ISR reports | Pharmaceutical Market Research

Unraveling Hybrid Clinical Trials: **CHALLENGES AND OPPORTUNITIES**

Unraveling Hybrid Clinical Trials: **Challenges and Opportunities**

ED BILLER

Hybrid trials — in which patients participate from home for some visits/activities, rather than in a clinical setting — have undergone rapid evolution in the past few years. Conceived more than a decade ago and thrust into prominence during the COVID-19 pandemic, hybrid clinical trials now have become the rule, rather than the exception. Sponsors and their partners progress further every day into more effective implementation of decentralized methodologies, supporting technologies, and other tools to promote the generation of more accurate data and streamline regulatory review, as well as reduce investigator and patient burdens.

This e-book examines how hybrid trials' journey has taken place in recent years — the reasons for confidence and concern — and examines how hybrid trials may impact pharmaceutical development in the future. "Warming Up To Hybrid Trials" (pages 5-7) looks at the industry's effort to make accommodations that would enable clinical trials to continue while maintaining patient safety, with respect to both the trials themselves and COVID. Over the course of one year — seemingly overnight, in an industry not known for rapid change — the use of hybrid trial methods and technologies, as well as the industry's understanding of hybrid trial advantages and challenge areas relevant to various therapy areas, skyrocketed.

Throughout 2021, ISR produced a series of reports digging deep into the rise of hybrid trials, a trio of which are included in this e-book. "Interest In Hybrid Trials Increases" (page 8) tracks the aforementioned sharp rise in hybrid trial utilization, as well as optimism for the use of hybrid trials in greater proportion to traditional trials moving forward. "Managing Trial Components: Hybrid Vs. Traditional Models" (page 9) asked respondents to weigh in regarding whether the management of a variety of trial functions was made easier in a hybrid model, in a traditional model, or whether no appreciable difference existed.

"Hybrid Trials Are Impacting Clinical Research, But Do Patients Want Them?" (pages 10-11) features a discussion with Ken Getz, founder of The Center for Information and Study on Clinical Research Participation (CISCRP), which has spent nearly a decade focusing on the patient experience in clinical trials via its Perceptions and Insights study. It examines what is necessary to sustain hybrid methodologies. Meanwhile, "Hybrid Vs. Traditional Clinical Trial Costs" (page 12) analyzes each trial approach's perceived expense relative to the other, both now and in the future.

"Hybrid Trials Q&A" (pages 13-15), features a sit-down with Rebecca McAvoy, VP of market research at ISR Reports. The Q&A discusses key takeaways from a recent ISR report (*Hybrid/Virtual/Decentralized Clinical Trials Market Outlook*), as well as seeks additional insight from Rebecca. The e-book concludes with "Hybrid Trials Are Here To Stay" (pages 16-19), which acknowledges the speed at which hybrid trials came to dominate clinical research, gauges respondents' thoughts on the effectiveness of those trials, and speculates on hybrid elements that have improved over time or remain to be ameliorated.

Hybrid trials have become so common on the clinical trial landscape that it almost is difficult to remember a time when they were not so ubiquitous, even though it was only a few years ago. The industry can continue to improve the effectiveness of hybrid trials by recognizing the pressures that have led to a de facto "coming out party" for hybridized studies since 2020, understanding associated difficulties that have been overcome so far, and comprehending the challenges yet to be conquered. ISR

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About **The Authors**

ED MISETA
Chief Editor, *Clinical Leader* @EdClinical

Miseta studied business economics at Pennsylvania State University and holds a master's degree in business administration. He has been a writer for more than 15 years and has been covering clinical research since January 2013. In his current position, Miseta interviews clinical executives from pharmaceutical and biotech companies and shares their insights with readers. His primary focus is on best practices, challenges faced and overcome, clinical trends, partnering, and implementing new technologies. He has also moderated numerous speaker panels at industry conferences and trade shows.

REBECCA MCAVOY
VP of Market Research, Industry Standard Research @Twitter

McAvoy has been with ISR for nine years and has been conducting both qualitative and quantitative market research in the pharmaceutical industry since 2006. She currently leads the clinical development market research division at ISR, overseeing syndicated reports and custom studies. Much of her research has focused on brand perceptions, outsourcing behaviors, and customer needs. Prior to ISR, McAvoy spent six years at ZS Associates, conducting market research with physicians and patients.

CONTENTS

Welcome to

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Warming Up To Hybrid Trials

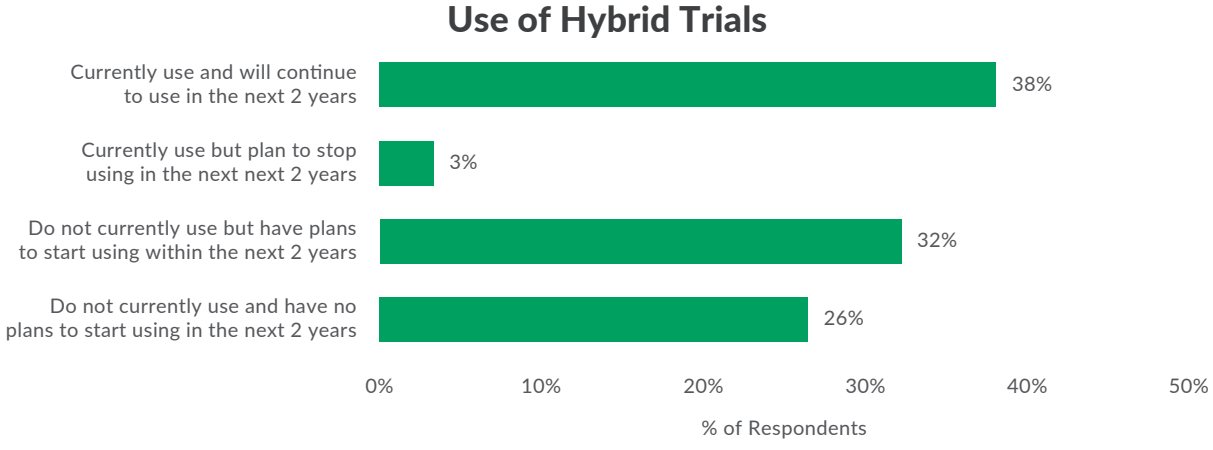
REBECCA MCAVOY VP of Market Research, Industry Standard Research @Twitter

The COVID-19 pandemic forced many industries to adapt to a strange new quarantined and socially distanced environment. The clinical trials space was no exception. Patients, especially very sick patients, cannot be expected to appear at trial visits as they once did. Accommodations needed to be made to enable trials to continue while maintaining patient safety – safety with respect to the trial itself and safety with respect to COVID.

