Not What Anyone Signed up for: Unnecessary and Insurmountable Barriers Encountered in Conducting Clinical Trials in COVID-19

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this took a few months, and mechanisms for safe monitoring to continue to be developed.

When the initial lockdown came, around March 12, 2020, we were confronted with safer-at-home orders but no guidance regarding research studies. Because our patients do not have the luxury of scheduling their diseases outside a pandemic epoch, we had to work around restrictions imposed by the County and the University. We somehow did that, and maintained many of our trials, and have accrued about 50 patients to our studies as of November 1, 2020. I was offered participation in several multi-center studies from industry for COVID-19 therapy based on drugs that we had used for patients with hematological malignancies and transplantation. Although these drugs were developed in a cancer setting, their mechanisms of action offered potential efficacy outside neoplasia. I turned these over to my colleagues in Infectious Diseases who are coordinating the research strategies of this academic institution. I did attend several conference calls prior to initiation of the studies, feeling some responsibility for bringing them here.

The challenges to our research initially consisted of the safer-at-home orders that did not define research personnel on clinical trials as essential workers. Fortunately, I was able to come to my office daily, and since I run a large clinical research program, I was able to supervise those studies still accruing patients. My team of physicians and I also consented many subjects, and my team of two research nurse practitioners and one study coordinator screened them. Many have gone on research protocols at this time. However, not having the regulatory staff on-site proved very difficult. Although they worked from home, many things were not done in a timely manner, documents were not signed, and amazingly, there were no easy electronic options. For example, FDA 1572 forms could not be signed electronically. Data management was doable from home, but interfacing with regulatory bodies in the academic structure was not easy and we could not furlough employees, so I, and the few of us on-site, did the bulk of the secretarial work—printing out forms, sending them, sending them electronically, etc. I have no idea whether any of these documents are being filed, and I know that we did not receive anything through the mail for months. Presently, we get mail about once a week, but the backlog is immense. Finally, after 3 months of confusion, we developed a rotation system by which all personnel were assigned days to come into an office, without other personnel present, in order to complete their work, answer phone calls from patients or trial subjects, provide support to the research nurses, and electronically meet with monitors.

IRBs and researchers will need to develop different standard operations based on what was learned during this critical period. Either we have to develop a system of electronic signatures, or a delivery system for hard-copy signatures. The research infrastructure will need to assess the value added by scientific peer review, by coverage analysis, and by contracts, by reviewing the large number of outside serious adverse events sent, pro forma to investigators, and the overhead costs of all those personnel who may be working from home. Zoom or other electronic platforms provided some help, but in the end, they merely added to the work of people on-site who ran multiple functions. Even today, I am writing this essay while intermittently checking email and while attending an on-line international academic meeting! The logistics of all the juggling of multiple responsibilities actually required more staff on-site, not fewer, and left many of us wondering whether our staffing models were correct prior to the pandemic.

Not What Anyone Signed up for: Unnecessary and Insurmountable Barriers Encountered in Conducting Clinical Trials in COVID-19

Westyn Branch-Elliman & Paul A. Monach

WBE’s perspective

My 2020 started with an email entitled, “Happy New Year! Have You Read about this Virus that’s Coming to Kill Us All?” 

I remember the last day my life was “normal.” It was the end of February, 2020 and I was on the phone with my father, and he was asking me my
thoughts about what we were seeing in the news about the novel coronavirus—then still regarded as a distant enemy in a faraway land. By way of background, I am an infectious diseases specialist with training in epidemiology, infection control, and implementation science. In the past, I was a hospital epidemiologist, in charge of local outbreak control, and more recently, I work in clinical research, focusing on weighing risks and benefits of different infection prevention and antimicrobial use strategies and on expanding infection prevention services to relatively uncovered aspects of the healthcare system. My father was calling to ask me my thoughts about the short- and long-term prospects for an epidemic in the United States, and what my thinking was on how this might impact the financial markets. In the middle of the call, I received word of the first “suspect case” in our hospital. I abruptly hung up the phone and did not look back. In fairly short order, cases began to peak, schools closed, my elementary school-aged children were suddenly house-bound, and the state was put under near-lockdown. I did not have another day “off” until sometime after Memorial Day.

