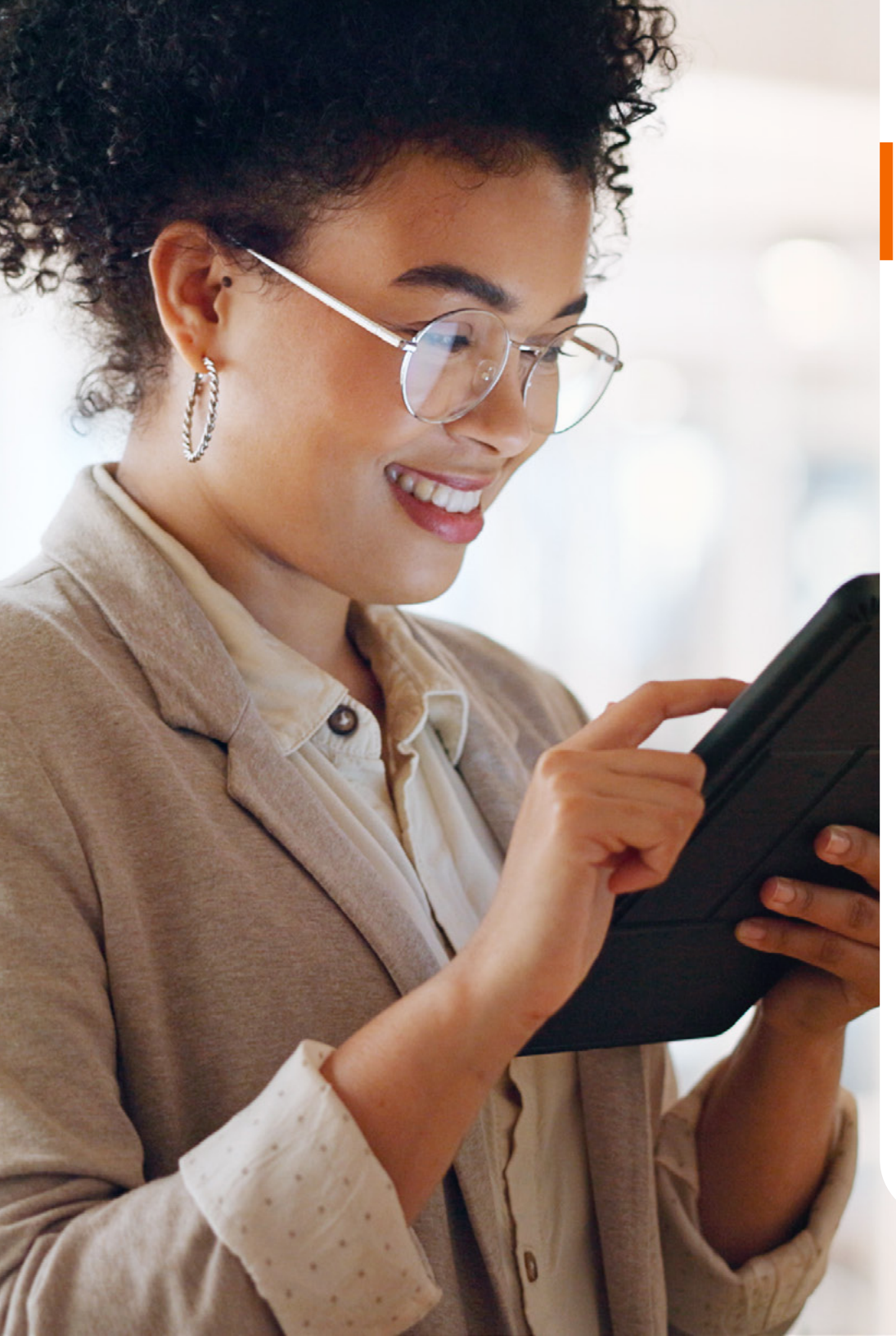
OpenClinica

EBOOK

Your Blueprint for Decentralized Clinical Trials

Decentralized, virtual, and hybrid trials: How to implement successful remote studies and get better data, faster



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Foreword from OpenClinica's CEO

Thank you for downloading our eBook! If you're here, you know the emphasis on decentralized clinical trials has been growing for some time. Renowned for their effective, safe methodology in clinical research, especially during the COVID-19 pandemic, decentralized trials have been promoted and adopted by some stakeholders. However, all new innovations have a learning curve. That's where OpenClinica comes in.

We believe that most clinical trials will never be fully decentralized, and a hybrid model is much more likely. Consider how you will implement hybrid trials that contain elements of decentralization with some on-site treatments and appointments still in the mix. This hybrid approach is much more likely to be adopted because of the flexibility that it offers both patients and clinical trial stakeholders.

To help you on your journey of decentralization, OpenClinica created this workbook to help you discover new strategies and best practices that you can implement to make the patient experience easier. This is the "why" behind decentralized and hybrid trials - to make it easier, more accessible, and frictionless for patients to participate in clinical research. I invite you to use this workbook as a tool to improve your clinical trials and welcome the opportunity to chat about your clinical research. Reach out any time. **Enjoy!**

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Digital transformation in clinical research

In decentralized clinical trials (DCTs), studies are being carried out using electronic patient reported outcomes (ePRO/surveys), eConsent, text messages, drug kits sent by mail, patient directed data sharing, and more. These tools greatly improve the patient experience and advance the traditional clinical trial model.

Decentralized clinical trials were on the rise before COVID-19, but their success in keeping drug development programs on track during the pandemic won these studies a renewed, leading role in mainstream clinical research. We've seen this type of digital transformation in many other areas. It's akin to what Venmo did for exchanging funds and QR codes have done for restaurant menus. These examples show that as digital, cloudbased tools and technology make their way into the mainstream, the benefits are tangible. And it's no different for clinical research.

