COVID-19

The Fine Balance: Adapting Clinical Research Into COVID-19 Response

Nicholas J. Giordano, MA[1], Naomi Alanis, MS, MBA[2], Jennifer A. Frey, PhD[3], Grace L. Hall, MS[4], and Wendy C. Coates, MD[5]

Quality clinical research remains a high priority during the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) coronavirus disease (COVID-19) pandemic response; however, the logistic barriers of conducting research across institutions with differing departmental policy responses and varying resources is a documented problem.[1,2] The COVID-19 pandemic has resulted in a surge of more than 1,000 newly formed clinical trials registered on clinical trials.gov with "COVID-19" in their study title as of May 8, 2020. While the need for new and innovative research remains high, traditional operations to support the execution of these studies must rapidly evolve to overcome the newly formed barriers of clinical research.[3] Most notably, reserves of personal protective equipment (PPE) dwindled and have forced hospitals to reevaluate the distribution of these supplies in an effort to conserve resources and minimize waste. Due to the lack of PPE, the logistics of screening and consenting patients in the emergency department (ED) must be revised while continuing to make safety of colleagues, patients, and the general public a main priority. Best practices need to be established to adapt clinical research into the rapidly changing environment of the COVID-19 response.

As the pandemic continues, new recommendations for conducting research have been made by the National Institutes of Health (NIH) and the U.S. Food and Drug Administration (FDA) for the COVID-19 public health emergency. These recommendations suggest that all ongoing studies during the COVID-19 pandemic should incorporate procedures that are compliant with regional management policies for controlling the spread of the disease; however, the logistics of executing that research is left to individual institutions.[4,5] We are hesitant to provide specific examples of studies relevant to emergency medicine that should be conducted during the COVID-19 pandemic due to the context-dependent issues across institutions and for fear that while an example might be suitable in one setting, it may be deemed inappropriate in another. Some variables such as the seriousness of the disease, investigational product supply, and whether there are reasonable alternative treatments will be relatively consistent across institutions, but other variables such as viability, available resources, and the ability to safely administer an interventional product might vary widely across sites. Instead, we want to detail who should be judging the criteria to continue research so that individual institutions can make an informed decision that best suits their specific scenario. The FDA has recommended that sponsors, in consultation with clinical investigators and institutional review boards/independent ethics committees, judge whether a study should be open to enrollment during the pandemic.[4]

Ongoing clinical trials raise an additional area of concern during pandemic response. Although there is

From the [1]Department of Emergency Medicine, Harvard Medical School, Massachusetts General Hospital, Boston, MA; the [2]Department of Emergency Medicine, Integrative Emergency Services, TCU and UNTHSC School of Medicine, Fort Worth, TX; the [3]Department of Emergency Medicine, The Ohio State University, Columbus, OH; the [4]Divisions of Trauma and Emergency Medicine, Department of Surgery, Duke University School of Medicine, Durham, NC; and the [5]Department of Emergency Medicine, Los Angeles David Geffen School of Medicine, University of California, Los Angeles, CA.
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Supervising Editor: Christopher R. Carpenter, MD.
Address for correspondence and reprints: Nicholas J Giordano, MA; e-mail: ngiordano@mgh.harvard.edu.
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some guidance from local and national organizations, the assessment of an appropriate response weighing ethical principles, staffing constraints, risk to participants, and ultimately the course of action to take resides on the principal investigator and the institutional review board.[4,5] It is widely believed that critical clinical care research during a pandemic must have a different approach than during nonemergent circumstances.[6] Logistic adaptations to mitigate risk for patients, health care workers, and the general public are paramount for fostering an environment for clinical research to continue during a pandemic. A review of the literature through PubMed using the search terms "COVID-19 research guidelines" and "COVID-19 research best practices" did not produce any guidelines or best practices pertaining to navigating the logistic barriers that emergency medicine (EM) research faces during the COVID-19 response.

Reevaluating how research is conducted in the ED and redefining clinical research operations has been necessary. Our objective was to evaluate the essential elements needed to keep clinical research operations open and active to enrollment and then systematically determine how research teams could immediately adapt these elements to the current pandemic environment while still maintaining safety measures for our workers, patients, colleagues, and families. The term "essential elements" was defined by our working group as the necessary measures that needed to be taken to conduct vital research operations. While financial support is a critical and a core component of research logistics, it was decided that funding was a byproduct of research enrollment and that defining safety measures for staff, colleagues, and patients should take priority; however, we acknowledge that in the long-term funding issues must be addressed to maintain research viability.

The Clinical Researchers' United Exchange (CRUX) is an innovative national interest group affiliated with the Society for Academic Emergency Medicine (SAEM) established in 2018. Participation is open to all SAEM members, but was designed specifically to engage nonclinical research staff in the execution of research within EM. On April 22, 2020, the group convened an emergency meeting to discuss operational logistics and share best practices related to staffing, screening, enrolling, and processing of biospecimens during the COVID-19 pandemic. A CRUX chair moderated the session in which each topic was addressed systematically, while providing members a platform to share their institutions' newly adapted procedures and concerns. Following each section, members were able to discuss best practices for each topic. Comments were recorded and subsequently circulated among CRUX members to confirm consensus. Responses were reviewed and collated into recommendations that are summarized by Figure 1.