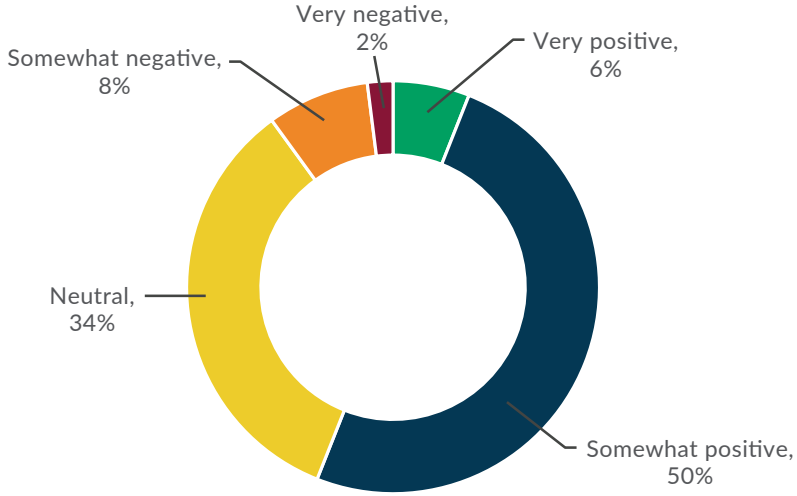
The pharma industry is not known for rapid change. A recent interviewee mentioned that she feels like she is tapping into stone tablets with chisels given the slow rate of change in clinical trials. Prior to 2020, a toe was dipped into trials with online components. However, the COVID pandemic brought push to shove, and many trial sponsors and CROs had no choice but to take the plunge into hybrid trials.

In a recent survey, Industry Standard Research (ISR) asked 121 clinical trials outsourcers at sponsor companies a series of questions about their company's use of hybrid trials. Hybrid trials were defined as the category of trials in which patients participate from home for some visits/activities rather than in a clinical setting. Forty-one percent of respondents indicated that their companies were currently using hybrid trials, and another 32% say their companies have plans to start using hybrid trials in the next two years.

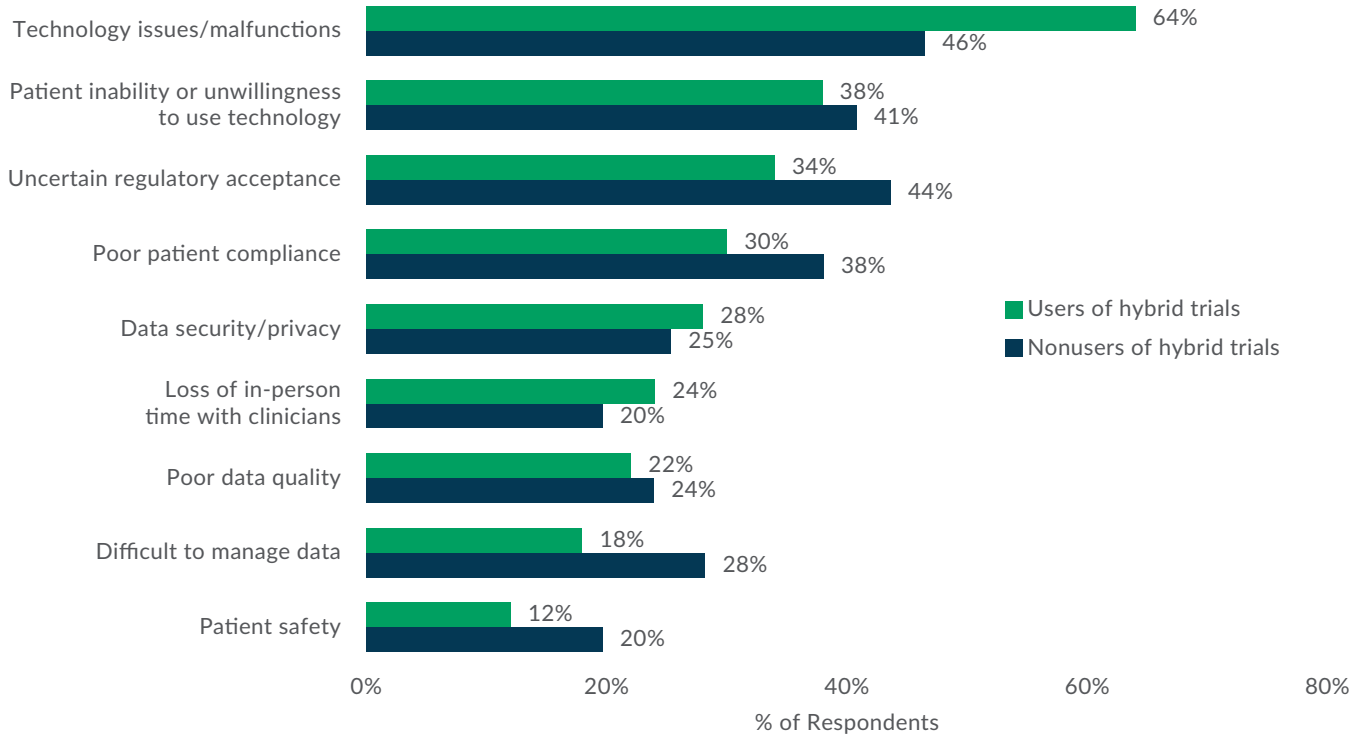
Compare this to results from a different study ISR ran the previous year: only 3% of respondents from sponsors and CROs said their companies were currently running hybrid/virtual trials and only 11% reported that their companies were even in the planning stages. The COVID pandemic in the 15 months between these surveys facilitated a large jump in the usage of hybrid trials.

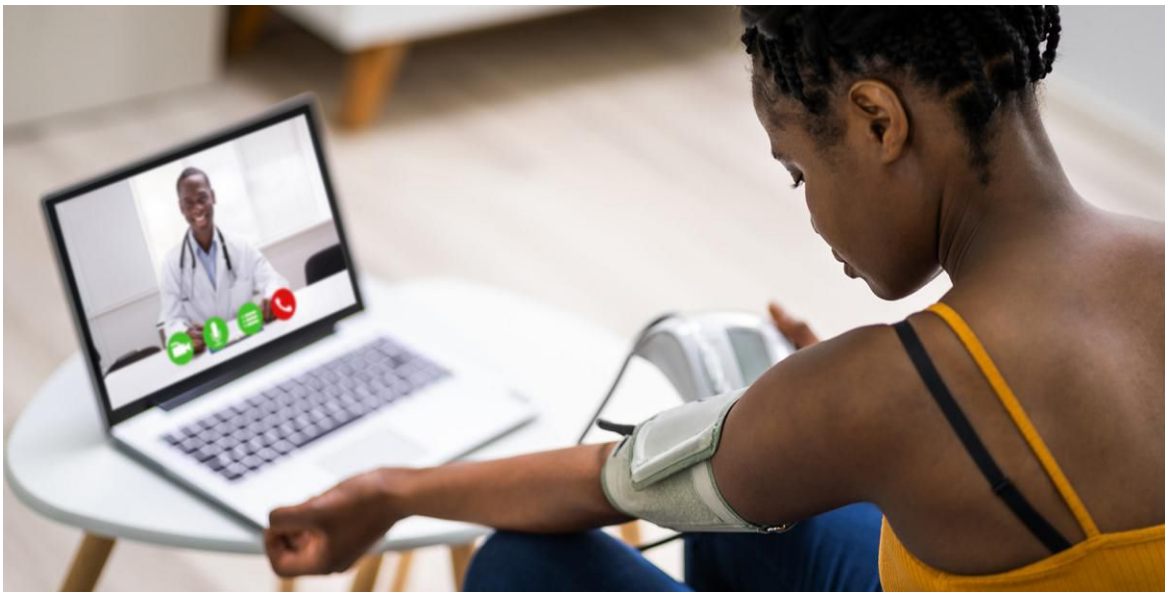


Overall Impression of Hybrid Trials



Concerns/Downsides about Hybrid Trials





So the use of hybrid trials has increased substantially, but how have these trials been working in practice? Among respondents whose companies are currently using hybrid trials, over half (56%) have a positive overall impression of hybrid trials. Another 34% report a neutral impression, and only 10% have a negative impression.

