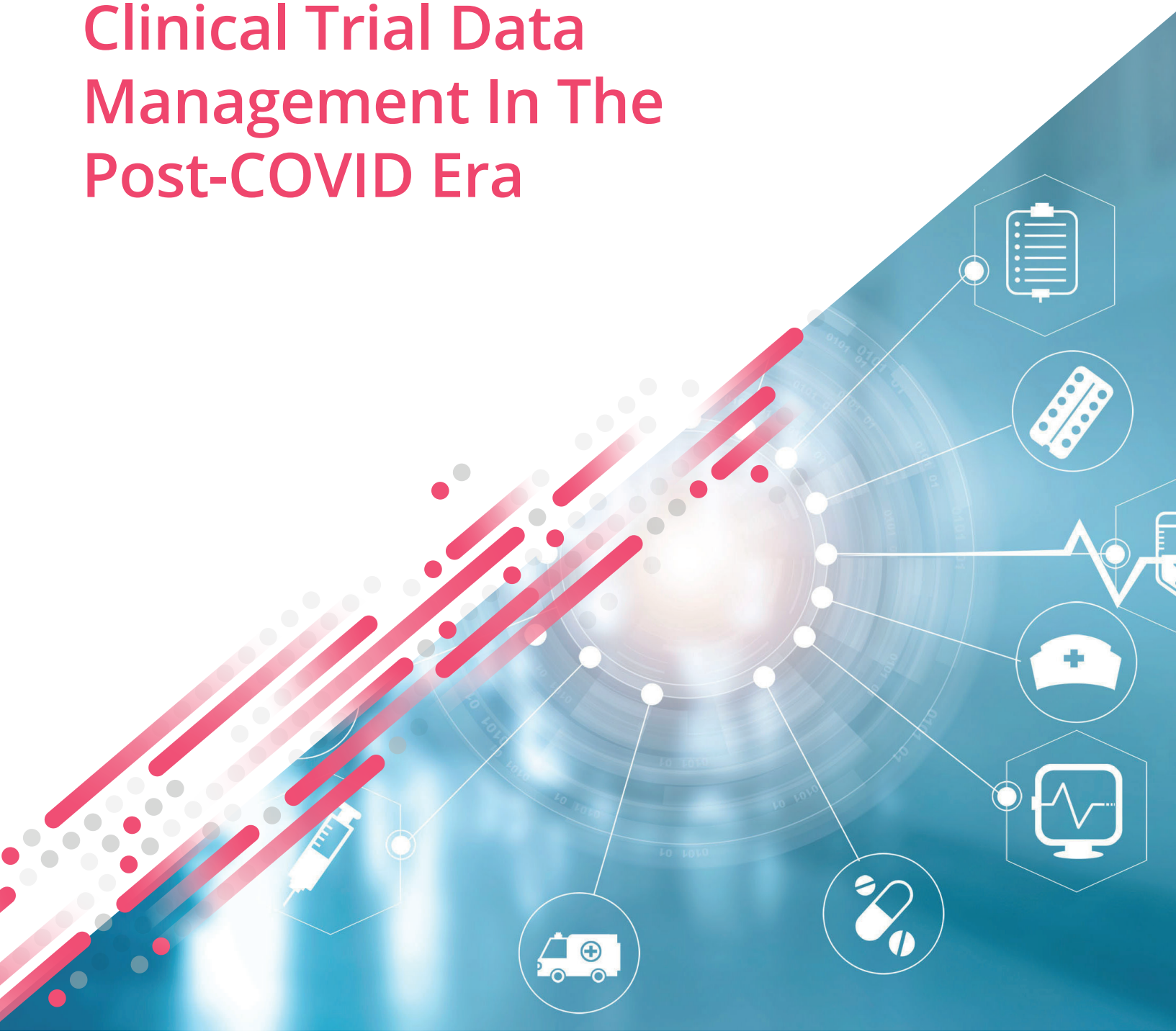
Pharma Intelligence
Informa

Clinical Trial Data Management In The Post-COVID Era



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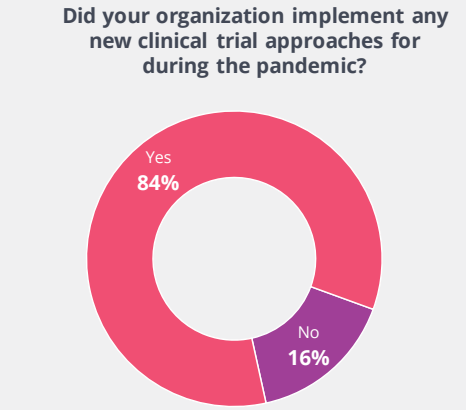
Clinical Trial Data Management In The Post-COVID Era