PM’s perspective

I remember exactly where I was on the morning of September 11, 2001, and also when I heard that the Challenger had exploded in 1986. I had no “COVID moment,” but over the course of March my obsession with the pandemic grew exponentially until it peaked at the point of controlling everything I did other than activities of daily living (ADLs). I knew I would be low on the list of people to be called in for “risky” inpatient work, having one of those “pre-existing conditions,” but I had to do something; with apologies to the patients I take care of at the VA who really did risk their lives for something in the past, I had to enlist. The opportunity arose when Westyn, whom I knew only because we served together on the local institutional review board (IRB), asked for my input on the use of rheumatologic drugs, specifically hydroxychloroquine and tocilizumab, in an institutional “treatment guideline” she was developing to advise inpatient teams on what labs to follow and what medications to use, based on very limited anecdotal evidence, to help the droves of patients we expected to descend on our hospital. As it turned out, my experience with clinical trials, including the plethora of bureaucratic processes and acronyms and numbered forms, would come in handy. Strangely, one of the few specific times where I remember where I was is when Westyn called to tell me she was being pushed to do a clinical trial.

WBE and PM: Designing and Implementing a Clinical Trial

In March, faced with a deadly disease descending upon our city and our hospital, there was an urge to be able to offer our patients “something” beyond the under-appreciated supportive care. Clinicians widely acknowledged that no available drug had sufficient evidence to support indiscriminate use in a purely clinical setting. The question was whether to use medications off-label based on limited anecdotes or to conduct a clinical trial—the first of many ethical issues we have confronted in the half-year since then. There was a desire by many, both among research leaders and some clinicians, for a “clinical trial” banner, so that patients would be appropriately informed about the potential for a lack of benefit—and potential for harm—associated with almost any COVID-19 intervention. With these realities in the background, the two of us, both clinical researchers and members of our facility’s IRB, received our marching orders: designing and implementing a clinical trial in time for the “first wave.” Why were we chosen? Partially because of our position on the IRB—one of the providers assigning us this Herculean task specifically said, “We picked you because we think you are the only ones who will be able to get the paperwork approved.”

Under normal circumstances, the process of designing, refining, and conducting a clinical trial would take months, at least. However, with COVID breathing down our necks, time was short. We reviewed the evidence available, limited to advice from our more experienced overseas colleagues—and then found ourselves constrained by which medications were available for purchase. We were lucky to have pre-existing relationships with the important institutional stakeholders—including the leaders in Research and Development, the clinical trials Coordinating Center, the IRB, and the
pharmacy—to move the trial from conception to implementation. We designed a pragmatic, adaptive randomized controlled trial comparing the addition of IL-6R inhibition to standard care for hospitalized patients with a confirmed diagnosis of COVID-19. With members of the team working literally around the clock—emails and approvals were flying during the hours between 2 and 4 AM—we were able to advance from a 2-page summary “pitch” to IRB approval in 6 days and enrollment of the first patient 4 days later.

After securing a medication amidst supply chain barriers, which necessitated completely revising the study within the 6-day period of design, the regulatory and ethical challenge we noted immediately when moving the study to the real world was: how do we weigh the research requirement for documentation of informed consent against the need to keep staff safe, while also limiting use of personal protective equipment (PPE)? Problems with PPE shortages in the clinical setting are well-known, but the impact on the research service line is not. Although questions about whether a wet signature was required were under review, all agreed that the patient should receive a paper copy of the consent form. A member of the staff doing this strictly for research purposes would risk exposure and have to use PPE to simply hand the sick and potentially morbidly ill patient a 7-page stack of paper—at a time when providers were instructed to wear their masks “for as long as possible.” We solved this first dilemma through collaboration with our clinical colleagues, who were working in the COVID units. They agreed to bring the consent forms to the patients’ bedsides during morning rounds, so that we could avoid redundant exposures and use of PPE.

After the dust settled on the problem of delivering a paper copy of the informed consent form, we experienced another: what were the requirements for the informed consent processes? As a VA facility, we are required to abide by FDA regulations, but early in the pandemic, when we were at our peak caseload, these “regulations” (technically Guidelines) were muddy at best. During an early online presentation, we were heartened to learn that the FDA would allow a remote consent process, with an impartial phone witness signing the consent form to affirm the patient’s desire to participate—a process not dissimilar to what has led to the highly successful RECOVERY Trial in England. This appeared to solve our PPE and staff risk problem: we could conduct the entire process over the phone, not worry about “poison paper” (that was more of a concern then than it is now), and limit exposures. Unfortunately, only a few weeks later, the FDA issued an update clarifying that the witnessed consent process could only be used for clinical consents, not research consents (particularly in interventional trials), and we were forced to develop more complicated and cumbersome processes, all in the name of collecting proof of a wet signature on a page from the patient or legally authorized representative (LAR).