One commonly mentioned theme for what has worked well in hybrid trials is that they enable easier participation for patients, resulting in good patient compliance.

- "Recruiting and retention of the patients has worked well as it is easier for the patients to have the study visits at home — a nurse coming to them rather than the patients going to the clinic."
- "Patient experiences are very positive."
- "More patient retention and compliance."

A second positive reported outcome of hybrid trials is the speed of data collection. The online model enables fast data collection and results tabulation.

- "Reporting of data in a timely manner as data entry burden is taken off of site personnel."
- "Speed of data analysis has been fairly good."
- "We have had real-time data."

However, the positive feedback on what has worked well doesn't mean that running hybrid trials is without challenges. Survey respondents also shared what has been frustrating in their experience with hybrid trials. Many responses were technology-related (technology not working properly, no available technologies to meet needs, expensive technologies), but they also ranged from extensive training needs and long setup times to challenges integrating in-person data with online data and high turnover in nursing staff.

Because hybrid trials are still quite new to the industry, there are many unknowns and concerns about running these trials. To get a sense for any discrepancy between the reality of running these trials and assumptions, we asked respondents from all companies to select up to three biggest worries or downsides regarding hybrid trials and then compared results between those whose companies are using hybrid trials and those that aren't.

Technology issues/malfunctions proves to be the area with the biggest difference between users and nonusers. Sixty-four percent of respondents whose companies are currently running hybrid trials list technology issues as a downside, compared to only 46% of respondents from companies that aren't using hybrid trials, a difference of 18 percentage points. This indicates that respondents whose companies aren't running hybrid trials may be underestimating the technology-related issues that arise when actually implementing hybrid trials.

On the flip side, Uncertain regulatory acceptance, Poor patient compliance, Difficult to manage data, and Patient safety prove to be more concerning to respondents whose companies don't run hybrid trials compared to respondents whose companies do. Respondents whose companies are inexperienced with running hybrid trials may be more concerned with these potential downsides than actual experience with these trials dictates. ISR

Interest In Hybrid Trials Increases

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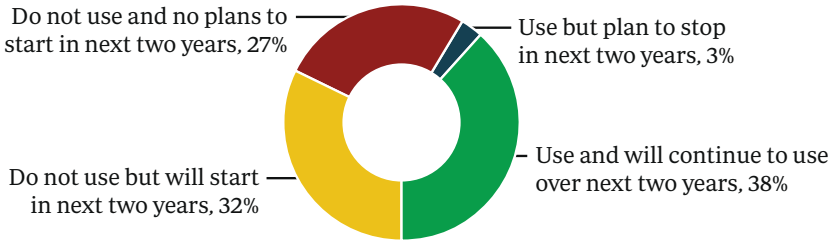
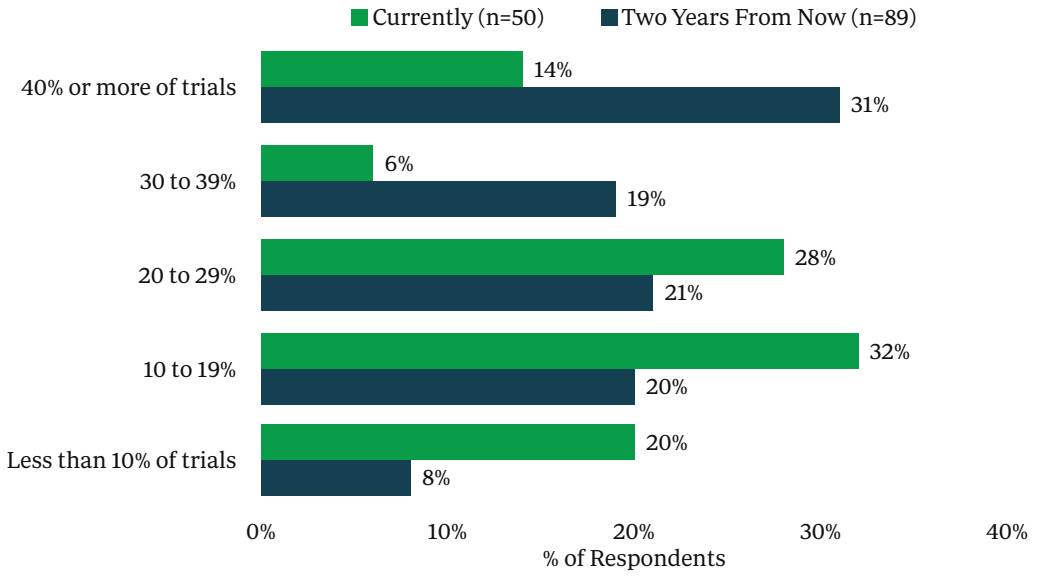
While outsourcing respondents currently hold mixed opinions on conducting hybrid trials (some traditional and some decentralized components), over two-thirds either currently use or plan to use them in the next two years. Respondents also anticipate that hybrid trials will make up a greater proportion of their studies two years from now. This is starkly illustrated in the bar graph below, where 14% of respondents currently — and 31% two years from now — use hybrid strategies for at least 40% of their trials.

"Please indicate your organization's current and future use of trials where patients participate from home via apps, monitoring devices, and online platforms rather than in a clinical setting. These trials may be called 'virtual,' 'decentralized,' 'remote,' or 'hybrid' trials." (n=121).



"What percentage of your organization's current trials would you estimate is being conducted as hybrid trials?" (respondents whose companies are currently using hybrid trials, n=50)

"Two years from now, what percentage of your organization's trials would you estimate will be conducted as hybrid trials?" (respondents whose companies are currently using or plan to use hybrid trials, n=89).

