Building a Strong Data Foundation for Decentralized Clinical Trials with an FSP Model

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By bringing trials directly to patients, decentralized clinical trials (DCTs) offer a host of compelling benefits, including reduced patient burden, such as travel and financial obligations, making it easier for patients to participate in clinical trials, which, in turn, results in faster recruitment, more diversity and increased retention. DCTs also can include environmental benefits through less travel and paper-based processes, which can help reduce the carbon footprint of the trial.

However, previously, perceived or actual regulatory or ethics committee hurdles, operational complexities — including significant data-handling challenges — and a lack of willingness to try something novel have slowed the adoption of DCTs.

Then came COVID-19. By necessity, DCTs were rapidly adopted across therapeutic areas as a means to allow clinical trials to continue, with advancements and accelerations in digital technologies serving as a key enabler. During the pandemic, developers gained significant experience in the appropriate application of DCTs, strategies that are now taking greater hold. In a survey conducted by the PPD clinical research group of Thermo Fisher Scientific in 2022, current users of DCTs anticipated that upwards of 40% of their trials will employ DCT strategies by 2024, as compared to 20% only a year prior.[1]

Though industry terminology has yet to be standardized, DCTs can be defined as clinical trials that include the flexibility for patients to participate in a trial remotely for some or all of a trial. While some trials are entirely virtual, the vast majority of DCTs include a mix of visits in the home and/or in the community and/or at a traditional investigational site.

DCTs can provide greater efficiency and reduce patient burden, but they're not formulaic. A wide range of decentralized elements (e.g., home health visits, televisits and remote monitoring) and technologies (e.g., electronic consent, wearables, electronic clinical outcome assessments and more) may be selected within the DCT spectrum, as illustrated in Figure 1.

DCTs may be well understood as a concept, however, their implementation is still relatively new within the industry. Given that DCTs also entail a significant lift in data complexity and volume, the traditional data management operating models need to evolve so they are less reactive and, instead, engage at the pre-protocol design stage, focused on proactive planning and the application of risk-based quality management methodologies.

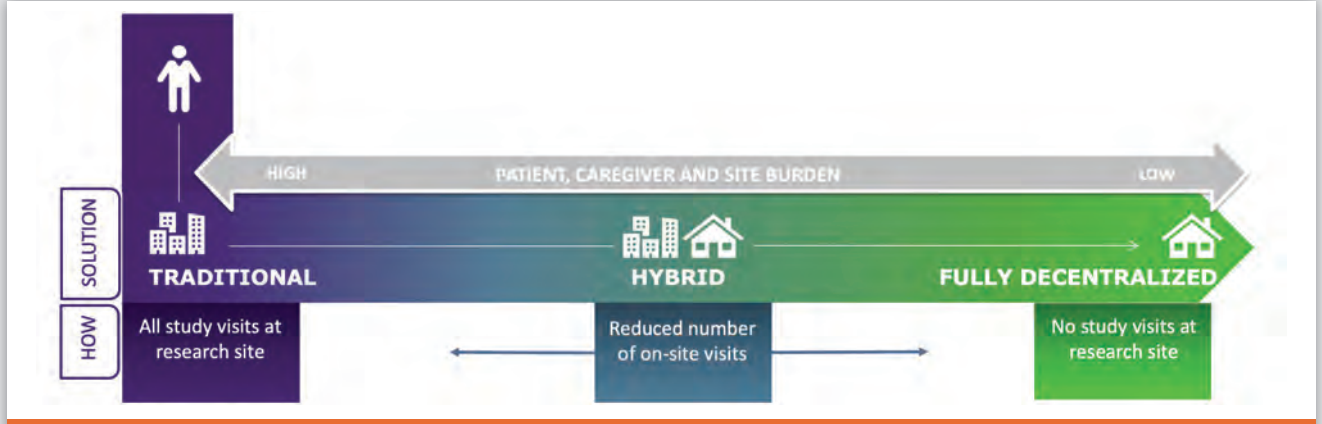

Figure 1. The DCT spectrum

To meet the needs of this new approach, specialized data management and digital and decentralized solutions teams have continued to expand to support sponsors through functional service provider (FSP) sourcing models. With this expertise, sponsors get access to the know-how they need to evaluate four key decision points made early in the development life cycle that are critical to the success of a DCT strategy. They involve choosing the right:

1. Outsourcing model
2. Patient experience
3. Site experience
4. Data journey

Making those right decisions—while understanding the tradeoffs involved in each—translates to a more consistent and quality experience both for patients and sites, a study that is delivered on schedule, and assurance of data integrity and reliability of studies.

