Patient Centricity and Virtualizing Technologies in a COVID-19 World

Measuring how the pandemic is driving adoption of digital tools in fully virtual, hybrid, and traditional clinical trials

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As the COVID-19 pandemic rages on, clinical trial conduct is being reimagined in ways few thought possible not so long ago. Stakeholders are rethinking how to develop protocols, consent patients, ensure compliance, and gather quality clinical trial data when patients and staff are remote, rather than located at traditional trial sites. As this shift is unfolding, patient centricity has stepped to the forefront, allowing studies to continue, and helping researchers move closer to developing greatly needed vaccines and therapies for COVID-19, and for many other conditions.

Patient centricity is a growing and important movement within clinical trials, and although an official industry-wide definition is lacking[1], sponsors often refer to it as adopting a culture that puts patients first. This means embracing processes that enable fewer protocol assessments or involve greater use of virtual patient-facing technologies in clinical trials.[2] As part of this effort, digital tools enabling remote participation in trials are being introduced to simplify how patients participate in studies and communicate with sites. Some examples include tools for electronic clinical outcomes assessments (eCOA), wearables, and televisits. These solutions give patients a voice in ongoing studies at a time when many aspects of clinical trials are quickly becoming decentralized, meaning they are being conducted either completely or partially outside of a traditional trial site via telemedicine and other remote mobile solutions.[3] Although these virtualizing technologies have been available for several years, adoption has been slow. All of that changed with the pandemic, resulting in a stunning transition to digital tools designed to keep studies going[4] as patient centricity is being repositioned as a standard practice.

Fueling this effort are a spate of recent guidances from regulatory agencies, advising stakeholders on conducting clinical trials during the pandemic, and highlighting technology as key to adopting practices that do not compromise study quality while keeping participants and staff safe. In March 2020, the Food and Drug Administration (FDA) released the first of several versions of its guidance, stressing that the safety of participants is paramount,[5] and since participants may be unable to visit the sites, sponsors should evaluate alternative methods for studies to continue. Examples of other agencies that have released guidances[6,7] appear in Chart 1.

This is a fast-changing picture, with new information constantly filtering in as to how sites are adapting to the COVID-19 era, and how patient-centric solutions are playing a growing role. To quantify this trend, the Society for Clinical Research Sites (SCRS) recently collaborated with Medidata (a Dassault Systemes Company) to conduct an online survey. It measured current and anticipated levels of adoption of patient-centric tools, and the sites' perspective on how patients have reacted to them. Importantly, results counter the belief of many sponsors that sites are resistant to more digital tools. The survey revealed that sites are receptive to virtualizing technologies that facilitate their work while enhancing the patient experience.

Guidances on Clinical Trials in the COVID-19 Era

FDA:

- Sponsors planning to use remote electronic assessments as part of a clinical investigation should use appropriate technology and develop procedures for provision of technology and technical support to trial participants, investigators, and/or other trial personnel to facilitate those assessments.

European Medicines Agency (EMA):

- Sponsors should consider in their risk assessment… conversion of physical visits into phone or video visits, postponement or complete cancellation of visits to ensure that only strictly necessary visits are performed at sites.

Health Canada

- Investigators may need to evaluate whether alternative methods for safety assessment are feasible should participants not be able to come to the investigational sites as specified in the study protocol…alternative methods may include phone contact, virtual visits via telemedicine or alternative care sites.

Chart 1

About the Survey

An online study on how sites view the tools that encourage patient centricity was conducted between May 19 and July 10, 2020. This time frame is meaningful, as the survey took place several months into the pandemic, allowing sites to respond to questions through a "COVID lens".

The survey included 25 questions that evaluated:

- How sites define patient centricity
- Demographics of participants
- How often in the past two years sites used tools to facilitate patient centricity
- Tools sites plan to start adopting over the next two years
- Sites' opinions of technology designed to improve patient centricity
- Willingness of patients to use patient-centric tools
- Factors limiting adoption of tools

The technology examined in the study was a wide-ranging list of today's tools, namely eCOA, phone text alerts, decentralized or virtual trials, and more. For the purposes of this survey, "decentralized or virtual" referred to studies that are fully virtual, meaning that all study visits are remote. "Hybrid" trials, an increasingly common term, refers to studies that have a combination of onsite and remote visits.*

Survey questions were largely multiple choice, asking respondents to select all technologies they have used or are currently using, or plan to implement over the next two years. Other questions sought opinions on the tools, using a scale of 1 – 5, with "1" indicating "do not agree at all", to "5", which indicated "strongly agree". The survey also included open-ended questions, which encouraged respondents to voice their opinions.

