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Clinical Research after COVID-19: Embracing a New Normal



Joel M. Gelfand^{1,2} and Brooke E. Hefele¹

The coronavirus disease 2019 (COVID-19) pandemic is a grave public health crisis, causing massive disruption to daily life. Dermatology clinical trials in psoriasis, atopic dermatitis, and hidradenitis have been suspended, terminated, or otherwise disrupted. Clinical investigators need to embrace a COVID-19 new normal and adjust research procedures to mitigate the risk of transmitting severe acute respiratory syndrome coronavirus 2 and depleting personal protective equipment while maintaining scientific rigor.

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The coronavirus disease 2019 pandemic: A grave public health crisis disrupting daily life activities

The coronavirus disease (COVID-19) pandemic is the gravest public health crisis facing the world in over 100 years (Gates, 2020). Pandemics result in disruptions of daily life activities for everyone. Clinical researchers certainly are not immune to disruptions in activities that include shaking the hand of a coworker for a job well done; sending our children to school or daycare; greeting a patient in a crowded waiting room; carefully explaining the risks, benefits, and alternatives of consenting to participate to a potential study subject in a cramped examination room; helping a study participant complete their surveys and handing them their medication; and having timely access to medical evaluation and procedures.

Desai et al. (2020) shed light on the early impact COVID-19 has had on clinical research in dermatology. They queried [ClinicalTrials.gov](https://www.clinicaltrials.gov) for the months of April 2019 through the end of May 2020 to evaluate the status of interventional trials in dermatology. The investigators identified 1,010 active (not recruiting), recruiting, and enrolling by invitation trials for dermatological conditions, with estimated

enrollments of 284,881 patients. They found that 92 of 1,010 (9.1%) of ongoing dermatology-related clinical trials were suspended, withdrawn, or terminated during this time period. Over half of the suspensions, terminations, and withdrawals occurred in March, April, and May of 2020 ($n = 57$ of 92, 62%), with estimated enrollments of 7,141 patients. There were 17, 21, and 7 excess dermatology trial suspensions, terminations, and withdrawals that occurred in March, April, and May of 2020 in comparison with March, April, and May of 2019, respectively. Among affected trials, 5,607 patients (79%) were enrolled in 32 trials (56%) listed as suspended specifically because of the COVID-19 pandemic. The most common COVID-19 trial suspensions were for atopic dermatitis ($n = 7$), psoriasis ($n = 7$), and hidradenitis suppurativa ($n = 5$). A substantial percentage (44%, 14 of 32) of the COVID-19-affected trials had estimated enrollments greater than 100 patients. Most (63%, 20 of 32) of COVID-19-affected trials were phase 2 and 3 trials (Desai et al., 2020). It is worth noting that phase 1 trials do not have the same reporting requirements and, therefore, the disruption in this stage of research may not have been

captured (U.S. Food and Drug Administration, 2020).

Evaluation of data from [ClinicalTrials.gov](https://www.clinicaltrials.gov) demonstrates COVID-19 disruption of dermatology-related clinical trial

Although the efforts of Desai et al. (2020) are laudable, they have described just the tip of the iceberg of the massive impact the pandemic has had on the clinical research community. [ClinicalTrials.gov](https://www.clinicaltrials.gov) reporting is notoriously delayed and incomplete (Anderson et al., 2015). Moreover, studies could technically be active and open to recruitment but for all practical purposes have enrollment suspended, which would not require reporting to [ClinicalTrials.gov](https://www.clinicaltrials.gov). This later scenario is exactly what we experienced in March 2020.

We are the principal investigator (JMG) and lead coordinator (BEH) of the Light Treatment Effectiveness (LITE) study, which is the largest academic dermatology lead interventional trial for the treatment of skin disease conducted in the United States to date (NCT03726489). LITE is a pragmatic noninferiority trial of 1,050 patients randomized to home versus office phototherapy in patients 12 or older with plaque or guttate psoriasis at approximately 35 sites across the United States.

A case example provides deeper insight and solutions to COVID-19 disruption of clinical trials in dermatology

Before the COVID-19 shutdowns, the LITE study had 30 active sites and was enrolling 30 patients per month. On 12 March 2020, sites began to report COVID-19-related closures, with peak site suspensions on 20 April 2020 ($n = 26$ of 30, 87%). Four sites remained open for enrollment (and thus no changes were made to the study status on [ClinicalTrials.gov](https://www.clinicaltrials.gov)) but saw no new recruitment during this time. Clinical volumes dropped dramatically, and many patients who preferred phototherapy for the management of psoriasis expressed concern over coming in for visits, either because of their own health or the health of family members. In some cases, patients who were in screening before the pandemic declined to be randomized once the pandemic hit because they were afraid

¹Department of Dermatology, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, USA; and ²Department of Biostatistics, Epidemiology, and Informatics, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, USA

Correspondence: Joel M. Gelfand, Department of Dermatology, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, USA. E-mail: Joel.Gelfand@penncmedicine.upenn.edu

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Clinical Implications

- Analysis of [ClinicalTrials.gov](https://clinicaltrials.gov) data and a detailed case example from the Light Treatment Effectiveness study demonstrates major disruption of dermatology-related clinical trials because of coronavirus disease 2019 (COVID-19).
- Clinical researchers must embrace a COVID-19 new normal, breaking down ordinary functions into principal components to determine which are truly essential while engineering solutions that lower the risk of severe acute respiratory syndrome coronavirus 2 transmission and relieve the burden on personal protective equipment, which is in short supply, all while maintaining scientific rigor.

phototherapy treatment closures. During the suspensions, enrolled patients (n = 149) remained active, and they were followed via telemedicine and through the collection of patient-reported outcomes on their mobile application, regardless of whether or not they continued to receive in office phototherapy per standard of care for site closures.

