SURVEY REPORT

Leveraging Technology in Phase I Clinical Trials

medrio + ISR reports

Executive Summary

It’s an old adage in clinical development that “every study is different.”

In the past, Phase I trials had a straightforward purpose: testing for basic safety and toxicology. However, in the past few years, early-phase clinical research has become a lot more complicated. In fact, in the last five years, Medrio has identified a 35% increase in variables compared to the preceding five years.

At the same time, Phase III philosophies are creeping into early phase trials. This, too, adds complexity. But Phase I trials can’t risk being weighed down with bloated protocols or too many endpoints.

Although Phase I trials benefit from modern eClinical technology solutions, these study teams are often constrained by limited budgets, tight timelines, and small teams. In short, the industry faces unique challenges in crossing the chasm of technology adoption in early phase research.

Contributing experts

Ana Palijan

Director of Early Phase and Translation Research at Innovaderm Research

Courtnay Buonomo

Associate Director of Data Management Systems and Standards at ADARx Pharmaceuticals

Éric Hardy

Senior Director of Biometrics at Innovaderm Research

Nicole Latimer

CEO at Medrio

In This Guide

The Research

Medrio contracted ISR to survey industry experts involved in Phase I research to understand how we can best support our early-phase clients.

Based on responses from 88 individuals working in Phase I clinical research, it's clear that early phase studies vary dramatically among companies. However, respondents all had one thing in common: they needed flexibility and expert guidance from their technology partners to keep up with the evolving terrain of Phase I research.

This report includes the research results and industry expert insights that explore the "why" behind the data.

Trial complexity

Are more data points better? And what if data comes at the cost of speed? Those are the questions our contributors explore as they unpack the survey stats around Phase I trials—and how companies have vastly different tolerances for complexity.

The need for speed

How can sponsors get to database lock faster? How can they set themselves up for a successful transition from Phase I to Phase II? Industry experts examine how data cleaning and data transformation play a role in speed. They also lay out best practices, including why a clear business case for each variable is the key to unlocking speed.

Data collection and management

How are sponsors navigating technology selection for Phase I trials? Experts unpack how sponsors are making progress in collecting data cohesively. They also share insights on why some companies opt for a hybrid approach to technology, straddling the fence between old and new methods.

Research methodology

- ISR conducted a web-based quantitative **survey with 88 respondents** and in-depth telephone **interviews with 8 participants.**
- ISR's proprietary Health Panel recruited research respondents from **North America and Europe.**
- The research was conducted in Q1 2024.
- Medrio was not identified as the sponsor of the research.
- Respondents were heavily screened to ensure they had the appropriate level of decision-making experience.

How Increasing Variables Affect Early Phase Research

Early phase trials are becoming more complex, sometimes for good reasons and sometimes to the trial's detriment.

In the past, Phase I trials primarily focused on toxicology and safety, providing a first look at how new drugs interact with human biology. However, sponsors have broadened the objectives of early-phase research in recent years.

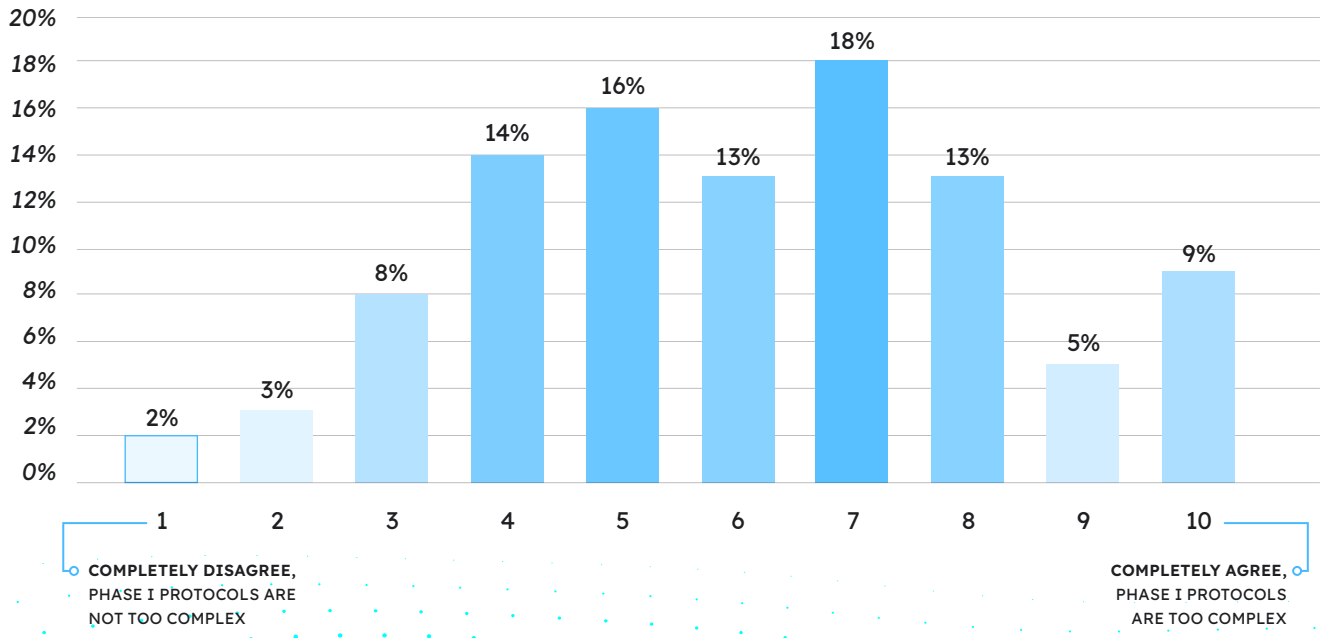
Sponsors face the challenge of balancing the need for robust data collection with the efficiency of trial execution.

Increasing complexity can sometimes be essential—such as when adaptive designs or complex biomarkers are introduced. However, introducing too many variables can overwhelm the trial process, increasing costs, timelines, and the risk of failure.

Here's what industry experts had to say about finding the right balance between depth of data and operational simplicity.

Are Phase I studies becoming too complex?

FIGURE 1.1 Thinking of Phase I studies you've recently been involved in and any other Phase I protocols you've recently seen, please rate your level of agreement with the following statement using a 10-point scale where 1=completely disagree and 10=completely agree.



Are Phase I studies becoming too complex, cont.

When asked if Phase I trials are becoming too complex, respondents offer a diverse set of responses. However, it seems that **most respondents believe Phase I protocols are too complex.**

Beyond these survey results, **Medrio's internal data backs up the claim of increasing complexity.** When comparing our clients' Phase I trials conducted in 2018-2023 to those in 2012-2017, the number of subjects decreased by 50%.

In the last five years, Medrio's clients saw a:

~35% in the number of variables

16.2% in the average number of forms

10.9% in the number of data points

21.1% in the number of form rules

> Complexity is relative. But if you simply look at the volume of data, we've seen a huge increase in variables within Phase I trials."