Accelerated by COVID-19 restrictions, the shift to decentralized or hybrid clinical trials is expanding the scope of drug development at multiple levels. It has implications for demographic reach and diversity, patient experience and convenience, cost-efficiency, and the range and granularity of clinical measurements and data available in real time from remote devices.

Decentralization has also brought a wealth of new technologies and methodologies into the clinical trial arena. Despite their undoubted advantages, though, these innovations can mean increased workload and complexity for trial managers. One challenge is ensuring that disparate technologies provide as seamless and integrated an experience as possible, enhancing speed and efficiency while optimising the value of patient-generated data.

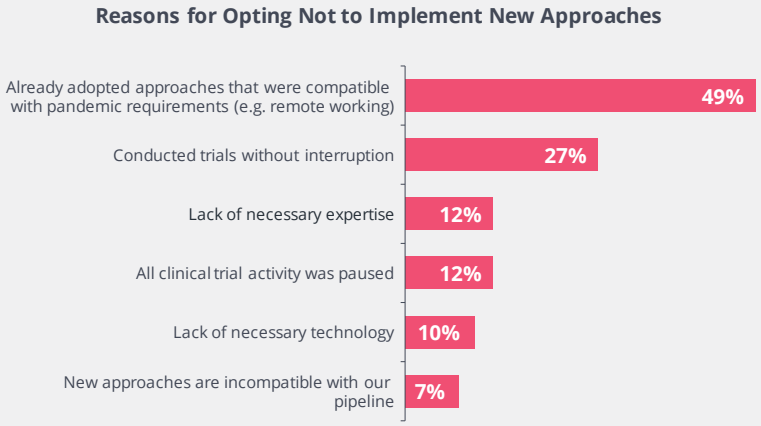
As one participant in a recent survey by Oracle and Pharma Intelligence noted, electronic patient-reported outcomes (ePROs) devices or interactive voice response systems (IVRS) impose additional burdens such as new logins, specialized training needs or compliance issues. In future, all of these sources may be integrated into a single data universe, the respondent said. For the moment, though, they continue to function independently and have to be reconciled.

Figure 1: Implementing New Approaches During the Pandemic



Question: Did your organization implement new approaches in order to continue existing clinical trials, or start new trials, during the COVID-19 pandemic?

Base: All respondents (n=251).



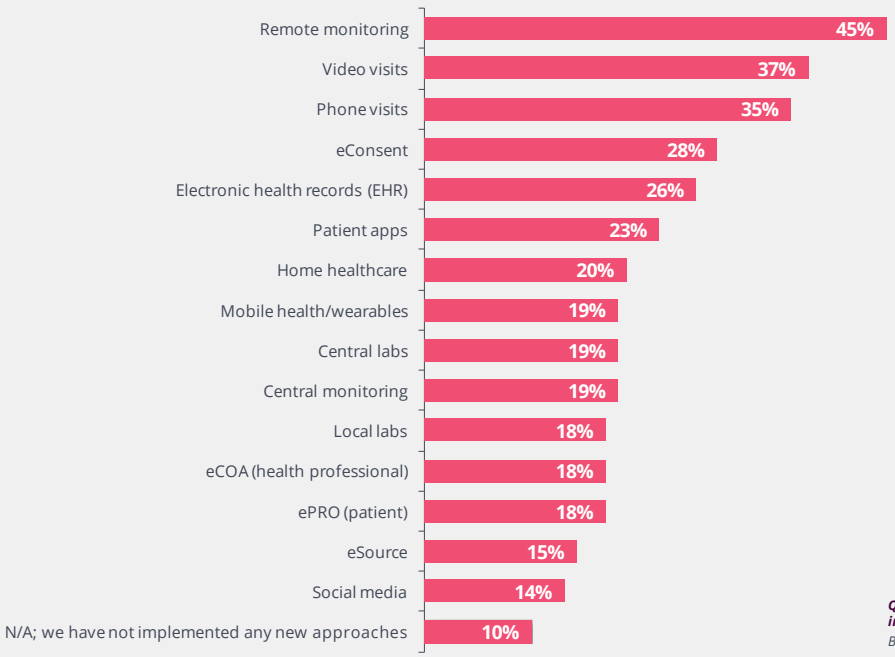
Question: Why didn't your organization implement any new approaches in clinical trials during the COVID-19 pandemic?

