Decentralized and Hybrid Trials 2020

Global research study into adoption and technologies

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Presenters

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Agenda

Introduction and definitions
• Decentralized and hybrid trials
• Informa Connect and survey methodology
• Clinical Trials Europe 2020

Key survey takeaways
• Current adoption of DCTs
• The COVID-19 effect
• Digital technologies and perceived benefits
• Challenges and barriers to adoption

Decentralized trial trends
• Regional perspectives
• Therapy area views

Conclusions
Introduction and definitions
“Decentralized clinical trials are defined as those executed through telemedicine and mobile/local healthcare providers, using procedures that vary from the traditional clinical trial model”

Clinical Trials Transformation Initiative
Decentralized clinical trials

Digital trial capabilities as a continuum rather than an absolute

- Digital technologies and enablers are shifting the point of care into the patient’s home
- The simplest of these are increasingly pervading “traditional” clinical trials
- Decentralization of trials can be now seen as a continuum

Source: Trialtrove; In Vivo

**J&J’s 2020 virtual trials**

Heartline: Mobile app and Apple Watch for stroke reduction

CHIEF-HF: Invokana real-world study

*Explicitly stated in trial description/notes/protocol*
In May 2020, Informa Connect surveyed clinical trial professionals on the adoption of DCT and technologies involved

- Representation across wide range of organizations and stakeholders
- Sample contains half European and one third US respondents
- Broad therapeutic area coverage, with majority of respondents indicating >1 area of focus

Source: Informa Connect
Key survey takeaways
**Current DCT adoption**

Balancing on the cusp of mainstream clinical research

Decentralized and virtual trials still represent the *minority of clinical research*

- Over three quarters of respondents report very little current use
- A small number of specialists are incorporating virtual components into all studies

Biopharma industry is generally lagging behind clinical service providers

Weighted average suggests approx. **one quarter of ongoing trials feature DCT components**

- Likely overestimated, but nevertheless speaks to huge opportunity

*Source: Informa Connect*
Immediate effect of COVID-19

COVID-19 is largely spurring on efforts to increase DCT adoption

Clear consensus emerges that COVID-19 is necessitating acceleration of DCTs

- 76% suggest pandemic is leading to increased DCT use among their workload
- Both biopharma and service providers increasing emphasis on these technologies as direct result

Trialtrove notes more confirmed DCT starts in June 2020 than any other month on record

"Where previously sponsors were reticent, they are now asking for some hybrid trial solutions."

"COVID is catalysing of our transformation process towards DCTs. All players in the trials ecosystem must adapt to the new situation and speed up the implementation of new procedures that vary from the traditional clinical trial model."

"It has pushed most of the data collection to be done remotely, hence future trial designs will be more robust to allow most procedures to be done virtually."

"COVID-19 is placing additional demand for decentralized trials. Modifications for protocols to allow for more decentralized visits and the need to de-couple some site based procedures to allow more visits to be remote."

Source: Informa Connect; Trialtrove
Longer-term effect of COVID-19

Inflection point creating lasting change in trial practices

Over 9 out of 10 respondents expect COVID-19 to catalyze increased adoption of DCT in the long term

- Further gains from 76% increase on current workload
- No rebound once initial disruption of pandemic is over
- Sentiment equally expressed across organization type and geography

Within individual organizations, adoption will likely be variable, depending on immediate business needs

Nevertheless, strong expectation that momentum towards DCT will continue over next two years

- 85% likely or certain to see increases
- Just 4% indicating further adoption is unlikely

Source: Informa Connect
DCT technologies

Technologies that enable a point-of-care shift feature prominently

Mobile technologies are clear enablers for the shift of clinical trials into the home

- Such technologies are harnessed in 77% of current DCTs
- Mobile technologies: eConsent, EHRs, wearables
- Mobile HCPs for assessment and treatment
- Mobile phones: PROs, telemedicine, digital Tx