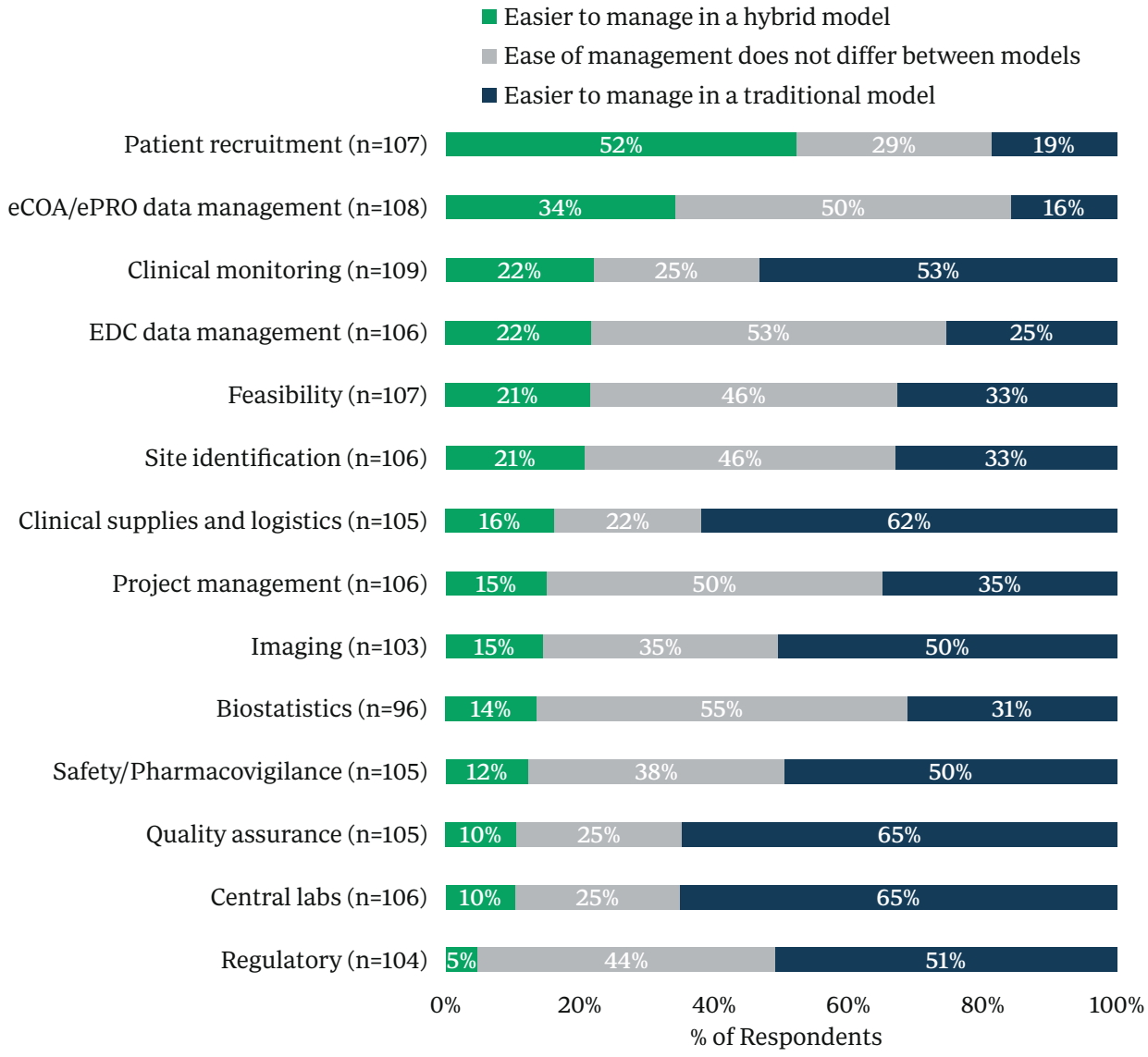


Managing Trial Components: **Hybrid Vs. Traditional Models**

INDUSTRY STANDARD RESEARCH

Respondents were shown a variety of trial functions and asked to opine as to whether management of each function was easier in a hybrid model, traditional model, or does not differ. To get an overall sense of managing hybrid vs. traditional trials, we averaged responses across functions. This analysis showed Easier to manage in a hybrid model at 19% and Easier to manage in a traditional model at 42%, meaning functions are over twice as likely to be considered easier to manage in the traditional model than the hybrid model.

"How does the ease of managing each of the below trial functions compare between a hybrid clinical trial and a traditional clinical trial?" (responses of 'don't know/not applicable' have been removed)



Hybrid Trials Are Impacting Clinical Research, But Do Patients Want Them?

ED MISETA Chief Editor, *Clinical Leader* @EdClinical

Clinical trials continue to evolve and have become increasingly complex. Studies now have more procedures, visits, and time spent at clinics during those visits. Studies also have narrower inclusion criteria and longer travel times to clinics. Those factors have been building for years and have created additional burdens for patients.

The Center for Information and Study on Clinical Research Participation (CISCRP) is celebrating its eighth year of focusing on the patient experience in clinical trials via its *Perceptions and Insights Study*. Founder Ken Getz notes the mission of the nonprofit group is to educate and engage patients, the public, and other stakeholders.

The survey is conducted worldwide, and CISCRP works with many organizations, pharma companies, patient advocacy groups, foundations, government agencies, and research centers to reach a large number of patients. Approximately half of respondents are from North America and another 30% to 40% from Europe.

The world has had to deal with COVID-19 since the last time the survey was conducted, and the pandemic made it more difficult for patients to participate in trials. Although media coverage of vaccine development in 2020 helped educate the public on the need for clinical research, what surprised Getz the most is that the pandemic did not have a measurable impact on the attitudes and perceptions that patients have about clinical trials.

"We saw high ratings in terms of the quality of patient's experiences in clinical research along with a high willingness to repeat participation," says Getz. However, despite the industry shift toward patient-centric practices, Getz notes, "the fundamental measures around the burdens of participation and their influence on the decision to participate only changed slightly."

One example of the changes that took place was the move to decentralized and hybrid trials. Those changes also raised concerns for patients, such as whether remote visits would replace the personal interactions patients had with study staff. Getz believes patients are looking for a balance between personal interactions and the use of new technologies. He notes patient preferences vary based on the therapeutic area, geography, and other factors.

WHAT DO PATIENTS NEED TO KNOW?

One of the questions patients were asked is what they want to know when deciding whether to participate in clinical research. Most patients express the greatest interest in understanding the purpose of the research. That is followed by the desire to understand inherent risks in the trial, benefits of the study medication, and costs/reimbursement. Once patients begin participation in the trial, logistics become an even more important consideration.

"Reimbursement plays a key role in trial participation," says Getz, "especially in virtual (decentralized) trials. It's an important factor that makes patients feel connected and valued. In North America close to 60% of trials offer cost reimbursement to patients. The form of reimbursement varies, with the most frequent being cash, check, and debit card."

Travel was another issue that generated a good amount of feedback. When compared to prior surveys, there was no major change in the willingness of respondents to travel. However, clinical trial participants still view travel as being disruptive to their daily routines. Survey respondents expressed high interest in minimizing travel and having more flexibility regarding when to participate.

For patients who were forced to travel, that journey generally took between 30 and 60 minutes. For 25% of patients, the travel time was more than an hour. Although travel is disruptive to work and family time, when asked if they would like their site visits replaced with virtual trial components, patients indicated they were willing to trav-

*"There's so much we can ask patients to help us learn how to optimize our relationships with them," says Getz, speaking with CEO Jim Murphy during a Phireside Chat at Greenphire's Patient Convenience Summit. "*Our Perceptions and Insights Study *is conducted every other year. We typically receive responses from 12,000 people."*

KEN GETZ
Founder, CISCRP

el. Even patients with the most severe medical conditions were willing to travel to appointments.

"That seems almost counter intuitive," notes Getz. "It tells us patients value personal relationships. They want to have some in-person engagement with a specialist or study team. That preference for personal engagement also coincides with unmet medical need and participants wanting to manage the burden of their disease. When patients are dealing with a diagnosed medical condition, particularly one for which there is not an adequate therapy, there's a much greater need to do whatever it takes to advocate for oneself and to integrate a trial into their daily life."

TRUST BRINGS LONG-TERM PARTICIPATION

Drug companies want to recruit patients who will engage with a trial for the duration of the study. So what factors will keep patients engaged for the long term? The studies conducted by CISCRP have found the most critical factors to be quality of the relationship with study staff and the amount of trust that exists between staff and the study participants.

"A lot of it has to do with whether their expectations were met," states Getz. "Did their expectations coincide with and affirm what they were expecting when they completed the informed consent process? Their relationship with and trust in the study staff played a role. The feedback they received throughout the study and communication with site staff is very important. A high percentage of respondents noted they had a positive experience participating in their trial even when the investigational therapy offered no benefit to them."

Over the last two years, respondent perceptions of their quality of care in the clinical study was up materially. Still, for some subgroups, fewer patients participating in a trial noted they would do it again. That finding may again show that while patients value the convenience of decentralized trials, remote engagement may result in fewer interactions with site staff.