Nicole Latimer
CEO, Medrio

"We are seeing an increase in complexity," says Éric Hardy, Senior Director of Biometrics at Innovaderm. "The actual structure of many Phase I trials is staying the same, but what is changing is the number of endpoints."

All of these additional endpoints, however, come at a cost. According to Éric, some sponsors mistakenly focus on the number of subjects rather than the number of endpoints when designing a Phase I trial. "They may assume that the trial should not be expensive since it's only ten subjects. But the **statistical analysis remains expensive whether a trial has ten or 100 subjects, as it is based on the end points analyzed."** explains Éric.

With a strong push towards greater complexity within early phase research, sponsors face the challenge of maintaining a balance. As they navigate decisions, it's helpful for sponsors to remain aware of the factors driving this shift.

What is driving this complexity in Phase I trials?

According to the experts we interviewed about the survey results, several aspects are driving complexity in Phase I trials.

PHASE III PHILOSOPHY

There's an increasing transfer of Phase III expectations into the early phase world. Many small biotech startups are hiring pharma consultants who have successfully led global Phase III studies.

"Some Head of Operations bring global expectations to Phase IA/IB," reports Ana Palijan, Director of Early Phase and Translation Research at Innovaderm. "But this later phase approach sometimes translates into over-engineering their Phase IA/IB."

MULTIPLE ENDPOINTS

Sponsors are increasingly looking for anything useful. Éric notes that sponsors may "try to fire in all directions" if their primary endpoint doesn't work. This approach, in terms of global data and statistics, ultimately means a lot of analysis.

CHANGE IN IP

Another complexity driver is the type of IP required due to more tailored drugs with new mechanisms of action.

"For example," says Ana, "there are different safety signals associated with biologics, which changes how Phase I trials need to be conducted to assess toxicology."

> If people have experience with Phase III trials, they may bring that philosophy to Phase I trials. But instead, they need to concentrate on what's most important, such as safety.
>
> Collecting too much data in a Phase I trial can be risky."

Éric Hardy
Senior Director of Biometrics, Innovaderm Research

What is driving this complexity in Phase I trials, cont.

FUNDING CONSIDERATIONS

Venture capitalism is changing. Biotech companies, in particular, are under pressure to assure their investors and show some level of efficacy as they move from preclinical to clinical.

“Some companies,” says Nicole, “may try to collect more data early on to demonstrate the superiority of their therapy as compared to others as early as possible.”

PATIENT EXPERIENCE

Regulatory agencies are pushing harder for data about patient experience in Phase I trials. Ana noted that as more Phase I studies require patient-reported outcomes, sponsors face new decisions about paper versus digital.

“Our data shows that more people are collecting patient-reported outcomes earlier,” confirms Nicole.

NUMBER OF SITES

A few years ago, it was common for an early phase trial to rely on a handful of sites. Today, Phase I trials often include many sites to recruit adequate participants.

“Today, depending on the indication being studied and the saturation of the clinical space, a Phase I study may have 20 sites,” says Ana. “A few years ago, it only took 5 to 6 sites.”

Best practices to manage trial complexity

AVOID OVER-ENGINEERING: Make your study protocols simple. Design a study to collect only the required information. Over-engineering your study design translates into extended timelines in reaching trial closeout.

COLLECT ONLY THE DATA THAT IS NEEDED: Avoid the temptation to collect data just for the sake of collecting data. “At first,” explains Éric, “collecting extra data may not seem to have a big impact. But it creates a lot more work upon data review.”

Nicole adds, “Collecting data is time-consuming and expensive. So don’t collect more than you actually need.”

How Sponsors Navigate the Pressure to Move Quickly

Speed is the key challenge when transitioning from Phase I to Phase II, and flexibility in technology is needed to unlock speed.

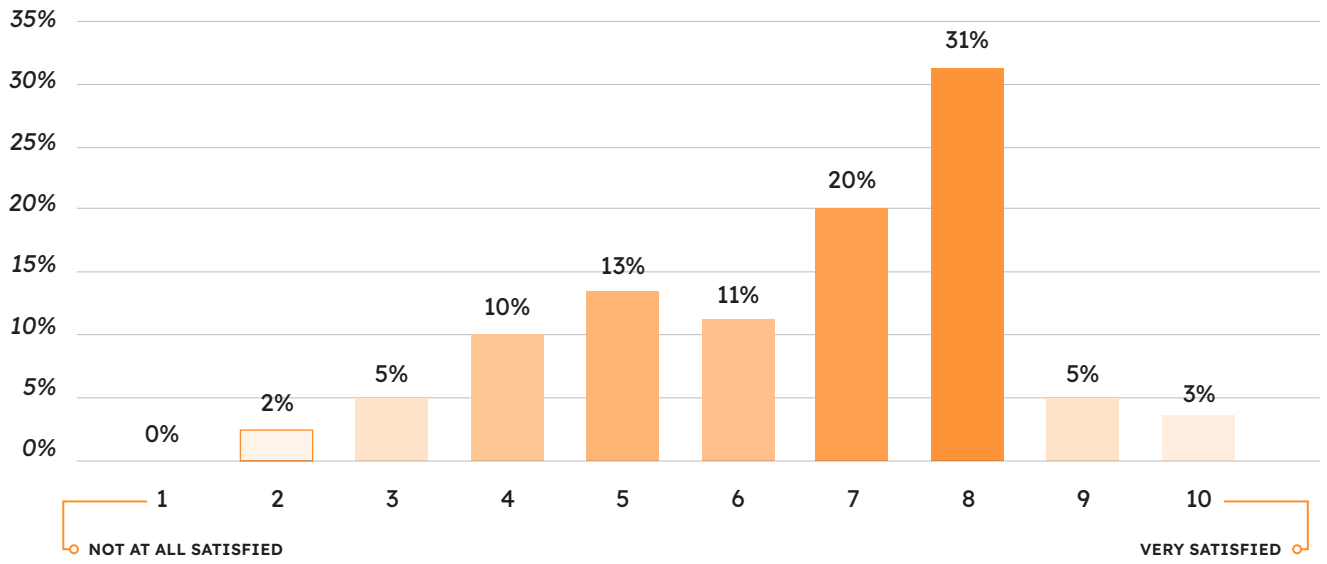
Once Phase I establishes safety, sponsors must move quickly into Phase II to maintain momentum. However, moving quickly in Phase I trials can be challenging, especially when ensuring data integrity and post-study readiness for Phase II.

While sponsors are often under pressure to accelerate timelines, this speed can sometimes come at the cost of thorough data collection. Early data is essential for decision-making, and rushing through a Phase I trial may result in overlooking crucial insights needed for designing Phase II studies.

Balancing the need for speed with comprehensive data collection is essential to ensure the trial's success and avoid future delays. Here's what industry insiders report on speed in Phase I research.