Decentralized vs. virtual vs. hybrid trials

Decentralized clinical trials

A decentralized trial is one in which the sponsor doesn't rely on the traditional role of the site to carry out the study protocol day-to-day. DCTs use technology to communicate with study participants and to collect data. Although all the activities of a decentralized clinical trial are conducted remotely and away from central study sites, they don't have to be fully virtual. By partnering with community doctors and even mobile health networks, caregivers can perform patient treatments in person. However, this still requires the support of virtual technologies, such as: remote learning on the clinical trial protocol for practitioners and caregivers; digital transmission of data and collected outcomes; and virtualization of patient enrollment and other processes. These technologies can be more challenging and time-consuming and therefore push study stakeholders away from implementing a DCT model.

Decentralized vs. virtual vs. hybrid trials

Virtual clinical trials

A fully virtual clinical trial is completely technology-based. This means there are no traditional sites, no physical locations used, and no face-to-face interactions. As you can imagine, this modality poses some major challenges.

First, the nature of the investigational treatment itself may prevent the trial from being virtual (e.g., requiring surgery). Outfitting participants with the necessary tech (such as medical grade sensory/wearable devices like the Dexcom Continuous Glucose Monitoring (CGM) System or Orpyx, an ambulatory gait monitoring pressure sensor) and ensuring these tools are working and used appropriately is a hurdle.

Patients tend to be busy people. While the convenience of not having to travel to a site may be appealing, the bar is higher for ensuring quality and compliance and the lack of caregiver contact could have an unintended adverse impact on the patient. Although the virtual model may be tempting given the concerns around the global pandemic, it requires extra upfront work and investment from the sponsor.

Decentralized vs. virtual vs. hybrid trials

Hybrid clinical trials

The promises of decentralized and virtual trials include expanding the pool of potential participants, accelerating recruitment, streamlining data collection, and cleaning, and cutting out middlemen.

The way you carry out your trial will likely fall somewhere on the spectrum between no virtual components to all virtual components. What if you see an opportunity for your trial to be decentralized or virtual, but still require some central sites? Or maybe you need at least one in-clinic visit for a procedure or test? This is the most common scenario for clinical trials today, and it's why OpenClinica talks so much about hybrid clinical trials.

Rather than thinking about technology use as an all or nothing proposition, a hybrid approach is often easier for study stakeholders to adopt. Especially if you are new to virtualization/ decentralization, start by identifying which components might be the easiest to virtualize. Perhaps a follow-up outcomes assessment can be performed digitally and remotely via questionnaires. Or perhaps a single blood draw is needed, in which case a mobile phlebotomy service might offer a lot of value.

The current clinical research landscape points to the necessity of decentralized, virtual, and hybrid clinical trials

76%

In a recent survey, **76% of respondents** (professionals working in CROs, biopharmaceutical organizations, and medical device companies) indicated that the COVID-19 pandemic has accelerated their adoption of decentralized clinical trial methods.[1]

50%

In **50% of clinical trials**, participants find it difficult to stay enrolled due to poor health.[2] This is especially true when travel to a site is required.

85%

85% of clinical trials fail to recruit enough patients and 80% are delayed due to recruitment problems.[3]

70%

70% of potential clinical trial patients live more than two hours from a study center, making participation in trials that require site visits less appealing.[3]

Promises of virtualization in clinical research

A look at the stakeholders

For Sponsors and Contract Research Organizations (CROs)

- Gain faster access to higher quality source dat
- Accelerate recruitment and improve retention; increase pool of potential participants
- Reduce reliance on sites, utilize virtual sites, improve site satisfaction
- Reduce or eliminate source data verification (SDV)
- Automate alerts (e.g., when a patient may be at risk or experiencing an adverse event)
- Improve participant and site compliance
- Obtain real time, actionable study metrics
- Decrease overall time to database lock

For Patients

- Reduce or eliminate travel to the site
- Enhance opportunities for participation
- Alleviate burden for patients with limited mobility or extreme illness
- Increase safety by mitigating the risk of exposure to COVID-19 or other diseases
- Engage with clinical trial staff when and where they are most comfortable

For Sites

- Access a larger, more diverse patient pool
- Streamline eligibility process
- Automate enrollment
- Increase patient engagement & retention
- Increase patient care and research capabilities
- Decrease staff travel and burden
- Increase ability to participate in more studies

