831458 – Trials@Home

Centre of Excellence – Remote Decentralised Clinical Trials

WP1 – BEST

D1.3 Updated set of recommendations based on ongoing case studies running in parallel to the WP3 pilot

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Document History

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Plain language summary

Researchers use clinical trials to assess how safe and effective medical treatments are. However, taking part in a trial as a participant may be challenging and inconvenient, as it can mean multiple visits to hospitals or trial sites. Decentralised clinical trials (DCTs) offer a solution by letting people take part from their homes or other convenient locations. These trials often use technology tools like mobile apps, wearable devices, and sensors to make participation easier.

Since 2019, we in the Trials@Home project have been researching how best to conduct DCTs. To address this, the BEST work package of the Trials@Home project produced a report in 2020 called **D1.1 First set of recommendations for RDCTs (to be implemented in the pan-EU pilot RDCT).**

You can find that report here: https://trialsathome.com/deliverables/.

The current report is the planned update of the 2020 report as the Trials@Home project nears its end. It contains new findings and recommendations from the careful study of specific DCT examples, including interviews with people involved in running these trials. If you are interested in DCTs, we encourage you to read both reports.

In 2020, our first set of recommendations for RDCTs (D1.1) were to:

Answer an important research question

All clinical trials should aim to answer important questions that help patients and healthcare professionals make informed decisions in the future.

Keep the focus on participants

Researchers should always consider the safety, needs, and preferences of the people taking part in a trial.

Simplify the participant experience whilst maintaining quality and scientific rigour

Researchers should make it as simple as possible to take part in a trial without compromising the ability of the trial to answer the research question.

Involve stakeholders early

Everyone involved in making a trial happen, from healthcare professionals and patient groups to those responsible for approving trials and new medicines, should be involved in discussions about the trial plans early, so that their opinions and advice can be taken into account.

Share knowledge and experiences

Some DCT approaches are still relatively new, and we can learn how to use them more effectively if we share our experiences, challenges, and solutions.

Research implementation and improvement of DCTs

We should use scientific methods to learn more about when and how DCT approaches work best so that we can improve trials in the future.

In 2025, our updated recommendations (D1.3) are:

Design trials for ease of participation and conduct

It is not just participants who benefit from simpler trials; the staff who work on trials can do their jobs better when trials are designed with them in mind.

Test processes, devices, and software thoroughly before deployment

DCTs can be complicated and involve many technological and organisational aspects. All of the things needed for the trial must be tested to check that they work before the trial starts.

Facilitate dialogue between participants and researchers

In addition to providing participants with information in a way they can understand, researchers should also make it easy for participants to communicate with trial staff and access support during the trial, so that they feel confident in carrying out trial activities at home.

Build trusting relationships

DCT approaches can involve many different people, and they need to work well together. It is worthwhile to take the time to build trust among those involved in different aspects of the trial.

Plan for effective communication between trial personnel

Clear communication becomes even more important when there is less in-person contact. Careful planning of communication methods and timing can make things run more smoothly, both for routine trial activities and when unexpected events occur.

Agree roles and responsibilities

Everyone involved in a DCT has a role, from participants remembering to complete questionnaires to the person responsible for ensuring that blood samples arrive in the laboratory on time. Knowing who is responsible for what and when ensures that tasks are not overlooked and that participants are kept safe.

Consider site readiness for DCT approaches

DCT approaches are still new to many healthcare professionals. Anyone planning a DCT needs to ensure that all the staff working on it will be appropriately trained and supported for any new ways of working.

Plan for the unexpected

No matter how well-designed a DCT is, external events like changes to laws and regulations, problems with delivering trial materials, or even global pandemics should be prepared for.

Allocate sufficient resources

Some people have suggested that DCTs should be less expensive than conventional clinical trials because they require fewer staff and fewer clinic sites. However, our research shows that DCTs still need a lot of resources to ensure that everything works, that medications and trial materials are where they need to be at the right time, and that everyone involved has the training and support they need.

