Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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THE CONDUCT OF CLINICAL TRIALS

Clinical Research in the Time of COVID-19

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I am writing about what I know—clinical trials. That said, I think you could substitute "clinical practice" anywhere you see "research" or "clinical trials" in this essay.

The COVID-19 pandemic is unprecedented. Our response to it is rapidly evolving as we learn more about the pathophysiology of this virus, how to mitigate its effects on public health, and our ability to adjust to new cultural norms. Ultimately, a new normal will be established, and this pandemic, in its acute form, will end.

But cancers will remain. Necessary cancer treatments, such as radiation, will remain. The need for clinical trials, the improved treatments they elucidate, and the US Food and Drug Administration (FDA) approval providing public access to these new and better treatments will remain. The pandemic does not end medical research, and it may, in fact, point us in a new and better direction for implementing clinical trials.

Research is an important aspect of any academic institution. Research productivity is a cornerstone of faculty advancement and promotion. This pandemic has already had a huge human and economic toll, globally stopping us in our tracks. It has greatly affected medicine in general, and disrupted new and ongoing clinical trials, prompting the FDA in mid-March to issue new guidance for industry, investigators, and institutional review boards.[1] Academic institutions will do robust research again, and those institutions most prepared to pick up research at pre-pandemic levels will be those that follow FDA guidelines to facilitate and continue running clinical trials even during the spread of COVID-19.

Medical research necessitates collecting large amounts of clinical and other data over a long period of time to determine the safety and efficacy of a given regimen. A whitepaper published in March 2020 by Science 37, a pioneer in virtual clinical trials, estimates that there are currently more than "40,000 ongoing clinical trials made up of thousands of trial sites, tens of thousands of investigators and hundreds of thousands of study subjects."[2] Furthermore, billions of dollars are invested into these trials, which are critical for bringing new and improved treatments to the public. Thus, there is a real need for continuity in medical research.

Until an effective vaccine for COVID-19 is established, consider that we will likely need to keep in place new social norms such as social distancing and wearing masks. Packed clinics and crowded boardrooms will be out of the question. We will also need to consider the psychological effects—the fear this virus creates—on our staff and especially our patients. So, how do we run clinical trials in the time of COVID-19?

The model for doing this can be taken piecewise from the clinical trials network model that we have been building over the last 2 years in the UCLA Department of Radiation Oncology. Our network demands the ability to remotely conduct and monitor research at participating sites for any specific protocol. To do this virtual or remote research, we need a system that can provide the following[1,3]:

1. Continuity of study visits, virtual or otherwise
2. Patient and investigator/study team connection in real time
3. On-demand telemedicine
4. Investigational product tracking
5. Electronic consenting

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6. Electronic patient-reported outcomes (frequently in the form of questionnaires)

7. Electronic clinical research folders

8. Adverse event and serious adverse event reporting in real time

9. Remote safety oversight (progress reports, monitoring, auditing)

10. Congruent data collection across participating institutions

These virtual research methods combined with mobile phlebotomy services and, when feasible, shipment of supplies directly to patients, make research accessible in the time of COVID-19 and may be better for patients as well. Often, research participants are difficult to recruit into trials, citing the inconvenience of coming to UCLA for multiple visits. Research participants who do consent to participate in trials frequently note the commute time, traffic, costs of parking, and inconvenience of coming to Westwood. Due to this pandemic, many patients fear (with good reason) coming in at all. Research participants, especially those who live further away or even in other states, regularly ask if they can do research procedures near their homes.

In creating our nascent network, we have started to implement many of the tools necessary for virtual research, but there is more to do. For the last year, we have been working with UCLA's Jonsson Comprehensive Cancer Center, investigating essential clinical trials management systems that we hope will be rolled out in the near future. COVID-19 certainly ramps up the demand for it. In addition to having this clinical trials management system for running remote and multisite clinical trials, changes will likely need to be made at a higher level: in staffing.

Adaptation is the key to success in any evolution. Although going back to where we were might seem most comfortable, it should not be the goal. New, smarter, more efficient, more cost-effective, and cleaner solutions will be the way forward. Implementing virtual visits and staggering work schedules so that fewer people are in the workplace at any given time seem like obvious solutions as a way to some normalcy. On May 11, Uri Alon and Ron Milo, both professors of computational and systems biology at the Wiezmann Institute of Science in Israel, collaborated with Eran Yashiv, a professor of economics at Tel Aviv University and the London School of Economics, to write a compelling piece for *The New York Times* entitled "10-4: How to Reopen the Economy by Exploiting the Coronavirus's Weak Spot."[4] The virus's weak spot in the title refers to is its latency period—on average, there is a 3-day delay from when a person is first infected to the time that person can infect others. These authors suggest

1. splitting staff into 2 working groups that alternate shifts; and

2. working in 2-week cycles of at work for 4 days and remote work from home for 10 days.

As transmission rates drop or increase, the balance of at-work days and at-home days can be adjusted. The benefits of implementing this model include the following:

1. It predicts the viral contractibility score will reduce to $R_0 < 1$.

2. It reduces the number of staff in the department at any given time, making social distancing easier and curtailing transmission.

3. It allows sustainable clinical and economic activity.

The model works regardless of the accessibility or even accuracy of testing. It is based simply on what we know about the virus' latency period and on social distancing and stay-at-home measures that have proven efficacy.

A more hidden benefit is that this model prevents the economic and psychological costs that would be inevitable if research, or any business for that matter, had to regularly reinstate and then shut down every time COVID-19 cases resurged.

This viral pandemic is daunting, but there is a way forward. Until a vaccine is developed, and likely even after that if COVID-19 becomes a seasonal norm, we will have to weigh the risks and benefits of everything we do, including medical visits and research appointments. However, the risk can be mitigated. Intelligent staff scheduling that takes into consideration what we know about the virus' transmission, combined with virtual research and clinical capabilities, at least in part gives us a path for conducting clinical trials—and perhaps medicine in general—through this health, economic, and social crisis.

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