831458 – Trials@Home
Center of Excellence – Remote Decentralised Clinical Trials
WP5 – CODE

D5.4 Report on changing stakeholders' roles and responsibilities, and proposals from stakeholders to overcome any challenges

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Document History

Version	Date	Description
V1.0	31 Jan 2023	First draft (PN)
V1.1	3 Feb 2023	Second draft with consolidated comments from team
V3	9 Feb 2023	Third draft for ExBo approval
V4	15 Jul 2023	Fourth draft for PMO and CODE review (AB)

Summary of the task

The present report details the Trials@Home deliverable D5.4, which included the administration of surveys regarding decentralised clinical trials (DCTs) to key stakeholders. The aim of the surveys was to identify the benefits and downsides of DCTs these groups perceive, as well as their current knowledge and familiarity with DCTs. This work feeds into the larger goal of determining where there is a need for education and training tools among these groups if there were to be widespread adoption of DCTs. Work Package CODE, the team responsible for communication and dissemination within the Trials@Home consortium, mapped and identified key stakeholder groups and developed the surveys as part of D5.3. The report for D5.3 describes how these stakeholder groups were identified as well as how the three surveys were developed in detail. The aim of D5.4 is to administer the surveys and report on the results, measuring and quantifying the paradigm change inherent in a move from traditional trial methodology towards DCTs.

The surveys were distributed through the Trials@Home network, and by approaching external organizations and networks when necessary. A key finding from the PI survey was that most respondents had never heard of DCTs, however they characterized them as increasingly important and relevant in the clinical trial world. They expected the change to more DCT approaches to take place in the short or mid-term timeframe. The patient survey revealed strong patient interest in a variety of topics related to DCTs, however very few patients in this sample had heard of DCTs, and even fewer had participated in one. Despite a nearly 2-year effort to broadcast the GP survey to providers across Europe, the sample size was not powered to draw conclusions. The insights from these surveys provide input for future development of training and education activities (D5.5, Education and Training Sessions).

Methods

Stakeholder Identification and Survey Development

As part of D5.3, stakeholders who might require training and education with the adoption of a decentralised trial approach were defined. Briefly, WP CODE selected patients, clinical site staff and General Practitioners (GPs) as the three stakeholder groups who could potentially require training and education tools. Three different surveys were then designed using the online tool SurveyMonkey. The surveys examine understanding and knowledge of traditional trials and DCTs, probing experiences, expertise, and any potential training and educational needs for DCTs, but were tailored based on the stakeholder group and how familiar they were expected to be with DCTs. For more information on this process and the surveys themselves, see the report for D5.3. The full question sets for all surveys are also available in the Annexes to that report.

Survey Administration

➤ PI Survey. Participating Trials@Home pharmaceutical companies and Contract Research Organizations agreed to distribute the survey through their networks. As noted in the report for D5.3, the survey probed study site staff and was not limited to only PIs. However, it has been referred to as the “PI Survey” for brevity. The survey was launched October 2020 and closed February 2021.

➤ Patient Survey. Patient organisations (disease-specific or otherwise) were approached and asked to distribute the direct link through their networks. As the survey was aimed at individual patients and/or patient advocates, patient organisations were not approached as an entity. Several Trials@Home consortium members also made use of existing contacts and available channels to disseminate the survey further. It was

also broadcast on Twitter and LinkedIn, with continuous attempts to increase awareness of the survey. The survey was launched in December 2020 and closed February 2021. Although the survey received over 400 responses, a much smaller number of patients indicated that they had participated in a DCT before (n = 13), making a proper, representative analysis difficult. In an attempt to gain a more in-depth picture of these patients' experiences and knowledge, those who consented to being contacted were invited to participate in a focus group. Six patients replied, however further follow up resulted in no further interaction so the focus groups were not performed.

➤ GP Survey. The Training & Education working groups approached various GP associations across Europe, as well as GPs in the Trials@Home consortium. The survey was launched on SurveyMonkey June 2021. Due to low response rates, members of the Trials@Home consortium were also asked to share with GPs in their network and to contact their personal GPs to complete the survey. There were extensive efforts throughout 2021 and 2022 to promote the survey before it closed February 2023.