Which brings us to the third, and most troubling, major ethical issue we faced: therapeutic misconception. One of the tenets of conducting clinical trials is that there should be “clinical equipoise,” and in line with that, patients should be deterred from expecting benefit from participation. Our experiences conducting a trial in COVID patients laid bare why these concepts are unrealistic, particularly for fatal diseases with no known effective treatments, such as COVID-19 in elderly patients. High mortality coupled with lack of evidence creates a perfect storm: patients and providers desperate to receive or prescribe “something,” whether in the context of a clinical trial or not. No one was willing to accept the idea that they would just let patients die without trying to do something more than the “supportive care” recommended in early societal guidelines.

Research consent processes require that investigators emphasize to patients that they may not benefit from participation in a clinical trial. However, this concept is divorced from reality: except for comparative-effectiveness studies, the reality is that patients participate because they hope for benefit, and providers refer their patients because they hope that the trial will help their patients more than will standard care. We encountered this challenge first-hand during our own trial. Because our study included a standard care arm—meaning no active therapy—we witnessed psychological distress not only among patients and their relatives, but also among treating physicians as evident in immediate abandonment of the scientific principles that they had supported during design of the trial. When
patients were randomized to standard care, physicians quickly revolted, and requested open-label use of the unproven study drug within 24 hours—even in stable patients. Honestly, we felt the same thing ourselves: as a clinician, and even as a researcher, it is very difficult to tell a patient that you have nothing to offer them, particularly when you feel responsible for that limited choice. Plus, we have been on the other side.

WBE

At age 33, I was diagnosed with early-stage, HER-2 positive breast cancer. Because of my “extremely” young age, and the aggressiveness of the tumor, there was a long discussion about how I should be treated: Standard chemotherapy regimens? Clinical trials? Something else? My oncologist and I considered enrolling in a clinical trial of chemotherapy plus Herceptin versus TDM-1, a newer, more expensive option that linked the chemotherapy agent to the Herceptin. The upshot of the trial for patients was that TDM-1 did not cause hair loss, and based on trials in other populations, there was hope that the medication would be more effective than the current standard of care. The prospect of avoiding hair loss is a big draw for most cancer patients, and especially young women: no one wants to look “sick.” In this trial, patients, with high hopes of not losing their hair, and for the opportunity to receive a potentially more effective therapy, were randomized 3:1 to the novel treatment arm. Not surprisingly, despite being fully informed about the possibility of randomization to the standard of care arm, patients randomized to the taxol-herceptin arm were disappointed—they were hoping for a better drug, fewer infusions, and a tangible benefit (no hair loss) that they didn’t receive.

Ultimately, I was conservative and opted for a standard (and more aggressive, although not the most aggressive) chemotherapy option, and lost all of my hair. Having been through that trauma and having to walk around that way for far longer than I ever would have imagined, many years later, I followed up on the trajectory of the trial, and learned that it did not meet its primary endpoint of improved safety in the TDM-1 arm, although interestingly, one of the important “clinically relevant toxicity” endpoints—hair loss—was not included as one of the measured adverse events.

PM

I spent the first two months of COVID in Boston with a WBC count averaging 3000 cells/ul, a lymphocyte count averaging 900, and transaminases high enough that I would have been kicked out of a clinical trial of any drug on the basis of hepatotoxicity. The offending drug was probably lomustine/CCNU, although procarbazine was also in play. The reason I had been taking them since October was that the low-grade glioma in my right motor cortex, initially dormant after treatment with temozolamide in 2013–14, was growing again. These treatments, along with the proton radiation therapy I received in 2019, are the only standards of care, and on average they are effective—temporarily. The median survival after diagnosis of a low-grade glioma with a favorable cytogenetic profile is 15 years, with a steady ongoing risk of transformation rather than some period of risk after which one is safe. At some point I am going to need a different treatment. It is of more than academic interest to me for new treatments to be studied, so that another proven approach is available when I need it. I would prefer that companies not be deterred from studying such treatments by the regulatory burden. If I need a treatment that is still in the investigational phase, I would prefer to not have a high risk of randomization to placebo, or to be excluded from the study based on having already received standard-of-care treatment—design elements often included because that is what is most likely to meet FDA requirements with the smallest number of patients.