With its sharp focus on patient centricity, the survey opened by asking respondents if they agreed with the following definition: "Patient centricity means putting the patient first in an open and sustained engagement in a clinical trial". A large majority agreed with this definition (90.51% strongly or somewhat agreed), but there was a litany of open responses such as, "Patient centricity refers to focusing on the patient over all else, and meeting the patient at his/her current place in life", and "Patient centricity means patient-direct data collection". Other definitions appear in Chart 2.

How Sites Define Patient Centricity

- Focusing on the patient over all else, and meeting the patient at his/her current place in life
- Patient-direct data collection
- Designs geared toward patients or subjects
- Adopting a culture in the design and development of clinical research projects aimed at meeting the needs of the patients/target groups whose challenges you hope to solve or resolve
- Partnering with the patient and their families to have their input into clinical trials
- Including and engaging with patients from decisions about the study concept/question, through study design, data collection and analysis, marketing, outreach, recruitment, retention strategies…through to dissemination and implementation of study results

Chart 2

Results

Survey respondents represented 321 sites, which were largely urban (63.2%), and overwhelmingly from North America (84.8%). The largest groups of respondents were composed of study coordinators (29.03%) and site managers (17.74%) (Figure 1). They mostly represented

* The survey did not distinguish between fully virtual and hybrid trials.

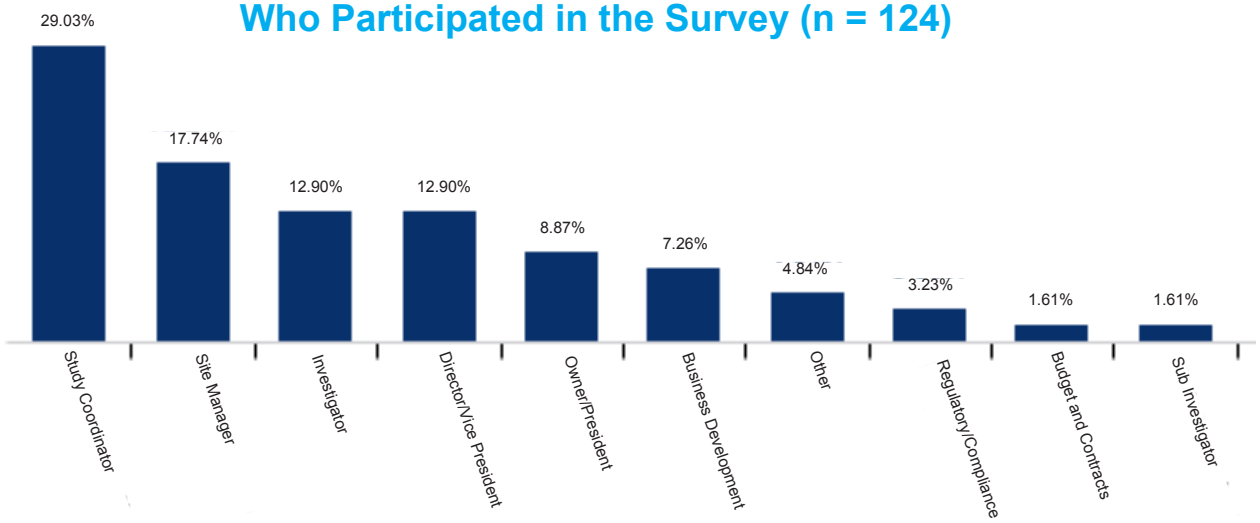


Figure 1

private practices that conduct clinical trials, freestanding research centers, or hospital-owned research departments. Also, they were an experienced group, with 74.8% claiming to have > 10 years of clinical research experience.