Base: Respondents not implementing new approaches (n=41).

Strong Uptake Of New Approaches

The Oracle/Pharma Intelligence survey of clinical trial professionals at biopharmaceutical/ medical device companies and contract research organizations worldwide found that 84% of respondents had implemented new approaches to clinical trial management during the pandemic, whether to continue existing trials and/or start new trials. Among the 16% of respondents who had not introduced new approaches, by far the most common explanation (49%) was that pandemic-compatible approaches had already been adopted (see Figure 1).

Figure 2: New Clinical Trial Approaches Implemented During the Pandemic

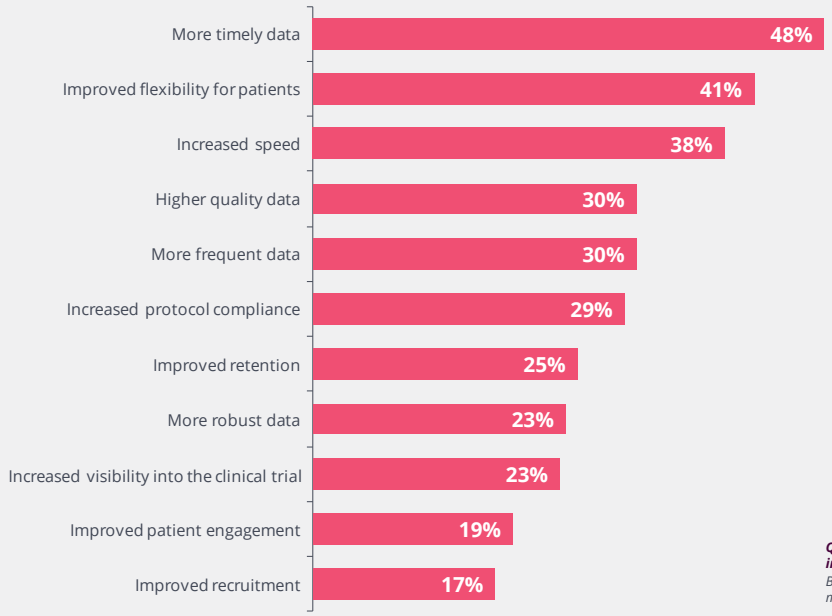


Question: Which new approaches did your organization implement during the pandemic?

Base: All respondents (n=251); multiple answers permitted.

Of the new approaches to trial management implemented during the pandemic, remote monitoring was most favored (45%), followed by video visits (37%), phone visits (35%), eConsent (28%), electronic health records (EHRs; 26%) and patient apps (23%) (see Figure 2).

