular scientist diagnosed with COVID-19

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ARTICLE INFO	A B S T R A C T
Keywords: COVID-19 Sepsis Research	The 2019–2020 COVID-19 outbreak resulted in widespread suffering along with major changes in the ways that researchers carry out their work. This article profiles the experiences of an early-career investigator in thrombosis research who worked through the COVID-19 pandemic and a COVID-19 diagnosis. The aims of this article are to normalize concern regarding COVID-19 in the research community, to provide a perspective on maintaining productivity during stay-at-home periods, and to discuss how the COVID-19 pandemic might alter common research practices in the future. While the COVID-19 outbreak was clearly disruptive and debilitating on a global level, some research practices that were heavily employed during the pandemic may continue to be utilized in

scientific research for many years to come.

## 1. Background

The 2019–2020 COVID-19 pandemic has resulted in global suffering [1] and unprecedented alterations in the ways that clinicians and scientists carry out their research. The widespread consequences of this global outbreak have included travel restrictions and job losses [2], mental and physical illness [3,4], and death [4]. In response to the outbreak, nationwide stay-at-home orders have been implemented, and healthcare visitations replaced with telemedicine appointments [5,6]. In the state of Illinois, USA, for example, a stay-at-home order was implemented on March 21st, 2020, and remained in place until May 29th, 2020. During this 70-day period, all non-essential workers were limited to working from home, and outdoor activities restricted to essential trips, e.g., for exercise and food shopping. In the scientific research community, many buildings were closed, and research activities halted, except for those investigating COVID-19 and COVID-19 treatments. The current narrative profiles the experiences of an early-career investigator (C.E.E.) as he attempted to navigate a dramatically changing research environment and work through the COVID-19 pandemic as a vascular scientist diagnosed with COVID-19. The aims of this article are to normalize concern regarding COVID-19 in the scientific community, to provide a researcher's view on maintaining productivity during periods of downtime, and to question how the pandemic might alter common research practices in the future.

## 2. Clinical perspective

The patient (C.E.E.) was a 35-year old male with no history of major illnesses or chronic medical conditions who gave consent for identifiable features to be published. The patient presented on day 1 with headache, body aches, and sore throat. The patient rested in isolation as soon as symptoms started. Fever began on day two, while symptoms progressed to a peak at day 4 (Table 1) and were completely resolved by day 10. Respiratory symptoms included a dry cough and sore throat but no shortness of breath, difficulty breathing, or chest pain.

At day 3, the patient tested negative for influenza A & B and streptococcus A. At day 4, the patient tested positive for COVID-19 (SARS COV-2-RNA, RT-PCR, Quest Diagnostics, USA). Accordingly, the patient was advised to rest in isolation until at least 3 days after fever had completely resolved without the use of fever-reducing medication, and for at least 7 days since the onset of symptoms. For pain and fever relief, the patient took an over-the-counter pain reliever, NyQuil (650 mg acetaminophen, 20 mg dextromethorphan, 12.5 mg doxylamine succinate, 10 mg phenylephrine HCl, orally 2 times per day) and Advil (200 mg ibuprofen, orally 2 times per day). The patient also took vitamin C (orally, 1g per day) and applied oral anti-septic pain relief, Orajel (0.13% benzalkonium, 20% benzocaine, 0.26% menthol, 0.15% zinc chloride, topically, 2 times per day), to oral ulcers.

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#### Table 1

Progression of symptoms during the COVID-19 diagnosis.

Symptom	Day									
	1	2	3	4	5	6	7	8	9	
Headache	•	•	•	•	•	•				
Sore throat	•	•	•	•	•	•				
Body aches	•	•	•	•						
Fever (Temperature)		• (101.3 °F)	• (99.9 °F)	• (98.7 °F)	• (99.1 °F)	• (100.9 °F)				
Dry cough				•	•	•	•			
Oral ulcers				•	•	•	•	•	•	
Hypogeusia							•	•	•	