According to the survey, the most widely used technologies over the past two years were eCOA/electronic patient reported outcomes (ePRO) (72.95%), email notifications (64.25%), and online recruitment (63.29%). Figure 2 illustrates how the technologies rank.

With the pandemic driving interest in purely virtual as well as hybrid clinical trials, the survey sought to measure their expected growth in the near future. Currently, the fully virtual approach has limited use, with only 15.46% of respondents claiming to have used decentralized or virtual trial tools in the preceding two years. Moreover, nearly three-quarters of respondents (71.88%) stated that they rarely used this technology, but looking ahead, 42.11% reported that they expect to add decentralized or virtual trial tools over the next two years—almost tripling today's level of use.

As for tools that enable the virtual/decentralized trial trend, big increases in eConsent and televisits are anticipated (Chart 3). Other tools showed smaller projected increases because they are already in wide use.

In delving deeper into which patient-centric technologies

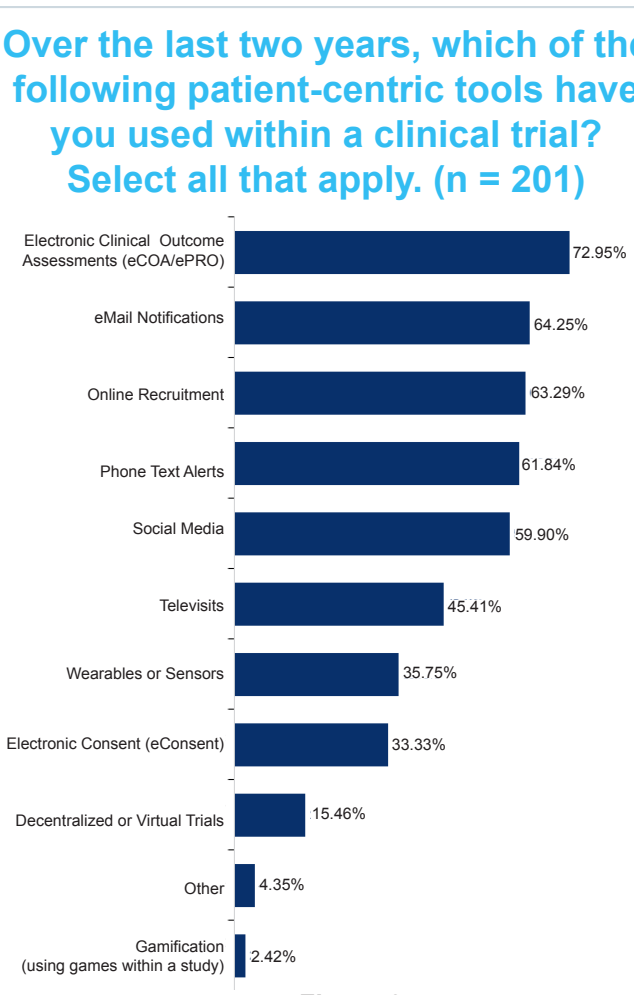


Figure 2

Change in Use of Patient-Centric Tools Over the Next Two Years

Technology	Used Over the Past Two Years	Expect to Start Using Over the Next Two Years
Decentralized/Virtual Trials	15.46%	42.11%
eConsent	33.33%	49.71%
Televisits	45.41%	39.18%
eCOA/ePRO	72.95%	11.11%
Phone text alerts	61.84%	20.47%
Online recruitment	63.29%	16.96%