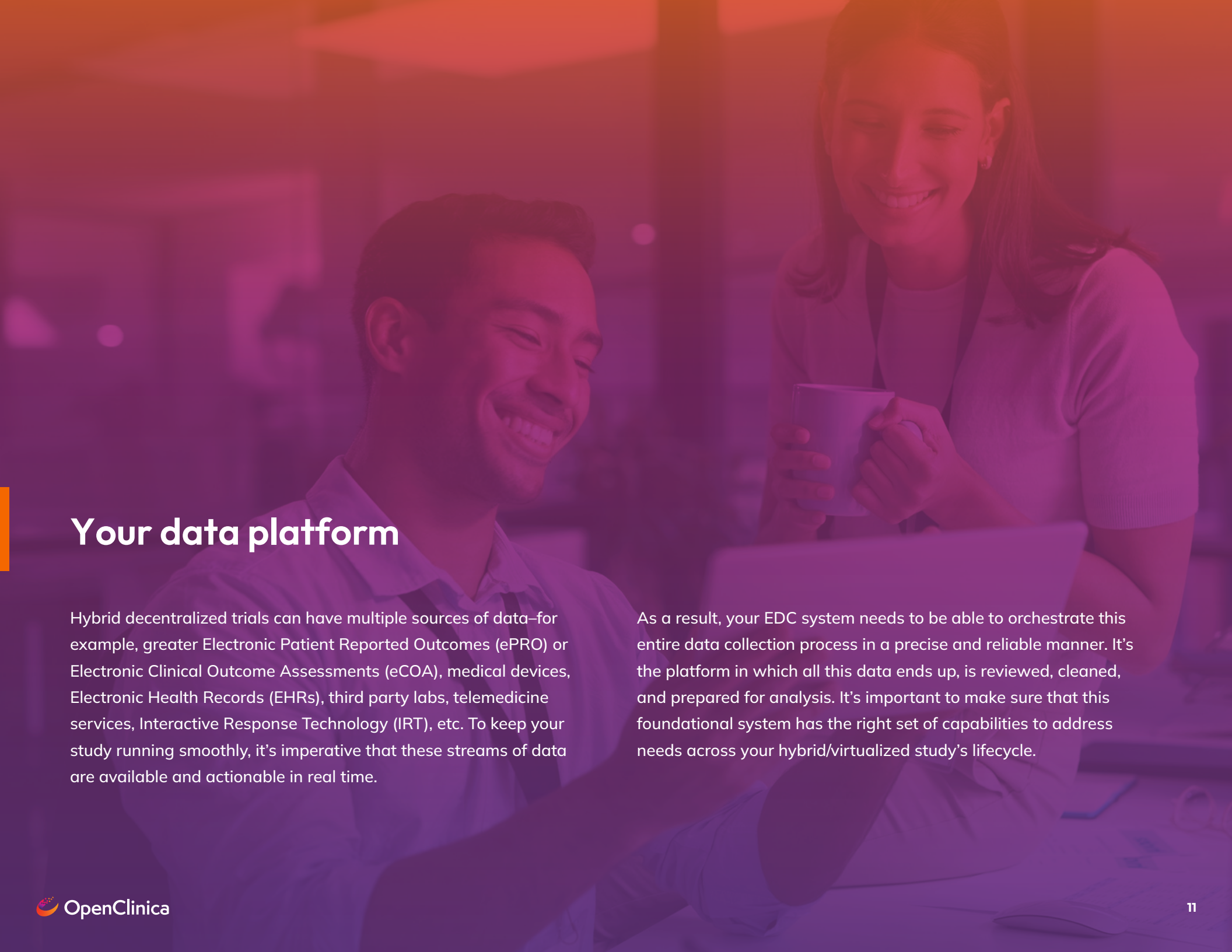
Implementing a hybrid clinical trial

How to utilize technology to improve the participant experience and streamline clinical workflows

The following chapters discuss the technologies typically used from start to finish throughout a clinical trial and showcase how adopting these technologies and processes can accelerate your move to decentralization/virtualization, leading to increased participant engagement, workflows that make clinical data management easier, and reduced burden on clinical researchers.

> *Virtualizing your trials doesn't have to be an all or nothing proposition. In fact, most virtualized and decentralized trials are a hybrid of more traditional and modern methods. You can often achieve an outsized benefit from simply virtualizing certain aspects of the trial. So, think about the parts you can decentralize now and start there. As your experience, systems, and process mature you can decentralize more and more.*

Ben Baumann
COO, OpenClinica



Your data platform

Hybrid decentralized trials can have multiple sources of data–for example, greater Electronic Patient Reported Outcomes (ePRO) or Electronic Clinical Outcome Assessments (eCOA), medical devices, Electronic Health Records (EHRs), third party labs, telemedicine services, Interactive Response Technology (IRT), etc. To keep your study running smoothly, it's imperative that these streams of data are available and actionable in real time.

As a result, your EDC system needs to be able to orchestrate this entire data collection process in a precise and reliable manner. It's the platform in which all this data ends up, is reviewed, cleaned, and prepared for analysis. It's important to make sure that this foundational system has the right set of capabilities to address needs across your hybrid/virtualized study's lifecycle.

Eleven key EDC capabilities

Your electronic data capture platform (EDC) is the backbone of your research data. To best support all your research, look for these key capabilities

- [ ] Ability to incorporate disparate data sources seamlessly and in real time (e.g., from EHRs, labs, devices, etc.).
- [ ] Adaptability to different, unpredictable usage environments. The system should be usable on any device, screen size, and browser (both by participants as well as study team members).
- [ ] High quality end-user experience: little to no training required, real-time edit checks, calculations, and dynamic logic, automatic saving of data. Support for collaboration. Different teams in charge of different aspects of the trial should be able to work together asynchronously.
- [ ] Robust change management to ensure data integrity across changes and a smooth user experience.
- [ ] Flexibility to adapt to changing virtualization. You should be able to launch your study with certain parts virtualized and change this as time goes on.
- [ ] Flexible notifications and messaging. With more parties to coordinate, your system should be smart about prompting users about what they need to do and when.
- [ ] Unfettered analytics. The increased number of digital moving parts in your virtualized study produce data that you can use to enhance the study itself. You can use this data to measure compliance rates, look for bottlenecks/breakdowns in process, and identify unintended consequences before they become real problems.
- [ ] Ease of configuration. Can your team be self-sufficient in building out their hybrid trial? Can they easily make changes and iterate quickly? How easily can they take a change from design, to test, and finally to production?
- [ ] Targeted review and verification of data. As more of your study becomes eSource, there's less data to review and verify. Thus, the ability to granularly define what needs to be reviewed can help monitors save time.
- [ ] Ability to incorporate best-of-breed point solutions. You never know when you'll find that one piece of technology you really want to use to do something very specific in your study. Your EDC platform should be able to play well with others via a robust web services API.
- [ ] Remote data monitoring. Access to data within the EDC so that monitors can ensure source data follows ALCOA principles (attributable, legible, contemporaneous, original, and accurate).

Don't forget - the whole idea behind EDC should be that the people involved in your clinical study are less burdened and more empowered, especially when conducting research virtually.

Check out OpenClinica's EDC Platform →

EDC benefits by stakeholder

Sites

Whether you are using virtual or physical sites, EDCs should give sites an easy and intuitive way to provide accurate study data, auto-notify users with actions required, auto-manage study calendars, and apply electronic signatures.