Conclusions

The research findings and recommendations we have presented in D1.1 and here in D1.3 will be combined with those from the other work packages of the Trials@Home project to produce a final overall set of recommendations for DCT approaches arising from the Trials@Home project.

Introduction

This report provides an update on the D1.1 Recommendations for Remote Decentralised Trials (RDCTs) and the accompanying D1.2 Criteria for selection of appropriate trials, both published in 2020.[1,2] It reflects the findings of further research conducted by Work Package 1 (BEST) of the Trials@Home project, which explored the opportunities, benefits, challenges, and solutions associated with decentralised clinical trial (DCT) approaches. This report does not replace the earlier publications (D1.1 and D1.2) and should be read alongside them.

The findings included in all three reports will be combined with outputs from the other work packages in the project to produce a final set of recommendations from Trials@Home at the end of the project.

DCT approaches enhance the accessibility of clinical trials for participants by minimising or eliminating the need for physical visits to trial centres. These approaches can be integrated with conventional site-based methods in hybrid trials, where some activities occur at a clinical site and others at home. Alternatively, DCT approaches can enable fully decentralised participation, with all trial activities being completed without the need for participants to visit a site. In this report, “DCT” refers to any trial using DCT approaches, whether hybrid or fully decentralised.

The recommendations presented in this report are relevant to anyone involved in the design and conduct of clinical trials using DCT approaches, including sponsors, researchers, site staff, and vendors. Additionally, this report may serve as a valuable resource for patient engagement or patient and public involvement (PPI) groups contributing to clinical trials.

Readers should note that the terminology used in clinical trials has evolved throughout the Trials@Home project. Earlier documents and publications refer to "RDCTs," while more recent outputs, including this deliverable, use the term "DCTs" to align with current usage. These terms are synonymous.

This document incorporates learnings from a systematic review and a qualitative research study that interviewed stakeholders involved in completed and ongoing clinical trials using DCT approaches.[3–5]

D1.1 and D1.2 established a framework for conducting effective DCTs, and it was recommended that this be followed in the Trials@Home RADIAL proof-of-concept clinical trial. The six recommendations made in D1.1 were:

Answer an important research question

DCTs, like all clinical research, should address a clear and important research question that is of value to public health and potential research participants. The research question should be central to the trial design and choice of methods used.

Keep the focus on participants

Meaningful engagement with patients and the public is essential to ensure that clinical trials are relevant, acceptable, and beneficial to the people they are intended to serve. By actively involving potential trial participants in all stages of the clinical trial process, researchers can improve the design, conduct, and impact of their work. Such involvement can be even more critical to the success of decentralised clinical trials due to a relative lack of opportunities for in-person contact between researchers and participants.

Simplify the participant experience whilst maintaining quality and scientific rigour

Decentralised clinical trial teams should direct their expertise towards maintaining scientific quality while simplifying the interactions between participants and the trial. This may mean selecting user-friendly technologies or minimising requirements for participant data entry.

Involve stakeholders early

It is particularly important to engage with stakeholders early when planning a trial using non-conventional methods. Researchers should allow sufficient time to discuss their plans with the relevant authorities, such as research ethics committees and regulatory bodies.

Share knowledge and experiences

Clinical trial practitioners can promote learning from the DCT experiences and expertise of others by sharing methods and learning points. Investigators and sponsors are encouraged to publish protocols, methods evaluations and results.

Research implementation and improvement of decentralised clinical trial methods

It is essential that the clinical trials community tests and evaluates DCT approaches.

Background

Since 2020, there has been a notable acceleration in the adoption of DCT approaches. This shift has been driven by continued technological advances and societal pressures, not least of which was the need to minimise physical contact during the COVID-19 pandemic. As a result, trials have increasingly incorporated decentralised approaches, such as home trial support, telemedicine-enabled visits, direct-to-participant delivery of trial medications, electronic consent processes, and app- or web-based e-diaries to support at-home data collection.