Chart 3

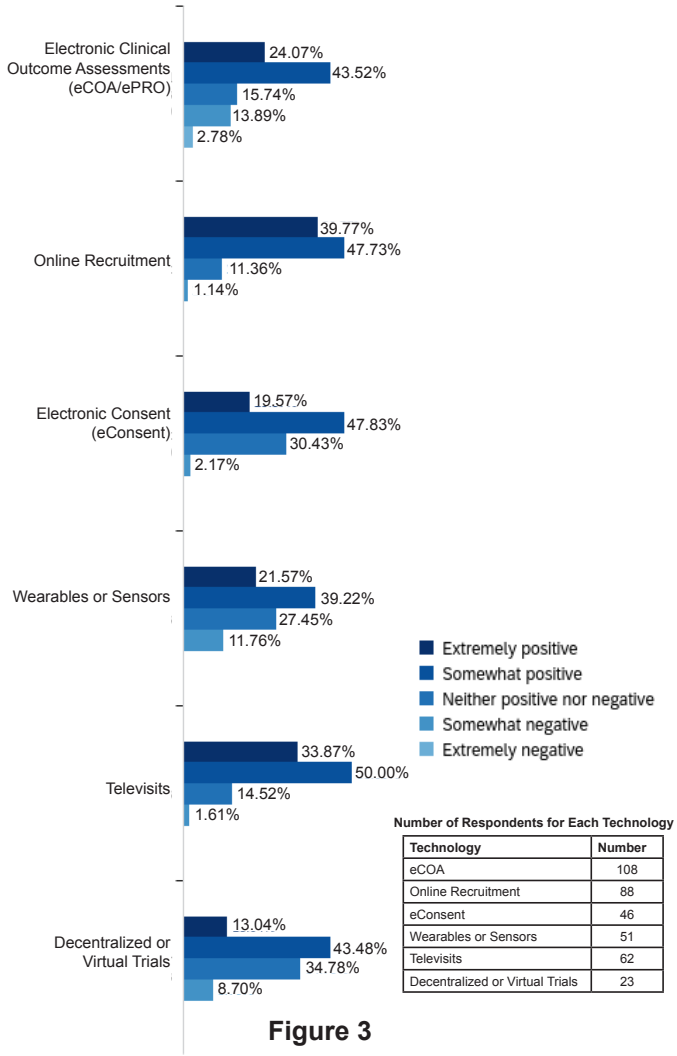


Figure 3

are slated for future use, it is worth noting that some tools named as *already in use* were actually used rarely or no more than half the time. For example, while televisits were reported as being used by 45.41% of respondents over the past two years, at the same time, 91.86% of them claimed to use televisits rarely, or no more than half the time. This is expected to change, however, as 39.18% of respondents anticipated adding televisit technology over the next two years (Chart 3). Wearables or sensors provide a similar example. More than one-third of respondents (35.75%) reported using them, but of that group, 91% stated that they rarely used them or used them no more than half the time. But, going forward, 25.73% are looking to add these virtualizing tools over the next two years.

Patients' Experiences With Patient-Centric Tools

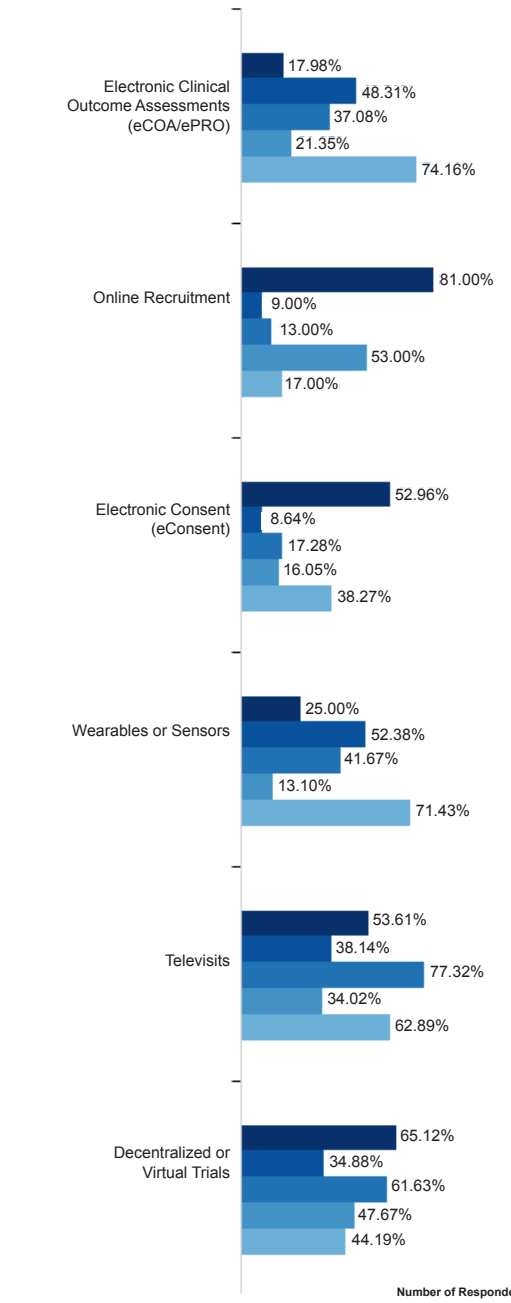
Participants represented sites that have used patient-centric tools in studies across a vast array of therapeutic areas. With this perspective, they were asked to rate their patients' experiences with those tools, using a scale ranging from "extremely negative" to "extremely positive" (Figure 3). The survey found that online recruitment technology garnered the most positive feedback with 87.5% (77 out of 88 respondents) claiming their patients' experiences were extremely or somewhat positive. Televisit technology was also well received—83.87% (52 out of 62 respondents) reporting extremely or somewhat positive results—although as stated earlier, its use remains limited.