- Let sites leverage data they already have (e.g., from the EHR)
- Make it easy for them to support their patients (don't force your sites to be in the tech support business)

Participants

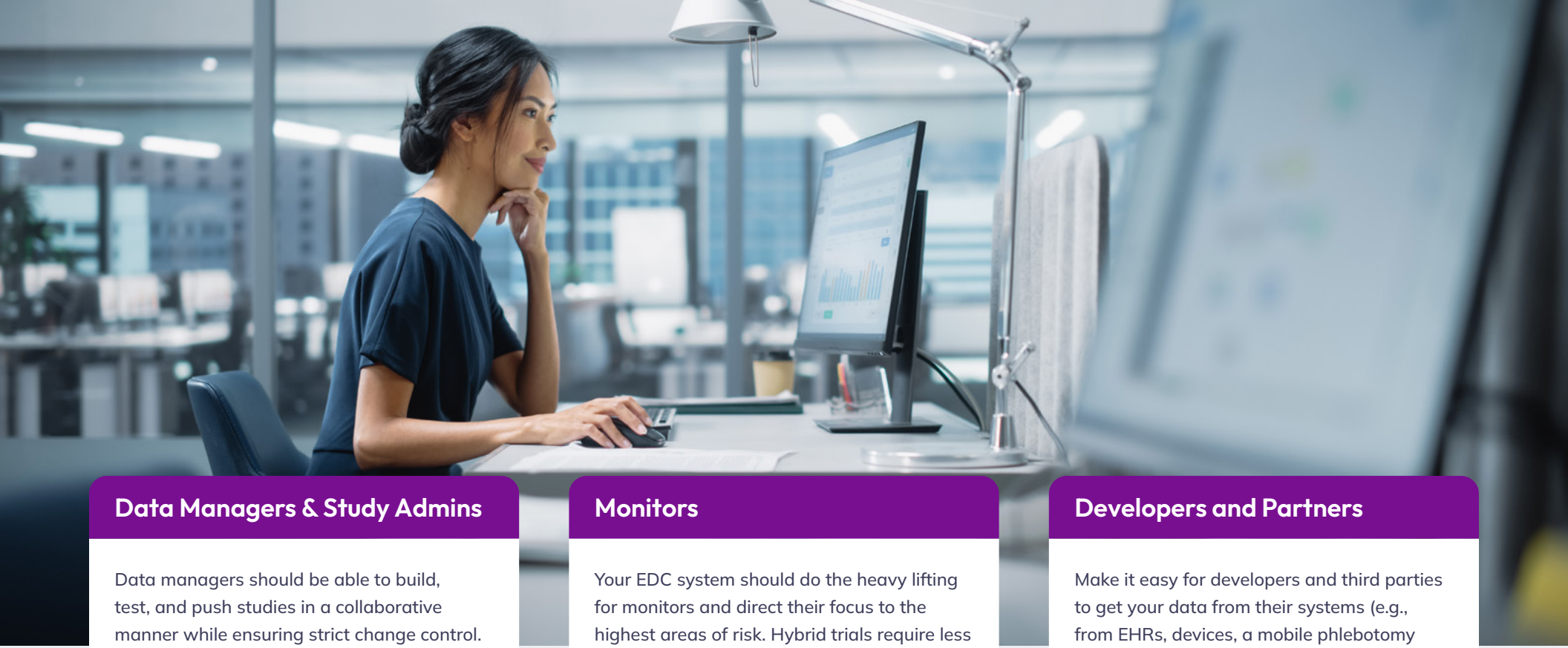
Allow patients to provide data anytime, anywhere from their own device. Think frictionless.

- Don't tie participants to a particular device, let them use the device already in their pocket
- Configure automatic push notifications to send participants text messages and emails when data is required
- Let participants leverage data they already have (e.g., Apple Health)

Sponsors

Keep up to date with study progress. Save time and money. Maintain regulatory compliance. Rest well knowing your data is secure and clean.

- Cast a wider net with regard to recruitment
- Accelerate study timelines (less wrangling with sites, less cleaning) while obtaining higher quality, more timely data
- Obtain real-time insight into study progress



Data Managers & Study Admins

Data managers should be able to build, test, and push studies in a collaborative manner while ensuring strict change control. They should also have a good toolset for provisioning sites and users, resolving queries, and creating datasets.

- Make it easy to build and change case report forms (CRFs)
- Data review should be highly efficient to ensure that data is flowing smoothly and at maximum quality

Providing business intelligence to different stakeholders should be easy and flexible. Data from external sources should be available in real time for optimal decision making

Monitors

Your EDC system should do the heavy lifting for monitors and direct their focus to the highest areas of risk. Hybrid trials require less source data verification, allowing monitors to focus on higher value activities.

- Help monitors identify issues before they become problems (dashboards and notifications looking at key risk indicators)
- Reduce monitor effort (less travel, less SDV), allow for upload of source documents to support remote monitoring
- Target SDV to only necessary portions of data

Developers and Partners

Make it easy for developers and third parties to get your data from their systems (e.g., from EHRs, devices, a mobile phlebotomy service, etc.).

To do this, your EDC system would have an extensive, reliable, and well documented web services API based on the industry CDISC standards.

This is the technical toolset developers can use to get external data into your study database in real time.

How to interface with participants

How you engage and communicate with participants in a decentralized trial is particularly important, especially if you're not relying on sites to facilitate. Capturing data directly from participants is hard enough–most are leading busy lives and aren't anywhere near as focused on the study as you are. So, as you strive to achieve a frictionless experience for your participants, think about eliminating all the seemingly little things that, collectively, could create a big barrier to obtaining your participant reported data.