Figure 3: Positive Impacts of New Clinical Trial Approaches

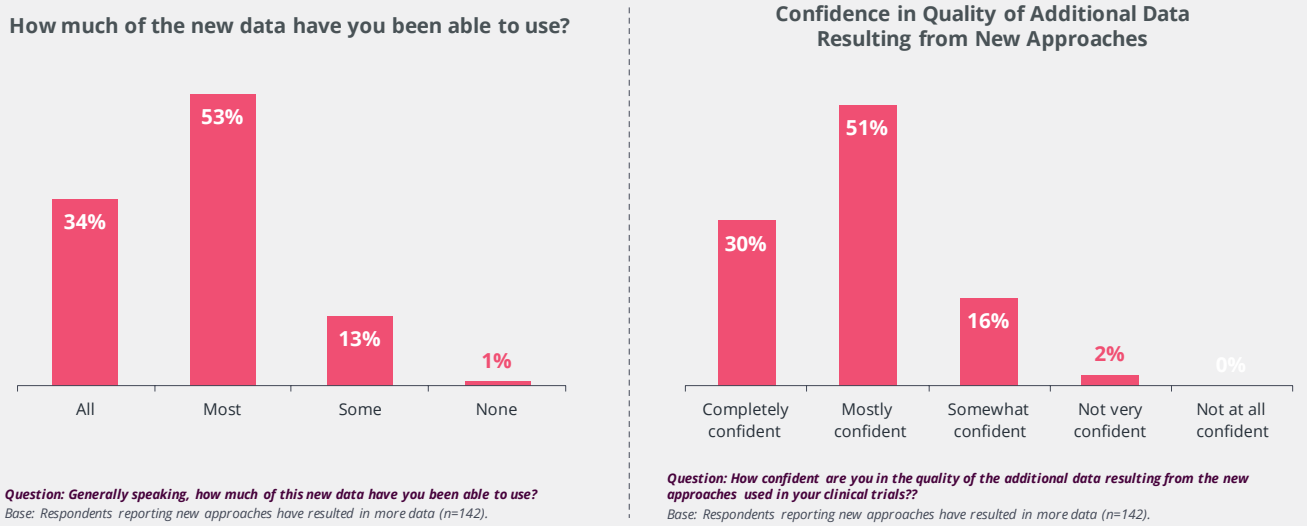


Question: How have your clinical trials been positively impacted? (Select all that apply.)
Base: Respondents reporting positive impact of new approaches; multiple answers permitted (n=183).

A large majority of respondents were enthusiastic about the effect these newly adopted approaches were having on clinical trials overall, with 26% seeing a significantly and 56% a somewhat positive impact.

The effects were particularly evident in more timely data (48%), improved flexibility for patients (41%), higher-speed delivery (38%), better quality data (30%) and more frequent data (30%) (see Figure 3). Moreover, 87% of respondents had been able to use most (53%) or all of the additional data generated through new approaches. And 97% of respondents were completely (30%), mostly (51%) or somewhat confident in the quality of these data (see Figure 4).

Figure 4: Use & Quality of Additional Data Resulting from New Approaches



Question: Generally speaking, how much of this new data have you been able to use?
Base: Respondents reporting new approaches have resulted in more data (n=142).

Question: How confident are you in the quality of the additional data resulting from the new approaches used in your clinical trials??
Base: Respondents reporting new approaches have resulted in more data (n=142).

Faster Data Turnaround

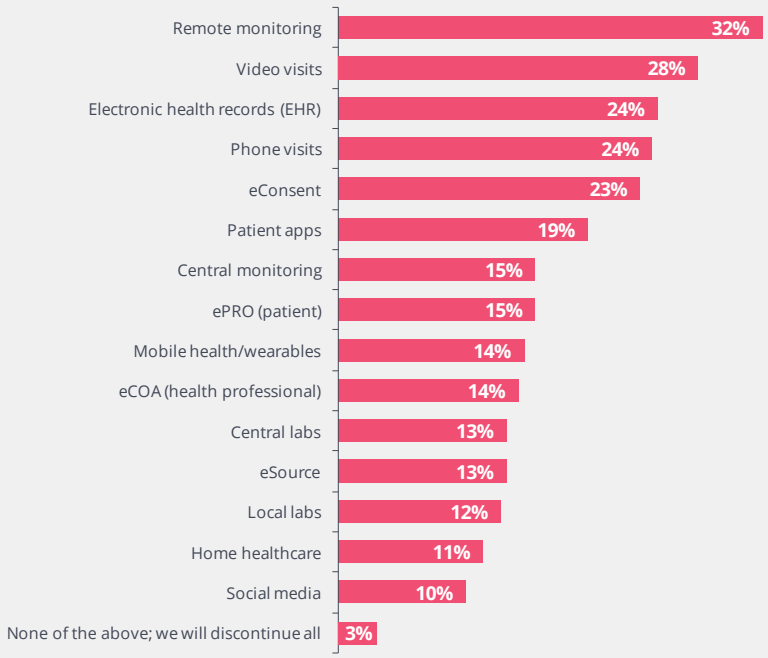
Talking to survey participants individually, though, the benefits of new technologies were not so clear-cut. One organization, for example, had adopted only electronic case report forms (eCRFs) to date. This shift was driven more by a general need for faster data turnaround than by COVID-19 specifically, the respondent said.

Nonetheless, more timely availability, evaluation, cleaning and presentation of trial data had undoubted advantages, such as shortening overall time lags. That was especially valuable in trials of serious conditions that called for regular presentations to a data safety monitoring board. Moreover, COVID-related barriers were driving a shift to more remote, risk-based data monitoring and reviews, the respondent noted. These were more likely to pick up outliers, irregularities or data gaps less discernible with conventional site-monitoring visits and source-data verification (SDV).