An interesting finding is that decentralized or virtual trial tools, while not widely used, had a split reaction. Specifically, 56.52% of sites referred to patients' experiences as either extremely or somewhat positive, while the remaining 43.48% had "neither a positive or negative" response or a "somewhat negative" response. This non-conclusive split may reflect the fact that there were only a handful of responses (n = 23) to this question as compared to other questions, which had far more answers, and therefore, a more definitive set of results. Re-evaluating this point in the future will provide data and further insight into patients' changing views of this growing approach to clinical trials.

Respondents were asked to identify the benefits of incorporating these technologies into clinical trials, using factors such as "improved patient enrollment", "improved patient investigational product (IP) adherence", and more, as shown in Figure 4. Not surprisingly, given today's COVID-19 environment, televisits were named most often as improving patient retention—77.32%, followed by decentralized or virtual trials at 61.63%. Also noteworthy is the finding that more than any other technology, online recruitment was credited with improving patient enrollment—81%. As for improving patient engagement to protocol activities, eCOA and wearables were deemed the most useful at 74.16% and 71.43%, respectively.

Finally, the survey inquired about patient-centric technologies that respondents currently are NOT using, and attempted to pinpoint factors that seem to be limiting their use. Respondents were asked to choose among answers such as time, cost, staff overload, and others (Figure 5), and

Which of the following do you see as the biggest benefits in incorporating these patient-centric tools into your clinical trial?