Decision Point #1: Selecting the Right Outsourcing Model

DCTs offer the potential for transformative benefits to the clinical research industry, including faster and more efficient trials and enhanced patient experiences. However, when designing a DCT trial, sponsors must navigate multiple types of approaches and technologies while also balancing the different needs of a range of stakeholders.

To minimize the risk of issues and disruptions, DCTs must be designed with the end in mind. This means that from the pre-protocol design stage, DCT and data management experts are needed with the experience and expertise to critically think through the full ecosystem to evaluate potential implications of decisions. To this end, it is essential to engage partners at the earliest stages to embed the necessary subject matter expertise. Ideally, a partner should have the experience and expertise to help drive the overall DCT strategy design and implementation plan and – understanding that data management is one of the critical underpinnings of the overall success of a DCT – should assist in driving an integrated data management plan.

When outsourcing the implementation of DCTs, there are several options. Full-service models offer end-to-end clinical development services across a trial, while FSP models involve the outsourcing of some or all of one or more functions, potentially across a portfolio. And finally, there are hybrids of both models.

In our experience, the FSP approach is often an ideal model for DCTs. Every DCT is unique, and the FSP model offers the flexibility to complement a sponsor's existing capabilities with dedicated functional expertise in targeted areas critical to DCTs. An FSP, for example, could be designed to deliver an end-to-end data management solution that encompasses all needed expertise, services, technologies, and processes. Or the FSP solution could incorporate a blend of sponsor, CRO and vendor tools, technologies, and processes. The strength of the FSP model is that it delivers the flexibility to meet the specific needs of a DCT while also embracing the rapidly changing evolution of our industry (e.g., by adopting a vendor's new wearables/data collection device or incorporating artificial intelligence and machine learning technologies like robotics process engineering to automate repetitive tasks.)

Additionally, in cases where a sponsor is implementing multiple DCTs across a portfolio, an FSP model is capable of scaling to incorporate DCT capabilities and best practices consistently across all trials in the sponsor's portfolio instead of on a limited trial-by-trial basis.

FSP models also enable engagement with functional subject matter experts who provide the right expertise at the right moment, including operational, clinical, and regulatory experience, to help guide the strategy, identify and mitigate risks, and drive accountability. These experts provide on-demand knowledge and consultation, as needed, around how to incorporate best practices, country-specific parameters

and evolving global regulatory frameworks into the design and deployment of the solution, thus empowering the study teams to make faster/smarter decisions and meet critical milestones.

Decision Point #2: Optimizing the Patient Experience

Patient centricity is an approach to health care that prioritizes the patient's experience, satisfaction and outcomes while considering their individual circumstances, preferences, and values. DCTs inherently offer several patient-centric advantages by bringing the trial to the patient. Many patients find that home visits by nurses or via televisits are more convenient, comfortable, and affordable than traditional site visits. DCTs also may provide enhanced abilities to support patients on trial. For example, if a patient's heart rate is continuously monitored by a wearable device, an alert flag could be put in place for certain low and high thresholds that may be able to pre-emptively detect any safety issues with the patients.

However, the trial also needs to ensure that no extra burden is imposed when traditional site tasks are transferred to the patient. For example, while a range of patient-centric data collection technologies can be deployed for the patient that potentially allows for near real-time monitoring of patient safety and improved insights, on the other hand, patients with fine motor issues may struggle to use the devices.