Post-study data readiness

FIGURE 2.1 Thinking of the Phase I studies you've recently been involved in, after last-patient-last-visit (LPLV), and using a 10-point scale where 1=not at all satisfied and 10=very satisfied, how satisfied were you with the time it took before the data were ready for analysis? (n=88)



Post-study data readiness, cont.

Interestingly, only 8% of respondents were “very satisfied” (9 or 10) with the time it took before the data was ready for analysis after last-patient-last-visit (LPLV).

Two main tasks contributing to delayed post-study readiness are:

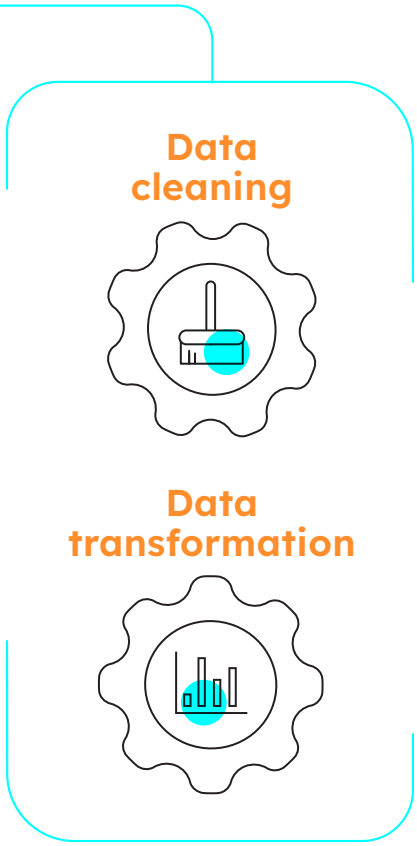
Firstly, **cleaning the final data** before database lock can create a lot of back-and-forth with sites. And oftentimes, the data isn’t actually changed.

“If you are imposing 100% SDV, of course, it is going to take a while to clean data,” says Ana. “**Risk-based monitoring can help reduce the time it takes to have data ready for analysis.** Sponsors need to assess their reasons for wanting to do 100% SDV.”

Overly restrictive acceptable data ranges can also slow data cleaning. For example, if sponsors place too tight of bounds on acceptable blood pressure or pulse ranges, this approach may generate many extra queries.

“Often, the issue is that sponsors have placed too tight of bounds around what is acceptable,” says Nicole. “But if a data point isn’t a primary or secondary endpoint, they should re-consider why there are such tight bounds.”

Nicole explains that **the best teams justify their must-have data.** “Every data variable should have a business case to justify its collection. If you can’t develop that yourself, look for someone to help. Sponsors can hire consultants or collaborate with their CROs to pressure test whether you really need all your proposed variables.”



Sponsors can ask consultants or CROs specific questions like:

- How are you going to decide on appropriate ranges?
- How are you going to clean the data?
- In your last five studies, how much data changed due to queries?
- How are you going to incorporate CDISC and SDTM on the front end?

Post-study data readiness, cont.

Secondly, **data transformation** can delay post-study readiness. According to Courtnay Buonomo, Associate Director of Data Management Systems and Standards at ADARx Pharmaceuticals, all phases of clinical research should **focus on using Clinical Data Interchange Standards Consortium (CDISC) standards. These standards include the Study Data Tabulation Model (SDTM).**

Transforming data into SDTM standards can be time-consuming. However, sponsors can create efficiencies in early-phase research by embedding data standardization into their study-build processes.

Choosing an **EDC vendor that offers pre-formatted forms with SDTM standards can greatly expedite the process** and help sponsors achieve post-study readiness faster.

"Some study builders ignore pre-formatted SDTM forms due to the notion of flexibility—but these forms can save a tremendous amount of time at the end to map the data back to a standard set," says Nicole.

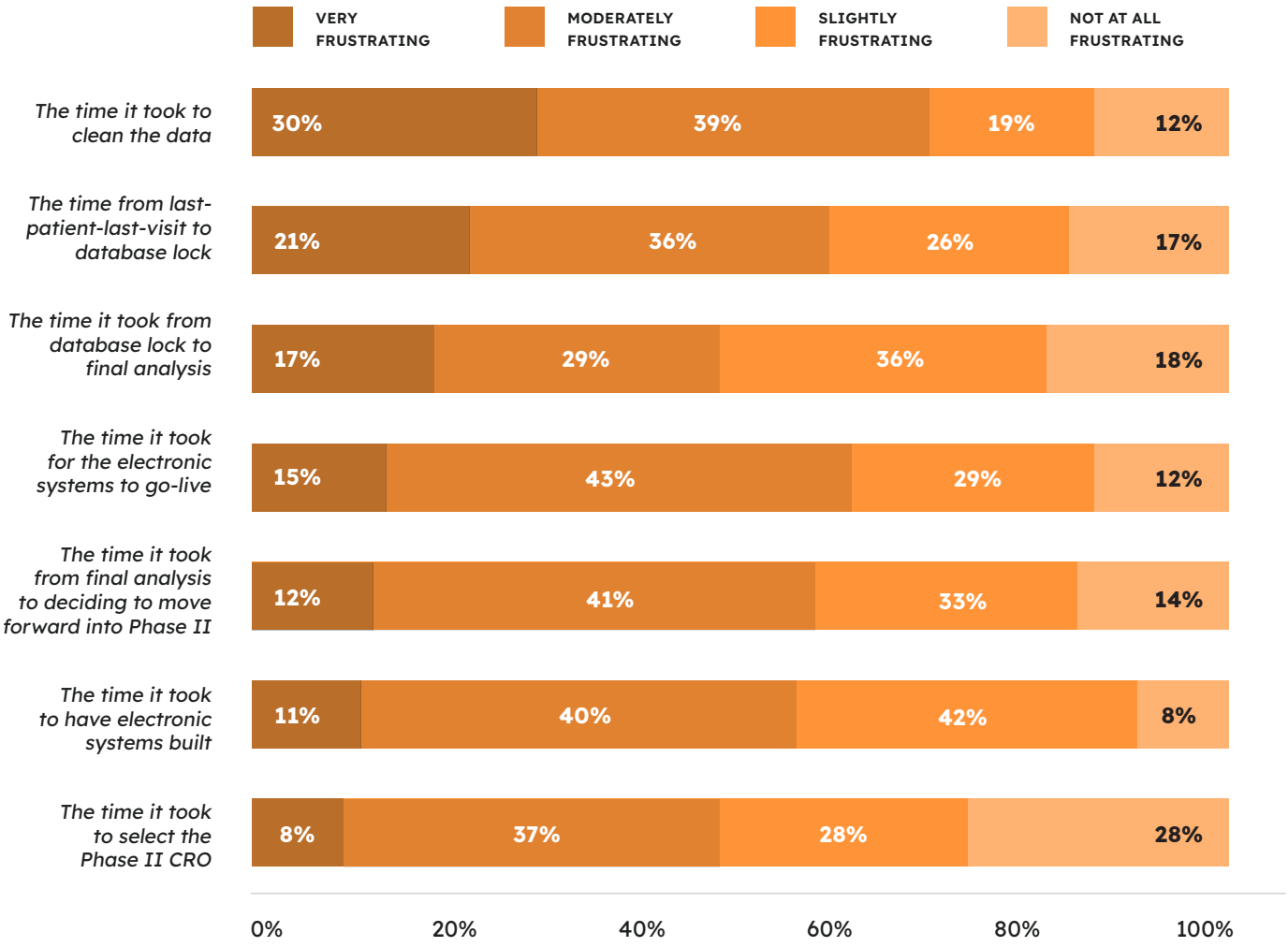
> "Your choice of EDC has a great impact on how much time post-study readiness takes."