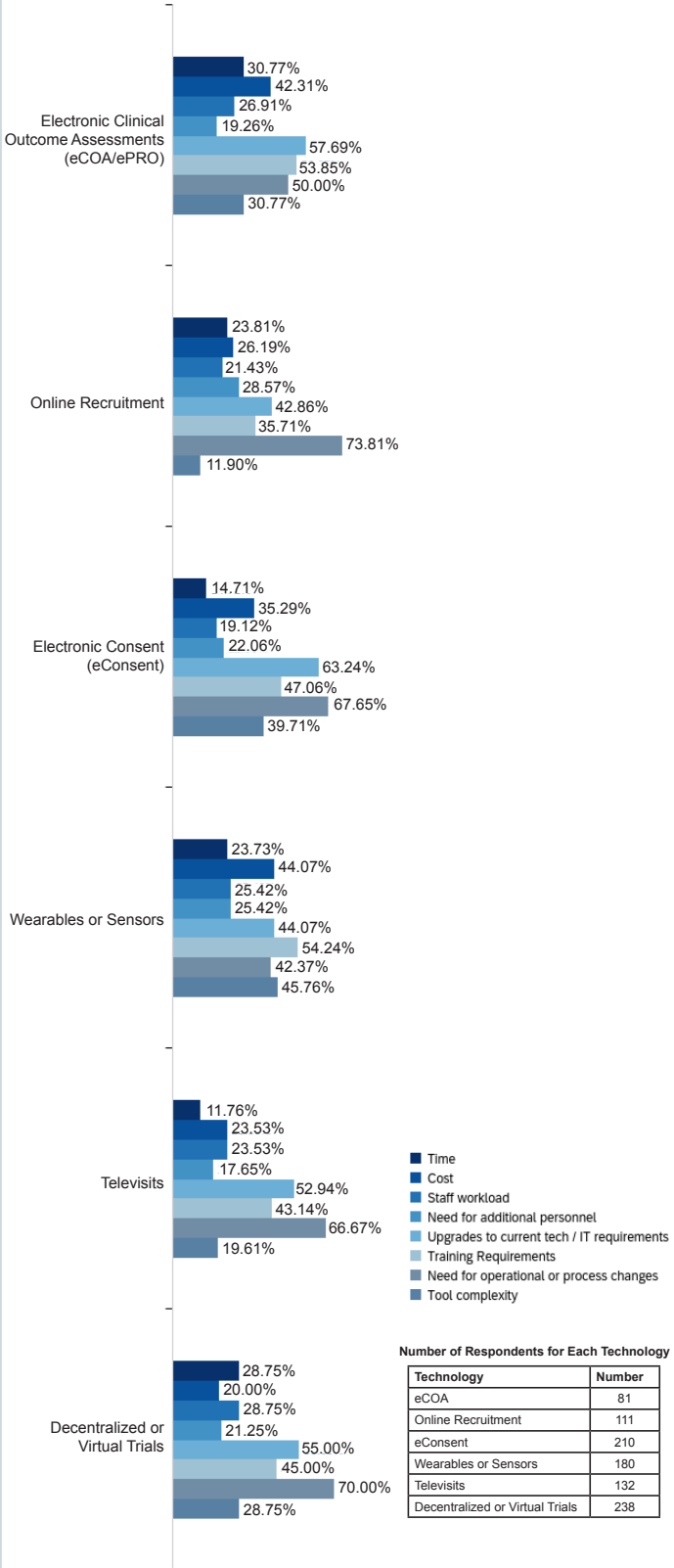


Number of Respondents for Each Technology

Technology	Number
eCOA	177
Online Recruitment	173
eConsent	116
Wearables or Sensors	171
Televisits	258
Decentralized or Virtual Trials	218

Figure 4

For the patient-facing digital solutions you do NOT currently use, what factors, if any, would limit your usage of these solutions in the future?



Number of Respondents for Each Technology

Technology	Number
eCOA	81
Online Recruitment	111
eConsent	210
Wearables or Sensors	180
Televisits	132
Decentralized or Virtual Trials	238

Figure 5

while all of these factors played a role, "need for operational or process changes" emerged as the most often cited across all of the technologies listed, led by online recruitment at 73.81%, followed by decentralized or virtual trials at 70%.

Interestingly, despite sites often being viewed as heavily burdened with work, "time" was the least cited barrier, with only 11.76% and 14.71% of respondents claiming it as a barrier to televisits and eConsent, respectively.

Interpreting the Results

On March 11, 2020, the World Health Organization declared COVID-19 a global pandemic[8], and its subsequent rapid fire spread upended longstanding clinical trial practices. Early on, the challenges posed by COVID-19 halted many clinical trials, but shuttered studies eventually started re-opening in revised formats, and more than 4,000 new studies have emerged for all aspects of preventing, treating, vaccinating, or testing for COVID-19.[9] The subject of this SCRS-Medidata collaborative survey was to understand which digital technologies were facilitating patient centricity by easing the transition to a more virtual realm, whether fully virtual or hybrid. With the help of these tools, patient's health, safety, and convenience have moved front and center by limiting the number of onsite visits while maintaining data quality, and active communication with the site.

Key results indicate a major uptick in use of virtual trials is expected, jumping from 15.46% of respondents claiming to use this technology over the past two years to 42.11% anticipating its use over the next two (Chart 3). Moreover, 83.9% of respondents stated that their patients had "extremely" or "somewhat" positive experiences with televisits. This finding aligns with 87.1% of respondents claiming that they, too, had similar experiences with televisits. There were an array of factors limiting acceptance of technology, ranging from time and cost to tool complexity, but the most often named barrier was the need for operational or process changes. For technologies currently being used, 47.37% stated it impacted greater use of virtualized trials, and 35% identified this issue as limiting use of eConsent.