WBE and PM: Even the Curse of the Billy Goat Will Be Broken

When it comes to serious diseases, patients enroll in clinical trials with the hope of benefit. Pretending otherwise and adding barriers to try to ensure this does not happen is a fool’s errand. Use of placebo controls can avoid immediate psychological distress in addition to bolstering scientific validity for subjective outcomes, but the use of placebos in diseases in which standard care is inadequate is
Table 1

Ethical issues that have arisen in the planning and conduct of our clinical trial.

1. Should we provide approved medications off-label or conduct a trial? Our original plan was to give tocilizumab IV in a sensible manner to very sick patients and be alert for new literature, rather than conducting a trial.

2. How could we maximize the amount of study drug available for the trial? In order to retain as much tocilizumab as possible for IV use, whether in a trial or open-label, one of us (PM) obtained the names of the small number of patients who normally receive tocilizumab IV monthly and contacted the prescribing MDs and asked them to consider switching the patients to self-injected tocilizumab every 1–2 weeks.

3. What was the most ethical trial design? When conceiving a trial design, we wanted to maximize benefit to participants while obtaining scientifically valid information to help future patients. We chose a “randomized play the winner” design with two active arms (tocilizumab and anakinra) and one standard-of-care (SOC) arm.

4. What was the most ethical trial design in the face of drug shortages? As the protocol was being finalized, we learned that neither anakinra nor tocilizumab was available in sufficient quantities to conduct the trial. We rapidly changed the design to a 2-arm trial of sarilumab (an anti-IL-6R antibody similar to tocilizumab) versus SOC. This decision forced us to allocate a larger proportion (50%) of patients to SOC at the start and design a trial similar to many being conducted around the world, rather than asking a novel and important research question.

5. What was the most ethical trial design to open the trial quickly? We chose to use sarilumab in its usual form (200 mg delivered subcutaneously via a pre-filled syringe) so that we would not risk needing to go through the time-consuming process of operating under an Investigational New Drug application (IND) from the FDA. This meant using anti-IL-6R treatment at a lower dose and less-aggressive means of delivery than what had appeared in the anecdotal literature.

6. How should we respond in the face of regulatory barriers that impede research? When one of us (PM) pushed later, based on press-releases rather than scientific publications, to increase the sarilumab dose to 400 mg, the FDA initially refused (6 days after being asked) to grant an IND exemption even though the drug’s manufacturer had trials in progress using that dose, and then assigned us to a pre-IND process that is used to assist developers of new drugs with trial design. We determined for ourselves and then convinced the FDA that this was unnecessary (6 days), then rapidly (within 2 days) submitted an IND, and 14 days later were granted the exemption for which we had argued previously. The study was thus on hold for 28 days while awaiting decisions by the FDA, during which many patients who would have been eligible could not be enrolled. Initially we were averaging almost one enrollment per day. Since re-opening the study, we have not enrolled another patient for 4 months, because the disease has temporarily abated in our region.

7. Why is it important to make trial results available as soon as possible? The two announcements that led to changing the dose in our protocol—one reporting discontinuation of the 200 mg arm in the manufacturer’s own study of sarilumab, and another reporting benefit of IV tocilizumab at a high dose analogous to 400 mg sarilumab—have not yet been followed by publications even in pre-print form. Subsequent announcements by the manufacturers of sarilumab and tocilizumab have reported negative results overall, in studies that included large numbers of intubated patients. The details, not yet available to the community, are relevant because the patient population targeted in our study (requiring oxygen but not mechanical ventilation) has been the one most frequently showing benefit, even if only minor benefit, in studies of other drugs.

8. What expectations do patients, family members, and clinicians have regarding fidelity to a research protocol? During the short time our trial was enrolling, we heard about expressions of disappointment from patients’ family members when the patient was randomized to SOC. Also, our colleagues on several occasions wanted to use a “rescue” dose of sarilumab (which was in the protocol as an option in either group before the protocol was amended to change to a single, higher dose) within 24 hours of randomization to SOC, or to use the small stockpile of IV tocilizumab that was available for use outside the trial.
Table 1 (continued)

Ethical issues that have arisen in the planning and conduct of our clinical trial.

9. How should informed consent be obtained in the face of a pandemic in with PPE is in short supply? We felt it was important to avoid direct interaction with potential subjects if done strictly for research purposes, to avoid risk of infection with SARS-CoV-2 and to conserve PPE for clinical use. This meant that informed consent had to be done by phone one way or another, which we would guess is inferior to doing so in person.