Staffing for clinical research projects during the pandemic was one of the largest barriers to research we identified. Variables such as personal heath and living situations came to the forefront of staffing discussions as comfort levels and continuation of job duties for nonclinical research staff was evaluated. The group identified that these types of difficult conversations were best fostered by creating the environment for managing up. This was accomplished by informing teams of what tasks need to be done and allowing them to volunteer for roles that they feel comfortable executing. It was suggested that those who do not fit into the current needs of the department be transferred into institutional labor pools to fill new or vacant roles. Members on the call described filling emerging roles in newly adapted research studies with furloughed non-EM health care providers. Those who were interested received research training to support ongoing clinical studies with their clinical skill sets. The CRUX discussion group identified that even when staffing needs are met, a hand-off strategy should be developed with standard operating procedures to ensure that the experiences of newly adapted roles are passed on through the anticipated summer turnover of staff leaving the department. Additionally, many institutions have undergone hiring freezes, and once the immediate needs of critical research studies have been met, efforts should be shifted toward reestablishing paused studies in a timely manner.

Screening procedures of patients who met criteria for ongoing clinical studies were impacted by institutional restrictions. At some hospitals, nonclinical research staff were not allowed in the ED and limited to electronic medical record review studies. For institutions that did allow research staff into the ED, virtual study screening through electronic medical chart review or analyzing electronic screening surveys via tablets in patient rooms were recommended as remote alternatives to in-person discussions for determining study eligibility. Action at a distance may continue to be the new normal for clinical researchers in the time of COVID-19.[7]

Study enrollment procedures required the greatest number of modifications during the pandemic

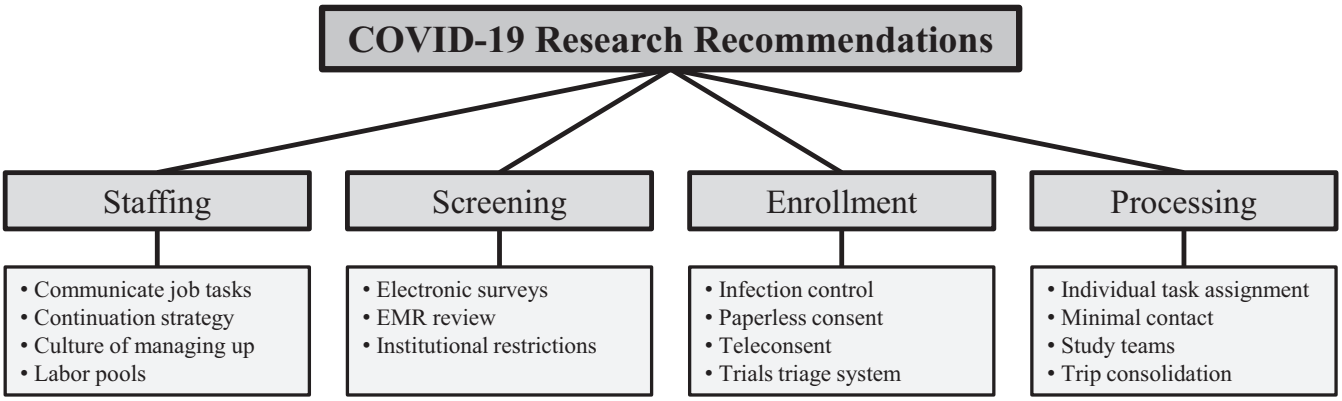

Figure 1. A summary of the CRUX recommendations for research during the COVID-19 pandemic. CRUX = Clinical Researchers' United Exchange.

response. Institutions with many COVID-19 research studies should incorporate a COVID trials' triage system, which could be as simple as a phone number to call at time of screening, staffed by a clinical research professional versed in all the ongoing research studies in the ED. The triage system can act as a central processing unit for identifying which research study would be most beneficial for the patient, the institution and the pursuit of knowledge. To save PPE and reduce the number of people exposed to COVID-19, all institutions should consider implementing telemedicine devices, whether it be a tablet, smartphone, or a landline telephone to gauge a patient's interest in participating in a research study without making physical entrance into the room. Some institutions reported utilizing research physicians who are working clinically to conduct discussions of consent; while this is convenient and can minimize excess contact with a patient, it is not sustainable as research efforts grow. Teleconsent was found to be most well received at hospitals that already have telemed services integrated into their current standard of care.[8] Paperless enrollment is recommended, but when not possible, the recommendation to use disposable pens, sterilize clipboards, and minimize entrances into the patient room were cited as strategies that could aid in infection control. Where appropriate, instead of leaving to make a photo copy of a signed consent form, consider holding the document up to the window and having a colleague taking a photo using a HIPAA-compliant device to document consent. If the paper consent form must be removed from a patient's room, do so in a sealed bag that could be decontaminated upon exit.

Procedures for processing biospecimen samples and study data needed to adapt to newfound recommendations of social distancing for COVID-19. At the consequence of cross-functional training, larger institutions with multiple people working per shift should look to have individual task assignments with the same employees working together during shifts (i.e., team A or B). Staff working in the ED should have minimal movement throughout the hospital and should be limited to duties within the ED. Administrative tasks or laboratory processing should ideally be done by another team member. Coordination of necessary work among teams should be done to minimize entry or egress to parts of the hospital as well as the individual patient rooms. Trip consolidation should be applied where enrollment windows permit. Contact with one another when not necessary (i.e., biospecimen sample handoff) should be replaced with a designated, safe location drop-off. Communication of staff location should be maintained throughout the workday to minimize staff cohorting in laboratory or office settings.

With the outbreak of COVID-19, we have seen unprecedented changes, innovation, and reevaluation of our health care system. During these tumultuous times, one thing that remains steadfast is that health care workers in the ED continue to do what they do best—adapting and overcoming any situation that presents itself. Some things will be forever changed by this pandemic, but the innovations and reevaluations of workplace efficiencies and operational logistics can propel us to the next level of innovative care for the future. We advocate that every institution have an open discussion of their essential research operations and use some of the recommendations presented here to find a revised, innovative solution to the challenges presented by COVID-19 that best suit their research endeavors.

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