"There seems to be a natural tension we picked up on in the study," says Getz. "Patients and the public have a desire for options, but there is a need to balance options with the need for personal connections. Decentralized and hybrid trials offer convenience, but that convenience must be balanced with individual preferences. We are entering an age of more personalized and customized participant experiences, and we have to figure out how to manage that."

SITES HAVE A SACRED RELATIONSHIP

Getz notes the relationship between the patient and the clinical site is sacred, and that relationship is important to study recruitment and retention. There is a comfort level that exists between the site and patients, which enables the site to understand patients and make accommodations that are appropriate for each patient. With a hybrid trial, sites can offer alternate mediums of interaction for each study participant. Although that may be convenient for patients, Getz believes this juggling hybrid options will present challenges for sites as they move along the learning curve.

"A hybrid approach will allow sponsor companies to collect clinical research data and to offer more participation options for patients," says Getz. "But offering more options for patients will require study staff to accommodate and execute multiple models simultaneously. That will present challenges and opportunities moving forward."

Data privacy is another area that is very important to patients. Researchers are collecting more genetic and biomarker information in trials and relying more on personal health information and electronic medical information. In North America, 60% of patients expressed concerns over data privacy, but that does not appear to interfere with their willingness to participate in trials. Although patients seem to have a high comfort level with sharing data, approximately 20% of patients interviewed indicated data privacy is a major barrier to their participation in trials.

"When it comes to remote and virtual trial models, data privacy concerns become elevated," states Getz. "There is a sense that as we use more technology, we may have to address a different set of expectations. Patients are also concerned that an increased use of technologies would increase their out-of-pocket costs, especially if the trial involved the use of a handheld device or mobile app. There is a lot of communicating and educating that we have to provide as we transition to more remote and virtual support in our studies." ISR

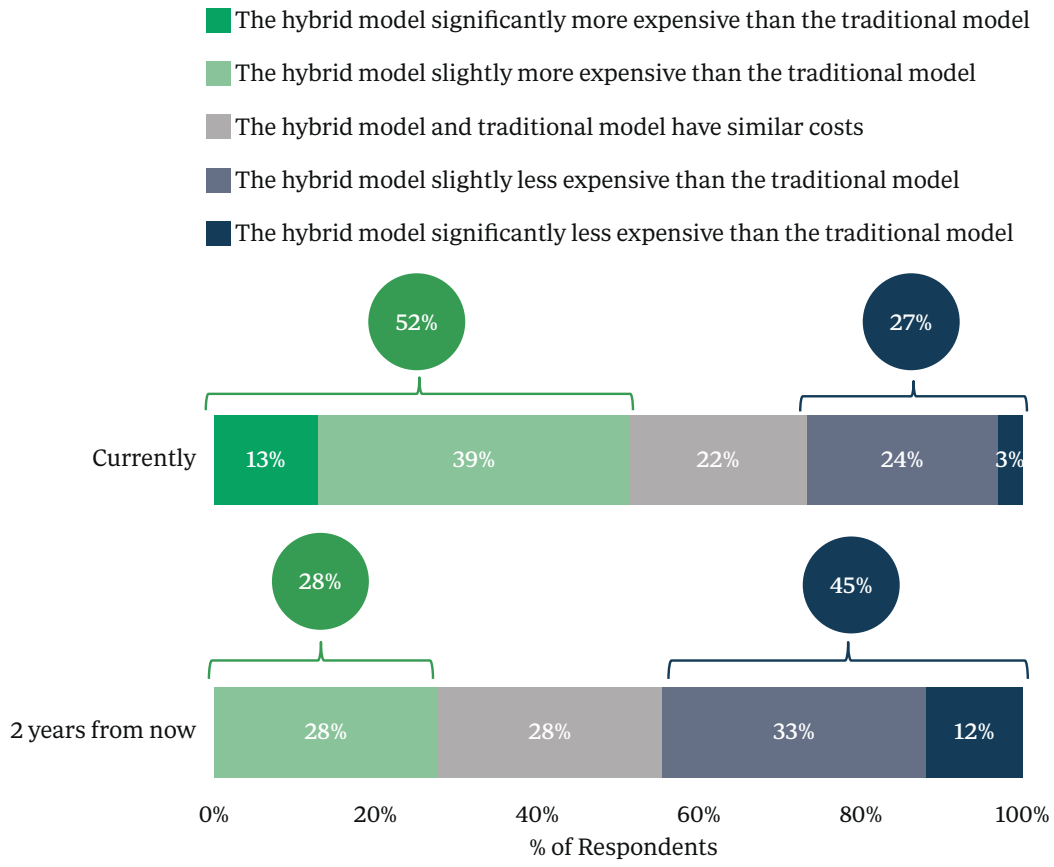
Hybrid vs. Traditional **Clinical Trial Costs**

INDUSTRY STANDARD RESEARCH

In a recent survey about hybrid trials, over half of respondents reported that hybrid trials are currently more expensive to conduct compared to trials in the traditional model, while only one-quarter considered hybrid trials to be less expensive than traditionally run trials. However, there is an expected flip in this sentiment. Two years from now, almost half of respondents expect the hybrid model to be less expensive, while only about a quarter think that hybrid trials will be more expensive than traditional trials.

"We understand there are many factors that can affect a trial's cost. We are looking to understand your general impression regarding the cost of traditional trials compared to hybrid trials. Currently, how do the costs of the hybrid trial model and the traditional model compare?" (n=109)

"Two years from now, how will the costs of the hybrid trial model and the traditional model compare?" (n=109)



Hybrid Trials: **Q&A**

ED MISETA Chief Editor, *Clinical Leader* @EdClinical

ISR Reports has released a new report titled Hybrid/Virtual/Decentralized Clinical Trials Market Outlook. *The report looks at the adoption of these trials and the components that are gaining the most traction.*

To gather the insights, ISR surveyed 109 respondents at sponsors and CROs regarding their experiences with hybrid trials and providers of these services. Though not all reported a smooth, pain-free experience, nearly two-thirds of respondents came away with a positive overall impression of hybrid trials. Furthermore, respondents do not seem to consider the hybrid trial model as a temporary solution to be discarded after the pandemic has subsided. A whopping 83% of respondents expect the hybrid trial model will be used more frequently than the traditional trial model three years from now. These data are saying loud and clear that hybrid trials are here to stay.

I spoke to **Rebecca McAvoy, VP of market research at ISR Reports**, to gain additional insights into hybrid trials and to discuss some of the key takeaways from the report.

REBECCA MCAVOY, VP of Market Research, *Industry Standard Research*

ED MISETA: Survey respondents noted which remote components are currently being used and which ones they expect to be using in two years. A couple of the findings surprised me. For example, even though decentralized trials allow patients to participate in studies from their homes, only 16% of companies report direct-to-patient shipment of investigational medicinal products (IMP). Only 18% are using wearable sensors/connected health devices. Any thoughts on why those numbers are so low?

REBECCA MCAVOY: There certainly was a rush to convert traditional trials to decentralized trials at the start of the pandemic. Although these remote components can facilitate the ability to participate in some parts of clinical trials from home, implementation of these remote components isn't easy and doesn't come without risk. Directly shipping IMP to patients comes with concerns about patient safety, patient compliance, cold chain/distribution issues, etc. Using wearable sensors or connected health devices introduces challenges of training patients/sites on use of the devices, device/technology malfunctions, patient compliance, and analyzing massive datasets, to name a few. I expect there to be an uptick in usage of these remote components, but it does take time for companies to get these functionalities up and running and to feel comfortable with these new approaches.