Deliver a frictionless participant experience

- Strive for an ultra-reliable user experience that doesn't require any training for the participant, can be used from any device the participant may happen to be using when the study needs something from them.
- Set-up automatic notification rules that let participants know when they need to do something. If you can send these notifications via both SMS text messaging and email you have a better shot of more timely interaction.
- Incorporate images, videos, and other multimedia content to provide participants with engaging information on how to accurately perform tasks and report outcomes.
- Engage patients and patient advocates in the design of your trial. Involving them in the design helps you understand what is important to them, and where there are barriers to participation that you may be able to remove.
- Avoid apps that must be downloaded and installed. These tie the participant to only the device that has the app. You'd also be relying on the participant to ensure the app is installed, is running, and stays updated.
- Ensure patient reported data gets into your core EDC platform in real time to facilitate decision making and automated logic (scheduling the next activity, sending reminders, etc.).
- Your platform should have technical capabilities to support the integration of wearables and mHealth devices such as a smartwatch or Fitbit, digital blood pressure monitors, and implantables.

Check out OpenClinica Participate™ →

In terms of participant-facing technology, sponsors often rely on an ePRO/eCOA toolset so that patients can report medical data anytime, anywhere.

eCOA

There are many different types of eCOA, including Electronic Performance Outcome (ePerfO), Electronic Clinician-Reported Outcome (eClinRO), Electronic Observer-Reported Outcome (eObsRO), and Electronic Patient Reported Outcomes (ePRO). All these options offer benefits for decentralized clinical trials, but ePRO is the most common and beneficial for patients.

ePRO

One of the most common types of eCOA, and certainly one that's very beneficial during decentralized clinical trials, is ePRO. ePRO enables you to receive data directly from your subjects - anytime, anywhere, on any device. If done correctly, ePRO offers a frictionless way for patients to engage and comply with your study.

Stakeholder benefits from a frictionless participant experience

SITES

Reduce burden on site staff. Take them out of the tech support business. Deliver source data in real time.

SPONSORS

Improve diversity, enrollment, engagement and retention.

DATA MANAGERS

Increase confidence in data quality and timeliness.

PARTICIPANTS

Deliver convenience and ease.

MONITORS

Reduce or even eliminate SDV, improve patient safety and compliance.

Tips for recruitment, screening, and enrollment

The beginning of the clinical research workflow involves recruitment and enrollment of trial participants. This is your opportunity to make a good first impression on participants. Think visual-first and include things like images and video on your forms. Apply the previously described techniques to achieve a frictionless experience and set a positive tone for the entire study.

Four considerations

- [ ] Make it easy for potential participants to indicate their interest in the study. Let them complete an initial intake form online to see if they'd be eligible. This data should then be directly leverageable in your study database (EDC) so that if the patient ends up going forward with the study, you don't have to ask for the same information again.
- [ ] Design participant-facing forms to be simple and intuitive, and readily usable on any device and web browser.
- [ ] Rethink the consent experience. Rather than presenting the participant with an electronic version of a dense legal document, break out the consent topics into engaging nuggets of information, graphical layouts, and quiz questions along the way to verify understanding.
- [ ] Make sure the data captured during this part of the study are well integrated with your EDC system. All your data should be in one place (and get there in real time) to make it as actionable as possible.

Stakeholder benefits from well executed electronic recruitment, screening, and enrollment

PARTICIPANTS

Empowered participants feel more engaged with the study. Self-service screening and enrollment enable patients to perform tasks without the added effort of interfacing with the site unless they have a question or concern.

DATA MANAGERS

Greater automation and smart, well designed forms mean data managers get high quality data right out of the gate and have less downstream cleaning work.

MONITORS

Save on travel to the site, answer queries regarding patient registration or enrollment faster, and reduce efforts around study startup. Eliminate the tedious and costly practice of SDV.

SITES

Reduce site burden by casting a wider net for recruitment, opening the pool of potential participants. Enable sites to register and enroll participants without an inperson appointment, saving them time and effort and increasing efficiency.

SPONSORS

Meet enrollment goals faster, increase compliance, reduce risk, and save on costs.

Innovative technologies like **OpenClinica Unite™** solve the problem of tracking and managing source documents by transferring data directly to your EDC system in a quick, reliable, and regulatory compliant manner.

Leverage existing data from medical records

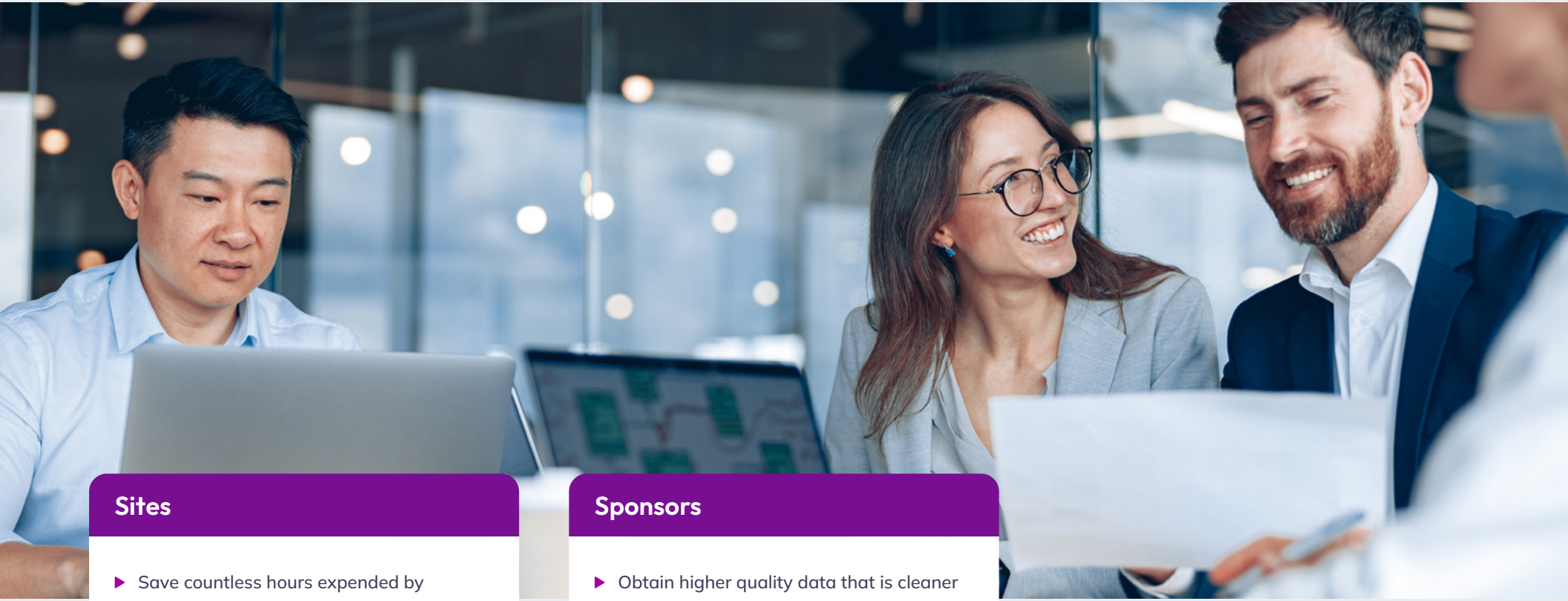
We all know that the source record for your clinical trial data matters a lot. We also know that it's a real pain to have to track and manage source documents (especially paper ones!). The approaches mentioned earlier all enable your data to be electronically sourced. Such "eSourced" data means there is no separate source of the data in your study that must be manually reconciled and could introduce data quality risks.

