Science 37®

MARCH 2022

CNS Clinical Trial Survey

How Agile Clinical Trials are Impacting CNS Research

New data sheds light on how trends in clinical trials will impact CNS studies over the next 12 months

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How Clinical Research Trends are Impacting CNS

By bringing studies to the patient, agile clinical trials — which move fluidly between traditional and decentralized components — have delivered significant benefits.

We already know that clinical research is undergoing transformation across the board. The traditional, site-based model for clinical trials is slow, costly, and inaccessible to more than 90% of the population.

Our previous research, published in November 2021, revealed a pivotal shift in the way clinical trials are approached across the entire industry, with more biopharma respondents expecting to run an agile (hybrid) clinical trial this year (77%) than were planning to execute a traditional, site-based study (69%). This was a major swing from the previous year, when 92% of the same sample ran a traditional study and only 59% ran an agile trial.

By bringing studies to the patient, agile clinical trials which move fluidly between traditional and decentralized components, taking advantage of the benefits of both — have already delivered significant enhancements, including universal access to patients and providers anywhere, faster enrollment times, higher retention rates, increased diversity, improved patient experience, and better data. The clinical trial of the future will not revert to traditional, site-based models, post-pandemic.

Our research shows that CNS (central nervous system) clinical trials will be among the highest adopters of decentralized components this year. And, according to Evaluate Pharma, CNS R&D spend will top US$32 billion in 2026 alone, resulting in more than 4,000 clinical trials. It's a sprawling therapeutic area of multiple conditions, including Major Depressive Disorder, Migraine, ADHD, Epilepsy, Schizophrenia, Alzheimer's, Parkinson's, Multiple Sclerosis, PTSD, and more. Many of these sub-categories require the use of sensors and wearables to extract data, and "data quality" is a key consideration for clinical trial sponsors across all categories and models. Clearly, a one-size-fits-all approach is not the answer in CNS.

To define the trends in clinical research within the CNS space for the year ahead, Science 37 surveyed research executives at trial-sponsoring organizations. This report conveys our findings.

CNS clinical trials will be among the highest adopters of decentralized components this year, and many of these sub-categories require the use of sensors and wearables to extract data.

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CNS Clinical Trial Survey

New data sheds light on how trends in clinical trials will impact CNS studies over the next 12 months.

Two-thirds of execs will run either an agile (hybrid) or fully decentralized clinical trial in the next 12 months, while just 57% will run a traditional, site-based clinical trial.

- A Science 37 report published in November 2021 revealed a pivotal shift in how clinical research is undertaken, with more respondents planning to run Agile (hybrid) Clinical Trials in 2022 than expected to run traditional, site-based studies.
- That study pointed to the CNS (Central Nervous System) therapeutic area as one of the fastest-growing adopters of DCT methodologies and tools. Consequently, we conducted another survey to explore clinical trial trends exclusively within the sprawling CNS category, which includes conditions such as depression, migraine, ADHD, epilepsy, schizophrenia, Alzheimer's, Parkinson's, MS, and PTSD.
- Of the qualified respondents to the CNS study, two-thirds are are from the pharmaceutical and biotech industries, 4% are from the medical devices sector, and the remainder is CROs. Almost nine out of ten of the 72 are active in the CNS space, with the rest looking to enter CNS in the future.
- Two-thirds (67%) of execs plan to run either an Agile (hybrid) or Fully Decentralized Clinical trial in the next 12 months, up from 49% for the previous 12 months. Conversely, just 57% plan to execute a traditional, site-based clinical trial in the next 12 months (compared to 74% in the previous 12 months).
- "Unexpected delays," "Data quality," and "Limited patient populations" all ranked highly among the issues keeping respondents up at night regarding CNS trials. Meanwhile, the greatest single perceived obstacle (by far) of running an effective CNS study was "Patient Recruitment," with 46% of the vote.
- ePRO/eCOA will be the most prevalent DCT component in CNS over the next 12 months, with more than two-thirds of respondents planning to use it. Among the biggest-growing DCT elements in CNS are Mobile/home nurses, up 40%, and Metasites/remote sites, up 38%.
- The three greatest perceived benefits of including DCT components in CNS clinical trials are "Increased patient retention" (56% ranked this in their top 3), "Increased patient diversity" (54%), and "Faster patient recruitment" (52%).

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DCT Adoption Trends, Projections, and Attitudes Within CNS

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DCT Adoption in CNS Clinical Trials

More respondents plan to run agile (hybrid) or fully decentralized clinical trials in 2022 than traditional studies.

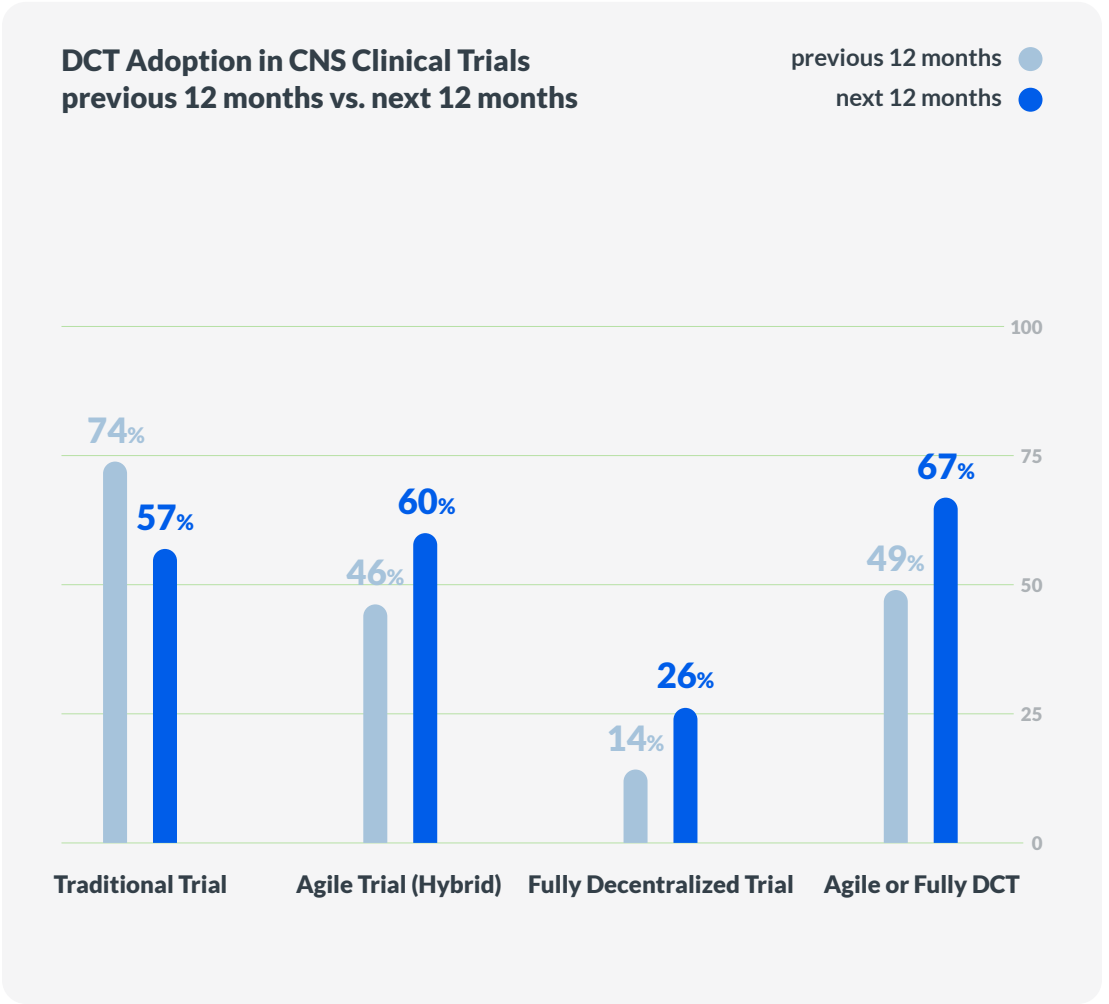
We asked respondents: ***Within CNS, what types of clinical trial activity has your organization done in the previous 12 months, and what does it plan to do over the next 12 months?***