For this reason, the specific needs of each patient population must be evaluated. For example, it may be worthwhile to engage with patient advocacy groups early in the development process to investigate and assess the accessibility of devices to ensure they are fit for purpose.

A patient-centric DCT design requires a full understanding of the DCT solutions, patient population, implementation, and data flow. An end-to-end patient journey helps to elucidate how patients will interact with and use different solutions. Considerations such as age, diversity, disease severity, socioeconomic status, and access to the Internet all should be incorporated within the design. It's also important to ensure the use of DCT solutions does not exclude any patient populations that are less able to access digital technology and that internet-enabled devices are provisioned to these patients as part of the planning.

Optimally, designs also offer patients some level of choice on how they wish to participate without excluding those who may wish to complete their visits at a site in the traditional manner.

Decision Point #3: Optimizing the Site Experience

DCTs can pose many challenges for sites that are often understaffed, already shouldering heavy workloads and, as they are operating in an intensely regulated environment, may understandably be resistant to change. In a survey by the PPD clinical research business of Thermo Fisher Scientific that included questions about site staff, the majority reported significant change management challenges when transitioning to DCTs, as noted in Figure 2.[2]

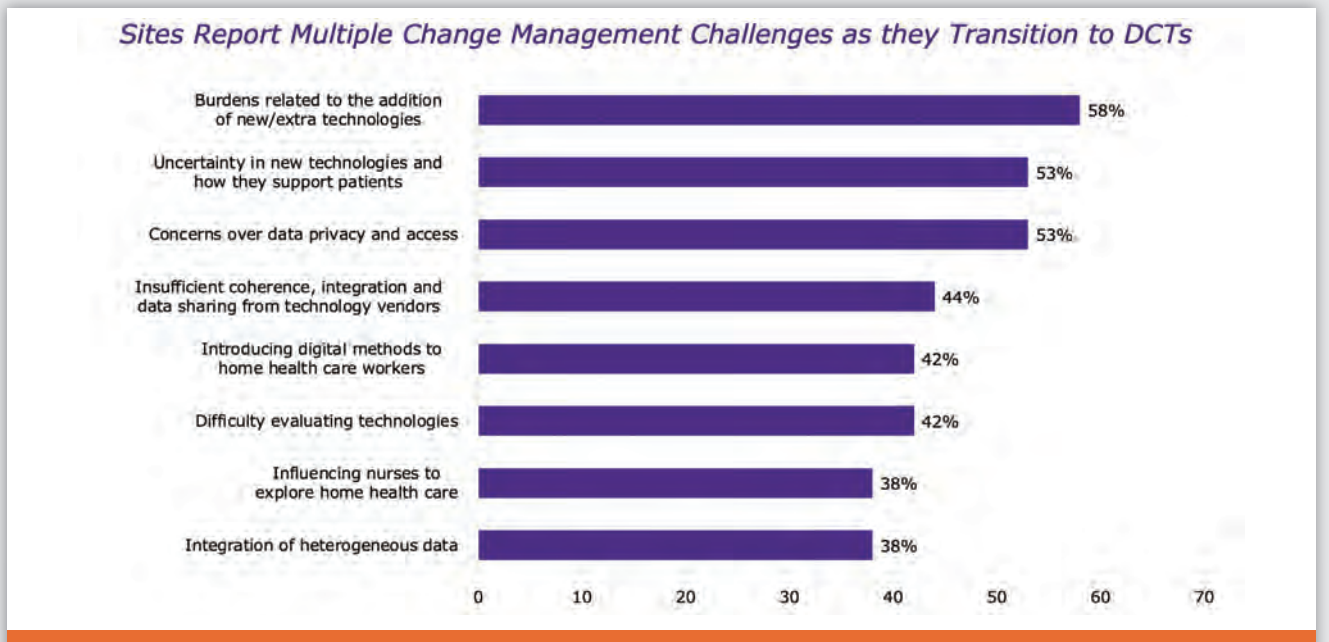

Figure 2. Sites report multiple change management challenges as they transition to DCTs

Recognizing the burden for site staff to adapt to work in different and sometimes altogether new ways compared to their tried-and-true processes, it is critical to consider all facets of the site's experience with the trial during the design stages. Every new piece of technology and process change holds the potential to compound the complexity for sites. If sites don't readily adapt, the result could be slower trial timelines, lower data quality, higher staff burnout and disengagement from the trial.