Clinical researchers must embrace a COVID-19 new normal, breaking down ordinary functions into principal components to determine which are truly essential

The pandemic made us rethink how we execute clinical research (Table 1). First, we accounted for all points of face-to-face contact in the prior

to come to the office for phototherapy and withdrew consent to pursue home phototherapy outside of the trial. During March, April, and May 2020, nine sites reported institutional holds on all non-COVID-19 research, six reported

reduced staffing including furloughs, three indicated state-level limitations, one site was forced to close pending staff quarantine after a COVID-19 exposure in clinic, and most (n = 25) reported temporary clinic or office

Table 1. Proposed Solutions for COVID-19–Related Barriers to Clinical Research

COVID-19–Related Barrier to Clinical Research	Proposed Solutions
Risk of COVID-19 transmission	<p>Reduce need for in-person or face-to-face contact:</p> <ul style="list-style-type: none"> • Virtual informed consent process with approved platforms such as DocuSign, REDCap • Collection of patient-reported outcomes via cell phone–based applications or survey links through e-mail or text message <ul style="list-style-type: none"> • Assessment of physician-reported endpoints via telemedicine when possible <ul style="list-style-type: none"> • Dispense study medications by mail <p>For patients who must be seen in person:</p> <ul style="list-style-type: none"> • Schedule in staggered manner to allow extra time to sanitize rooms, avoid patients having to congregate in a waiting area • Take history via the office phone system from a separate room to reduce face-to-face time and thus lower the risk of aerosol or droplet transmission • Universal use of masks, consideration of face shields, eye protection, meticulous hand sanitizing <ul style="list-style-type: none"> • Point-of-care COVID-19 testing if feasible • Eliminate the need for coordinators to be in clinic, executing their tasks remotely
Research staff furloughed or laid off	Utilize centralized coordinators to support understaffed teams at local study sites while ensuring the informed consent process addresses privacy concerns
Accurate remote physician assessments	<ul style="list-style-type: none"> • Use a hybrid method of store and forward and live videoconferencing and follow best practice guidelines: https://www.aad.org/member/practice/telederm/toolkit • Provide patients guides to photographing skin for televisits: https://static.skindsight.com/Photo-Guide-for-Teledermatology.pdf?mtime=20200413103122
Collection of physical samples, that is, blood draws	<ul style="list-style-type: none"> • Embed or align with standard-of-care visits as much as possible <ul style="list-style-type: none"> • Utilize in-home or traveling phlebotomy services
Administrative barriers, IRB delays, institutional restrictions	<ul style="list-style-type: none"> • Prioritize studies for continuation, consider each study’s ability to adapt to COVID-19 conditions <ul style="list-style-type: none"> • Address institutional regulations by working with IRB and understanding potential exemptions for deviations • Document impacts of COVID-19 on data collection and study execution to allow for post hoc analyses

Abbreviations: COVID-19, coronavirus disease 2019; IRB, Institutional Review Board.

workflow and transitioned coordinator responsibilities to function remotely, thus eliminating the need for them to be in clinic. Second, the LITE study is somewhat unique in dermatology because it is a pragmatic (real world) study that is embedded in routine clinical care (Hefelee et al., 2019; Loudon et al., 2015). Therefore, when tele-dermatology suddenly became a widely accepted standard of care that was reimbursed by insurance, we were able to pivot to collecting physician-reported endpoints through telemedicine visits (Gupta et al., 2020). These adaptations allowed us to reduce risk of transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) while preserving limited personal protective equipment (PPE). The most challenging research procedure to implement after the pandemic was allowing for a robust informed consent process to occur in a virtual environment. To address this, we developed a new supplemental electronic consent through REDCap (<https://www.project-redcap.org/>) that is emailed to the patient and reviewed via phone call or videoconference. After a standard-of-care visit with the physician, either in person or through teledermatology, a patient could sign the informed consent form from their home and immediately complete baseline activities with the coordinator who signs and

enters data into the study application on their end, maintaining no points of face-to-face contact. This adaptation allowed us to enroll our first new patient entirely remotely (the patient, coordinator, and physician investigator were all at home with no in-person contact in the clinical setting) after the onset of the pandemic-related site closures on 4 May 2020, initiating a new phase of recruitment for the LITE study.

We are all now living in a post-COVID-19 new normal. The pandemic demands that we break down ordinary functions into their principal components and determine which tasks are truly essential and thus justify the risk of spreading the virus and the use of PPE, which is in short supply, versus those which can be reengineered to eliminate the risk of spreading SARS-CoV-2 to our patients, staff, colleagues, and their families and communities while preserving scientific rigor that we must maintain to advance the cause of medicine and the care of our patients (Ranney et al., 2020).

ORCID*s*

Joel M. Gelfand: <http://orcid.org/0000-0003-3480-2661>

Brooke E. Hefelee: <http://orcid.org/0000-0001-8789-5377>

CONFLICT OF INTEREST

The authors state no conflict of interest.

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