Overlapping definitions, but all allow for increased mobility and reduced burden

- Shared technology may also be across in-home devices, sensors and wearables

AI-ML becoming more routine in trials

- Facilitates diagnosis, patient stratification and even evidence generation

Source: Informa Connect; CTTI
Benefits of DCTs

Patient centricity is recognized as the biggest asset of a decentralized study

Main benefit for the adoption of DCT

- Patient convenience and engagement: 53%
- Shorter trial timelines: 13%
- More diverse/representative patient populations: 11%
- Reduced cost: 10%
- Real time data: 8%
- Other: 5%

Patient convenience and engagement is recognized as the leading benefit of DCTs
- Half of respondents identified this patient centricity as the main driver
- Shorter trial timelines driven by biopharma R&D productivity demands

DCT technologies can also be a double-edged sword...

Source: Informa Connect; NEJM Catalyst
Challenges and barriers to adoption
Myriad obstacles to navigate for DCTs to enter mainstream practice

**Little consensus** emerges among respondents for the **key challenges facing DCT**

- Challenges concerning regulators, data security and quality, technology and stakeholder engagement all highlighted by at least one third of respondents
- Ease of patient use is only minor challenge, reflecting patient centricity benefits as previously described

Wide range of responses reflects diversity of opinions and organizations surveyed

- Geographic and role-specific differences begin to emerge, particularly concerning data...

<table>
<thead>
<tr>
<th>Biggest challenges to overcome for running DCTs</th>
<th>Proportion of responses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regulatory acceptance</td>
<td>44%</td>
</tr>
<tr>
<td>Data protection and privacy</td>
<td>43%</td>
</tr>
<tr>
<td>Technology functionality</td>
<td>39%</td>
</tr>
<tr>
<td>Stakeholder buy in</td>
<td>38%</td>
</tr>
<tr>
<td>Quality of data</td>
<td>34%</td>
</tr>
<tr>
<td>Ease of use for patients</td>
<td>27%</td>
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<tr>
<td>Staff training</td>
<td>17%</td>
</tr>
<tr>
<td>Other</td>
<td>6%</td>
</tr>
</tbody>
</table>

Source: Informa Connect
Regulatory acceptance

Guidance from regulators will ease uncertainties and facilitate much greater adoption

“That DCTs can be considered equivalent to in-site trials as a rule; define the exceptions not the conditions for use.”

“Published list of mHealth approved medical devices for taking readings. There is a great deal of confusion on what equipment can be used and what not.”

“What would they expect to see during a study audit of data captured in mix models (in-clinic vs remote).”

“Which systems can we use for virtual patient visits: Skype, FaceTime, Zoom, Teams, ClickDocs?”

“Can remote assessments become gold standards in support of endpoints?”

“Clearly articulate what is allowable to be conducted outside of the traditional site and how those activities need to be managed under the investigator responsibilities.”

“Strongly encourage sponsors to include decentralized/virtual and hybrid trials in all phases, starting with pre-IND meetings all the way through.”

“Reassure sponsors what is acceptable. We work closely with regulators and generally find them very open to hybrid trial options, but sponsors always assume regulators will not approve.”

Source: Informa Connect
Decentralized trial trends
Regional DCT landscape

North American sponsors, service providers and regulators are leading the DCT revolution

Respondents in North America report higher use of DCTs among current studies

<table>
<thead>
<tr>
<th>Region</th>
<th>Sample size</th>
<th>Weighted mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average</td>
<td>152</td>
<td>23%</td>
</tr>
<tr>
<td>Europe</td>
<td>86</td>
<td>21%</td>
</tr>
<tr>
<td>North America</td>
<td>51</td>
<td>29%</td>
</tr>
<tr>
<td>RoW</td>
<td>15</td>
<td>23%</td>
</tr>
</tbody>
</table>

Fewer North Americans yet to embrace DCT technologies, while 16% employ virtualization across all trials

“Other health authority jurisdictions are not as amenable as the FDA. Some of our challenges, even with patient acceptance, have been very different in different parts of the world.”