Whether the changes had actually improved data quality was a moot point. The organization needed more experience in using algorithms and other modern methods to clean and interpret data, the respondent said. For the moment, it was happy just to maintain data quality and see whether this improved in the future.

In future, it would continue using eCRFs for data collection, as well as more dynamic, risk-based monitoring, depending on the comparative quality and consistency of data coming out of individual sites. At the same time, manual data input from hospital records to eCRFs remained the norm in the majority of European hospitals, which did not have the necessary systems for data linkage or direct flow into the case report form.

Figure 5: New Approaches Planned for Continued Use Post-Pandemic



Question: Once the pandemic is behind us, which new approach(es) will your organization continue using?

Base: Respondents implementing new approaches; multiple answers permitted (n=225).

In the survey, 97% of respondents who had adopted new approaches to clinical trial management during the pandemic aimed to continue using at least some of them post-COVID, with remote monitoring (32%), video visits (28%), phone visits (24%), EHRs (24%) and eConsent (23%) topping the list (see Figure 5). One interviewee predicted that the trend to remote monitoring would only accelerate, encouraged by improved data quality, regulatory guidance and better understanding of the technology.

For another respondent, the new methodologies were a boon for data volume and timeliness but the impact on data accuracy needed clarifying. While electronic data were more easily captured and could be delivered in almost real time, data managers had less control over a decentralised process, even if it was more convenient for patients.

One participating organization had navigated the COVID-19 restrictions by introducing telehealth visits, patient questionnaires filled in remotely by study participants on their own devices, and virtual informed consent in some instances. It also planned to use electronic patient-reported outcomes (ePRO) devices in future trials. These initiatives had boosted confidence in the quality and timeliness of the collected data, with more granularity and better compliance data, the respondent said.

Barriers To Continued Use

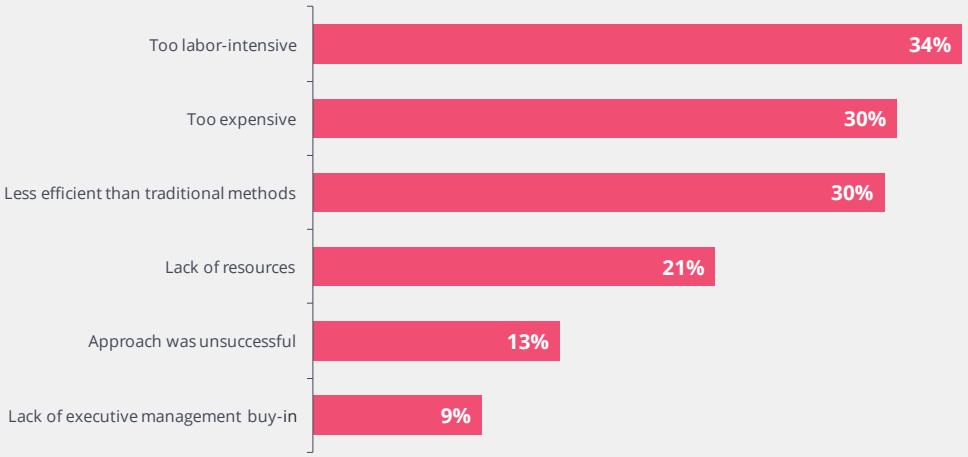
Addressing the relatively low scores in the survey for continued use of technologies such as ePROs (15%), eCOAs (electronic clinical outcome assessments: 14%) and eSource (13%), one participant suggested these technologies were still in an evaluation phase. Another noted that ePRO could be quite costly to implement, considering the need to programme and validate devices (see Figure 5).

Consequently, ePROs were probably best reserved for situations where they could really add value,

such as primary endpoints that required home-based patient data (e.g. pain scores). Among survey respondents planning to discontinue at least one of the newly implemented approaches post-COVID, 34% felt the new strategies were too labor-intensive, 30% too expensive and 30% less efficient than traditional methods, while 21% lacked the resources to maintain new approaches (see Figure 6).

At least one interviewee's clinical trial operations were now almost fully digital, including remote access to eCRFs and associated systems, eTMFs (electronic trial master files) and, in the US market, eConsent. The majority of European countries currently do not accept eConsent, for legal reasons, the interviewee pointed out.