MISETA: Respondents were asked what components of a trial are easier to manage in a hybrid approach and which were easier to manage in a traditional trial. Only patient recruitment and electronic patient-reported outcomes (ePRO were cited as easier to manage in a hybrid trial. Seven components were cited as easier to manage in a traditional trial, and six components were noted as not differing between the models. Are some respondents feeling that certain functions are not easier to manage in a hybrid model simply because they have not had sufficient time to evaluate them?

MCAVOY: One thing to remember about hybrid trials is that only some of the activities take place at home while other activities still take place in a clinical setting, meaning that those responsible for running the trial need to account for both home-based activities and clinic-based activities, further complicating the already complex process of trial operations. The components that were considered harder to manage in a hybrid setting will likely become easier over time as the folks in charge of the trials become more well-versed in the hybrid trial design and execution.

MISETA: I think the best statistic in the report was the satisfaction level noted by companies using a hybrid approach. Sixty-three percent of respondents noted a somewhat or extremely positive experience using a hybrid approach. Another 24% noted a neutral experience, while only 13% reported a negative experience. Companies are not using most of the capabilities available in a hybrid approach, and there are only a few capabilities that they note are easier to manage in a hybrid trial. That being the case, to what do you attribute that high satisfaction rating?

MCAVOY: Based on responses in other areas of the survey, I have a few thoughts. The top 'lesson learned' is that the hybrid approach can work. I think people are pleased that their trials didn't have to completely shut down amid the pandemic. There had been dabbling in these types of trials prior to the pandemic, but the pandemic forced companies to jump in with both feet, regardless of apprehension. Some aspects of hybrid trials that have gone well are higher quality/faster data, easier patient recruitment, improved patient compliance, and easier/more flexible for patients. I suspect those qualities of hybrid trials played a role in the positive satisfaction rating.

MISETA: The most important lesson learned by respondents is that the hybrid approach can work, followed by that approach requiring significant planning and project management and patients being open to them. Were you able to determine from respondents what some of the additional planning and management requirements were that do not exist in traditional trials?

MCAVOY: As we all know, hybrid trials were new for many in the industry prior to the pandemic, so this was not a space in which people had a lot of prior experience to draw from. Also, as I mentioned before, hybrid trials are designed to have both in-clinic and remote components, creating additional challenges related to setup, coordination, and communication. The following quote about 'lessons learned' sheds light on several of these ideas: "Extreme planning for each visit required, advance patient reminders, provide opportunity for direct person-to-person communication with patient together with their physician before and after each visit …"

MISETA: I feel like one of the primary concerns about hybrid trials that I hear from sponsor companies is the quality of the data that will be gathered from patients. Yet the report asked respondents what aspects of their hybrid trials have gone well, and the number one answer was higher quality and faster data. Are the concerns over data quality a bit overblown?

MCAVOY: Interestingly, perspectives on the quality of data in hybrid trials can vary. We asked respondents to share, in their own words, what has worked well with hybrid trials and what has been frustrating. "Higher quality/faster data" was the most mentioned response for aspects that have gone well; however, "data concerns" was tied for the second most mentioned response for aspects that have been frustrating. It all comes down to individual experience. If data collection and management has gone smoothly, the person responsible for that trial might say that higher quality/faster data is a great benefit of hybrid trials. On the other hand, if someone has had data-related challenges in their hybrid trials, they might not have as rosy of a perspective.

MISETA: When asked what aspects of their hybrid trials have been the most frustrating, the number one answer was technology-related issues. Number two was setting up the model. These issues may fade as the model gains increased usage, but it does make me wonder if many companies are attempting to set up these trials themselves rather than engaging with vendors who have the required expertise.

MCAVOY: Just as this trial design is new for sponsors, it is also new for service providers. CROs don't necessarily have all the answers either and may have a steep learning curve when it comes to hybrid trial design and execution. We didn't ask specifically about whether sponsors are attempting to set up trials on their own, but we do know that hybrid trials often involve additional vendors compared to traditional trials, which adds complexity to the overall trial management for the sponsor.

MISETA: When asked about the potential benefit to sponsors and CROs, respondents noted better patient recruitment, retention, compliance, and diversity. All of these are issues that have plagued clinical trials for years. As the adoption of these trials increases, can we expect to finally make a dent in these industry challenges?

MCAVOY: Yes, I think hybrid trials will be a great tool for improving some of the age-old challenges related to recruitment, retention, compliance, and diversity. Because of the ability to participate from home, patients in the more difficult-to-reach demographics will have increased participation opportunities. Improved patient compliance and recruitment come up frequently as benefits of these trials. Being able to complete at least some trial activities remotely facilitates easier participation and lower likelihood of dropping out, particularly for patients for whom travel is difficult.

Please visit ISR Reports for more information on the Hybrid/Virtual/Decentralized Clinical Trials Market Outlook. ISR

Hybrid Trials Are Here To Stay

REBECCA MCAVOY VP of Market Research, Industry Standard Research @Twitter

Hybrid trials. Decentralized trials. Remote trials. Virtual trials. No matter what you (or anyone else) call them, the rapid uptake of trials in which patients participate from home for some visits/activities rather than exclusively in a clinical setting has been a game-changer for continuing clinical research in the face of the COVID-19 pandemic. Though the industry has yet to settle on a uniform terminology for this type of trial, it does seem as though the industry is aligned on its expectations for the future of these trials.

In a recent ISR survey, 109 respondents with recent experience conducting hybrid trials were asked to share their outlook on hybrid trials' place in the biopharmaceutical industry over the next three years. The results leave no ambiguity. Over 80% of respondents expect that the hybrid model will be used more often than the traditional trial model within the next three years. And about half of those respondents anticipate the hybrid model will be used significantly more than the traditional model. These data may skew somewhat in favor of future hybrid trial use as the respondents were required to have been involved with running a hybrid trial over the last year. However, because these data are coming from users of hybrid trials rather than a random sampling across drug developers, the respondents are speaking from a place of experience rather than conjecture.

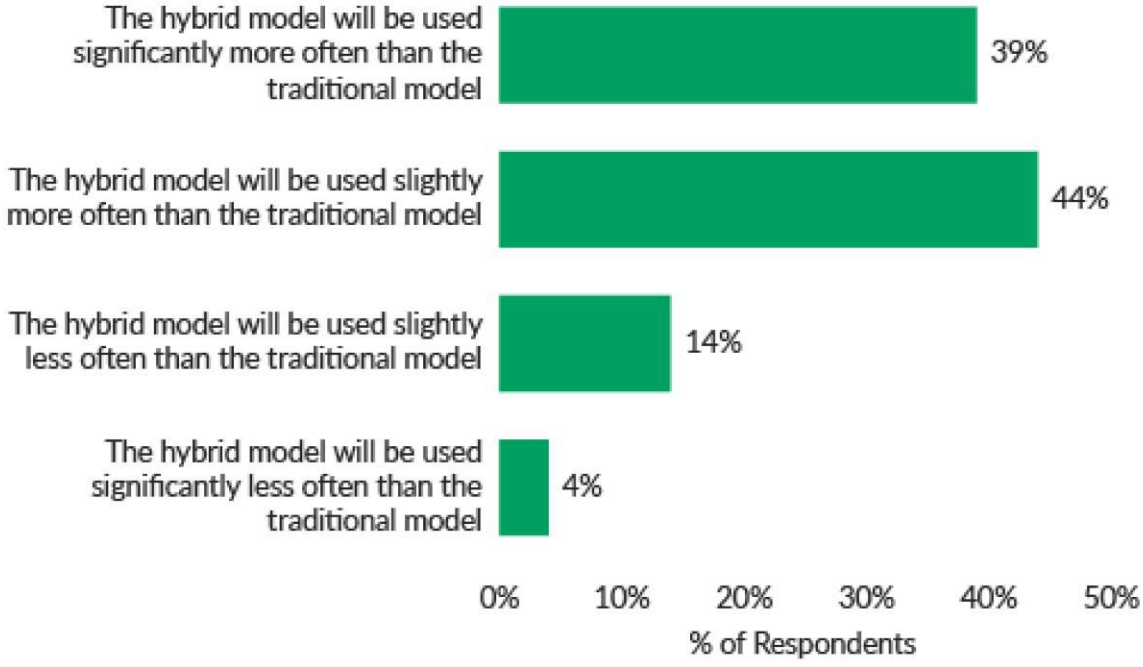
From these data, it is clear that not only do users of hybrid trials not expect the hybrid model to be relegated to the back burner once the pandemic has subsided, but they expect this model to quickly become the predominant model. In an industry known for its slow pace of change, there must be a strong belief that these trials are the wave of the future for there to be such consensus in this bold prediction.