The increasing availability and capability of digital technologies have provided opportunities for clinical trials to capture data in new ways. Wearable devices and sensors have become smaller and more sophisticated, offering the potential to collect rich longitudinal data from trial participants. Mobile apps can be deployed as data collection tools, trial communication devices, or interventions. However, this additional data can pose challenges to existing data governance and infrastructure, with efficiencies of scale balanced against possible risks to data quality.

There is a growing emphasis on designing clinical trials that prioritise the needs and preferences of participants. Some ways to enhance trial participation include delivering medications and materials directly to participants, collecting data remotely at home, and conducting visits via telemedicine services or using home nursing services. These DCT approaches can offer greater convenience, improved access, and a more active participation experience. However, it is crucial to ensure that the benefits of moving activities away from conventional trial sites are not outweighed by unintentionally increasing the burden of participation.

Innovations in technology can enhance access to trials by eliminating the need for in-person visits. Conversely, this change may lead to the exclusion of individuals and communities with lower digital literacy. Therefore, trial teams should assess the potential risks associated with technological developments to ensure equitable access for all participants.

The COVID-19 pandemic led to a rapid and significant shift in regulatory approaches worldwide, with some agencies producing new guidance or adapting existing guidelines to allow DCT approaches to be used to enable the continuation of clinical trial activity during the pandemic. Guidance documents released since by the US Food and Drug Administration (FDA), European Medicines Agency (EMA), and the current draft of ICH E6(R3) Annex 2 reflect an industry-wide shift toward DCTs. [6–8]

The goal of clinical trials is ultimately to improve health and wellbeing. Any research question must be both scientifically sound and of value to the population. The core principles of the D1.1 recommendations remain valid in 2025. However, research conducted since their publication in 2020 has provided further insights and highlighted additional areas of DCT activity that require careful attention and adaptation to ensure successful implementation.

Methods

The findings reported in D1.1 were derived from two scientific research studies: a systematic review of methods used to conduct DCTs and initial findings from a qualitative analysis of interviews from case studies that used DCT approaches in various therapeutic areas. Academic articles based on these studies have since been published, containing detailed information on the methods used (available open access).[3–5]

The updated findings and recommendations outlined below are primarily based on the case study research reported above, supplemented with additional new data collection and analysis.

Case study selection

A total of 31 case studies were identified as follows:

- A case study selection tool was developed to select a representative sample of 20 DCT case studies, identified through initial literature searches and suggestions from Trials@Home consortium members. Eleven of these twenty case studies were completed or terminated, and nine were planned or ongoing at the time.
- Eleven additional new case studies, addressing therapeutic areas, technologies, or patient groups that were missing or underrepresented in the original selection, were collected between 2021 and 2023.

Data collection

Data were collected through semi-structured interviews in all 31 case studies. Each interview was audio recorded and transcribed for analysis. The interviews were conducted in three phases:

Stage 1 – Initial case studies (n=20), first interviews

In early 2020, 48 individuals with diverse roles across the initial 20 case studies participated in 41 interviews. These individuals represented pharmaceutical companies, clinical research organisations, technology and logistics vendors, academic researchers, and patient representatives. The interviews focused on the interviewees' experiences with DCT approaches, examining the challenges encountered at various stages of the trials and the strategies employed to overcome these obstacles. Additionally, interviewees highlighted the successful aspects of the trials, which benefited both the trial team and the participants.

Detailed findings of Stage 1 are reported in two academic publications.[4,5]

Stage 2 – Initial case studies (ongoing or planned at the time of the first interview; n=9), follow-up interviews

Between May 2021 and July 2022, twelve follow-up interviews were conducted with participants from the nine initial case studies that were planned or ongoing at the time of the first interview. These interviews focused on the progress of the trials and any changes that had occurred since the initial interviews.