Ana Palijan
Director of Early Phase and Translation Research, Innovaderm Research

Transitioning from Phase I to Phase II

FIGURE 2.2 How frustrating were the following elements of transitioning the compound/asset from Phase I to Phase II? (n=67*)

(75 of the 88 respondents indicated they had experience in both Phase I and Phase II studies, and of those 75, 67 respondents had experience transitioning an asset from Phase I to Phase II)*



Transitioning from Phase I to Phase II, cont.

Transitions are hard. **Respondents found the majority of transition elements we tested to be either "moderately frustrating" or "very frustrating."** Of seven possible sources of frustration, they identified the time it took to clean the data as the most frustrating aspect of transitioning from Phase I to Phase II.

From a data perspective, three of the most frustrating parts of transitioning from Phase I to Phase II are:

- The time it took to clean the data
- The time from last-patient-last-visit to database lock
- The time it took for the electronic systems to go-live

Speed is decided by how efficiently data is collected, and queries are resolved. Ana adds that the speed of clinical research is largely driven by the human component. "Therefore, a lot of post-study readiness comes down to operations," she notes. "**The right EDC is foundational—but without the right clinical operations team in place, processes will be inefficient.**"

Courtnay also notes that sponsors can gain traction between Phase I and Phase II by reusing standard forms for things like demographics and Adverse Events (AEs).

> "Depending on how intentionally you've built Phase I, you may be able to reuse some components and gain efficiencies as you transition into Phase II."

Courtnay Buonomo
Associate Director of Data Management Systems and Standards, ADARx Pharmaceuticals

Prioritizing speed or data volume

Based on survey results, respondents are divided on whether they would like to collect more data or finish the study sooner.

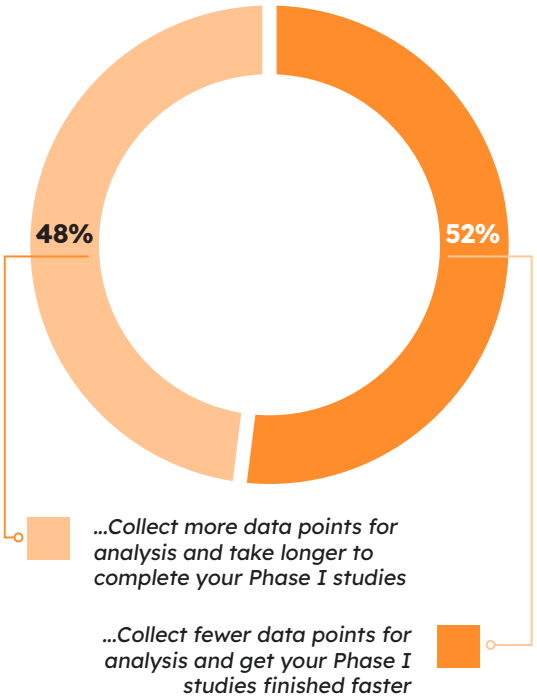
A deeper analysis of this data suggests that **smaller sponsors are more interested in collecting less data and finishing the study sooner as compared to larger organizations.** According to survey responses, companies with an average of 1900 employees prefer collecting more data, even if it means a slower timeline. Meanwhile, smaller companies with an average of 1200 employees prioritized speed over more data.

Of note, **60% of respondents from smaller companies with fewer than 500 employees prioritize speed over data volume** in Phase I research. But Éric acknowledges that it can be a struggle for smaller companies to make this decision. “Smaller companies usually aim for less expensive trials. But they often still really want more data while reducing costs.”

When deciding between collecting more data or moving faster through a Phase I trial, Nicole strongly encourages sponsors to focus on speed. “For Phase I trials, 70% of the time, sponsors will move on to Phase II. So, it’s highly likely that you’ll get through to the next phase. Since it costs an average of $15,000 per day, you want to move as fast as possible.”

Nicole warns that the more data is collected in Phase I, **the more data needs to be monitored, cleaned, and transformed.** More data also raises the chances of the FDA asking about any particular datapoint.

FIGURE 2.3 Would you rather...? (n=88)



Companies with:

~1,900 employees prioritized more **data** over speed

<1,200 employees prioritized **speed** over more data

Best practices to accelerate clinical trials

DEFINE YOUR MUST-HAVE DATA: Nimble teams want to move fast. But they may be so eager to get their protocol sent to the FDA that they don't take the time to review and streamline the required data critically. Teams should begin by identifying the data they cannot do without.

PRE-FORMATTED FORMS BUILT ON SDTM STANDARDS: Incorporating CDISC and SDTM on the front end of a study build can save time during closeout. "You'll thank yourself later for building a good standard library," reports Éric.

LEVERAGE THE WHOLE TEAM: Getting all hands on deck at the beginning can speed up a study. According to Nicole, many clients talk about the 'first draft' created by their medical monitor. "But when they bring in their data management and clinical operations team, they can whittle it down from wants to needs."

> "If you priced it by variable, would you think more deeply about which variable you would collect and which ones you wouldn't?"

Nicole Latimer
CEO, Medrio

Why Creating a Cohesive Strategy is Challenging

As trials grow more complex, creating a seamless data collection and management strategy becomes more important and more difficult. Without a cohesive approach, data can easily become fragmented across systems and platforms.