10. Which members of the study team should be available to perform the informed consent process? The informed consent discussion was conducted by phone after a full copy of the form was delivered to the patient (by clinical staff) and legally authorized representative (LAR). The LAR was always off-site, because visitors were not allowed in the hospital. Because the process was laborious and we had other patient-care duties, consent was usually obtained by research nurses on rotation to be available 24/7. Although they know general internal medicine and the study protocol in detail, this process meant that the members of the study team most knowledgeable about the disease (WBE) and the study drug (PM) were not immediately available in the event of detailed questions.

11. How should informed consent for patients lacking decisional capacity be obtained? Most patients were determined informally to be incapable of providing consent. In the case of patients who had been transferred from an inpatient psychiatric facility, the study team made the decision on several occasions to not even approach the patient about participation, based on reports of aggressive behavior and non-compliance with SOC measures such as supplemental oxygen. In the case of patients with dementia, which was typically exacerbated by COVID-19 disease and accompanied by somnolence, consent was obtained from the LAR by phone, without involving the patient significantly in decision-making.

12. How should an agent be allocated when it is in short supply? Separate from the trial, WBE sometimes discouraged colleagues from using the hospital’s limited supply of tocilizumab for patients who were reported to have advanced dementia at baseline, although there were no strict rules and decisions were made on a case-by-case basis with multiple physician review. In addition, clinical guidelines issued by VISN1 (the regional VA administrative unit in which VA Boston lies) and several other local medical centers advised initial use of tocilizumab at lower doses than had been used in China and Italy, due to low availability.

13. What should constitute valid documentation of informed consent? FDA guidance regarding the process and documentation of informed consent were cumbersome and had to clarified over time. The VA Office of Research and Development (ORD), in detailed discussions with the FDA, received clarification that physical evidence of a signature by the patient or LAR on the informed consent form had to be obtained and stored. We had already enrolled all 9 patients by that point, usually with oral consent by the LAR who reported having received and read the ICF and had no further questions. We are concerned, going forward, that placing the LAR in a position of having to return a photo or scanned signature page in a secure manner places undue burden under stressful circumstances and may exclude from participation persons without access to the necessary technologies.

14. Are the usual processes for obtaining and documenting informed consent slowing the progress of research and identification of effective treatments? VA ORD requested and received direct clarification of FDA policy. IRBs at academic institutions have all looked at the FDA guidance and made their own interpretations. We suspect that many institutions allowed the process that we originally followed (delivery of the full ICF to the patient or LAR, a consent process witnessed over the phone by an impartial third-party, and assurance that the patient wished to participate but without a requirement to return a signed form as documentation) and that many trials conducted in the US would not have been completed otherwise or would have excluded patients of low socioeconomic status and/or advanced age. In contrast, the RECOVERY study conducted in the UK explicitly allowed oral consent if written consent could not be obtained by the means required by the FDA [www.recoverytrial.net/for-site-staff/site-teams, www.recoverytrial.net/for-site-staff/site-set-up-1/recovery-trial-faqs-for-study-sites/#identification], and it enrolled 10-fold more patients than any US trial in the same time.
Table 1 (continued)

Ethical issues that have arisen in the planning and conduct of our clinical trial.

15. How can we balance rigor, patient protections, feasibility, and the urgent need to identify effective treatment? The RECOVERY trial is also pragmatic (simple eligibility criteria and outcome measures, no collection of samples for research purposes) and adaptive (data are interpreted after pre-specified numbers of patients have been enrolled), although the absence of a shared electronic health record meant that the study could not be embedded and required completion of electronic case report forms at the sites. The UK’s single National Health Service (NHS) owns the hospitals and employs the physicians and staff, so contracting was simplified and non-negotiable. The list of study staff at the 176 participating hospitals occupies 17 pages in the supplementary appendix of the peer-reviewed paper, funded by a grant of only 2.1-million pounds beyond the substantial core funding already in place to support research infrastructure. During the first phase of RECOVERY, 15% of all eligible patients in the UK were enrolled. The Chief Medical Officers of the NHS are hoping for 60% enrollment now that case numbers and the associated burden on the clinical workforce are lower.