Analysis

Planned analysis included summaries of the distribution of responses and measures of central tendency for rating questions, and a qualitative analysis for free text answers. A Chi square test was also performed to find a correlation between PI interest and knowledge. All analyses were performed by experts in the Training & Education group and, where possible, reviewed by stakeholders.

Results

Percentages presented in this report are rounded to the nearest whole number and represent a proportion of the entire sample for that survey, unless otherwise specified. The full datasets for all three surveys from SurveyMonkey are available in Annexes 1, 2, and 3, while only highlights and points of interest are presented in the main text of this report. Due to the low response rate for GPs (n = 28), it was not possible to perform a valid statistical analysis on the responses. Further, only about half of the GPs who were surveyed had ever heard of DCTs. As such, these results were aggregated with the PI survey, and will be reported on together in this report and referred to as the healthcare provider survey (HCP survey). The dataset for the GP survey can be viewed in Annex 3.

HCP Survey

➤ Subject Demographics. The PI Survey received 436 responses from healthcare professionals across many aspects of clinical trial conduct. Survey respondents were asked to select their role, with the ability to select more than one. The most selected role was that of investigator, which 70% of participants selected, followed by study coordinators (25%), study nurses (14%), and 'other' role (3%). Note that 28 of these responses were aggregated into these results from the GP survey, representing 6% of the results. About half of respondents worked for a university hospital (49%), while 24% were based out of general hospitals. The remaining professionals worked for private practice settings (12%), site management organizations (3%), or 'other' (12%). Respondents were able to select more than one answer for this question.

The next question, which asked about therapeutic area, received 644 answers, indicating that many participants represented more than one therapeutic area. Oncology was the most frequently selected disease group with 137 selections (31.4% of participants), followed by 21% selecting autoimmune diseases, 20% cardiovascular, 17% diabetes, and 16% respiratory. The areas of rare diseases, neuroscience, infectious diseases, and paediatrics were selected by less than 10% of respondents each. About 16% of respondents also selected 'other' therapeutic area. Most responders were either in the UK, Romania, Belgium, Poland, or Spain, while nine other countries were represented in less than 7% of responses. A full list of the countries can be viewed in Annex 1.

➤ Familiarity with DCTs. Over a third of respondents (35%) stated they had heard of DCTs before. Those 152 healthcare professionals indicated that they had heard about DCTs primarily through conversations with their peers (44%) or at conferences (38%). The full list of ways providers had heard of DCTs is available in the survey results in Annex 1. The survey also asked for a rating between 1 and 10 for how robust their level of knowledge is, with 1 indicating limited knowledge and 10 showing expert knowledge, which received an average score of 5.03. See Figure 1 for the distribution of scores. 41 participants in the sample reported that they had already been involved in a DCT at some point. This is 27% of those who had heard of DCTs, but only 9.4% of the full sample. About three-quarters of respondents had not heard of IMI, however 15% had previously heard of the Trials@Home project.