Thus, the details of how systems interconnect (for example, minimizing the number of platforms and data entry requirements by integrating DCT systems) will directly impact the time required by site staff to work on a DCT. The fewer platforms used and the use of integrations (for example, from an eConsent platform to the EDC) will reduce the time and burden for the site staff working on the study. Therefore, it is critical that, as part of the DCT strategy, understanding how sites interact with each platform is placed at the forefront of consideration during design.

Increased operational complexity at the sites is also an example of why an FSP engagement is an ideal outsourcing model for DCTs. Specialized expertise can be added through an FSP model to ease the site burden by providing support services and training to fill site capabilities/resource gaps and keep the study on schedule (e.g., by adding FSP-sourced site study coordinator roles or administrative support services).

Mapping out precisely how the site will interact with the different tools in a logical order, as illustrated in Figure 3, with a value placed on integration to avoid duplicate data entry, can go a long way to help reduce site burden.

With integration, data from one source can become the truth for all sources, eliminating the need for duplicate entry or integration of data and to reconcile it across systems. Without this interconnectivity, sites would need to use multiple platforms, potentially frustrating users.

In addition to avoiding redundant data entry through the integration of systems wherever possible, DCT data management designs also should strive for simplicity to minimize the number of vendors and DCT platforms, ensure that an agile change management process is in place, and provide clear training and support for site staff. Around-the-clock and multilingual service desk support to cover unexpected issues from the patients and sites is also often helpful.

Finally, proactive risk mitigation strategies should be incorporated to help sites gain comfort with a model, processes and technologies that were not part of their norm. As an example, the primary endpoint for a trial could be eDiary data that are then compared at baseline to a critical window during the treatment period. If a patient is completing an eDiary daily, a review of compliance could be performed across sites with outliers flagged for sites to remind patients of their commitments. Also, during the critical period, missed entries could be escalated for more prompt support to ensure compliance does not drop significantly, thus helping to protect the endpoint.

Decision Point #4: Optimizing the Data Journey

When designing a DCT strategy, the design must fit the needs both of patients and sites. It also needs to be able to collect and deliver all the data required to meet the primary and secondary endpoints for the study, so, the asset is more likely to be approved by regulatory agencies, wanted by patients, prescribed by physicians, and covered by payers at a price in line with the value it provides.