By comparing respondents' recent CNS clinical trial activity with their planned CNS activity for the immediate future, we are able to build an accurate picture of trends for the entire therapeutic area.

The data shows an ongoing shift away from traditional site-based clinical trials and toward Agile (hybrid) and fully decentralized clinical trials. However, this trend is not as pronounced for all indications, possibly due to the inherent complexities of CNS, which we will touch upon shortly.

Two-thirds of CNS execs (67%) plan to run either an Agile (hybrid) or fully decentralized clinical trial in the next 12 months, up from 49% for the previous 12 months. Conversely, just 57% plan to execute a traditional, site-based clinical trial in the next 12 months (down from 74% for the previous 12 months).

67% plan to run either an agile (hybrid) or fully decentralized clinical trial in the next 12 months, up from 49% in the previous 12 months.



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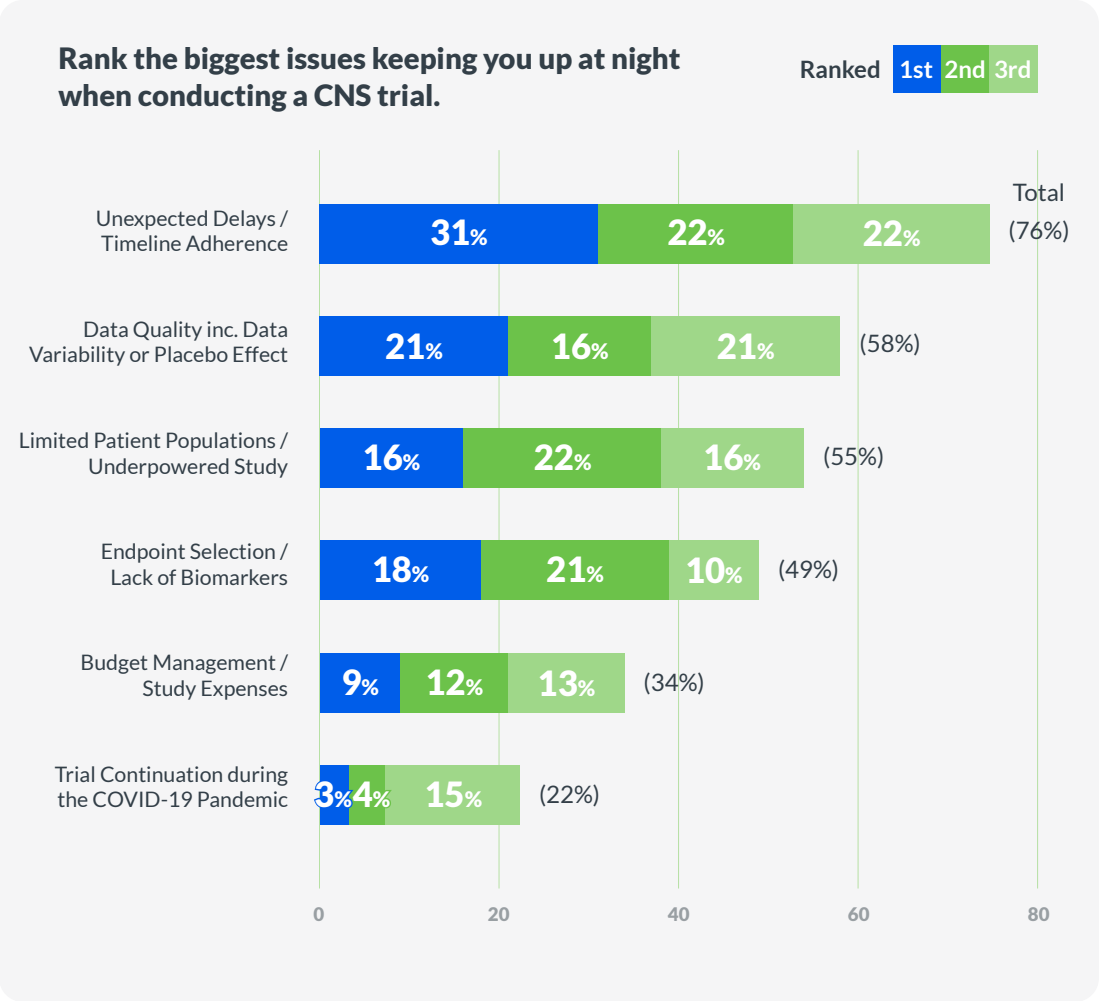
What's Keeping CNS Execs Up at Night

"Patient recruitment" was seen as the single greatest obstacle in CNS clinical trials.

We asked respondents: ***Rank the biggest issues keeping you up at night when conducting a CNS trial.***

We had a clear winner in the rankings, with 76% placing "Unexpected delays/timeline adherence" in their top 3 obstacles. Also scoring relatively highly was "Data quality/variability" (58% in top 3), "Limited patient populations" (55%) and "Endpoint selection" (49%).