Stage 3 – New case studies (n=11)

Eighteen interviews were completed with interviewees from 11 new case studies between October 2021 and December 2023. In addition to considering challenges or barriers to implementing DCT approaches, these interviewees were asked to reflect on their use of technology to facilitate DCTs and evaluate the interplay of stakeholder relationships in DCT conduct.

Analysis and Interpretation

Transcripts of case study interviews were coded and analysed thematically and supplemented with published information on trial conduct, such as protocols and results papers, where available.

A summary was created for each of the original 20 case studies, and the WP1 BEST team discussed how these cases could be improved. Each case study also underwent a SWOT analysis, assessing its strengths, weaknesses, opportunities, and threats. A list of potential solutions or mitigation strategies was developed addressing each identified weakness or threat.

Findings and Recommendations from Case Study Research

Much of our case study research since 2020 supports the original recommendations published in D1.1. The following new findings should be considered supplementary to D1.1 and not a replacement for the original recommendations.

Design trials for ease of participation and conduct

While D1.1 highlighted the need to simplify trial experiences for participants, our subsequent research has found that streamlining the experiences of trial staff can also improve trial conduct and the likelihood of trial success. Design techniques, such as journey mapping, can help researchers understand the experience of trial participation and minimise unnecessary burden. Experiences or expectations of difficulty by trial participants may deter them from adhering to required trial activities with implications for data quality and statistical power. Similar activities should be undertaken to plan staff activities so that individual trial staff do not experience frustrations or excessive workloads that may be a barrier to maintaining the scientific integrity of the trial and the clinical safety of patients. Attention should also be paid to supporting staff who work remotely to avoid experiences of isolation.

Test processes, devices and software thoroughly before deployment

In D1.1, we advised that trials should use tested and validated technologies. Our case study research has further shown that testing and validation should be extended to all planned trial conduct aspects, including devices, software, integrations, workflows and logistics. All intended users should be considered, or their representatives involved, in user-testing and dry run activities.

Facilitate dialogue between participants and researchers

In D1.1, we emphasised the importance of developing communication materials in appropriate languages and formats to suit participants' needs and preferences. Participants' need for clear and appropriate communication was identified in our case studies. Our interviewees reported that some participants required two-way communication or dialogue with trial staff to feel confident in carrying out trial activities at home. While this can be facilitated through telephone or email contact, alternative technology-supported modes of communication, such as 24-hour telephone helplines, video calls, technology helpdesks, or secure messaging, could also be used for this purpose.

Build trusting relationships

Our 2020 recommendations identified that early engagement with external stakeholders, such as healthcare professionals, patient groups, and regulators supported the approval and introduction of new DCT approaches. Another aspect of early engagement that we have since identified is its role in building trusting relationships between the people involved in delivering a trial and with the participants. DCTs can be complex, often with limited in-person contact and increased reliance on technology compared to more conventional trials. All parties, including staff, participants, and vendors need to understand the purpose of a trial and their respective roles within it. Early and effective engagement between sponsors, sites and vendors of technologies and services was seen as necessary to build trust between parties who need to work effectively together. Our case study interviewees believed that stakeholder engagement was essential to establishing trust with communities and healthcare professionals, thereby supporting successful recruitment. Establishing trust between the participants and the organisation running the trial was important in guiding decisions to participate and to remain in the trial for the duration.

Plan for effective communication between trial personnel

DCT approaches can challenge communication by reducing in-person contact, not only between participants and trial staff, but also between trial staff and other service providers, such as home nursing services or laboratory services. Case study interviewees reflected on the communication difficulties they experienced during their trials and suggested that more careful planning of communication strategies would have been beneficial. Communication planning should be included from the start of the trial design process to develop a transparent communications plan with clear pathways and expected response times. Clear and frequent communication within a trial can build a sense of shared purpose and connection between researchers, participants, and service providers.

Agree roles and responsibilities

Closely related to communication planning, case study experiences highlighted instances of confusion between parties about which organisations or individuals were responsible for ensuring that certain trial activities occurred at the right time. Interviewees agreed that the roles and responsibilities of everyone involved in delivering the trial should be clearly specified before it begins.