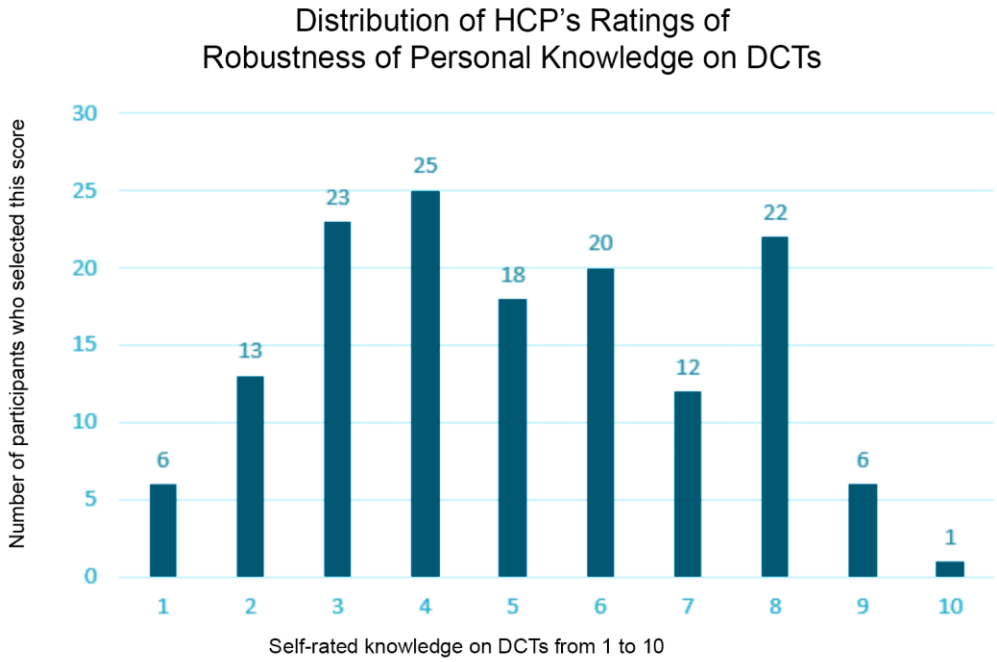

Figure 1 – The distribution of how participants rated the robustness of their current knowledge on DCTs from 1 (limited knowledge) to 10 (expert level knowledge).

➤ Interest in DCTs. On a scale from 1 to 10, with 1 meaning no interest and 10 representing very high interest, the average score was 7.02, with the majority of participants rating their interest at 5 or above. Figure 2 illustrates the distribution of scores. Over half of respondents stated that DCTs would positively impact their own willingness to conduct a trial and only 10% stated that a DCT would have a negative or rather negative impact on their interest to conduct a trial.

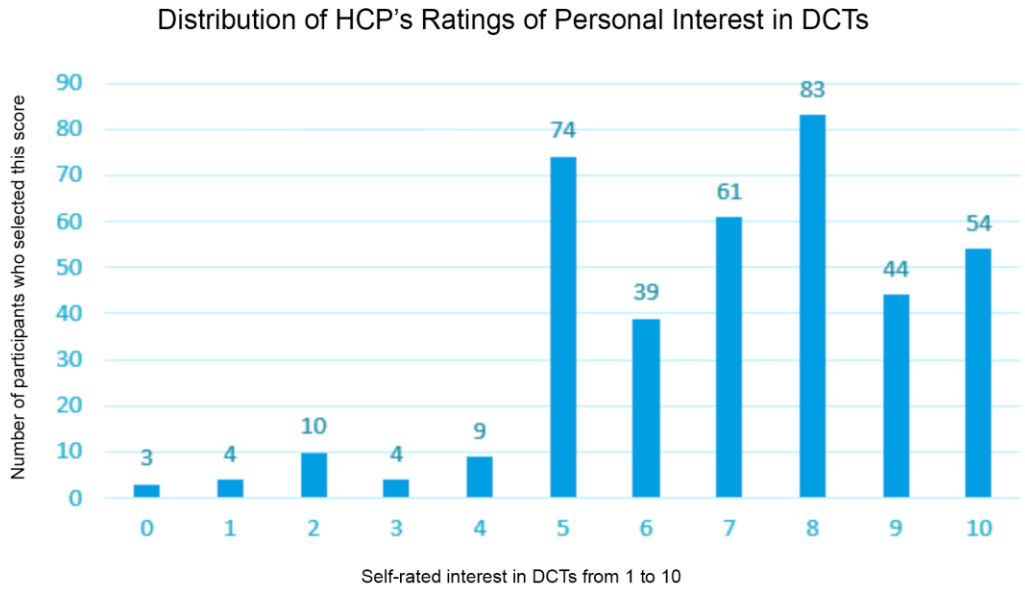

Figure 2 – The distribution of how participants rated their own personal interest in DCTs from 1 (not interested) to 10 (very interested).