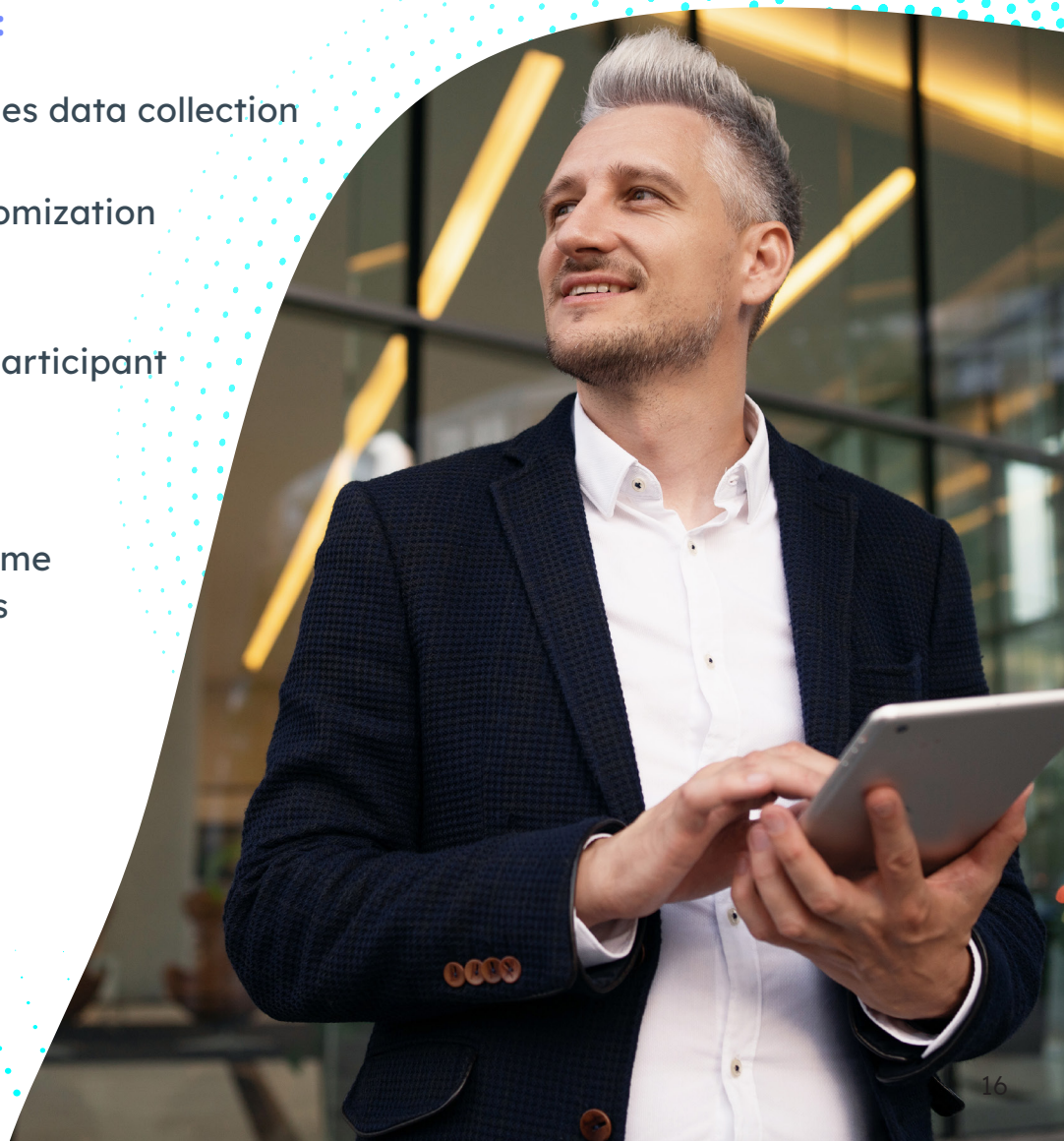
A fragmented approach risks data inconsistency, slow decision-making, and delayed critical insights.

Therefore, sponsors and CROs must prioritize building a unified data strategy to ensure that the information gathered is reliable, accessible, and actionable in real-time.

Building a cohesive data collection and management ecosystem is a growing obstacle for Phase I trials.

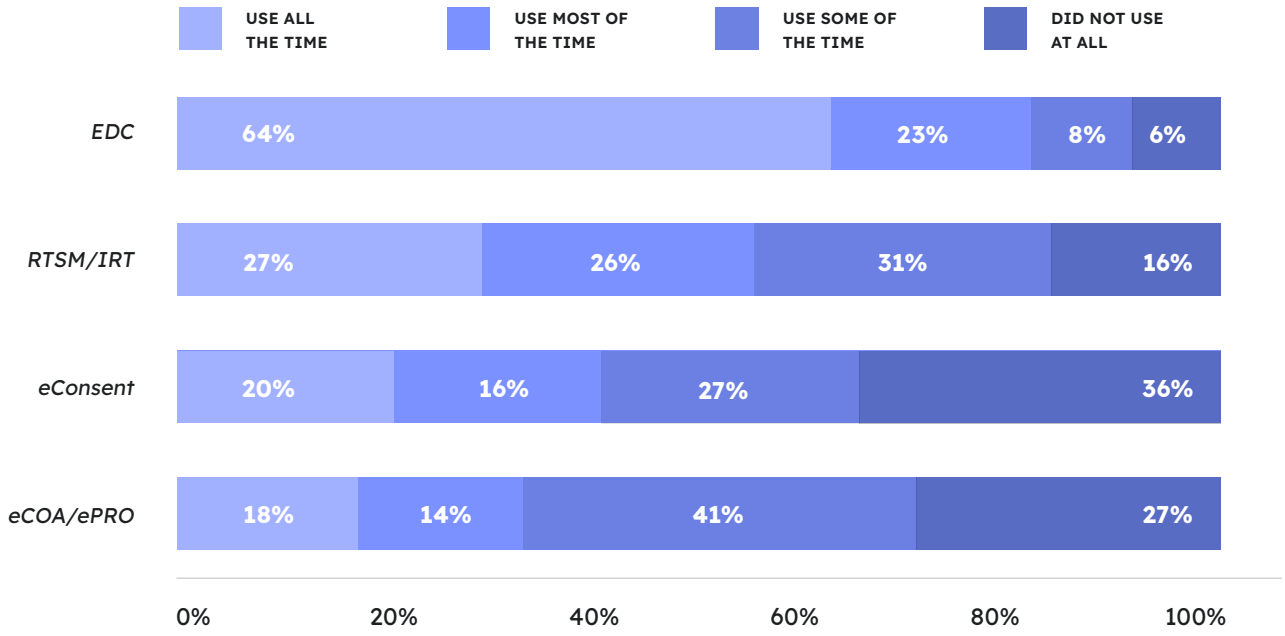
Many technologies can play a critical role in early-phase research:

- **CDMS/EDC** streamlines data collection
- **RTSM** manages randomization and supply chains
- **eConsent** enhances participant engagement and compliance
- **ePRO** provides real-time insights from patients



The use of technology

FIGURE 3.1 Thinking of the Phase I studies you've recently been involved in, how frequently do/did you use the following clinical technologies? (n=88)



"Each Phase I trial is a puzzle that needs to be solved," says Ana. "And part of that puzzle is deciphering which mix of technology will best support the trial's needs."

According to survey results, **Electronic Data Capture (EDC) is the clinical technology most commonly used in Phase I studies.** Today, EDCs are no longer just data entry systems. Modern EDCs can accommodate the growing complexity and speed of early-phase clinical research.