So what is driving this prediction for the use of the hybrid model overtaking the use of the traditional trial model in such a short time? First off, respondents rated their experiences with hybrid trials as mostly positive: 63% express a positive experience, 24% are neutral in their opinion, and only 13% consider their experience with hybrid trials to be negative. While their overarching impressions aren't solely positive, you can bet your bottom dollar that if those running hybrid trials were consistently experiencing disastrous results, we would not be seeing such strong expectations for future use.

To dig a little deeper into the experience of running hybrid trials, survey participants were asked to describe what has gone well when using this model. Higher quality/faster data was mentioned by one-quarter of respondents, while the next three most mentioned aspects were related to patients: Easier patient recruitment, Improved patient compliance, and Easier/more flexible for patients. As patient recruitment and retention are ongoing challenges in clinical trials, any improvements made in these arenas are likely to be welcomed with open arms.

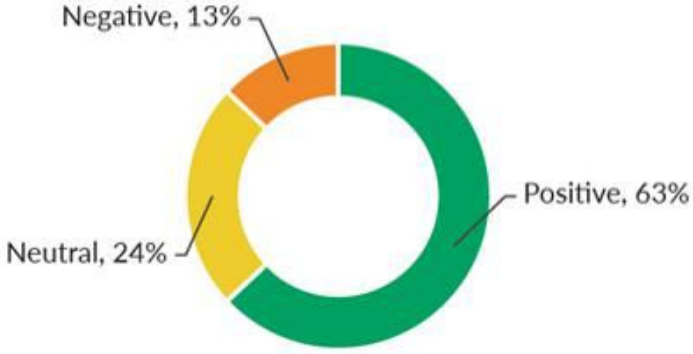
Predictions for Hybrid Trial Use in 3 Years

"What is your outlook on hybrid trials' place in the biopharmaceutical industry over the next three years"

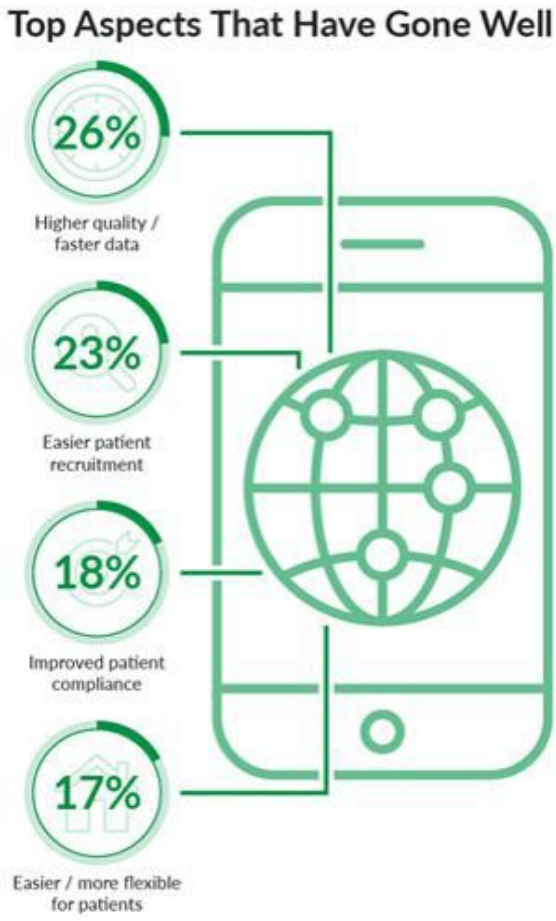


Overall Hybrid Trial Experience

"How would you classify your overall experience with hybrid trials?"



"PLEASE TELL US ABOUT YOUR EXPERIENCE WITH HYBRID TRIALS. WHAT HAS WORKED WELL?"



A few selected responses to the above question shed light on the most frequently mentioned aspects of hybrid trials that have gone well:

Higher quality/faster data

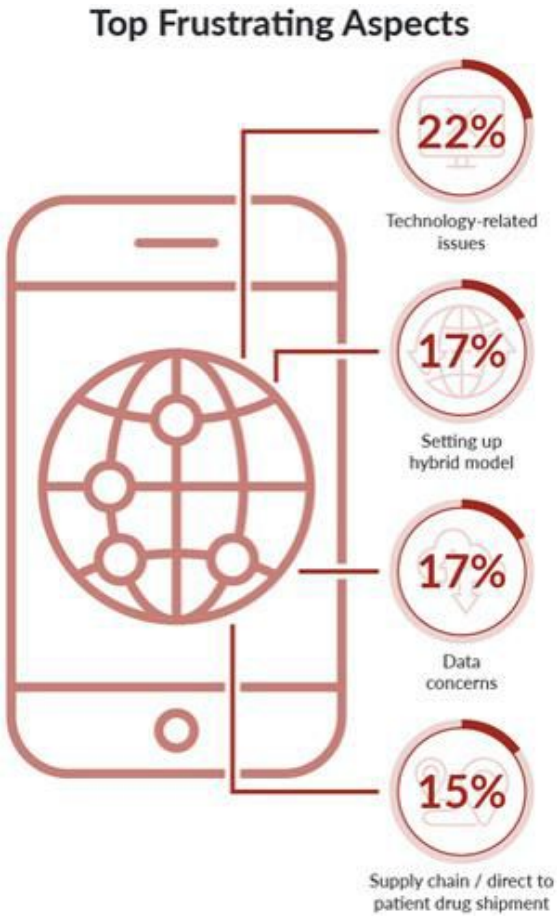
- "Use of emerging capabilities (ePRO, eConsent, eCOA, etc.), real-time and quick access to data, seamless document management"
- "PROs have been much more robust and timely"
- "Pace of data entry and accessibility of data and their processing"
- "Relatively easy setup, fast data generation, results available promptly"