➤ Correlation Between Prior Knowledge and Interest. To assess the correlation between PIs that are informed and PIs that are interested, participants were grouped into three ordinal groups: 'Not interested,' 'A bit interested,' and 'Interested,' as well as 'Not informed,' 'A bit informed,' and 'Informed.' We then performed a Chi-square (p = 0.02) and Kendall's rank correlation test (p = 0.02 and τ = 0.19) which indicated a mild but significant correlation between grades of information and interest of the respondents.

➤ Experience with DCT Elements. The next questions focused on participants' specific hands-on experience with elements of DCTs. Figure 3 summarises these results. Most participants (73%) indicated that they have worked with patient online diaries, while 54% had experience with telemedicine and 53% had experience with IMP self-administration at the patient's home.

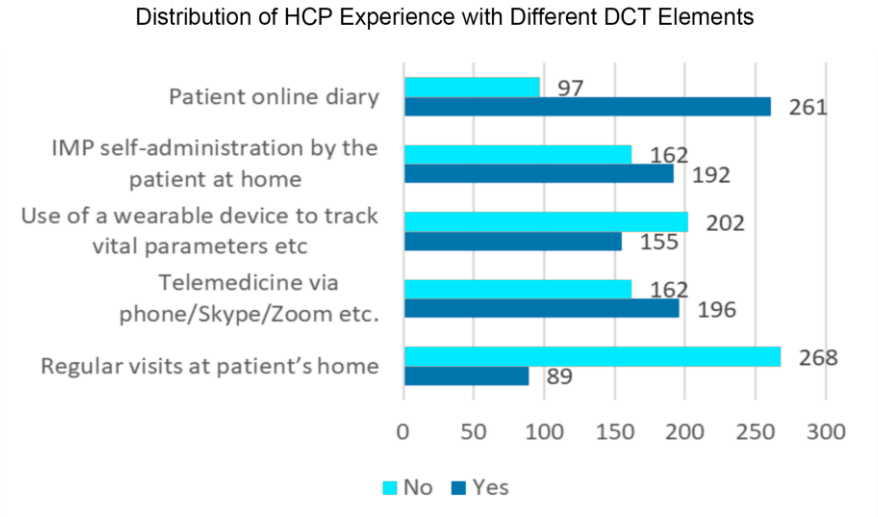

Figure 3 – The distribution of experience with different DCT elements.

➤ Experience with DCTs as a Whole. Participants were then asked about their experience with DCTs as a whole. They were given a scale from 0 (no experience) to 10 (= expert level). 356 responders gave details on their experience. The average experience score lies at 3.28, which indicates that most responders attest

themselves a rather limited experience. Indeed, less than 2% of participants reported having expert experience in DCTs, while over 20% said they had no experience. The second most common rating was 5, which 18% of respondents chose. See Figure 4 for the full distribution of scores.

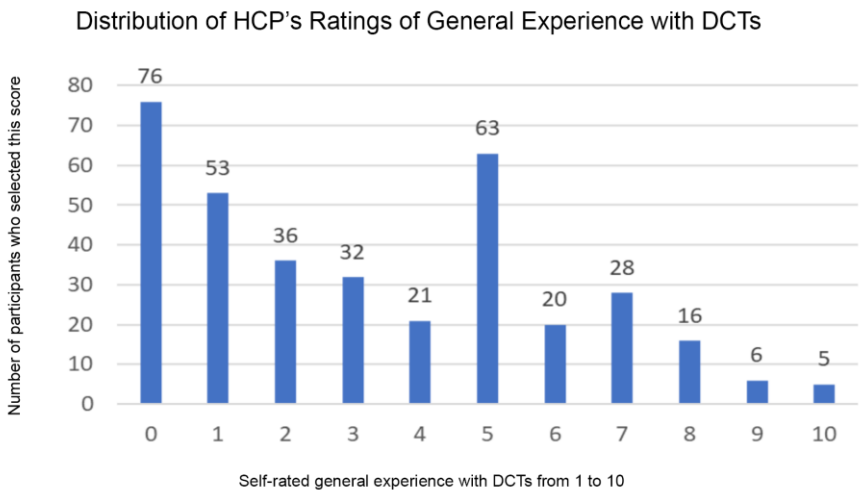

Figure 4 – The distribution of general DCT experience rated 0 (none) to 10 (expert).