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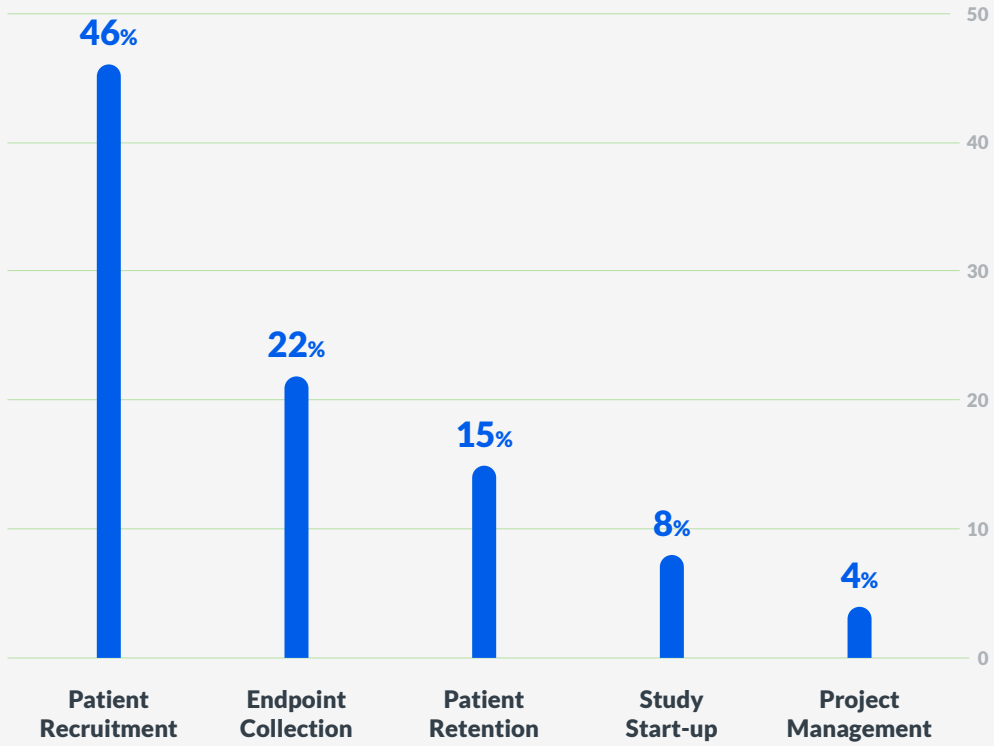
What's Keeping CNS Execs Up at Night (Cont.)

We asked respondents: *What is your single greatest perceived obstacle in running an effective CNS study?*

With respondents restricted to just one choice for this question, "Patient recruitment" was the clear winner with a whopping 46% of the vote.

"Patient recruitment" was cited as the single greatest perceived obstacle in running an effective CNS study with 46% of the vote.

What is your single greatest perceived obstacle in running a CNS clinical trial?



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CNS Categories with DCT Components in 2022

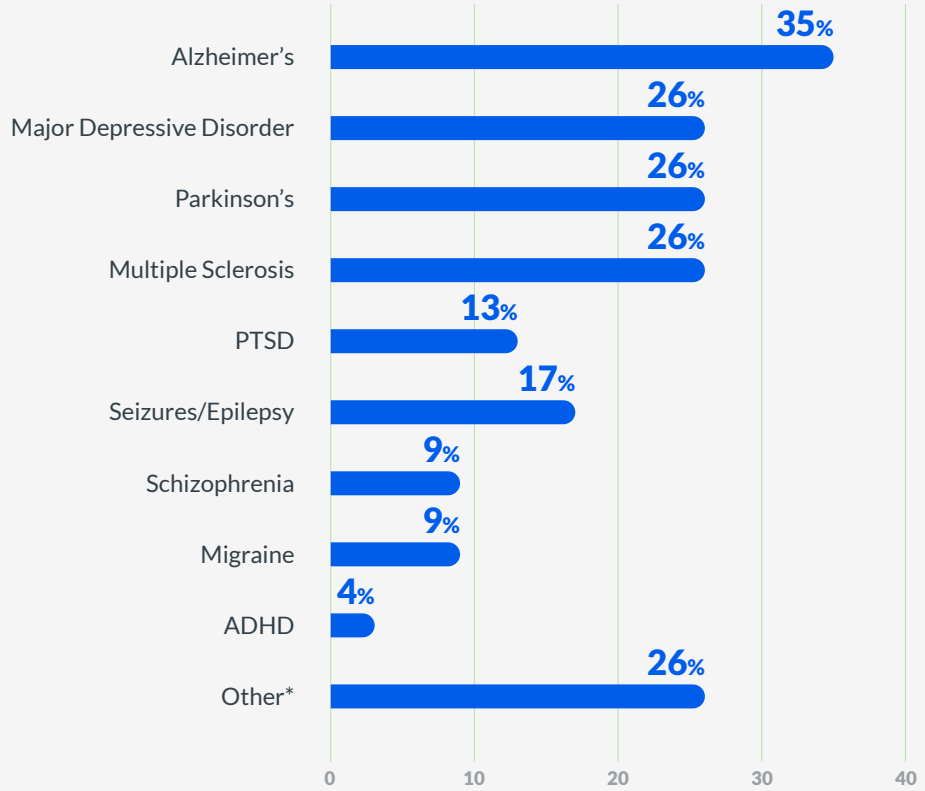
Clinical trials with DCT components will be executed across many different CNS indications.

We asked respondents: ***For which conditions within CNS have you conducted clinical trials comprising one or more DCT components in the previous 12 months or plan to conduct in the next 12 months?***

Alzheimer's topped the responses as the most prevalent CNS categories for clinical trials featuring DCT components in the next 12 months. This was closely followed by Major Depressive Disorder, Parkinson's and Multiple Sclerosis.

It should be taken into account that CNS is an umbrella therapeutic area that features many different types of disorders — including depression, migraine, ADHD, epilepsy, schizophrenia , Alzheimer's, Parkinson's, MS, and PTSD — and so there is a lot of variance in the pipeline, depending on a number of disease-specific factors. Note also that the sample size is relatively small for the responses to this question.

For which CNS conditions do you plan to use DCT components in the next 12 months?



*ALS, HD, Narcolepsy, Idiopathic Hypersomnia, OCD, Tourette's & Childhood Onset Fluency Disorder

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DCT Components Used in CNS Trials in 2022

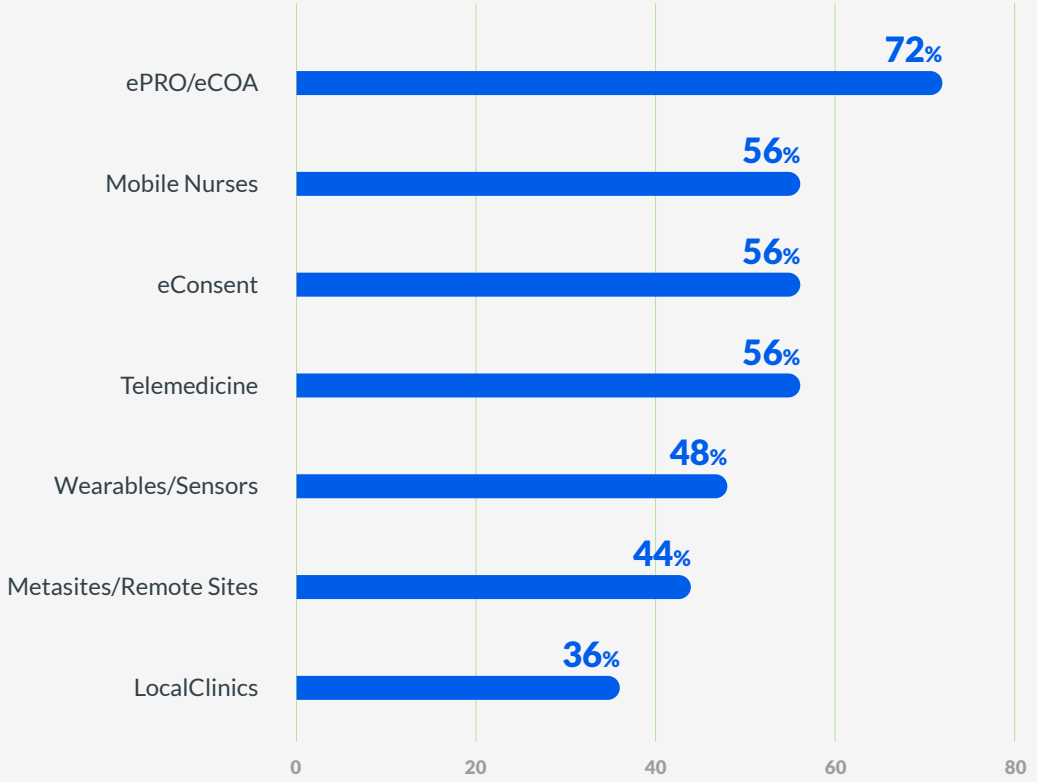
Metasites/Remote Sites and Mobile Nursing show the biggest gains.