16. What roles do practicality, feasibility, and speed play in the ethics of the conduct of clinical trials? One of the differences between the pre-print of the study of dexamethasone in RECOVERY and its publication after peer-review is that a statement in the discussion about the speed of the conduct and analysis of the study was changed from “just 98 days” to “nearly 100 days.” We presume that a reviewer or editor thought it was important to make this indisputable fact sound less impressive than it is. We are relieved that the statement describing the time between protocol approval to dissemination of results was allowed to remain at all.

also ethically problematic. Rather, we as a medical research community should recognize motivations behind treatment decisions and adjust how we conduct interventional research accordingly.

We will also add: cumbersome and changing recommendations, put in place by people who never have to interact with a patient or treating physician, has made the conduct of our trial nearly impossible. Everyone who could influence the trial from a distance slowed it down. Everyone whom we knew personally or was within one degree of separation was incredibly supportive and helpful. We are extremely grateful to our friends and collaborators on the IRB, R&D leadership, the coordinating center, the pharmacy, and at other VA sites in New England, who worked tirelessly and off-hours in order to bring an option—any option—to our patients. Without them—and without the underlying trust we had all established as members of a group—the study would never have opened.

In the end, in addition to being grateful, we are exhausted, over-saturated with information about SARS-CoV-2, and more than a little bit angry. But we are also motivated to effect change. Advocates of pragmatic trials and learning healthcare systems have been arguing that the need for change, on ethical as well as scientific grounds, is urgent—since at least 2015. Since that time, how many patients have we literally “protected to death”?

2020 started with an email about a new virus that was coming to kill us all, and then has featured thousands of emails related to our efforts to keep that from happening, which brings us to our final question: Can we start 2021 with a different email: “Happy New Year! We have new treatments and a vaccine!”? For decades, the best year in Cubs’ history was “next year.” And then they won.

Author’s Note: This story was submitted in October 2020. Much has happened since then, including that the trial re-opened and is finished, and the US has widespread availability of effective vaccines.

Related Work
Usually, I am a dual trained open and endovascular neurosurgeon. While working at a prominent academic medical center in New York City, my main focus has always been clinical care first. This all changed at the beginning of March 2020, when our city became inundated with patients severely ill with COVID-19. The health system had to restructure to manage the load, and elective surgeries were canceled and stayed canceled for 3 months while we collectively pivoted primarily towards managing the pandemic.

The research that I had done in the past primarily involved large dataset outcome studies for patients with brain aneurysms or acute ischemic stroke. We had a small team of very capable persons who were adept in curating electronic data from electronic health records. At the beginning of March, many of the early reports were coming in of COVID patients suffering major strokes and other neurologic symptoms. In the middle of March, with a large portion of my usual clinical activity suddenly restricted, we jumped into action designing a retrospective-prospective observational cohort study to try to identify which COVID patients were at risk for developing neurologic manifestations. In order to properly conduct this research, our group needed information on all COVID-19 patients presenting to our health care network.

We were one of the first research groups in our system to submit an IRB protocol, and thankfully through the major healthcare restructuring, the IRB stayed open. At the time, our local IRB had given utmost priority to COVID-19 related studies. These submissions were given immediate attention and the turnaround time on approval was quite rapid, particularly as it pertained to non-interventional observational studies. The rapidity of our approval gave us a head start and access to invaluable resources within our data warehouse group, which was able to ping us all the patients we were investigating with COVID-19. Probably about a week or two after starting, access to this data became restricted as nearly every research group in the system was having similar ideas. There were also growing institutional concerns about the public health message they were trying to portray, layered with the fear that outcomes in certain areas of New York City appeared worse than others. No one wanted to be considered the system that was doing a bad job managing the pandemic or their patients.

In tandem, it became apparent that many other clinician researchers wanted access to similar information. A counterpart in the Department of Neurology and I teamed up to create a research network of interested researchers who wanted to have access to information on COVID-19 patients. We were able to use Microsoft Teams as a centralized hub to help create networks of research groups for parties with similarly aligned research interests while also preventing overlapping research ideas. We could assign roles within specific projects and defuse any potential squabbles about authorship. As researchers expressed interest, we were able to easily addend our IRB to add additional team members with nearly same-day feedback. By the end of the project, there were over 50 researchers involved with various observational projects with clinician researchers looking at a variety of topics including COVID and ischemic stroke, COVID and hemorrhagic stroke, COVID and epilepsy, COVID and encephalopathy, COVID and race/ethnicity, and COVID and neuromuscular disease. While Teams was the hub for our centralized research machine, it was important to keep it maintained and protected and to ensure no patient information was placed in the group. This, in addition to managing the projects and making sure everyone who wanted