➤ Perceived Impact of DCTs. Survey participants were also asked to indicate what impact they would perceive DCTs to have on several aspects of the clinical trial landscape on a scale of 1 to 5, 1 being 'Negative' and 5 being 'Positive,' with 3 representing 'Neutral' impact. The results of this series of questions are summarized in Figure 5, which shows the distribution of these ratings across each aspect (patients' willingness to join a trial, the doctor-patient relationship, the participant's own willingness to conduct such a trial, the profitability of the participant's own business model, their operations and business procedures, and their team).

➤ Positive Impacts. Notably, 64% of participants believed that DCTs would result in a positive impact on patient willingness to join a trial, while only 10% believed DCTs would have a negative impact. The weighted average score for this category was the highest, at 3.81. This was also the only question where 'Neutral' was not the most common response. Like their ratings on patient willingness to join a DCT, participants forecasted an overall positive impact on their own willingness to conduct a DCT, with a weighted average score at 3.71. The ratings for this aspect were indeed distributed more towards 'positive,' with exactly 50% of participants giving either a positive or rather positive rating and less than 10% rating more negative than neutral. Lastly, participants were asked for their opinion on the expected impact on their own site's team. Participants revealed a tendency to see a positive impact (average score of 3.44), with a positive-skewed distribution to scores as well. None of the distributions of ratings showed a skew towards negative scores.

➤ Neutral Impacts. Many aspects were rated as having neutral, or no impact. The impact on doctor-patient relationship received a weighted average rating of 3.11 out of 5, which represents a neutral score. Indeed, the answers fit a Gaussian distribution, showing no impact was the most common answer, with a similar number of people perceiving positive and negative impacts. Other notable 'neutral' results include perceived impacts on site business model and profitability, with a weighted average of 3.33. Indeed, 3 was the most common score, with 41% of those surveyed giving this rating. The same was observed for perceived impact on site operations and business procedures, with a weighted average score of 3.42 and over a third of participants giving a neutral score.

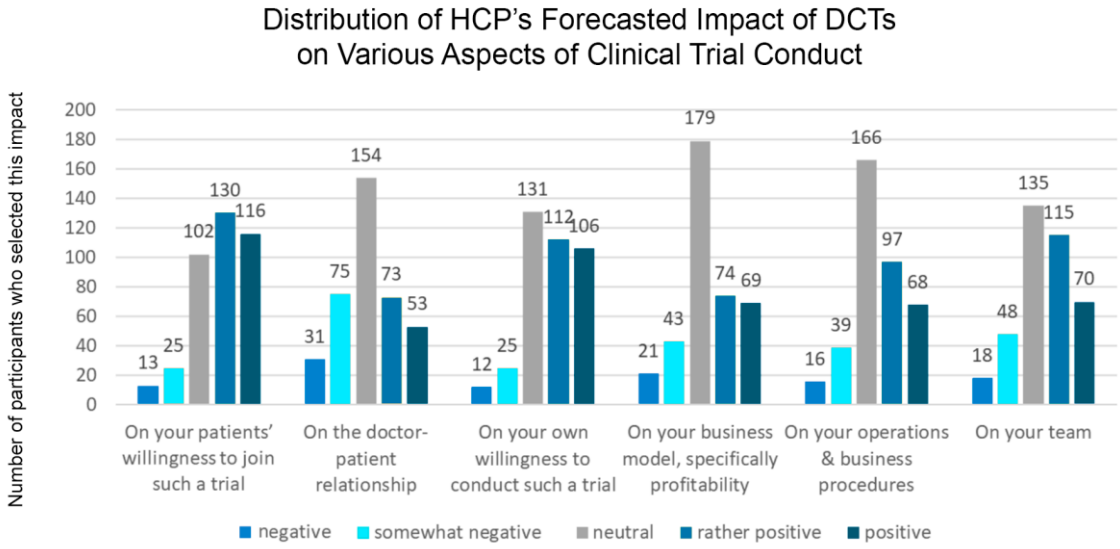

Figure 5 – The distribution of participants' assessments of the potential impact DCTs could have on various aspects of the clinical trial landscape.