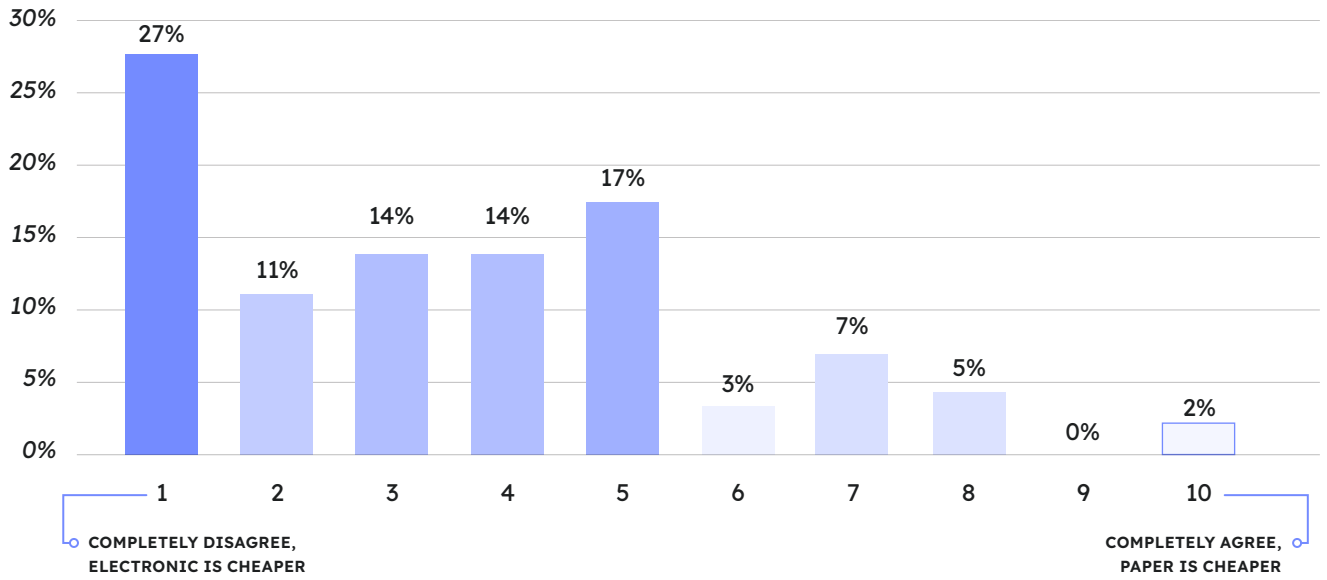
Rather than a single point of data entry, they can now absorb a huge range of data sources coming from many places at different times. They can also support study teams with data management and reporting.

Interestingly, the results also show that **RTSM is gaining traction as a technology in early-phase trials.** As trials become more complex, study managers need adaptive, unified RTSM technology to maintain real-time data and keep costs down.

According to Courtnay, using RTSM in Phase I trials can create efficiencies for later-phase research. "Your team gets used to the technology, and you gain efficiencies by figuring out your basic setup early on."

Recognizing the value of electronic data collection

FIGURE 3.2 Thinking of Phase I studies you've recently been involved in, please rate your level of agreement with the following statement using a 10-point scale where 1=completely disagree and 10=completely agree: Collecting data in Phase I studies is cheaper using paper, rather than using electronic data capture applications. (n=88)



When asked if collecting data on paper was cheaper than doing so electronically, the **vast majority of respondents chose electronic data collection as the more cost-effective option.**

This isn't surprising since back in 2022 the Tufts Center for the Study of Drug Development (CSDD) found that **inefficiencies in paper-based methods contribute to significant delays and increased costs.** Challenges include delayed data access and increased administrative burden.

"The true value of electronically collecting data becomes fully apparent as a Phase I trial progresses," says Nicole. "As study teams begin to face the costly challenges associated with data cleaning, protocol amendments, and reporting, the value of a robust EDC system shines."

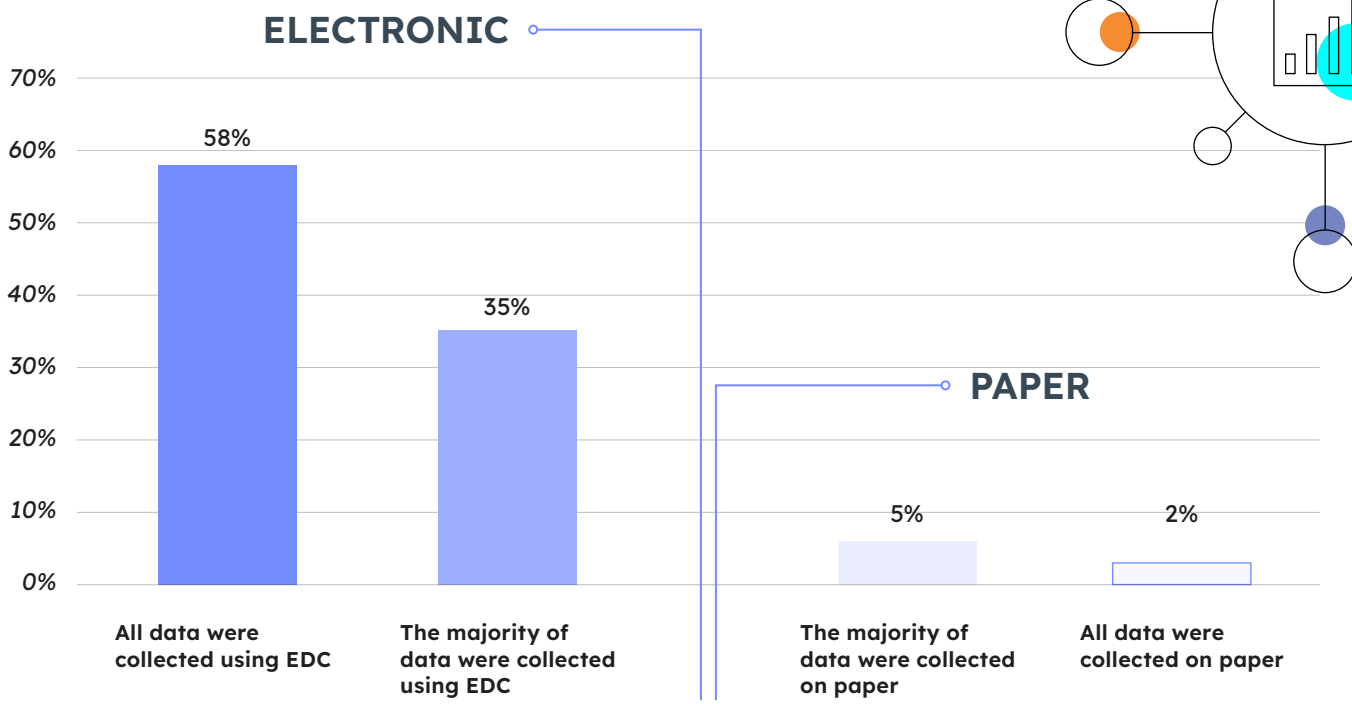
> "In an early phase trial, a system decision is an important one since it's such a big part of your budget."