Unfortunately, today, it is typical in clinical trials for research coordinators to manually transcribe data from the site's system housing the patient's health record (i.e., EHR system) into the EDC system. This, of course, is not eSource. The result is that your study's source lives in the EHR, placing an enormous burden on the sponsor to ensure that what's in the EDC system is consistent with what's in the EHR.

Integrated EHR eSource

Consider the value that data from the patient's chart pulled directly into your EDC could have on your clinical trial. Most sites must carve out considerable time and resources to transcribe EHR data into the EDC. Integrating directly with the EHR allows you to unlock latent data that sites would otherwise spend hours trying to input, data managers would spend hours cleaning, and sponsors might not be able to get their hands on for weeks or months.

Benefits of EHR eSource



Sites

- Save countless hours expended by overburdened coordinators and clinicians.
- Reduce routine tasks from hours to seconds.
- Redirect attention to patient safety and care as opposed to data processing.
- Participate in research more easily and profitably.

Sponsors

- Obtain higher quality data that is cleaner and more complete.
- Get access to finalized study data faster.
- Reduce the costly practice of 100% SDV.
- Increase site satisfaction and compliance.

Learn more about OpenClinica Unite for EHR eSource

Actionable intelligence via reports and dashboards

With all your data collection components in place, you'll need to consider how you will track study progress and identify possible issues. Good reporting is especially important in a decentralized trial because you'll be relying less on sites to help ensure things are happening in the right way. So, start by developing a list of key metrics that will matter. These could be organized into different categories, such as:

- **Safety** (e.g., relationships between treatment and AEs)
- **Protocol compliance** (e.g., number of events out of window)
- **Recruitment** (e.g., screen failure rate)
- **Data cleaning** (e.g., query resolution rate)

While you should start out with a target set of metrics, it's nearly impossible to predict what you might want to analyze as the study progresses. Therefore, it's important to have a flexible analytics toolset that gives you access to slice, dice, and visualize all your clinical data and metadata.

Reporting considerations

- Make sure you have immediate access to operational and clinical data (so team members can act quickly on everything from queries to adverse events). It should also be easy to access the data underlying a given report.
- Set-up different dashboards (collection of reports) around different themes and/or specific dashboards for specific stakeholder groups containing the set of reports most relevant to that stakeholder.
- Assign permissions to ensure you maintain appropriate confidentiality and enable users to access the reports they need to do their job.
- What's the best way to compare performance, trends, patterns, and outliers by cohorts? Be sure you're able to visualize a given set of data in flexible ways (e.g., via bar charts, scatter plots, stacked line graphs, goal lines, data tables, etc.)
- To ensure your reports are as actionable as possible, they should be able to push alerts and updates automatically to relevant stakeholders.
- The system should be easy enough to use so that you can quickly create new reports, update existing ones, and enable your colleagues to build their own reports without requiring specialized technical skills.

Check out OpenClinica Insight™ →

Stakeholders benefit from real-time, visual reports & dashboards

Data Managers, Monitors, Sites, & Sponsors

Historically these stakeholders have relied on Excel spreadsheets as the glue to fill in the gaps of rigid reporting systems. However, sites, monitors, data managers, and sponsors can now perform all their reporting in a collaborative manner online. This makes it easy to share and reuse reports resulting in better communication, organization, and faster decision making.

Statisticians

Statisticians are responsible for ensuring that the study is constructed in a way that will help the sponsor draw conclusions from the trial data. They focus on the questions the study needs to answer. A system that makes it easy for statisticians to understand and navigate the data, and provides flexible tools for interpreting this data, enables statisticians to maximize the value they deliver in their essential role.

Exploring integrations

Each decentralized clinical trial is unique and has its own set of requirements and may require integrations between systems, such as:

Remote patient monitoring: sensors, wearables, medical devices, and health apps

Enabling outside sources to contribute valuable, accurate patient data into the EDC can save clinical trial stakeholders tons of time. Plus, it reduces the burden on patients. With virtually every person utilizing a smart device, integrating with them may be a huge benefit for your study.

Telehealth technology

If you need to meet with patients but are not requiring that they visit a site, consider adding a telehealth component to your study. The COVID-19 pandemic greatly increased the number of appointments conducted over secure video conferencing, increasing patients' confidence and affinity for this type of technology.

Labs, IxRS, CTMS, EHR, payments

These are examples of technologies commonly used in clinical trials today that you may benefit from integrating into your study.