➤ Perceived Areas Needing Change. The survey also asked respondents how much change they expected would need to take place to facilitate a change toward DCTs. Participants were probed on five different areas: the participant's own education level, the education of their team, the technical equipment they have available at their site, their internal processes and, finally, an understanding of the value of DCTs by patients. These areas were presented, then participants were prompted to give a rating of 1-5. A rating of 1 meant 'No change needed,' then a 2 meant 'Some change needed,' a score of 3 was 'Neutral,' and 4 and 5 meant either 'Much change needed,' or 'Very strong changes needed,' respectively. For all five areas, the weighted average was higher than 3.0, suggesting a skew towards greater change needed. The highest average score was given for understanding by patients, at 3.99, while the lowest was given for participant's own education (3.55). Team education was given an average rating of 3.75, technical equipment was 3.9, and processes was 3.9.

➤ Training and Education Needs. Participants were asked to select at least one topic from a given list where they thought education would be most needed. Over three-quarters of participants who answered this question indicated that they thought more education was needed in the technical area (77%). Most participants also thought that legal and regulatory education would be useful (62%), with just over half selecting communication (52%). The survey also asked which source of education they would prefer. The most preferred option seemed to be interactive online training/tutorials, with 58% of responses, however a significant proportion of responses went to other methods as well. 44% selected non-interactive online webinars, 41% preferred face-to-face, 33% selected written training/reference material/FAQs, and 26% indicated online slide deck training. The complete results for both questions are available in Annex 1.

➤ Opportunities. 364 people provided an answer as to whether they see opportunities with regard to DCTs, with a near 50-50 split: 179 do see opportunities while 185 don't see any (49% vs 51%). Participants were also asked to briefly describe the opportunities they see in a comment box. All provided answers were then analysed and categorized. The decrease in patient burden was the most common opportunity, mentioned in 31% of responses, followed by higher efficiency, mentioned in 22%, and better recruitment, which was mentioned in 21% of responses. As another benefit, more research opportunities due to higher efficiencies were mentioned in 10% of responses.

➤ Concerns. 118 participants reported having concerns over DCTs, while 246 did not and 72 people skipped this question. Based on the analyses of the free text provided in the next question, the common themes identified included reducing patient trust in the procedure, as well as traditional thinking, which were

mentioned as the main concern in 28% of responses each. Accessibility (20%), organizational aspects (16%), patient safety (13%) and availability of medical staff (10%) were also common responses. Only six participants (5%) saw the legal or regulatory framework as a concern, followed by four responders (3%) who wrote that a lack of knowledge or experience was their main concern.

➤ Expected Change to the Trial Ecosystem. Participants were asked to rate how much change to the trial ecosystem a shift towards DCTs would bring. On a scale from 0 ('No change at all') to 10 ('Revolution-like changes'), the average score was 6.43. Just over half (53%) expect these changes to become prominent in a mid-term time frame (3-5 years), while 32% of respondents expect changes more in the short-term. Only 13% of responders see changes in a long-term frame (6 years or more). Figure 6 shows the distribution of ratings of how much change DCTs will bring.