Figure 6: Reasons for the Decision to Discontinue Using New Approaches



Question: Why is your organization discontinuing these approaches?
Base: Respondents planning to discontinue at least one newly implemented approaches; multiple responses permitted (n=148).

New Technologies Mean More Complexity

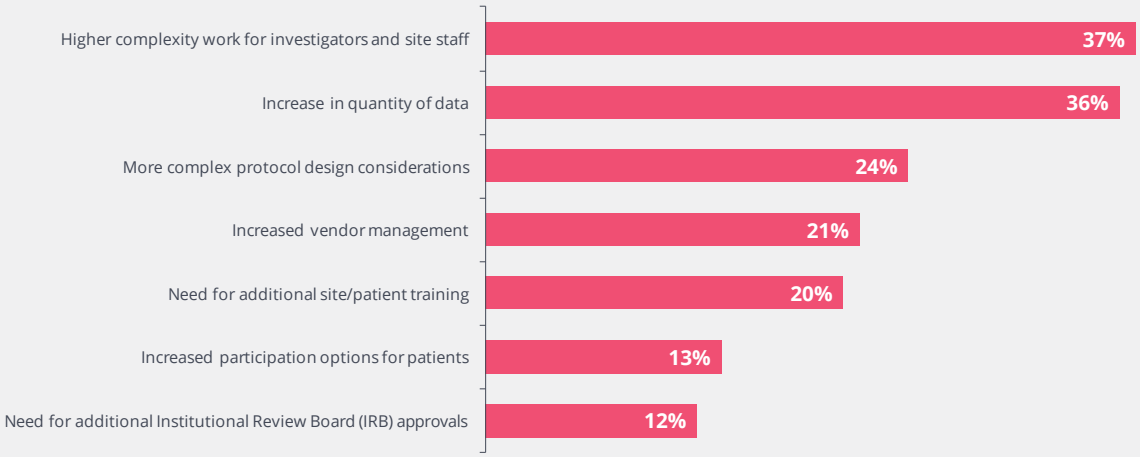
Where survey participants planned to continue using new methodologies in clinical trials, they felt the consequences were most likely to be higher complexity work for investigators and site staff (37%), increased data volume (36%), more complex protocol designs (24%), increased vendor management (21%) and need for additional site or patient training (20%) (see Figure 7).

"There is still this trend to extract more and more data, and of course it's a burden for the sites," one interviewee commented. They would come under even more pressure if data were collected via wearable devices: "what to do with, say, 100,000 data points if the patient is recording their blood pressure every 10 seconds."

All the same, if valuable information could be extracted from the general 'noise', the new strategies could be helpful, the interviewee accepted. It was useful, for example, to have data from continuous blood pressure monitoring, as opposed to potentially less representative once-a-day measurements.

Another interviewee said the feedback from site staff was that new approaches were making their lives far more complicated, particularly with current infrastructures and expertise. The rate of transition, though, was likely to vary by organization. At

Figure 7: Top Two Consequences of Continuing to Use New Approaches



Question: What are the most significant consequences of continuing to use these approaches in your clinical trials?
Base: Respondents planning to keep at least one newly implemented approaches; up to two responses permitted (n=217).

academic centres and universities, principal investigators were much more attuned to multiple trial management strategies. But sites in more rural areas, or distanced from centers of excellence, would find the transition more challenging.

Another survey participant described increased complexity as "the new reality" for trial sites. Data volumes would be a challenge in the short term. In time, though, investigators and site staff would adjust to the new requirements, particular if conducting clinical trials was their "daily bread and butter."

For one respondent, data complexity in clinical trials was more of a general trend reflecting diversification of external data sources. That meant additional databases and more data queries. Managing the proliferation of patient samples could be challenging as well, especially if patients withdrew consent to use samples further down the line.

New methodologies could also have consequences for vendor management, one respondent acknowledged. Once a vendor was properly onboarded, though, management would become much more straightforward. Vendor management might be more complicated if wearables were involved, another interviewee noted. That would add at least one more vendor and another channel for data flow into the clinical database.