We asked respondents: *Which DCT components for CNS therapies have you deployed in the previous 12 months or plan to use in the next 12 months?*

Almost three-fourths (72%) of our respondents plan to deploy ePRO/eCOA tools in the next 12 months in CNS clinical trials, while more than half (56%) are also planning to use Mobile Nurses, Telemedicine and eConsent.

In addition to these mainstay decentralized tools and methodologies, almost half (48%) say their CNS studies over the next 12 months will include wearables or sensors.

Which DCT components do you plan to use in CNS trials in the next 12 months?



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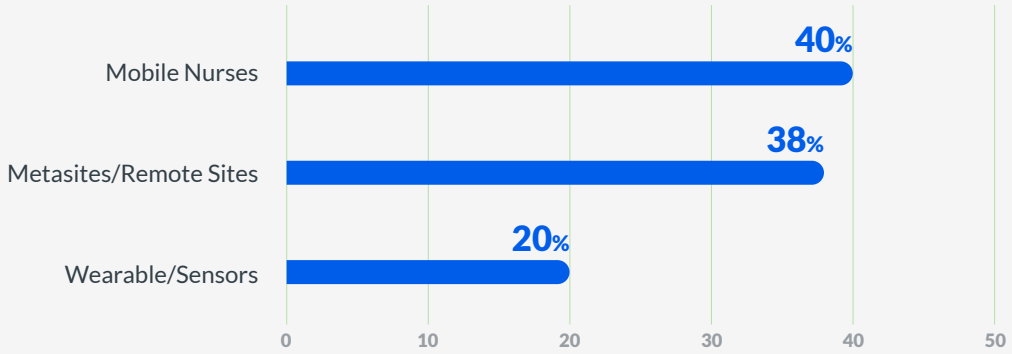
DCT Components Used in CNS Trials in 2022 (Cont.)

We expect a 40% increase in Mobile/Home Nurses in CNS in the next 12 months.

Mobile/Home Nurses recorded the biggest gain in DCT tools 2021 to 2022, with a 40% increase in expected use in CNS studies, followed by Metasites/ Remote Sites with a 38% increase in CNS.

Regarding the Metasite, the lure of a virtual trial site that enables 100% global coverage is clearly gathering pace in CNS.

Which DCT components will see the biggest increases in adoption in 2022 (in CNS trials)?



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Greatest Perceived Benefits of Including DCT Components in CNS Trials

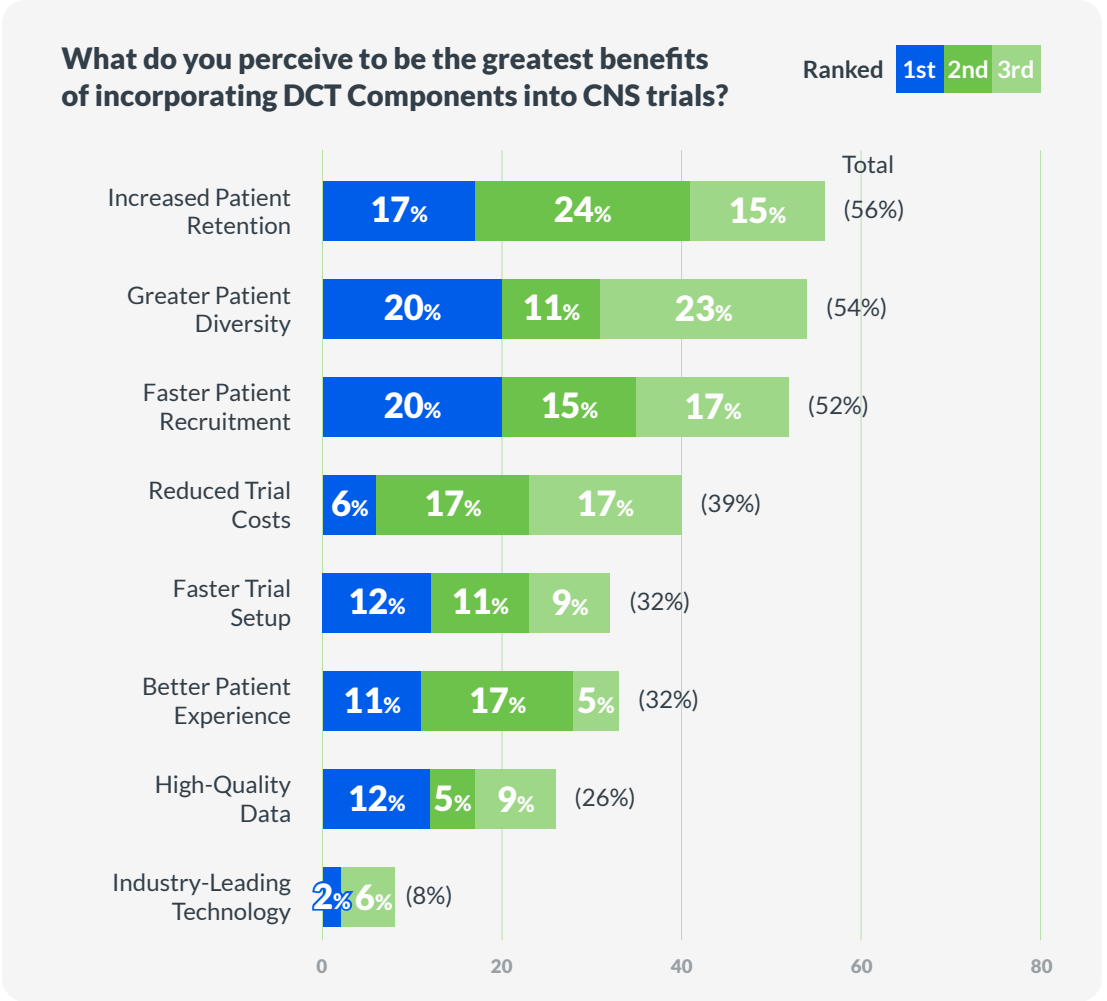
We asked respondents: ***What do you, or your organization, perceive to be the greatest benefits of incorporating DCTs into your trial design for CNS therapies only?***

Respondents were asked to rank eight benefits of DCTs, from biggest to smallest. To order the responses, we took the sum of the percentages of the top three rankings for each response (Fig. 5).