Complementing the data were a number of open responses from respondents that provided sharp insights into anticipated use of patient-centric tools over the next two years. When asked if there were to be one technology that could improve how sites could help patients, responses

highlighted a range of today's digital/remote tools, such as centralized texting as reminders for study visits, iPads or laptops to be used for virtual visits and eConsent, eDiaries, ePRO that can be completed on a patient's personal smartphone, and more. At the same time, a number of responses expressed a strong desire for a comprehensive technology with multiple functionality, rather than continued reliance on point solutions. Here are two examples:

- One piece of technology - NOT 10. Subjects alone have to use about three. That is not patient centricity.
- With too many technologies, patients have trouble keeping track of their usernames and passwords. Single sign-on would be important if multiple vendors are involved.

There is a clear interest among sites in virtualizing tools, but several respondents rightly stated that the sponsor or contract research organization (CRO)—rather than the site—is responsible for choosing the technology associated with studies. And, there is evidence that many sponsors, CROs, and collaborative groups are onboard with this trend. A small sampling of stakeholders that have voiced support for this transition includes: the National Institutes of Health (NIH) and the National Science Foundation, which put forth a white paper entitled, "Digitizing Clinical Trials"[10]; the SWOG Cancer Research Network, which has convened a working group to explore this issue[11]; and the growing wave of webinars and literature dedicated to this topic.[12, 13, 14, 15] These groups cite patient interest in safety and convenience as particularly fueled by the pandemic, and this sea change is expected to continue going forward. The "convenience factor" and reduced site visits enabled by telehealth are viewed as too attractive to relinquish[15], given their potential for boosting recruitment, retention, and compliance.[3]

The shift toward a more patient-centric style of clinical trials has been underway in recent years. In late 2019, just prior to the pandemic, the Clinical Trials Transformation Initiative (CTTI) released recommendations on how to adopt decentralized clinical trials, with a focus on protocol design, use of televisits, data integrity, and safety monitoring as investigators embrace mobile technologies.[3] Similarly, our survey showed that numerous digital tools were widely used over the past two years, with eCOA, and e-mail notifications leading the way (Figure 2). Use of decentralized or virtual trials has been limited, but the pandemic is expected to accelerate this trend, especially with hybrid trials.

Data from the Society for Clinical Research Sites' 2020 Landscape Survey document this finding.[16] Only 12% of participants claimed to have been approached by sponsors or CROs to conduct a fully virtual clinical trial. Of that group, 58% declined the opportunity, citing low budget, not comfortable with this style of clinical trial, and patient safety and privacy concerns. By comparison, 30% of participants reported having been approached to conduct hybrid trials, with only 26% declining the offer, largely due to low budget, and/or not having the right population.

Decentralized Trials Are Here

As clinical trial conduct is trending toward virtual and hybrid approaches, stakeholders are looking to participate and better understand how they are impacting patient centricity today, and in a post-pandemic world. Heading in this direction means sponsors and CROs are embracing technologies that will jumpstart this effort for sites, and for patients. Our survey shows that far from being resistant, sites are anxious to be part of this movement as long as the virtualizing technologies are user-friendly, can reduce the number of standalone solutions, offer ready access to training and IT questions, and most importantly, allow clinical trials to continue while keeping patients safe. For sponsors and CROs, re-designing protocols that allow for greater use of these tools is a critical step that is supported by regulatory guidance and industry alike, and is a key starting point.

Going forward, issues such as inadequate budget, discomfort with virtual or hybrid trials, lack of good connectivity, and the need for operational or process changes may be significant obstacles for stakeholders. To gauge progress, it will be meaningful to re-visit this subject and re-examine the adoption of various types of virtualizing technologies that will improve the patient experience, while also addressing longstanding challenges in clinical trial conduct.

SCRS acknowledges the contribution of Ann Neuer, MBA, in the development of this white paper. Neuer is President of Medical deScriptions, LLC, a provider of writing solutions and market research to the clinical trials sector. Contact her at aneuer@cinci.rr.com.

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16. Contact SCRS for further details on the 2020 Landscape Survey.

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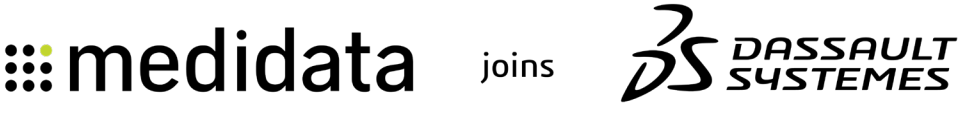

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