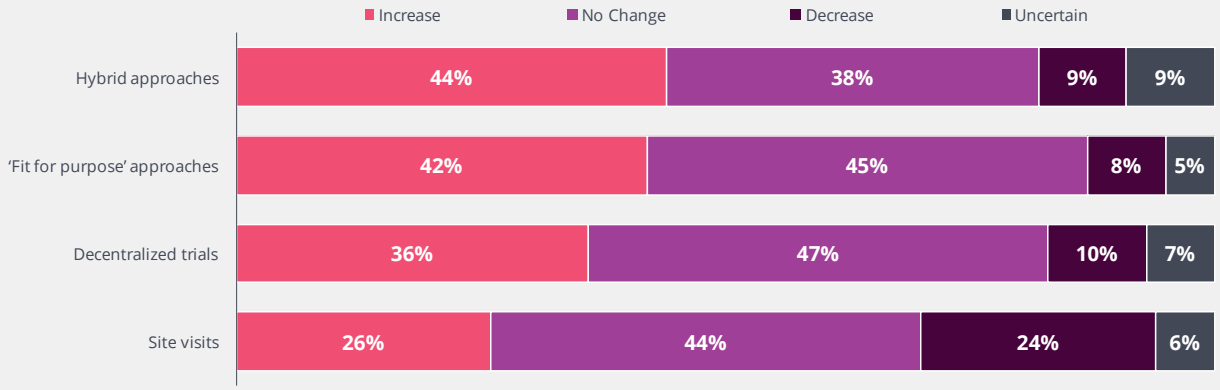
Additional training for either sites or patients should be limited, as most remote devices were largely self-managing, the respondent added. And, on the plus side, new approaches such as mobile apps could establish a "stronger bond" with the patient, together with better protocol compliance and adherence.

Not For Everyone

As one survey participant pointed out, the decentralized model will not suit everyone. For example, an organization focused largely on intensive care conditions (e.g., hematological disorders), where most of the treatment is onsite and requires complex laboratory assessments, may find decentralization a step too far.

One interviewee said their organization planned to adopt both centralized and decentralized trial models in years to come, rather than the fully remote strategy imposed by COVID-19. The balance of this hybrid approach would depend on the medication, therapy area and type of study, although resources such as EHRs, video visits and remote monitoring were likely to remain in routine use.

Figure 8: Expected Change in Use of Select Approaches Post-Pandemic



Question: How do you expect your organization's use of the following to change post-pandemic?
Base: Respondents implementing new approaches (n=225).

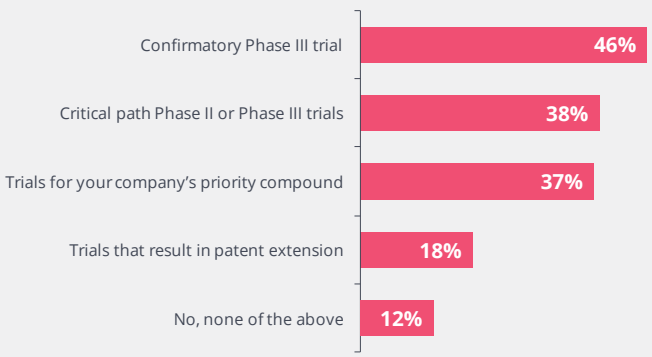
Indeed, 44% and 42%, respectively, of survey respondents expected their organizations to continue using hybrid or 'fit for purpose' approaches in clinical trials once the pandemic was over, while 36% envisaged more recourse to decentralised trials (see Figure 8). Most of the respondents said they would employ these strategies for both restarts of existing trials disrupted by COVID-19 (63%) and for new clinical trials (61%) (see Figure 9).

Figure 9: Trial Applications for Increased Usage & Priority Trials

Trial Applications for Increased Approaches

Question: For which of your organization's clinical trials will these new approaches be utilized?
Base: Respondents expecting an increase in decentralized trials, hybrid, and/or ft for purpose approaches; multiple responses permitted (n=148).

Incorporating New Approaches in Priority Trials

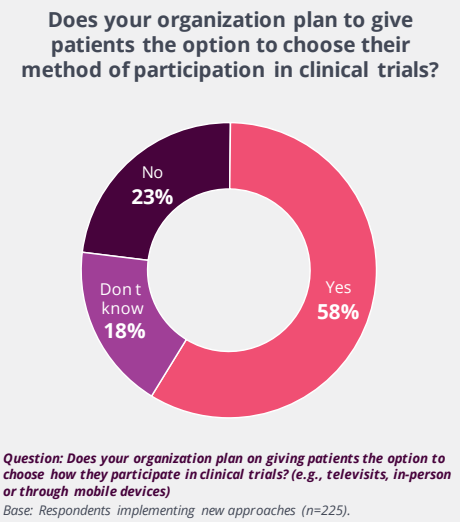


Question: Are you incorporating any of these new approaches in studies you would consider to be 'priority trials'?
Base: Respondents implementing new approaches; multiple responses permitted (n=225).

