The Enduring Impact of COVID-19 on Current and Future Clinical Trials

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The authors conducted a web survey in June 2020 to assess the impact of COVID-19 on clinical research and the clinical research community. Of the 149 respondents that completed the survey, 82 (55%) were from 51 clinical research sites, 25 (17%) were from 11 pharmaceutical and biotechnology companies, and 42 (28%) were from 16 contract research organizations (CROs). Most respondents were based in the United States. (See Figure 1 below.)

Over 80% of respondents were employed at the same organization they worked for in January of this year.

Results

Major findings of the survey include answers to the following three questions:

What are the top five challenging obstacles that the clinical trial community has encountered or expects to encounter in a COVID-19 study?

Over 60% of respondents from all the sectors of the industry said that COVID-19 testing accuracy and logistics and patient fear and anxiety are among the top-five challenging obstacles. (See Figure 2 below.)

About 50% of respondents stated that protocol design complexity, too many competitive COVID-19 studies, and lack of personal protection equipment are among the top-five challenging obstacles.

About 30% of respondents said that selecting the right endpoints, validity of patient reported outcomes, limiting inclusion and exclusion criteria, and lack of patient interest in completion of study are among the top-five challenging obstacles.

Less than 6% of respondents said that rushed processes and increased documentation, low incidence of COVID-19, site staff availability and safety concerns, patient transport to the clinical site, cumbersome startup phase, or SAE Reporting are among the top-five challenging obstacles.

How can the clinical and regulatory communities better gear up for a possible second wave of COVID-19 in Fall 2020?

Many respondents considered a Fall/Winter COVID-19 wave as a given. They provided many suggestions to proactively mitigate some of the risks.

The top two recommendations are using the lessons learned from the first round and creating contingency plans that consider closure of clinical research sites.

Respondents from sites wanted clear regulatory guidelines on what is and is not permissible based on the pandemic status of each site.

Most respondents wanted protocols to be updated to allow virtual/telemedicine visits, online questionnaires, personal protective equipment management and use, and access to on-site rapid COVID-19 testing.

Respondents made the following recommendations for protecting the health of site personnel and patients:

- Ensure a safe environment before and after contact between a patient and staff member.
- Tell patients in advance of a visit what to expect.
- In case of coronavirus exposure, employ a hazmat-certified cleaning crew funded by the study sponsor.
- Track staff/patient contacts during visits for subsequent tracing if needed.
- Making protections visible to staff and patients.
- Use "Now Serving" tickets to limit the number of patients in the waiting area and ensure adequate distancing.

Respondents also made the following recommendations:

- Update risk sections in the protocol and consent form.
- Increase compensation for patients.
- Accelerate protocol amendments to allow use of digital technologies.
- Accelerate IRB approvals of protocol amendments.
- Conduct virtual site qualification, monitoring and closeout visits.
- Work more closely with community groups, patient influencers, patient advocates, and the physicians and principal investigators that serve racial and ethnic minority populations to accelerate enrollment
- Develop alternative methods for distribution and return of investigational product.

What are the top five lasting changes to clinical trial design and conduct as the result of COVID-19?

Eighty-four percent of respondents said that a top-five lasting change would be the adoption of alternative methods for study assessments. (See Figure 3 below.)

Seventy-three percent of respondents said that a top-five lasting change would be more home/virtual visits (73% of respondents).

Forty-seven percent of respondents said that a top-five lasting change would be closer collaboration among research sponsors, research sites, and regulatory bodies.

Twenty-eight percent of respondents said that a top-five lasting change would be increased public interest in study participation, while another 28% said the opposite.

Twelve percent of respondents said that a top-five lasting change would be higher clinical research costs.

Over 75% of executives and functional directors said that fewer study visits and more home visits and the adoption of alternative study methods would be top-five lasting changes.

Many respondents predicted the following long-term changes:

- General acceptance of e-tools by sites and remote monitoring
- Greater public recognition of clinical study participation as a civic duty
- Longer visit times to allow for decontamination
- A permanent shift to more remote work by site personnel
- Sponsor preference for sites that allow off-site access to source documents (remote EMR access)

- Sponsor sensitivity to local COVID-19 incidence in selecting sites for both COVID-19 and non-COVID-19 studies
- Faster IRB and other regulatory review processes

Other Findings

Quantitative and qualitative data collected in the survey support the following additional findings:

- Survey respondents from all three industry sectors— sites, sponsors and CROs — had generally consistent views on COVID-19 effects, challenges and long-term solutions, although sites, as usual, expressed more interest in support from sponsors and CROs than the other way around.
- Respondents generally agreed that the COVID-19 pandemic would drive long-term adoption of technology and processes that support virtual and decentralized studies.
- Respondents were essentially equally divided on whether the COVID-19 pandemic would increase, decrease or leave unchanged public interest in study participation.
- Respondents in U.S. states, such as Texas, Arizona, Florida and North Carolina, that were relatively unaffected by COVID-19 at the time of the study were less concerned about its impact than respondents in states that were highly affected. A survey today would likely show less of a difference.
- Site respondents expressed frustration with the lack of detail and inconsistency in COVID-19 guidance they were receiving from sponsors, CROs, and governmental agencies. They would like this issue to be addressed before a new COVID-19 wave occurs.
- Site respondents would have liked paused studies to restart more quickly with updated protocols and processes (which may indicate a lack of understanding of the work required to do so by sponsors and CROs).
- Respondents were making detailed contingency plans for a possible second COVID-19 wave in the coming fall/winter. However, a new wave has occurred already.
- Respondents recognized the opportunity to leverage public awareness of the importance of clinical research but expressed concern that safety concerns, confusing information, and fragmented public education would dilute or more than offset the opportunity, especially in disadvantaged populations, which were under-represented before the pandemic.