Ana Palijan
Director of Early Phase and Translation Research, Innovaderm Research

Recognizing the value of electronic data collection, cont.

Case report forms

FIGURE 3.3 Thinking of the Phase I studies you've recently been involved in, how did you collect **case report form (CRF) data**? (n=88)



Paper case report forms (CRFs) involve manually filling out physical forms. **Electronic CRFs (eCRFs)**, on the other hand, **allow data to be entered directly into a digital system**, providing faster access to data, real-time validation checks, easier updates, and enhanced security.

Since eCRFs streamline data collection and improve overall data quality compared to paper-based CRFs, it makes sense that **93% of studies collected the majority or all of their CRF data via EDC**.

According to Ana, **all sponsors need to ask is whether paper or electronic data collection will serve them best.** "Look at your must, your need, and your budget—and work with that. An experienced team understands the tradeoffs of paper versus electronic. One also needs to keep in mind the end-user experience. Many study sites are not set-up to work with eSource and imposing such systems may impact trial engagement and overall study quality."

Recognizing the value of electronic data collection, cont.

Patient-reported outcomes

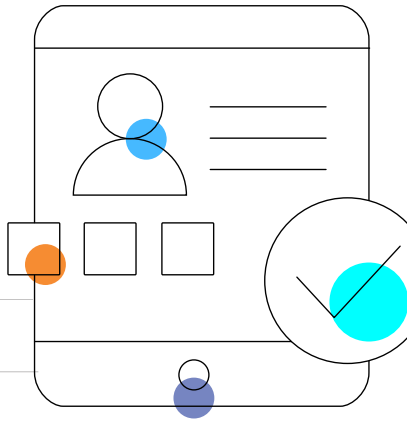
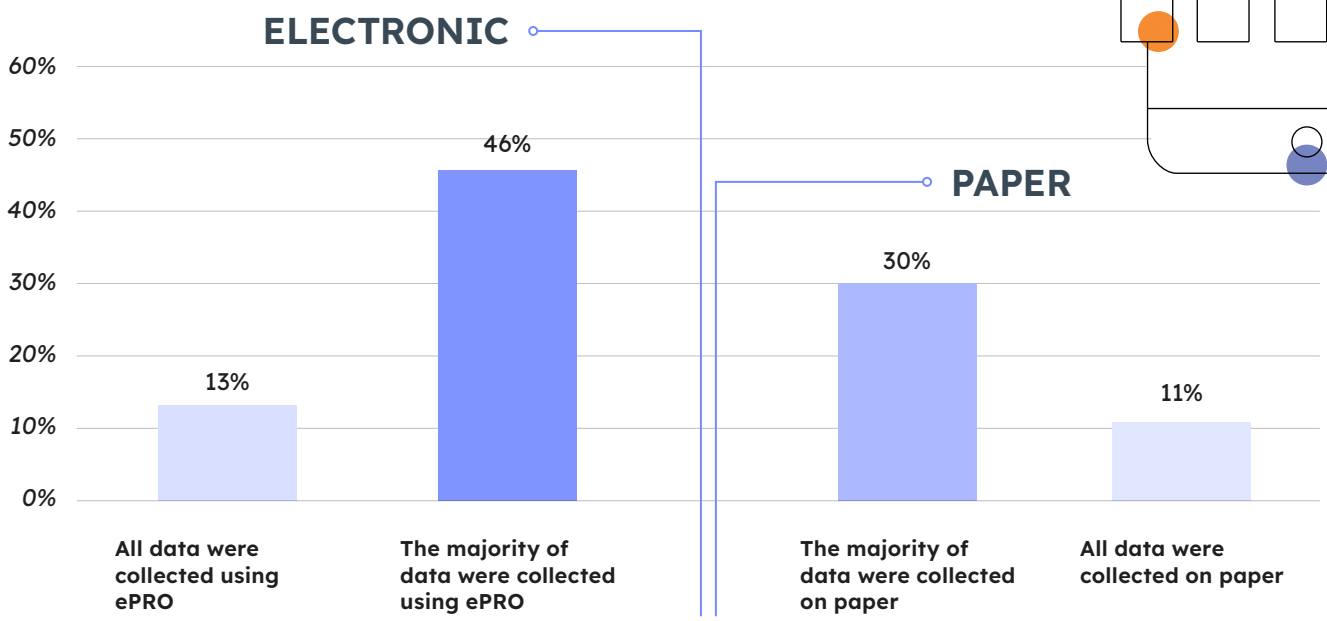


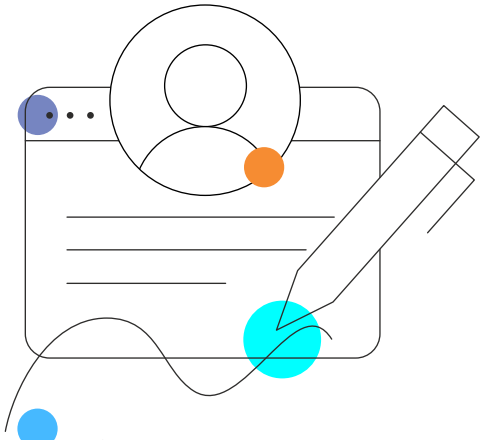
FIGURE 3.4 Thinking of the Phase I studies you've recently been involved in, how did you collect patient-reported outcome data? Asked only of respondents who have collected PRO data in recent Phase I studies. (n=82)



According to survey results, **59% of respondents reported using Electronic Patient-Reported Outcomes (ePRO) for the majority or all of their data collection.** Meanwhile, paper collection is still part of many Phase I trials, with **41% reporting that the majority or all were collected on paper.**

Courtnay notes that some of the **hesitancy around ePRO may be due to the perceived risk of not having source documentation.** Since the industry still emphasizes source data verification (SDV), some sponsors have not yet made the leap.