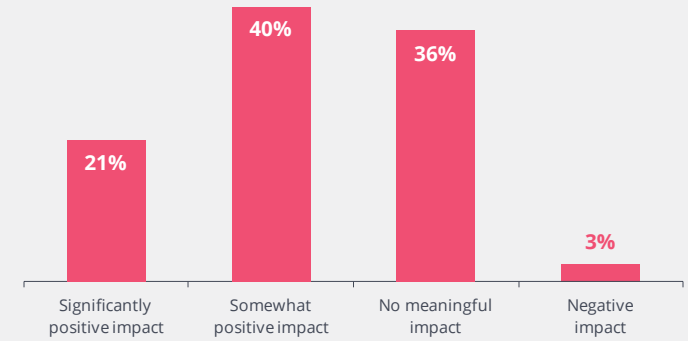
Letting Patients Choose

These trends also raise the question of how patient choice will influence trial management. In the survey, 58% of respondents said their organization planned to give patients the option of deciding how they participated in clinical trials. Moreover, 61% felt that giving patients this option would have a significantly (21%) or somewhat (40%) positive impact on clinical research (see Figure 10).

Figure 10: Patient Choice in Clinical Trials



Question: Does your organization plan on giving patients the option to choose how they participate in clinical trials? (e.g., televisits, in-person or through mobile devices)
Base: Respondents implementing new approaches (n=225).



Question: If patients are allowed to choose how they participate in clinical trials, what impact do you think that will have on clinical research?
Base: Respondents implementing new approaches (n=225).

Among respondents interviewed separately, there were mixed feelings on this point. The general consensus was that patient choice would depend on the type of condition addressed and the drugs used. With studies involving severe or acute conditions, there was really no question of patients not coming into hospitals, one respondent said. And in hematology trials driven strongly by blood parameters, there was little room for anything more than "minor tweaks."

In an indication like rheumatoid arthritis, probably more of the trial could probably be shifted to a home environment, the respondent added. Another interviewee cited diabetes and pain management, as well as trials for COVID-19 vaccines. Here, there might be an initial patient visit to measure antibody levels but everything else could be tracked remotely.

As one survey participant observed, there was still a basic obligation to follow the trial protocol and collect whatever data were needed for analysis. And even with remote patient visits, the assessment burden on the patient, including laboratory samples, remained the same. Moreover, a gain in patient convenience might be offset by increased burden on CRAs, while statisticians, might have to determine whether patient choice had influenced trial outcomes.

Another interviewee foresaw home-based care being offered initially for conditions where treatment was straightforward, simple to monitor and easily self-administered without nurse support. Once the sponsor felt confident patients had all they needed to complete trials remotely, the option would be available to everyone.

This was natural evolution that mirrored the

emergence of better informed patients over the last decade, the respondent added. It would improve the efficiency of clinical trial execution and, even more importantly, would drive recruitment of better selected, more engaged, more motivated patients. That also had implications for patient compliance, both within the trial and in the wider treatment environment once the trial was over.

Interoperable Environment

As the survey and discussions with participants made clear, decentralized and hybrid clinical trials are already well on their way into the mainstream. Much of the underlying technology is well established and cultural change will follow. Pandemic constraints and the accelerated development of COVID-19 vaccines have proved that overhauling the traditional site-based model is not only viable but desirable.

To reap the full benefit of all these advances, though, trial sponsors and their outsourcing partners need to ensure that clinical trial transformation is occurring in a genuinely interoperable environment. With decentralized trials, multiple technologies for collecting and processing clinical trial data should be seamlessly integrated to drive optimal outputs. Too often, this is not the case. Industry is moving in the direction of interoperability, but in different ways and at different paces.

In particular, the speed at which new technology for decentralized trials is evolving has outstripped the adoption of operational changes to manage this new environment optimally. Partnering with a specialist provider such as Oracle, with its advanced platforms for unified clinical trial management, may be the step into the future that enables decentralized and hybrid trials really to deliver on their promise.

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