As of November 2020, only a handful of treatments for COVID-19 have FDA approval or emergency use authorization. Remdesivir, for example, inhibits viral RNA-dependent RNA polymerase and thus viral replication. A mortality benefit of Remdesivir has not vet been established, but this treatment has been shown to improve time to recovery in hospitalized patients with moderate disease (NIAID ACTT-1 trial) [7,8]. A major limitation of this therapeutic is its requirement for intra-venous delivery, which limits its usage and investigation in the early stages of disease when hospitalization would not otherwise be necessary. Another example, Dexamethasone, is a systemic corticosteroid shown to reduce mortality in persons with severe and critical COVID-19 (RECOVERY trial) [9]. A meta-analysis also demonstrated a lower 28-day all-cause mortality in patients who received corticosteroids [10]. The use of corticosteroids is not fully supported, however, given that corticosteroid treatment in patients with similar viruses (e.g. SARS-CoV, MERS, and influenza) can result in undesirable effects including increased mortality, increased incidence of secondary infections, and impaired viral clearance. Convalescent plasma has also been granted emergency use authorization by the FDA for the treatment of hospitalized patients with COVID-19. While convalescent plasma therapy is well-tolerated, a mortality benefit of this treatment has yet to be shown [11]. One trial reported a reduction in time to clinical recovery but no mortality benefit in those receiving convalescent plasma, and this trial was terminated early [12], while another trial suggests that giving this treatment earlier in the disease course is favorable [13]. The FDA has also recently granted emergency use authorization to the monoclonal antibody, Bamlanivimab, for the treatment of mild to moderate COVID-19 in adults and pediatric patients. This treatment was shown in the ongoing BLAZE-1 trial to reduce hospitalization in those at high risk for disease progression [14]. Bamlanivimab is not, however, approved for individuals who are hospitalized or who are critically ill requiring mechanical ventilation. While clinical studies of novel COVID-19 treatments are ongoing, another limitation of experimental therapies that require monitored or supervised administration is the associated risk of disease transmission between patients and healthcare providers.

## 3. Personal perspective of the patient (C.E.E.)

My PhD training at King's College London provided me with a solid foundation in thrombosis research and triggered my interest in inflammatory vascular diseases [15–20]. During my postdoctoral training at the University of Cambridge, I received start-up grants from the British Heart Foundation and the British Society for Haematology to develop my research ideas and study the bi-directional interactions between lung tumorigenesis and thrombosis [21,22]. During my subsequent Parke Davis Fellowship at the University of Illinois College of Medicine, I began to assess how pulmonary thrombosis regulates the progression of acute lung injury [23]. As a Research Assistant Professor, I am currently continuing these studies at Ann & Robert H. Lurie Children's Hospital of Chicago and Northwestern University Feinberg School of Medicine, funded by a Career Development Award from the American Heart Association.

Apart from the worldwide coverage of the COVID-19 pandemic, I

guessed that changes to our typical research routines were imminent when we received an email reminding us that personal protective equipment for research use should not be taken for external use. Next, we were asked to restrict our animal breeding programs and refrain from starting new experiments. Then, in line with government and state orders, our institute was put on widespread shutdown and non-essential studies were completely stopped. In other words, all experiments unrelated to COVID-19 would cease. Access to our research building was prevented and in-person meetings prohibited.

My symptoms first appeared when I was resting at home. The onset of my symptoms was not expected, somewhat distressing, and led to a shift from my usual routines. It was unsettling that: (i) I was unsure where or from whom I had contracted the virus (one possibility is at the grocery store); (ii) the disease course and severity can vary substantially between individuals; and (iii) I was placed in isolation (including from my close friends and immediate family) until 3 days after my symptoms disappeared. After I had recovered and throughout the lockdown, it was very different to be working from home instead of in the laboratory; my work was forced to shift away from wet laboratory tasks and towards editorial and writing tasks. Even the most routine tasks including animal breeding and colony maintenance had to be drastically limited. Despite widespread disruption to my normal research practices (Table 2), I