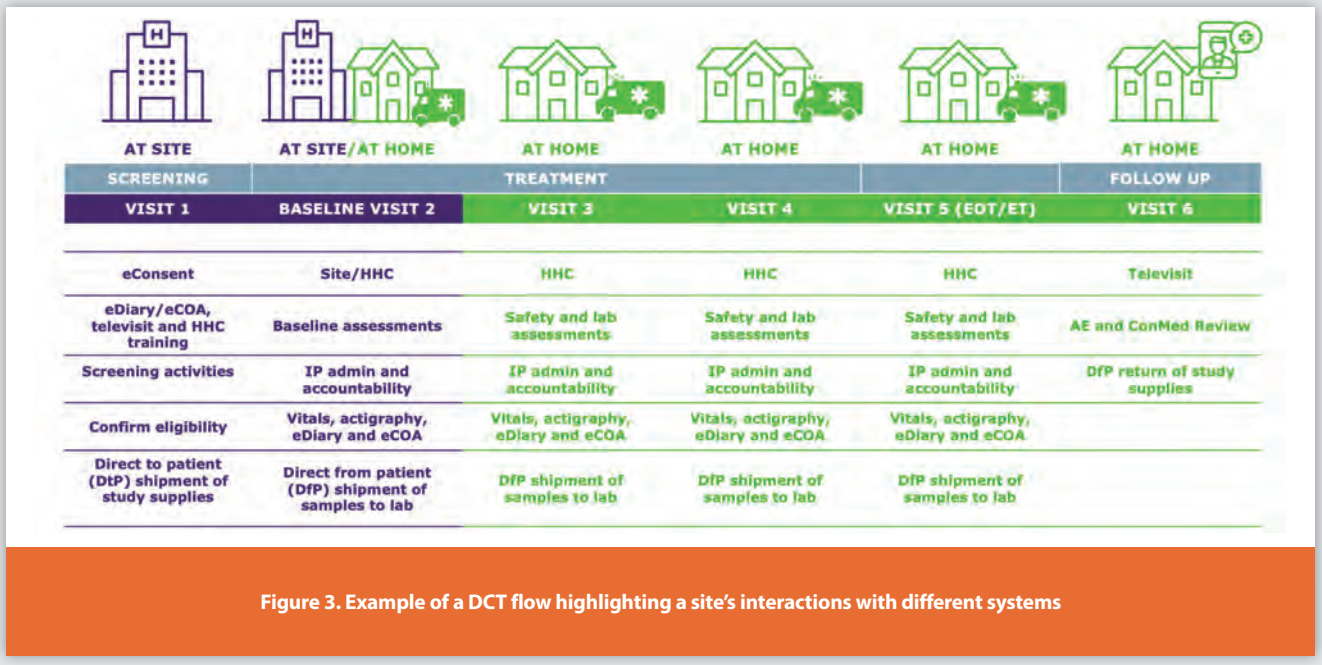

Figure 3. Example of a DCT flow highlighting a site's interactions with different systems

Table 1. Traditional approaches to collecting data versus DCT approaches

	Traditional Trial	DCT
Where is the data collected?	At the investigational site	Anywhere (at home, in the community, at an investigational site)
How is the data collected?	Primarily by site staff using observation/measurement	Via connected devices and/or patient engagement tools and/or by home health nurses or site staff
When is the data collected?	During site visits	During site visits or televisits or home visits and/or community

Indeed, data is the thread that connects the disparate aspects of a DCT. But, as illustrated in Table 1, the traditional model is shifting. In DCTs, data is collected in fundamentally different ways.

Using DCTs means data may be collected from regulator-approved sources that may not have been accepted just a few years ago. For example, millions of health data points are now captured on Fitbits, Apple Watches, and other e-data sources. As technology advances, trial designs need to keep pace, so FSP engagements that provide specialized expertise in DCTs and data management will help sponsors navigate this new environment to ensure the integrity of study data.

DCTs are primarily run through the implementation of digital technology such as eConsent, televisits, eCOA, wearables and supporting decentralized services such as home health care and direct-to-patient shipments that allow data to be collected remotely. Integrating, managing, and interpreting new data types, such as genomic, video, real-world data (RWD) and sequenced information from sensors and wearables, require new data technology strategies compared to "traditional" electronic data capture (EDC) systems.

For example, a vital signs device may be worn by a patient to help monitor safety and collect real-time data in the home. Because of the way it's implemented, the device would collect much larger volumes of data than the vital signs collected at a site visit as part of a traditional study schedule of events. Consequently, a detailed plan must then be in place to answer questions such as: What data points are being collected and where? Who is monitoring and reviewing safety signals? Are alert flags activated for certain low and high thresholds? What is the communication plan in the event of an alert? How is the data being reconciled? Finally, how will it be assimilated with other trial data sources and incorporated into analytics that both assess and predict operational risk?

Incorporating virtual elements also requires a clear vision of how the technologies, platforms and other "site-less" elements will work together with minimal intervention while, at the same time, without underestimating the potential challenges of managing multiple vendors.

During the vendor selection process, the flow of clinical data must be well understood. Mapping out the data flow (see Figure 4) can help the team align on a plan while providing opportunity to discuss concerns to help ensure the different elements of the vendor's pieces will integrate and be fit for purpose.