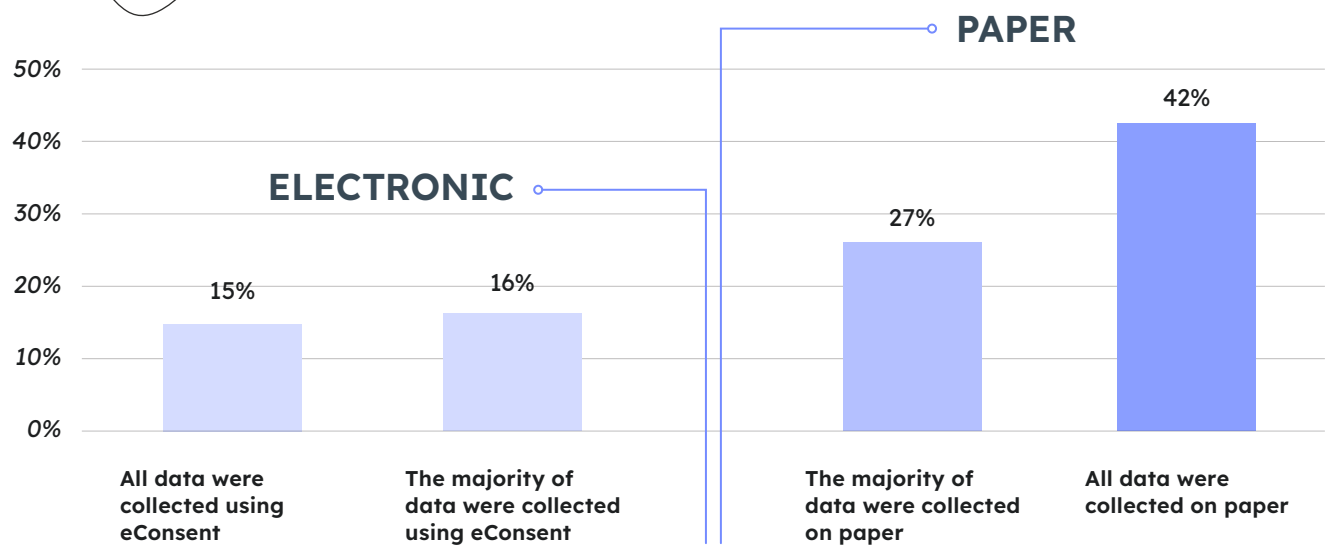
Nicole points out, however, that **ePRO is linked to improved regulatory compliance.** "Electronic patient-reported outcomes can reduce errors and missing data. They provide accurate, consistent, and traceable clinical data collection."



Recognizing the value of electronic data collection, cont.

Electronic consent

FIGURE 3.3 Thinking of the Phase I studies you've recently been involved in, how did you collect patient consent? (n=88)



According to survey results, **paper patient consent continues to be the most common choice for Phase I studies.** Two-thirds of respondents reported that in the most recent trial they'd been involved in, the majority or all patient consents were collected on paper.

Courtnay notes that the **hesitancy to make the leap to eConsent may often be tied to perceived cost.** With the pharma industry's slowness in taking up new technologies, she thinks there may not be a big push for eConsent in Phase I trials unless the FDA starts forcing the issue.

While some sponsors have fully embraced technologies like eConsent, ePRO, and RTSM, many have not. Since Phase I trials are typically smaller and focus on safety, many sponsors opt for hybrid systems that combine electronic tools with paper records. However, this cautious approach can slow down data collection and introduce fragmentation.

Best practices to promote flexibility

ASK CRITICAL QUESTIONS: Determining what technology and services suit your study requires thoughtful evaluation. These questions could include:

- What is the primary endpoint?
- Do you want to collect data in-clinic or remotely?
- What are budget limitations?
- What best serves you, your sites, and your potential patient population?

SEEK OUT FLEXIBLE TECHNOLOGY:
Phase I trials often encounter unforeseen challenges. Therefore, they need adaptable systems that support rapid changes in data collection, protocol adjustments, and trial management.

EXPLORE EXPERT SERVICE PARTNERS:
Working with multiple vendors can add more stress and complication in Phase I research. Look for partners who offer clinical data and project management services individually, allowing full customization to meet your specific needs.

About Contributing Experts

Ana Palijan

is the Director of Early Phase and Translation Research at Innovaderm. She is known for her scientifically robust and efficient approach to operations and study execution. Ana brings a wealth of experience in clinical research, including study design, project management, clinical operations, medical writing, and the development of training materials.

Courtnay Buonomo

is the Associate Director of Data Management Systems and Standards at ADARx Pharmaceuticals. Courtnay has extensive experience in data management, EDC development, and data management technologies. Throughout her career, she has developed mechanisms for efficient database builds to collect the highest quality data and actively serves as a subject matter expert in several data management technologies. Courtnay is passionate in her work and takes great pride in delivering, maintaining and supporting data collection.

Éric Hardy

is Senior Director, Biometrics, at Innovaderm Research. He has established himself as an industry specialist in clinical data management. His background includes proficiency in programming to numerous clinical trials, ensuring the integrity and accuracy of data collection and analysis. He is also well versed in managing vendors providing external services such as EDC, RTSM and ePRO.

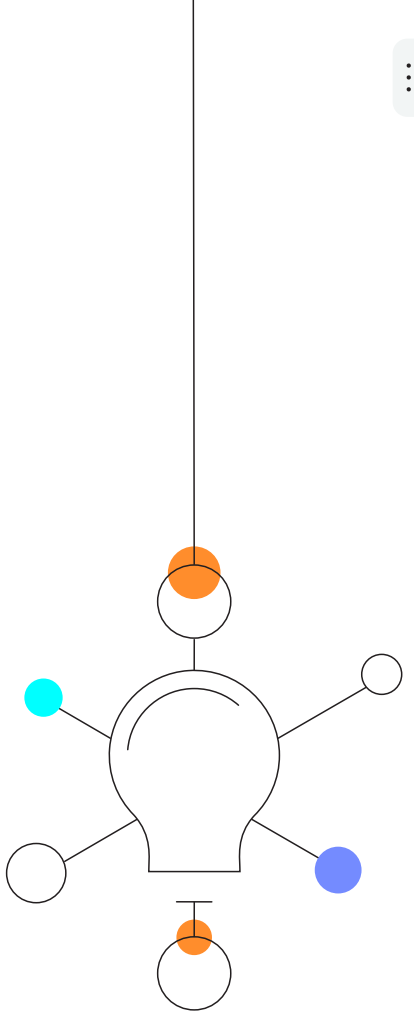
Nicole Latimer

is the Chief Executive Officer at Medrio. As CEO, Nicole carves out her time in three equally and critically important areas: studying the life sciences industry, making decisions about how Medrio can have a greater impact on that industry, and then focusing on the best way to communicate those decisions to employees and customers.

About medrio

Trusted by sponsors, CROs and sites worldwide, Medrio aims to improve 100 million lives through faster, more efficient, and secure clinical trials. With almost two decades of experience, Medrio delivers proven, scalable solutions, unrivaled customer support, and guidance to the industry's leading innovators, including pharmaceutical, biotech, medical device, diagnostics and more.

The company's suite of solutions, including **CDMS/EDC**, **eCOA/ePRO**, **eConsent**, **and RTSM**, enables the capture of quality clinical trial data while optimizing workflows for regulatory readiness. Experience the power of Medrio and realize the full potential of your clinical operations and outcomes.



Talk to a Medrio expert

to secure your data strategy.

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