#### Table 2

Restriction	Solution			
Novel techniques cannot be developed in the laboratory	<ul> <li>Attend video presentations of new techniques and technologies</li> <li>Read new articles and meeting abstracts to generate ideas for novel studies</li> </ul>			
Laboratory meetings are cancelled	<ul> <li>Maintain regular contact with lab member by email or telephone or video</li> <li>Take regular progress checks</li> </ul>			
Conferences and other events are postponed or moved virtual	<ul> <li>Attend virtual meetings and interact through message boards or video</li> <li>Expand online presence using social media and other networking platforms</li> </ul>			
Career development progress is difficult to monitor and achieve	<ul> <li>Attend online career development workshops and training</li> <li>Find and use online resources from professional development departments</li> <li>Complete academic service tasks such as manuscript and grant reviewing</li> <li>Communicate with senior colleagues to</li> </ul>			
Studies for grant applications are delayed	<ul> <li>identify areas for improvement</li> <li>Plan studies for the future and generate a prioritized list</li> <li>Search for new funding opportunities and begin new funding applications</li> <li>Improve grant writing skills using online resources and workshops and advice and feedback from peers</li> </ul>			
Studies for manuscripts are delayed	<ul> <li>Write the aspects of the grant that do not require pilot data</li> <li>Plan studies for the future and generate a prioritized list</li> <li>Focus on completing and submitting unfinished manuscripts</li> </ul>			

attempted to reduce the deleterious impact of the lockdown on my research productivity by maintaining at least some fundamental aspects of my usual working routine. For instance, I kept my working times and days consistent with my usual patterns. I worked from an office area of my home using software that allowed access to my work computer. I maintained remote communication with my Principal Investigator (PI) to discuss the tasks I was carrying out and the approximate amount of time for each task. I followed departmental advice and used the lockdown time to work on laboratory-free tasks such as manuscript reading and grant writing.

Although the changes were initially frustrating, the stay-at-home order and subsequent alterations in my research practices also gave rise to a diverse panel of solutions that I used to maintain productivity (Table 2). For instance, I used social media platforms to update my online presence and identify online research talks and workshops that could aid in my research exposure, critical thinking, and development of research plans [24]; these included ResearchGate, LinkedIn, and Twitter (@Colin E Evans). I searched online for live or recorded video presentations that were relevant to my research; these included talks organized by individual researchers, such as the blood and bone seminar series (htt ps://bloodandboneseminar.com/), and talks arranged by research societies including the North American Vascular Biology Organization (htt p://www.navbo.org/). Similarly, I attended annual meetings that were made virtual by large-scale organizations such as the American Heart Association and the American Thoracic Society. I used online tools to search for funding opportunities in the area of thrombosis research; these included ResearchGate, Funding Institutional, and the NIH/NHLBI webpages. I also had the time to review a higher number of manuscripts than normal for peer-review journals, which extended my academic responsibilities and editorial experience.

If my levels of motivation dropped during the period of remote working, I followed these tips to attempt to improve my levels of productivity: (i) I identified improvement opportunities by comparing my CV and track record with a typical profile that might be required for a more advanced position; (ii) I took break(s) from the task(s) I had been working on for the longest by completing other tasks in the meantime; (iii) I generated a list of tasks in order of priority; (iv) I took timeout to exercise outdoors; and (v) I continued to read the latest studies in my research area.

As with any debilitating illness, my COVID-19 diagnosis was concerning, but I was fortunate enough to suffer from relatively mild symptoms. The statewide stay-at-home order allowed me to focus on desk-based research activities including grant and manuscript writing. I was also fortunate to have a supportive team and advisor as well as several inprogress writing tasks. In other words, I was one of the COVID-19 patients that was able to continue my professional duties during the workplace disruptions, albeit in an unfamiliar manner. Other researchers may not be as fortunate. For example, the damaging impact of COVID-19 has been reported to be exaggerated in minority groups [25,26]. Furthermore, prolonged periods of isolation and/or severe COVID-19 symptoms can lead to mental health consequences including post-traumatic stress disorder and depression [27,28]. Behavioral and emotional changes including altered eating habits and perceptions of weight gain have also been reported to occur during COVID-19 lockdown [29]. For those seeking emotional support, there are an abundance of mental healthcare resources online, including from the American Psychiatric Association (http://wor kplacementalhealth.org/Employer-Resources/Working-Remotely-During -COVID-19), the Centers for Disease Control and Prevention (https: //www.cdc.gov/coronavirus/2019-ncov/community/mental-healthnon-healthcare.html), the National Safety Council (https://www.nsc.org/ work-safety/safety-topics/coronavirus/mental-health-and-wellbeing), and the Mental Health Foundation (https://www.mentalhealth.org.uk/co ronavirus/looking-after-your-mental-health-while-working-during-coron avirus). Individual research institutes also often have their own professional services and resources, such as those provided by the University of Michigan (https://www.depressioncenter.org/work/information-for-em

ployers/developing-an-employee-assistance-program; https://www. depressioncenter.org/toolkit/i-want-stay-mentally-healthy/coping-work) and Cincinnati Children's (https://www.cincinnatichildrens.org/patients /coronavirus-information/family-resources/routine-structure).