Consider site readiness for DCT approaches

Many investigators and sites are unfamiliar with DCT approaches, either in hybrid or fully decentralised trials. Willingness and readiness to adopt DCT approaches should be included in site selection and feasibility assessments. Case study interviewees described the considerable work required to support sites and healthcare professionals new to DCT approaches. When implementing DCT approaches in new trial sites, plans should be made to fully train and support site staff, for example, by providing named contacts or helpdesk support.

Plan for the unexpected

Like any clinical trial, those using DCT approaches are vulnerable to uncontrollable external factors, such as legal and regulatory changes, logistical and technical issues, and unexpected events such as pandemics and natural disasters. Case studies have demonstrated the critical importance of risk assessment and contingency planning, as well as the necessity for trials to adapt with agility to changing circumstances. Many of our case studies were able to progress through the COVID-19 pandemic due to minimal in-person visits and the use of technology; however, this same reliance on technology can leave DCTs vulnerable if technical issues arise. Similarly, the logistics that support at-home study participation, such as the delivery of medicines and materials and the coordination of home nursing, are vulnerabilities that should be addressed in risk assessment and mitigation plans

Allocate sufficient resources

While some have advocated for decentralised clinical trials (DCTs) as being more efficient than traditional trials, it is important to recognise that substantial resources are still necessary to plan and conduct a successful DCT effectively. Beyond the costs of providing and shipping medicines, materials, and equipment, as well as making provisions for the technological and data requirements of trials, additional resources may be required to facilitate preparatory testing and to support staff in transitioning to new working methods. If DCT approaches are combined with conventional methods within the same trial – for example, to provide flexibility for participants or sites – this will likely increase the required resources further.

Discussion

The findings of the research conducted by WP1 BEST since 2020 have reinforced and expanded on the initial recommendations in D1.1, emphasizing the need to focus on communication, trust, support, and risk mitigation. These findings will be combined with those of other Trials@Home work packages to produce a final set of overall recommendations from the Trials@Home project.

There have been several changes to the regulatory landscape in recent years, with regulators

clarifying requirements for DCTs. The COVID-19 pandemic has pressure-tested many DCT approaches and likely accelerated their long-term, widespread adoption in clinical trial practice. However, adopting a DCT approach still requires careful consideration, as it is not universally suitable and depends heavily on the flexibility and adaptability of teams, sites and vendors. The successful implementation of a DCT may necessitate specialised skills, particularly in using technology, which may not be required in conventional trial designs. Therefore, researchers should assess the suitability of the DCT approach against their existing resources and expertise.
DCTs remain a relatively new concept for many trial teams and sites, and the regulatory landscape is still evolving. To address this, the clinical research community should continue to share knowledge and experiences to help shape best practices and inform regulatory guidance and decision-making. This collaborative approach will contribute to the growing body of evidence supporting the potential benefits of DCTs.

Conclusion

Decentralised clinical trial (DCT) approaches affect how trial staff and participants experience trials. By prioritising effective communication, user-friendly technology, and streamlined logistics, DCTs should enhance participant-centricity and create a more positive trial experience. Greater accessibility and convenience may encourage wider participation in clinical trials, ultimately facilitating scientific advancements and providing more participants with opportunities to access innovative treatments.

As we reflect on the lessons learned in WP1 of the Trials@Home project, it is essential that we acknowledge the dynamic nature of DCTs. Looking forward to the next five years and beyond, we anticipate further technological advancements that will enable the collection of novel types of data and interaction with trial participants. Ongoing assessment and evaluation of DCT approaches will therefore be critical to ensure that they continue to meet the evolving needs of participants and researchers alike, paving the way for a more effective and inclusive clinical research landscape.

Data Availability Statement

The case study interview dataset that supports this report is held by the University of Dundee and access is limited to the study team in accordance with the ethical approval obtained for this research.

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