Conclusion

The COVID-19 pandemic has disrupted much ongoing clinical research, severely testing the viability of many study sponsors, CROs and investigational sites.[1,2] The clinical research enterprise has quickly diverted immense resources to numerous new studies related to COVID-19, with very uncertain financial or public health implications. Even with a possible upswell of public interest in study participation, many of the new studies will likely fail to enroll enough participants to generate statistically significant findings. In the midst of these dramatic developments, the clinical research enterprise — not known for its aggressive attitude to innovation — is also rapidly deploying technologies, instituting safety measures, and adapting processes to make clinical research even possible during a pandemic.

The survey findings above reveal a general consensus on the many steps the clinical research enterprise can take to deal with the COVID-19 pandemic and reinvent itself to be more resilient going forward. The clinical research enterprise is shining brightly in the

current emergency, but will its efforts pay off in effective tests, treatments and vaccines? And, can it maintain the current rapid pace of innovation once the crisis has passed?

References

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2. Improving Clinical Trial Enrollment - In the COVID-19 Era and Beyond, Crystal M. North, Michael L. Dougan, Chana A. Sacks, 16 July 2020; https://www.nejm.org/doi/pdf/10.1056/NEJMp2019989?articleTools=true

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Figure 1. Locations of United States respondents

Figure 2. Top-Five Most Challenging Obstacles Encountered or Expected to Be Encountered in a COVID Study (% of Respondents)

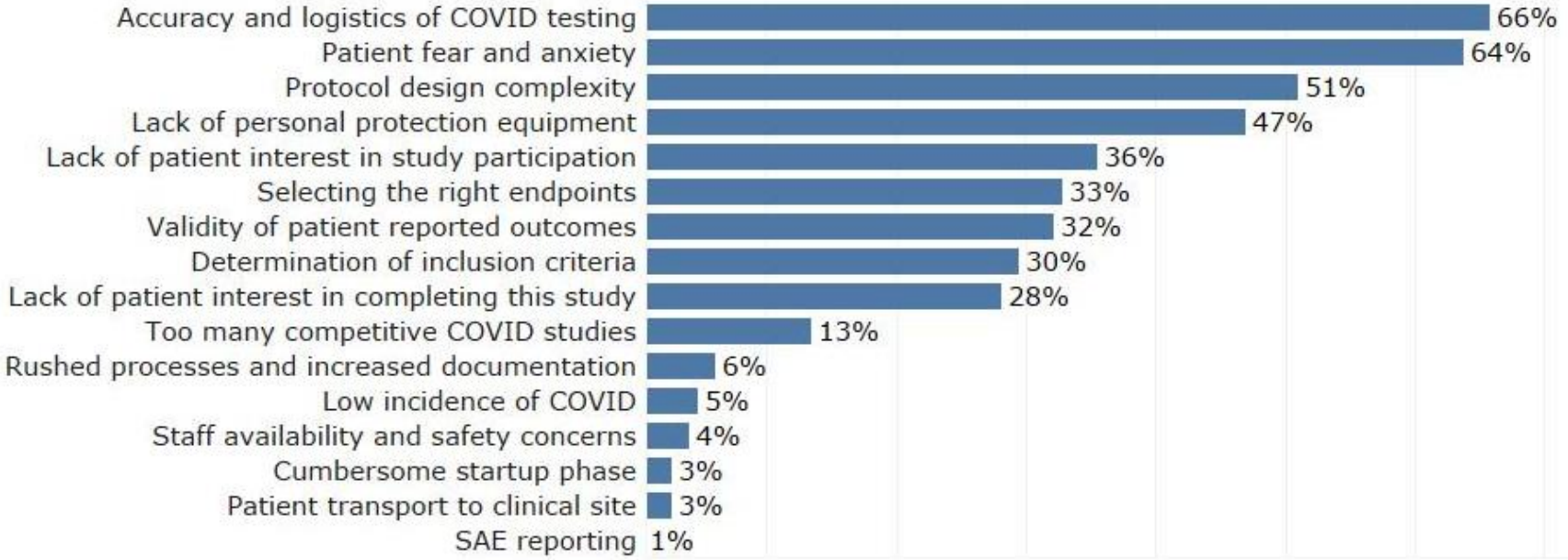

Figure 3. Top-Five Lasting Changes to Clinical Trial Design and Conduct Resulting From COVID-19 (% of Respondents)