`In the foreseeable future, there remains the possibility of further workplace restrictions and/or another complete lockdown. Despite the best efforts of researchers to maintain productivity during lockdown, remote working is not without its limitations. For instance, while virtual conferences and online meetings are common tools that have been widely used during the COVID-19 pandemic, they limit the opportunity for effective networking. This could be especially relevant to early-career researchers that are job seeking and/or looking to gain promotion [30]. What's more, many research institutes have suspended new hires during the pandemic and the number of advertised faculty positions has dramatically dropped compared with previous years. Similarly, training opportunities and fellowships that require international travel have been largely postponed or cancelled. All things considered, it is highly likely that most of the research community are hoping for a rapid return to pre-COVID-19 research practices as soon as this becomes safe and feasible.

#### 4. Role of the Principal Investigator

During such periods of difficulty, it is the responsibility of the PI to not only encourage and monitor the productivity of their group members, but also to ensure the well-being and safety of their laboratory personnel. During the COVID-19 outbreak, the PI should help laboratory members to maintain appropriate social distance by: (i) promoting the work-fromhome order for those carrying out non-essential research; (ii) ensuring that essential research is performed by individuals working separately and in staggered shifts; (iii) organizing disinfection and cleaning of working areas; and (iv) finding affordable and nearby parking so that laboratory members performing essential research can avoid public transport. If a laboratory member displays symptoms, they should be sent home by the PI to recover and stay at home to isolate per the guidance of local public health authorities.

Laboratory members that are worried about COVID-19 (or related matters) should be able to approach their PI for direction and support. It is also beneficial if the PI has fostered a sense of community amongst laboratory members [31]. From a research standpoint, the PI should maintain regular contact with group members and advise on methods of maintaining productivity when working from home, for example by providing suggestions for reading material and designating specific writing or data analysis tasks. The PI should also coordinate with institute officials and laboratory members to ensure a successful phased return to normal working routines.

## 5. Future perspectives

In the wake of the COVID-19 outbreak, many operational changes were implemented in the short-term, which may remain or be re-adopted in future. For example, working shifts have been staggered and the number of researchers per laboratory limited. Individuals have been required to wear personal protective equipment, distance themselves from each other, regularly disinfect working surfaces and handrails, and frequently wash their hands. Going forward, research institutes may choose to retain video communications in the place of in-person visits and video learning in the place of in-person workshops, which would reduce the carbon footprint of research-based travel and likely improve air quality in large cities [32-34]. Organizing committees have also become familiar with virtual meetings instead of large group gatherings. For example, large annual meetings organized by the European Hematology Association and the American Association for Cancer Research were conducted virtually in 2020. It remains to be seen to what extent remote practices will continue when widespread in-person gatherings can return.

Hopefully, biomedical research in academia and industry will lead to the development of an affective COVID-19 therapy or vaccine in the foreseeable future. Ultimately, the COVID-19 crisis highlighted the potential of home-based working for research activities that do not require wet laboratory space and informed senior management of efficient research practices that could continue to be used in future. Ultimately, this health crisis could also stimulate the number and quality of scholars that pursue biomedical research, thus providing a silver lining to the dark COVID-19 cloud. This possibility is especially plausible in the field of thrombosis, given that the high incidence of thrombotic events in COVID-19 patients [35–37] has not only increased public awareness and engagement with thrombosis research, but also generated additional funding resources, and helped facilitate new collaborations across the fields of infection, immunity, and thrombosis.

#### **Consent Statement**

The patient (C.E.E.) gave consent for the study to be performed and for identifiable features to be published.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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