APIs: The key to integration

API (Application Programming Interface) refers to the modern technical interface software developers use to enable real-time interchange of data between systems. Not all APIs are created equal, however. They can be based on different technical standards, which can make them difficult or easy to work with. The APIs on each side of the integration need to have the right "hooks" available to support the use cases most important to you.

How to pick the right partner for your hybrid trial

Four key considerations

1. Software

Write down and prioritize your requirements to serve as a "shopping list." But keep in mind that while it's important to check off a certain number of requirement boxes, it's also important to realize that the toolset itself isn't the sole determinant of a successful trial. Just because you have a box full of hammers, saws, and wrenches, doesn't mean you'll be able to build a house. How reliable is the system? Can the features you need sufficiently scale and adapt? Evaluating ease-ofuse is particularly difficult to distill into written requirements. Ask the vendor you're considering to provide a sandbox where you and your team members can get hands-on with the software.

2. Support

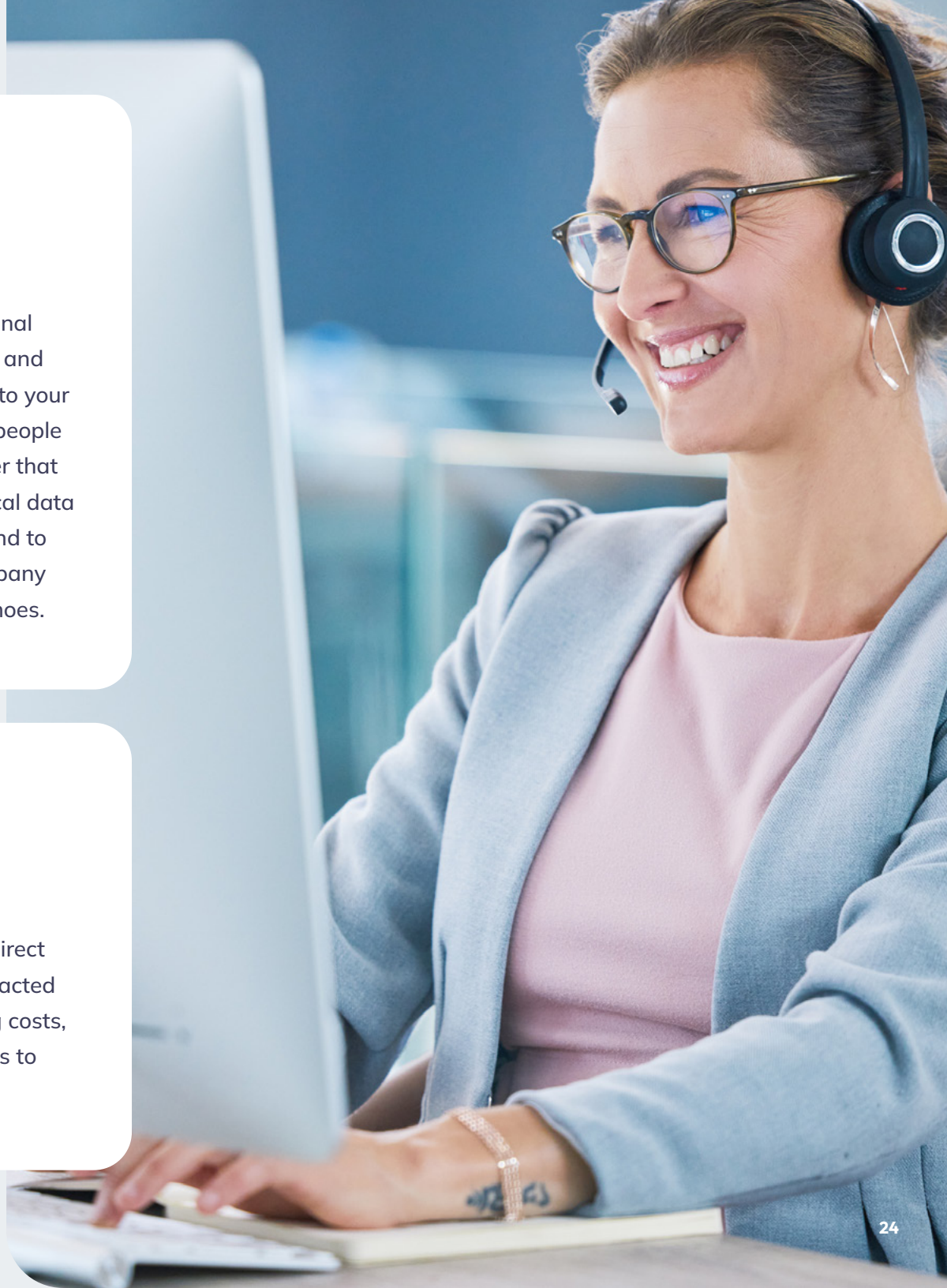
Every clinical study requires a certain level of support when it comes to onboarding new technology. How long does implementation take? What skills and resources are required? What does training look like? You'll need more than just responsive tech support. Your vendor should also make it easy to demonstrate ongoing compliance with regulations such as ICH GCP, 21 CFR Part 11, HIPAA, and GDPR.