Three perceived benefits rose above the rest: Increased Patient Retention (which 56% of respondents included in their top three rankings), Greater Patient Diversity (54%, top three), and Faster Patient Recruitment (52%).

Therefore, in terms of perceived benefits of DCT within CNS, the focus is very much on patient benefits in the realms of enrollment, retention, and diversity.

56% had Increased Patient Retention in their top three perceived benefits of using DCT components in CNS trials.



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Viability Assessments for Using DCT Components in CNS Trials

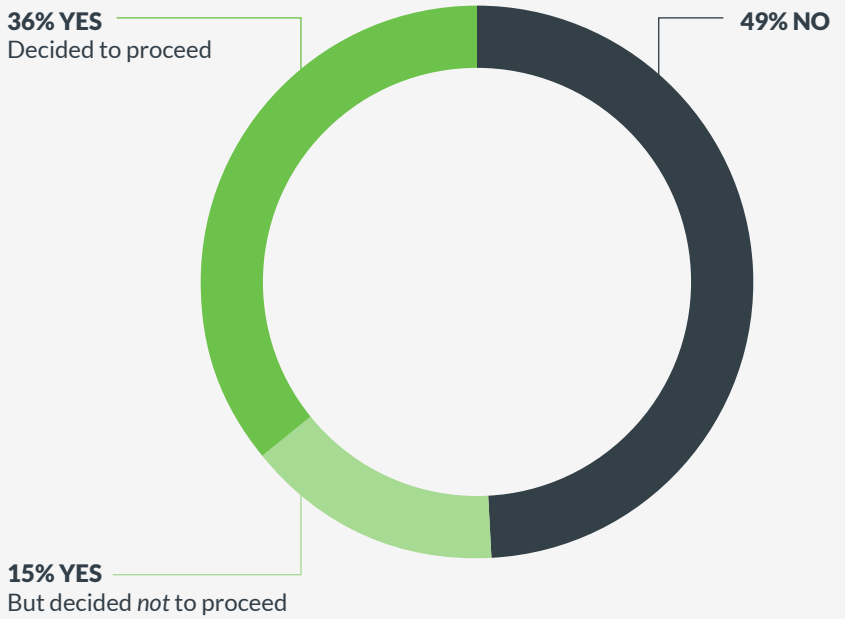
We asked respondents: ***In the past 12 months, has your organization conducted a viability assessment of decentralized elements for a clinical trial in CNS?***

Just over half (51%) of respondents in total said, yes, they had conducted a viability assessment of DCTs within CNS over the past 12 months, with 36% deciding to proceed with a clinical trial featuring DCT elements.

Their top-ranked reasons for adopting DCTs (page 14) were similar to the "perceived" benefits of DCT elements for CNS trials (page 12): Namely, 62% had Increased Patient Retention in their top three rankings; next was Greater Patient Diversity (50% in top three), followed by Better Patient Experience and Faster Recruitment (each 40%).

As for why organizations decided against adopting DCT elements following an assessment, 45% cited both the "Need for Human Interaction at Sites" and "Data Quality Concerns" in their top three rankings.

Have you done a viability asessment for using DTC components in a CNS trial in the past 12 months?



51% said they had conducted a viability assessment of DCTs within CNS over the past 12 months, with the majority deciding to go ahead with an Agile or Fully DCT trial.

ADDITIONAL DETAILS ON FOLLOWING PAGE >

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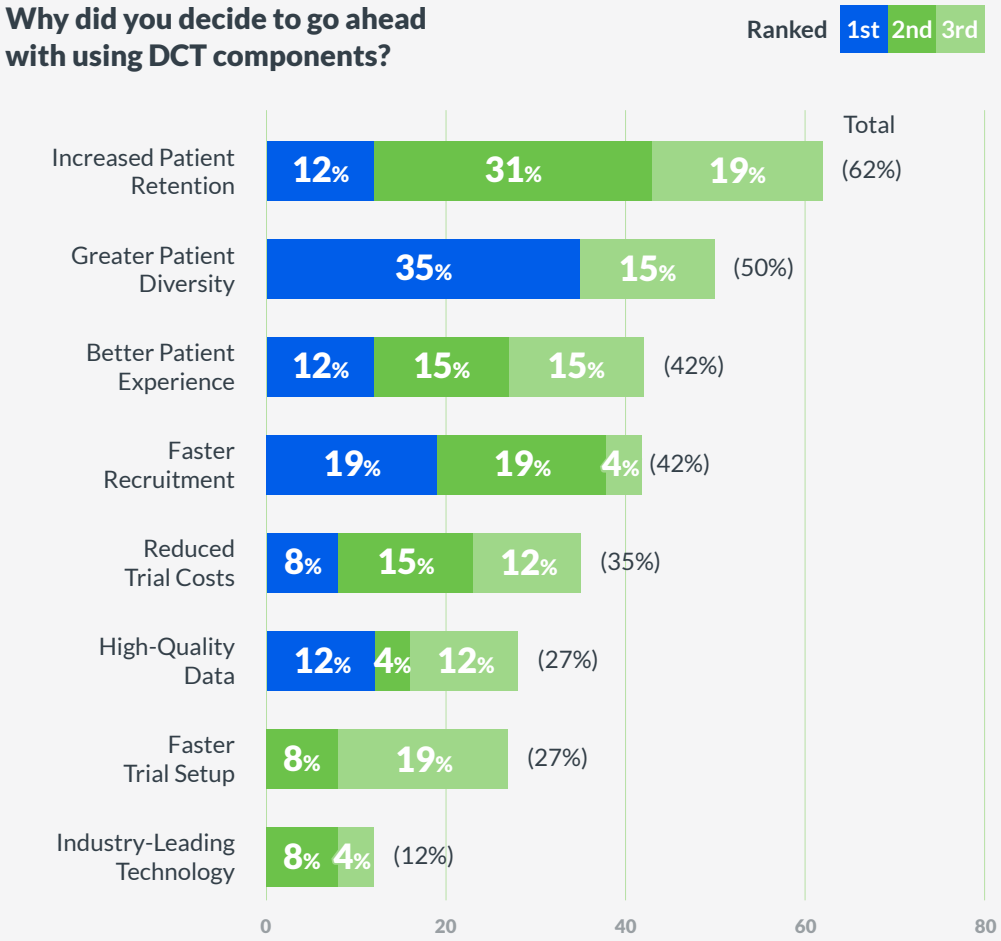
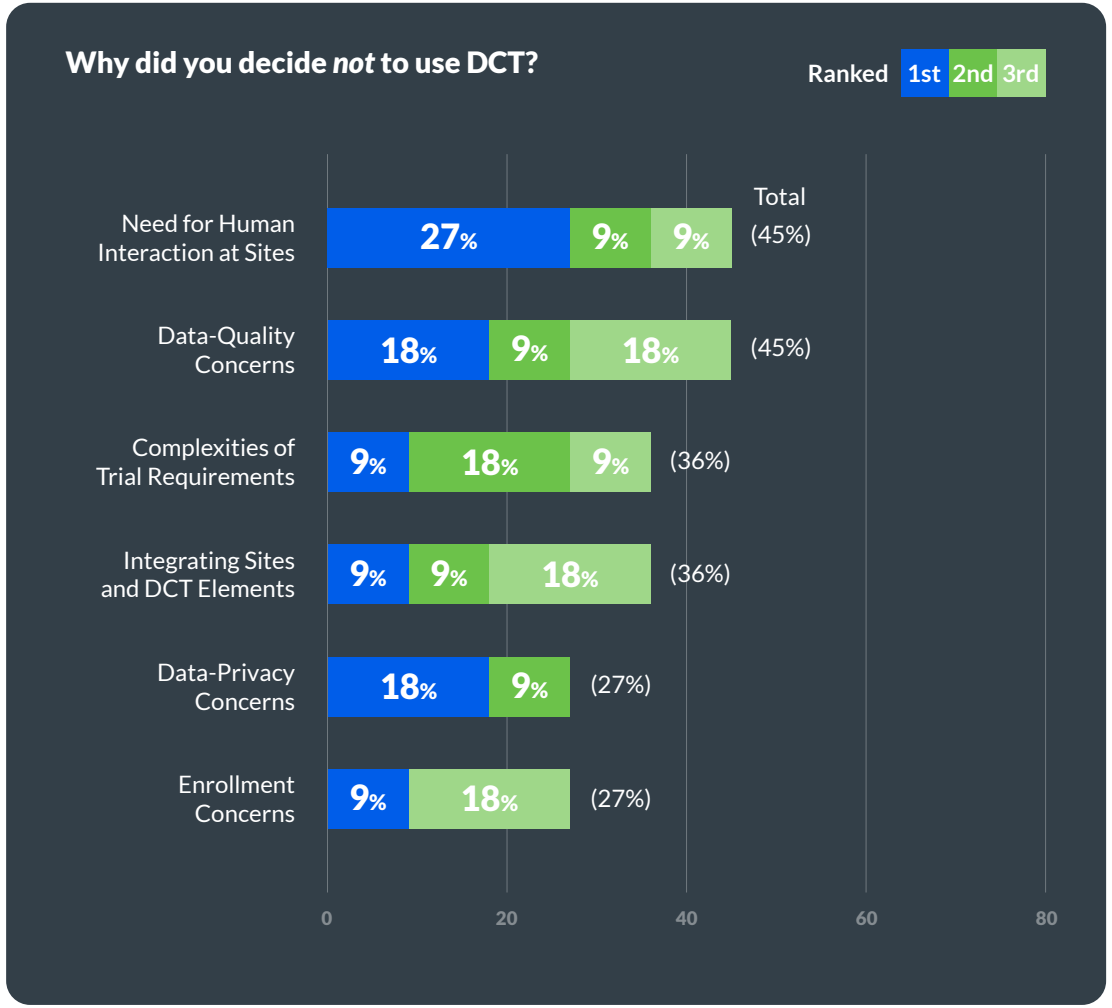
Viability Assessments for Using DCT Components in CNS Trials (Cont.)