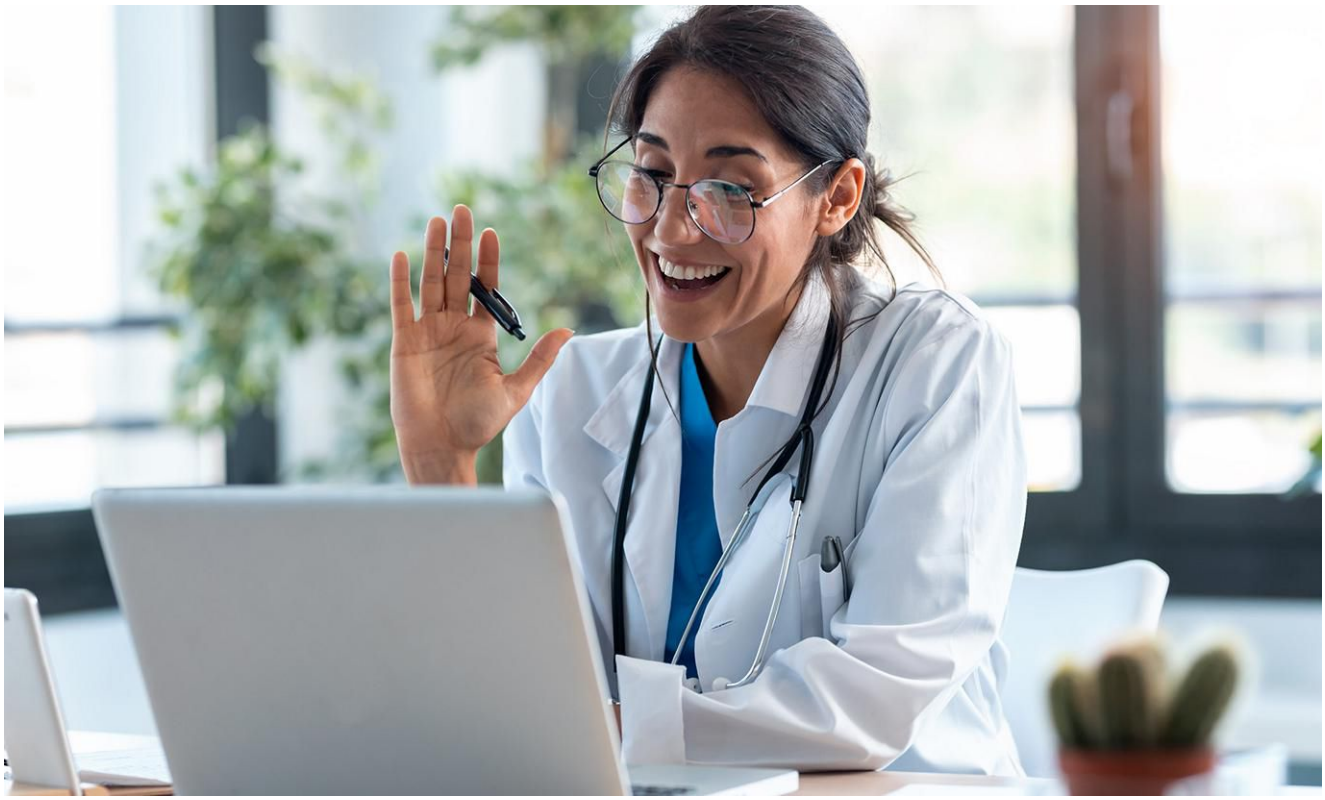
Patient recruitment/compliance/ease of use

- "Easier to recruit patients as can reach rural areas (no reliance on centers)"
- "Patient compliance with diaries, ePRO, etc. increased significantly. Patients save travel time and better balance private life"
- "Patient satisfaction; Prevention of patient drop-outs; Virtual visits involving patient-reported outcomes; Visits involving adverse event ascertainment can be done remotely very well"
- "Better compliance as no travel for patients involved, PROs better filled in, fewer dropouts due to nonsafety reasons, clinical monitors less exhausted"

This is not necessarily to say that everything has come up roses for hybrid trials. Respondents were also given the opportunity to expound on aspects of this model that have been frustrating. Technology-related issues came up the most often, followed by Setting up the hybrid model and Data concerns. Interestingly, we have seen a differing of opinions on the data gathered during hybrid trials — it is mentioned by some as an aspect that has gone well and by others as an aspect that has been frustrating. Not all users of the hybrid model have the same takeaways about its benefits and drawbacks.

"PLEASE TELL US ABOUT YOUR EXPERIENCE WITH HYBRID TRIALS. WHAT HAS BEEN FRUSTRATING?"





The following verbatim responses to this question provide more detail about what has frustrated survey respondents about hybrid trials:

Technology-related issues

- "Patients' understanding how to use technology; Home nurses not being able to correctly teach patients how to use tech or troubleshoot when there is a problem with a device; Lack of adherence over time with digital devices"
- "Connection issues with devices, user friendliness of the ePROs … translation of the manuals/screens for patient-related devices"
- "Increased responsibilities for patients (especially the elderly age group), data security, interconnectivity across various data platforms, training needs, and absence of seamless customer support and internet issues"

Setting up hybrid model

- "It added complexity and introduced a third party, which wasn't always properly trained. There were also frustrations with rescheduling and some samples that were not handled properly"
- "Setup is more complicated than in more traditional trials"
- "Putting in place a hybrid trial was very time consuming in terms of logistics. Everything about data collection was much more complex, IMP preparation and administration and all the agreements required to be amended. Actually, it was like setting up a brand-new study while the study was already ongoing (i.e., twice start-up activities…)"

Data concerns

- "Lack of reliability of data sources, less control on data input and quality, difficulties to reconcile data"
- "Data integration (which is difficult due to the volume of data collected)"
- "Technology has oftentimes been used to replace hospital and office-based measures and as such it is risky and remains an unknown as to the quality and nature of the data sets"

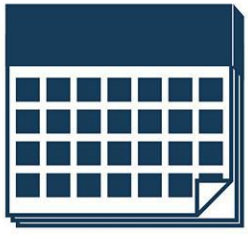
Though there remain some kinks to work out in the design and execution of hybrid clinical trials, there have been enough positive results for respondents to predict continued rapid uptake of this model. In the age of patient-centricity, this new trial model should offer a more appealing method of clinical trial participation for potential patients and hopefully make any growing pains worthwhile for the industry. ISR

Six Questions to Ask About Your Market Research

How do you ensure the research products and services you buy will make you confident in the decisions you make? Here is how Industry Standard Research ensures you are getting the value you should expect from quality market research.

How Many Participants Take the Study?
Understanding your margin of error allows for better expectation setting, making you more likely to hit your performance metrics. ISR provides a vast sample of participants by using our proprietary Health Panel to make sure our studies reach the correct amount of participants needed for accurate analysis.

Where Did the Participants Come From?
Eliminating sample bias translates into accurate competitive information and improves service quality by ensuring your decisions are the right ones. ISR's Health Panel provides an array of participants of all company sizes within the pharmaceutical industry.



When Were the Data Collected?
This should be the first question someone asks you during a presentation, and saying "I don't know" doesn't sound so good. Whether in custom research or our syndicated library, ISR collects up-to-date data relevant for the project at hand.

Who Sponsored the Research?
We are an independent, third-party data source. We provide clean, unbiased data, and clean data means you can confidently stand behind your analysis and presentations.

What is the Responsibility Profile for the Participants?
Nothing stops a presentation faster than senior management questioning the fundamental basis of your research. Confidently project the research to your decision makers knowing that ISR pulls information from key decision makers.

What is the Background of the Analyst Who Managed the Project and Reporting?
ISR offers experienced analysts with hands-on industry knowledge. Our analysts will produce insights that you can quickly turn into fit-for-purpose recommendations for your organization.