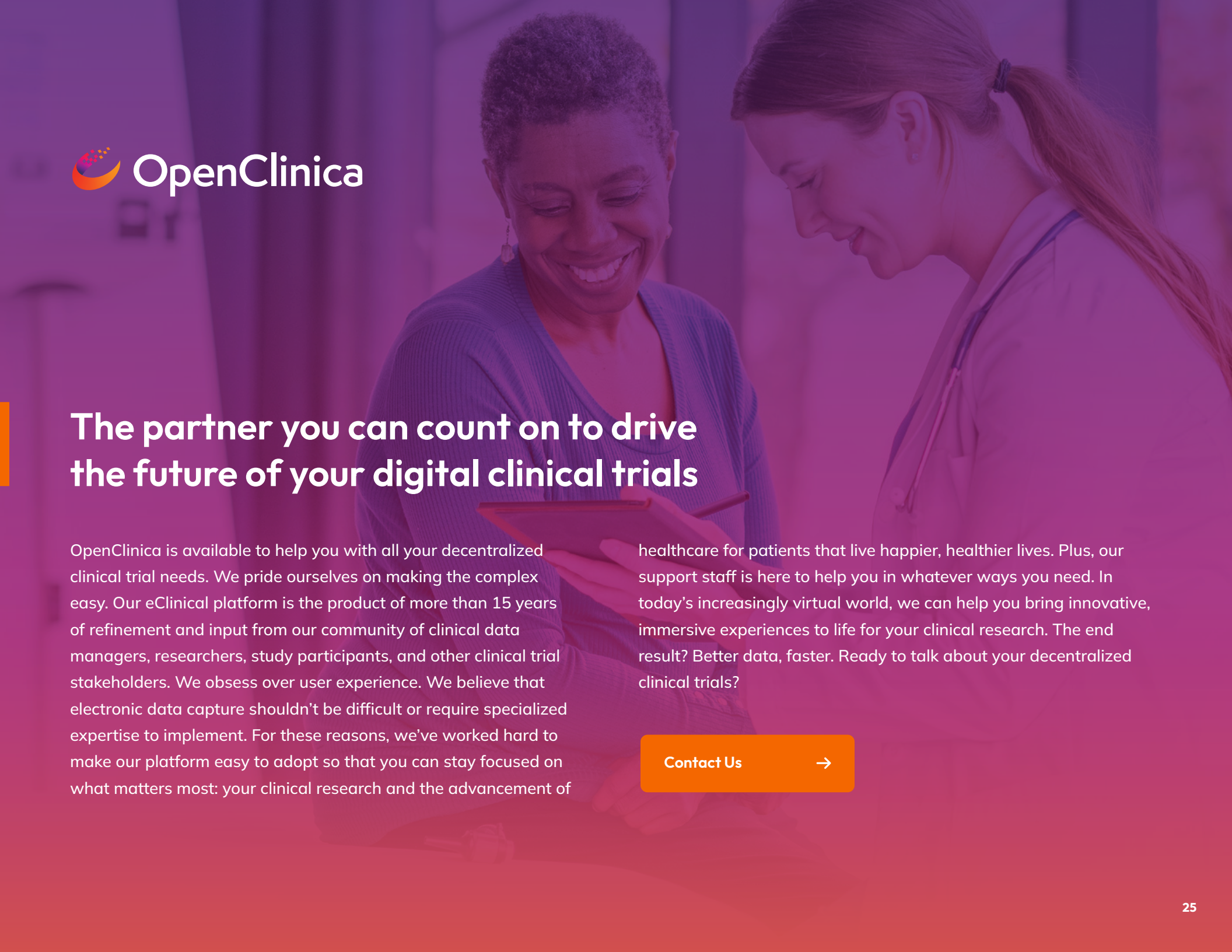
3. Professional Services

Most technology companies offer a variety of professional services, but make sure you investigate the availability and expertise of the support personnel that will be the key to your success. Believe it or not, some vendors hire and train people with very little industry experience. Search for a partner that hires people with field experience, such as former clinical data managers or clinical research coordinators. You're bound to have a much better experience by working with a company whose people understand what it's like to be in your shoes.

4. Cost

Cost is always a critical factor. Consider not just the direct cost of the software, but how other costs may be impacted as well (such as data entry/cleaning costs, monitoring costs, site payments, etc.). The correct way to assess costs is to look at them holistically.





OpenClinica

The partner you can count on to drive the future of your digital clinical trials

OpenClinica is available to help you with all your decentralized clinical trial needs. We pride ourselves on making the complex easy. Our eClinical platform is the product of more than 15 years of refinement and input from our community of clinical data managers, researchers, study participants, and other clinical trial stakeholders. We obsess over user experience. We believe that electronic data capture shouldn't be difficult or require specialized expertise to implement. For these reasons, we've worked hard to make our platform easy to adopt so that you can stay focused on what matters most: your clinical research and the advancement of healthcare for patients that live happier, healthier lives. Plus, our support staff is here to help you in whatever ways you need. In today's increasingly virtual world, we can help you bring innovative, immersive experiences to life for your clinical research. The end result? Better data, faster. Ready to talk about your decentralized clinical trials?

Contact Us →

OpenClinica

OpenClinica has delivered innovative and practical solutions for clinical trials since 2006. We continue to push the envelope by automating source data acquisition and workflows through our cloud-based platform. Offering a secure bridge between healthcare and research, OpenClinica is trusted by the world's foremost life science companies, academic institutions and government entities and has been used in more than 15,000 studies involving over three million patients worldwide.

We are proud to support thousands of small, midsize and large research organizations spanning biotech, pharma, academia, medical device manufacturing and contract research organizations.

OpenClinica, LLC is headquartered in Waltham, MA.

For more information on OpenClinica's solutions for automatic EHR to EDC data integration, electronic data capture (EDC), EHR eSource, ePRO/eCOA, randomization, and analytics and reporting – visit: **www.openclinica.com**.

Resources

1. https://www.oracle.com/oce/dc/assets/CONT2CC43C146CD14B52A0A103ABD34D70BB/native/oracle-report-11-17-20.pdf?elqTrackId=9416c79188ad4c50a7bd8beb10c9837b&elqaid=103092&elqat=2
2. https://mdgroup.com/blog/why-decentralisation-is-the-future-of-clinical-trials/
3. https://www.biopharmadive.com/spons/decentralized-clinical-trials-are-we-ready-tomake-the-leap/546591/
4. https://www.archemedx.com/corp-blog/decentralized-virtual-hybrid-clinical-trial-whats-the-difference/