Why did you decide to go ahead with using DCT components?



Why did you decide *not* to use DCT?



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How Wearables and Sensors are Used in CNS Clinical Trials

We asked respondents: ***How are you using wearables/sensors in CNS studies? How are you using wearables/sensors data in CNS studies? And which endpoints do you measure using wearables/sensors?***

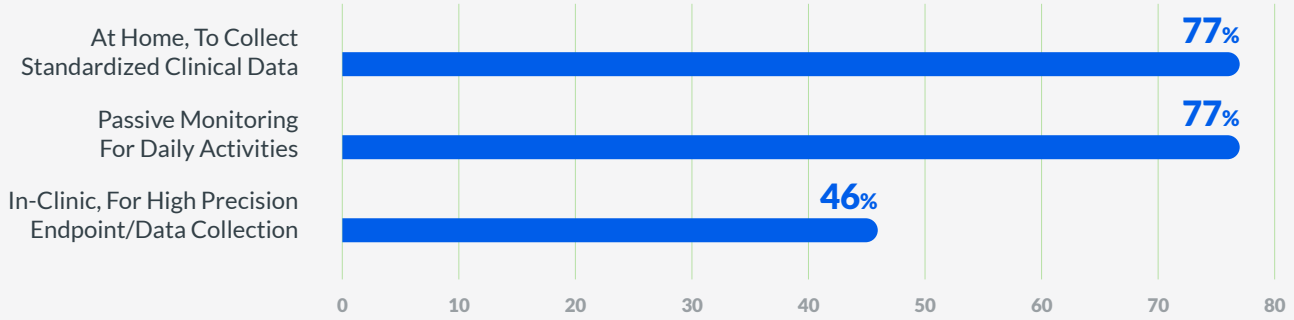
Note, while the sample sizes for these questions were relatively small, the responses were still of interest.

More than three-quarters of respondents said they use wearables/sensors in CNS clinical trials At Home To Collect Standardized Clinical Data, with the same number also using them for Passive Monitoring Of Daily Activities. A further 46% reported using them In Clinic For High-Precision Endpoint/Data Collection.

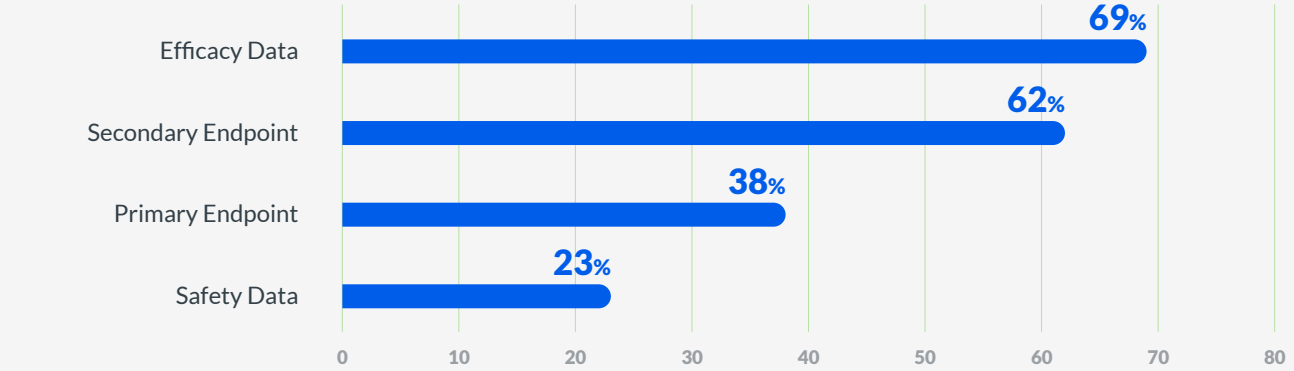
As for the data, more than two-thirds of those using wearables/sensors said they were collecting Efficacy data, with an additional 62% collecting Secondary Endpoint data.

And in terms of which endpoints are measured using wearables/sensors, 79% cited Activity (general), with a further 57% measuring Sleep.

How are you using wearables/sensors in CNS studies?



How are you using wearable/sensor data in CNS studies?