Conclusion

Having reflected on each of these four decision points, it's important to recognize there is no perfect blueprint that can optimize the data life cycle and associated data flow for every DCT. This is not a one-size-fits-all proposition, but factors that impact the quality of the decisions made will largely remain the same. The right voices need to be at the table from the very beginning, and FSP outsourcing models should be considered to obtain access to the specialized DCT and

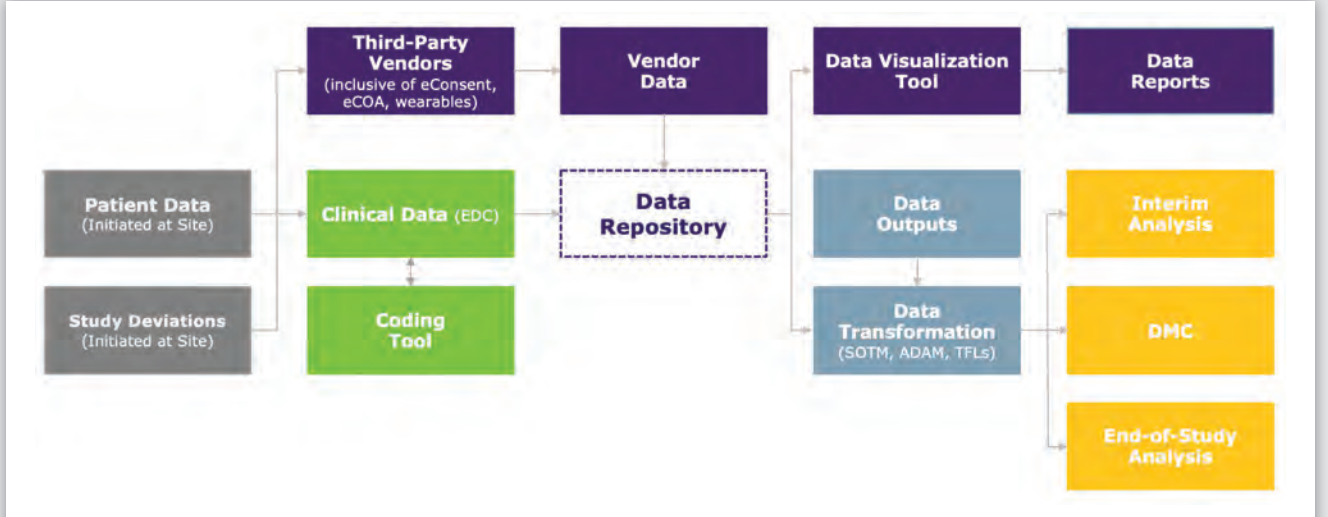

Figure 4. Example of a clinical data flow for a DCT

data management expertise necessary to make strong decisions from the onset.

DCT developers need to consider the distinct needs of protocols, patients and sites, map out desired patient and site experiences, and be agile to adapt to meet those highly variable needs. It is important to leverage advanced technologies, tools, and methodologies when appropriate to generate, manage, review, and analyze more and better data.

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Author Biographies

Robert King *serves as executive director, Functional Service Partnership (FSP) solutions, PPD clinical research business, Thermo Fisher Scientific. In this role, he is responsible for collaborating with clients to develop customized approaches to deliver resource continuity, increase productivity and drive value. Robert has more than 30 years of experience in clinical development and currently serves as a board member and secretary for the Association for Clinical Data Management. During the last 15 years he has had global leadership roles in data management/biostatistics and clinical development support functions. In all these roles he has been a key driver in developing and implementing corporate strategic direction across clinical development and eClinical technologies, as well as gaining significant experience in the FSP marketplace.*

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George Weir *serves as senior director, clinical data management (CDM), PPD clinical research business, Thermo Fisher Scientific. George has more than 25 years of CDM experience, covering both CRO and large pharma. George started his career with the PPD clinical research business in 1997 before leaving to take a position with pharma in 2000. George returned to the business in 2005, where he has held various management positions, most recently as senior director of CDM. George provides oversight to all CDM-related issues, with a particular focus on FSP, ensuring adherence to timelines, budget, procedural documents and deliverables.*