Rob Kowalski, EVP and US Head of Development, Novartis

Source: Informa Connect
Regional DCT statistics

Clinical trial databases paint the same picture, albeit with underestimated totals

Specific keyword search terms identify 332 ongoing or planned DCTs globally
- Small fraction (0.5%) of total clinical trial landscape (~65k studies)
- Considerable underestimate of total, but sizable sample to analyze

North America has most DCTs (208) and strongest DCT emphasis, with **two-fold increased adoption** over global totals
- 1% of total trials identified as DCT

Notably **fewer DCTs in Europe and RoW**, also minor shares of total trials
- 75 and 86 DCTs, representing 0.5% and 0.3% of total trials respectively

Source: Trialtrove
Regional DCT outlook

Survey suggests North America will extend its lead in DCTs

Even with a higher starting base, DCT uptake is expected to increase faster in North America than elsewhere

- 90% of respondents likely or certain to see increased adoption
- Just 10% neutral or negative vs 15% in Europe

Separation between North America and Europe is independent of COVID-19

- Identical responses between regions for immediate and long-term effect of pandemic on DCTs

Lower strategic priority in RoW countries, where clinical landscape is less competitive

Source: Informa Connect
Varying attitudes towards data protection

European stakeholders have greater concerns around data privacy and quality

Data privacy laws and accessibility are hindering DCTs particularly in Europe

- European subset recognizes data protection as the leading challenge (52%)
- Data quality also emphasized by 37%

GDPR framework is more restrictive than other data practices, introducing nuances when applied to clinical trials, consent and data sharing

North American respondents cite data protection and quality concerns much less frequently

Regional perceptions around DCT data challenges

Source: Informa Connect

“The EU privacy laws are a significant barrier in Europe to conduct remote monitoring.”

“How do we perform remote consent, especially in Europe where eSignatures are not that well accepted.”
**Therapy area landscape**

Decentralized trial innovations can be general or indication-specific

Many **DCT innovations are unique to particular therapy areas**

- Novel endpoints, wearables/sensors
- Certain diseases are more amenable to be treated and monitored remotely

However, overlap between therapy area focus of respondents precludes specific analyses from the survey dataset

- Differences between endocrine (#1) and CNS (#8) likely not meaningful
- DCT technology can be independent of the indication being studied

**Current decentralized trial adoption by therapy area focus**

Total sample n=180

Oncology most represented TA

Considerable overlap; few organizations operating in single therapy area

**Areas of focus**

<table>
<thead>
<tr>
<th>Area</th>
<th>0%</th>
<th>20%</th>
<th>40%</th>
<th>60%</th>
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<tbody>
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<td>Oncology</td>
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<td>Cardiovascular</td>
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<td>Neurology</td>
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<td>Respiratory</td>
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<td>CNS</td>
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<td>Infectious diseases</td>
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<tr>
<td>Endocrine</td>
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<tr>
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<tr>
<td>Not applicable</td>
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</table>

Source: Informa Connect
Therapy area statistics

Trials in CNS diseases with decentralized technologies feature prominently

**CNS trials** carry considerably higher likelihood of incorporating DCT components

- Most numerous (135) and 3-fold greater likelihood (1.5%) to be decentralized than the average trial (0.5%)
- Cross-section of ongoing DCTs and not necessarily fully representative

**Oncology notable by its lowly position**

- Just 16 DCTs represents 0.1% of wider total
- Complex inclusion criteria, in-person treatments and assessments

Top five specific indications for DCTs are **insomnia, smoking cessation, Parkinson’s, coronavirus and type 1 diabetes**

Source: Trialtrove; In Vivo
Conclusions
Concluding thoughts

COVID-19 will accelerate decentralization of clinical research and digital best practices

Key survey takeaways

- Wide variation in the uptake of DCTs, current adoption suggests balancing on the cusp of mainstream trial practice
- COVID-19 is necessitating adoption of supportive digital technologies, catalyzing long-term adoption
- Recognition for advances in patient centricity brought by mobile technologies; regulatory and data concerns

Decentralized trial trends

- North America is ahead of the curve in the adoption of DCTs and will continue to pioneer the technology
- Use across sites in Europe is constrained by stricter data privacy laws
- Trial innovation can be disease-specific, leading to varying rates of adoption and benefit for decentralization

Additional materials:
Thank you for your attention

Questions?

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