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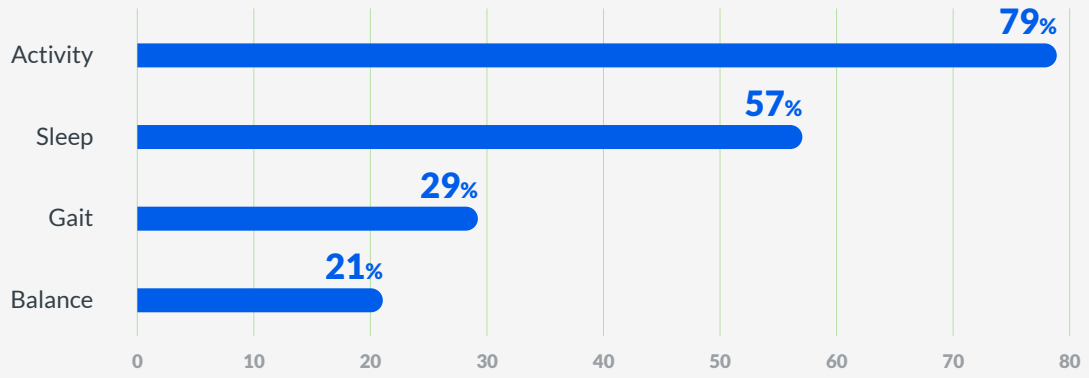
How Wearables and Sensors are Used in CNS Clinical Trials (Cont.)

77% of respondents using wearables/sensors in CNS trials said they use them at home to collect Standardized Clinical Data

Which endpoints do you measure using wearables/sensors?



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CONCLUSION

Five Reasons for Taking an Agile Approach to a CNS Study

We have seen how a shift away from traditional, site-based clinical trials and toward agile clinical trials has reached a pivotal point across CNS indications. Let's now pull it all together with our top 5 reasons for taking an agile approach to a CNS study.

1 The benefits of agile clinical trials.

Agile clinical trials enable significant enhancements across all therapeutic areas, including CNS. Respondents have told us that their single greatest challenge running effective CNS studies is Patient Enrollment (page 7). Science 37's own data shows decentralized approaches have enabled universal access to patients and providers and have accelerated the clinical research process — producing, on average, 15x faster patient enrollment, 28% greater patient retention, and 3x more diverse patient representation. And, despite the various idiosyncrasies within the numerous CNS conditions, these benefits will translate in large part to any disease state.

2 Wearables and sensors protect and enhance data quality.

Data quality and consistency are of utmost concern to CNS trial sponsors (page 7 rankings), and rightly so. Many conditions in CNS require wearables and sensors to collect and capture endpoint data. Science 37 partners with numerous leading biosensor data vendors to incorporate wearable solutions into the study design. Science 37's device-agnostic technology platform will harmonize and process all endpoint and safety data. This replaces a lot of costly in-person monitoring, reducing the number of visits and increasing accuracy. Meanwhile, continuous monitoring results in richer information. Science 37 has working examples of how wearables/sensors are a great fit for decentralized approaches to clinical trials in CNS conditions.

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Five Reasons for Taking an Agile Approach to a CNS Study

3 Regulatory bodies encourage agile clinical trials.

Regulatory bodies noted the benefits of incorporating decentralized components into clinical trials during the pandemic, and are on board with agile clinical trials across all therapeutic areas — and that includes CNS. The FDA, for example, recently issued guidance on the use of "digital health technologies" in clinical trials, supporting the idea that decentralized approaches may encourage participation for those who do not live close to study sites and acknowledging the need to test treatments on more representative populations. Science 37 will deploy its own regulatory experts to validate the data collection in agile clinical trials, which for a global study, will likely involve taking a country-by-country approach.

4 Metasites can improve retention and diversity.

Metasites (or virtual clinical trial sites) are a great way to consolidate patients and eliminate the need for using so many brick-and-mortar sites in many CNS studies, especially where patient enrollment is a concern. And our research has shown that reducing reliance on physical sites can remove friction in the clinical trial process, greatly enhancing the patient experience and subsequently increasing retention rates and the diversity of the study population. Initiatives, like Science 37's Community Provider Network — which has expanded sixfold and now reaches 28 million patients worldwide — are an important part of the solution. At present, less than three percent of physicians participate in clinical trials as investigators; by expanding our network of community providers, Science 37 enables providers to offer clinical research as a care option to patients without having to add expensive infrastructure.

5 An Operating System is available to enable Agile Clinical Trials.

This flexible approach of combining traditional and decentralized components can also add complexity, and it's only possible to get optimum results if the trial is powered by a sophisticated, agile clinical trial operating system that is configurable to the needs of individual studies. Science 37's Agile Clinical Trial Operating System is underpinned by a unified, end-to-end technology platform that orchestrates workflow, generates evidence and harmonizes data. It essentially works with all reliable biosensory devices and wearables to collect reliable, consistent endpoint and safety data, both of which are rightly concerns to CNS clinical trial sponsors. In combination with our specialized networks of patient communities — telemedicine investigators, mobile nurses, remote coordinators and connected devices — it powers a gamut of study configurations, from Metasites (virtual sites) to any combination of DCT elements. Ultimately, the objectives of the agile clinical trial are to put the patient at the center of all studies, and to accelerate clinical research so that we can get new treatments to market faster and into the hands of those who need them most.

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CONCLUSION

Five Reasons for Taking an Agile Approach to a CNS Study

Science 37®

1. The benefits of agile clinical trials.

The significant enhancements enabled by agile clinical trials — faster recruitment, better retention, increased diversity — apply just as much to specific therapeutic areas, like CNS.

2. Wearables and sensors protect and enhance data quality.

Many CNS indications require wearables and sensors to collect and capture endpoint data. Science 37 partners with numerous leading biosensor data vendors to incorporate wearable solutions.

3. Regulatory bodies encourage agile clinical trials.

Regulatory bodies noted the benefits of incorporating decentralized components into clinical trials during the pandemic, and are on board with adopting agile clinical trials across all therapeutic areas, including CNS.

4. Metasites can improve retention and diversity.

Metasites (or virtual sites) consolidate patients and eliminate the need for so many brick-and-mortar sites in many CNS studies, especially where patient enrollment and retention are concerns.

5. An Operating System is available to enable Agile Clinical Trials.

To get optimum results, CNS trials demand a sophisticated, end-to-end agile clinical trial operating system that is configurable to the needs of individual studies.

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APPENDIX

Methodology, Respondent Data, Author Bios, and About Science 37

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APPENDIX

Methodology and Respondent Characteristics

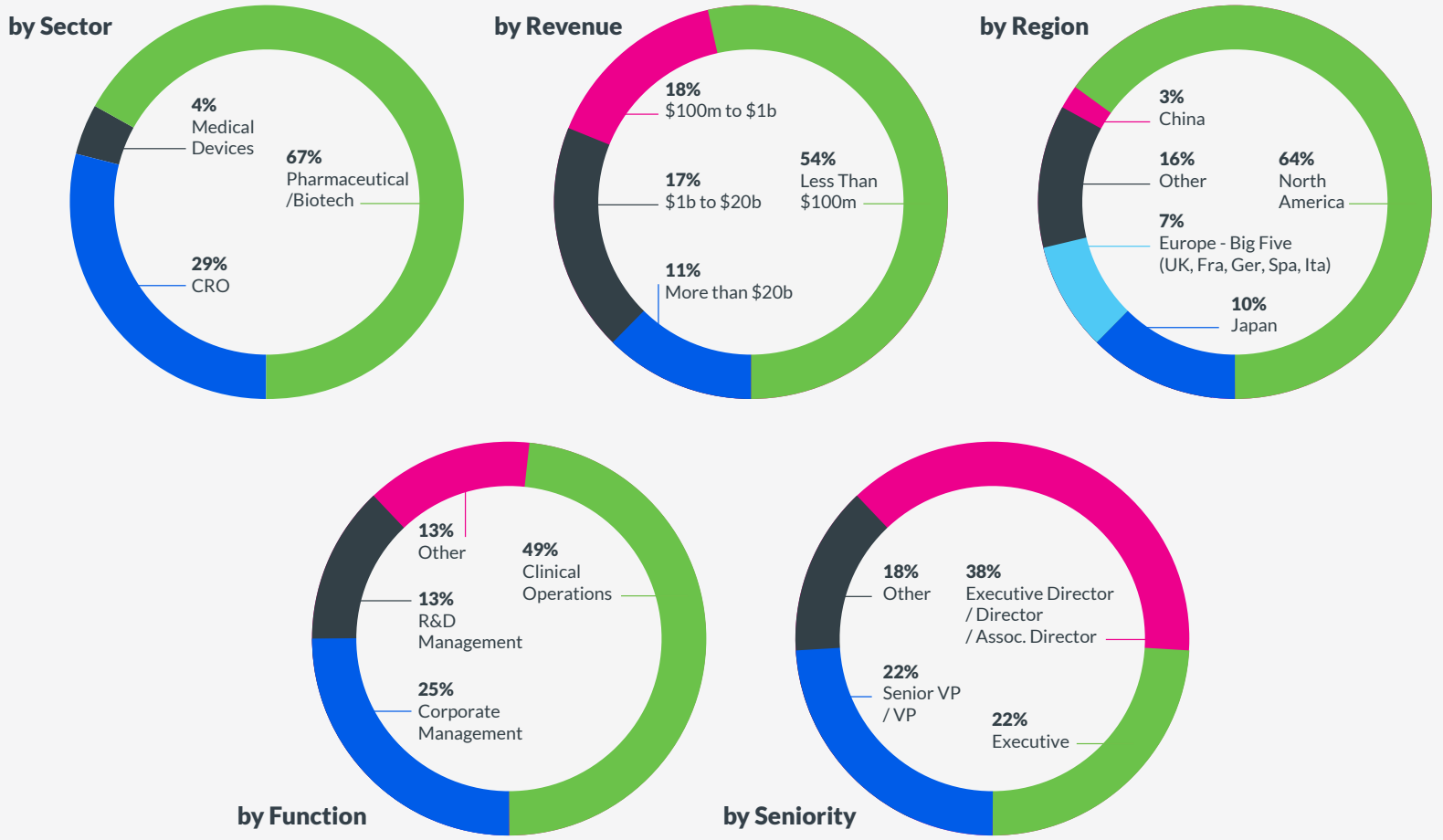
Science 37 executed this survey online in December 2021 and January 2022. Respondents were targeted almost exclusively by email, with some social media promotion, and responses were submitted via online questionnaires.

A total of 415 questionnaires was received, which generated a "qualified" respondent sample of 72.

We only included responses from senior executives who are either currently involved in sponsoring or managing clinical trials within CNS categories or planning to get into the CNS space.

All data published in this report are a percentage of the respondent sample for each question. Note, the sample for each question is the qualified respondent sample of 72.

Responses were analyzed by Life Science Strategy Group, and percentages were tested for significance at the 95% confidence level.



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APPENDIX

About the Authors and Science 37

David Coman
Chief Executive Officer,
Science 37

David is a pioneer of Agile Clinical Trials and came to Science 37 from ERT, where he was Chief Strategy Officer and ran its Data & Analytics business. Prior to that, he was CMO at Quintiles and Founder of the Digital Patient Unit where he pioneered some of the first decentralized clinical trials. Earlier in his career, David held a variety of marketing leadership roles in telecommunications, including at AOL, Excel Communications, and Aerial Communications.

Drew Bustos
Chief Strategy & Marketing Officer,
Science 37

An expert on innovation, design thinking, and technology, Drew currently leads Global Strategy, Marketing, Partnerships, and External Diversity for Science 37. He is actively engaged in helping drive the adoption of innovative technologies via patient-centric approaches within the life sciences industry. He has led corporate strategy, marketing, and product management throughout his career, successfully executing aggressive growth plans.

About **Science 37**

Science 37, Inc.'s (Nasdaq: SNCE) mission is to enable universal access to clinical research, making it easier for patients and providers to participate from anywhere. In 2014, we pioneered decentralized clinical trials— and we are now the leaders in the field. The Science 37 Operating System (OS) supports today's more agile clinical research design, enabling up to 15x faster enrollment, 28% better retention, and 3x more diverse patient population. To learn more about our solutions, and how we can help you implement Agile and Decentralized Trials, visit www.science37.com, or email science37@science37.com.

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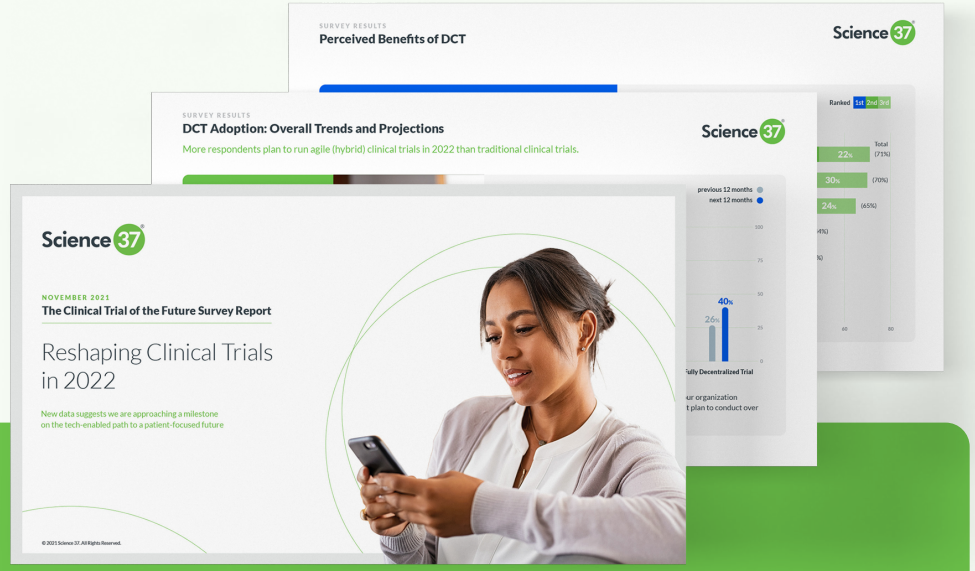

For additional reading on the Agile Clinical Trial visit **www.science37.com**

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