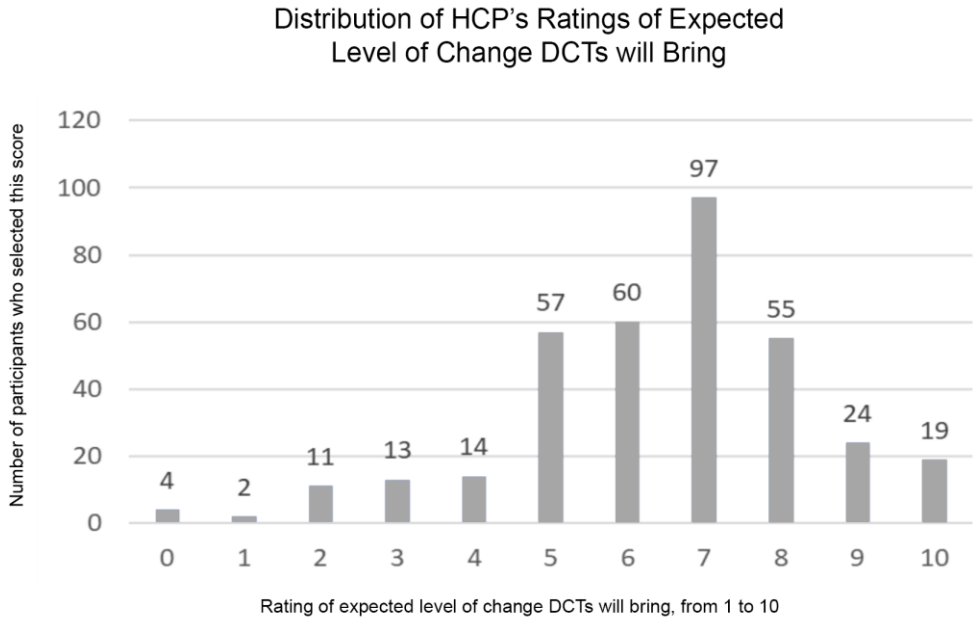

Figure 6 – Distribution of ratings of the expected level of change that DCTs will bring, from 0 (no change) to 10 (revolution-like changes).

➤ Trial Mix. Over two-thirds (67%) of respondents reported that they thought that DCTs would replace conventional trial models to some extent, while 83% thought that hybrid trial models would be the majority in the future. Only 16% believed that the future will involve fully virtual, remote, and decentralised trials. About half of participants stated that DCTs and hybrid trials would never replace conventional trials (49%). Most PIs (63%) see hybrid clinical trials (i.e., trials with some decentralised and remote elements) as the most important emerging clinical trial model, while only 9% answered that DCTs were the most important.

Patient Survey

➤ Subject Demographics. The patient survey received 406 responses, the majority of which based in Germany (30%), Italy (28%), or Belgium (20%). However, 20 other European countries were selected at fewer than 4% of respondents each. All but 2 respondents were adults, with another 8 people taking the survey on behalf of a child patient. Aside from this, there was wide distribution across each adult age group. Most respondents indicated they were female (62%). A more detailed breakdown of participant demographics can be found in Annex 2. Patients lived with a variety of chronic conditions, with the most common being diabetes (33%), followed by autoimmune diseases (19%), cancer (8%), and cardiovascular conditions (7%). Another 27% of patients indicated they had an unspecified rare disease, while another 30% of patients selected 'Other.'

➤ Previous Experience with Conventional Clinical Trials. Most of the patients (73%) had never participated in a conventional clinical trial. Of the 110 patients who had, slightly more had participated in industry-sponsored trials at 40%, while 33% had participated in academic-sponsored trials and 27% didn't know who the sponsor had been. Most participated for the entire duration of the trial (81%). Of those who didn't participate in the full trial, half dropped out during the first period, with 19% and 13% dropping out at the second and third periods, respectively. No patients dropped out in the fourth period and 19% didn't remember. These 16 patients gave a variety of reasons for why they terminated their participation in the trial. These reasons can be found in the survey results, presented in Annex 2.

The survey also asked participants which aspects of their participation they found most valuable or desirable, with the ability to select more than one. Over three-quarters selected 'Potential treatment for my disease' (76%), and most also indicated 'Value for other patients/society' (66%). 'Education on my disease' (44%) and 'Interaction with the PI' (38%) were less common choices. For those who hadn't participated in a trial before, the vast majority (92%) indicated that it was because they had never been invited to one, as opposed to the 21 patients who were invited but declined for some reason. These 21 patients had a variety of reasons for not choosing to participate, including concerns about health effects (29%), time investment (24%), and time constraints such as travel connections and logistics (19%). The full list can be reviewed in Annex 2.

➤ Previous Experience with DCTs. Most of the patients surveyed had never heard of DCTs, at 73%. The 100 patients who had heard of them mostly had never participated in one. The 13 participants who noted that they had participated in a DCT were asked a series of additional questions about their experiences, such as whether they had participated in the full trial, which aspects they found most valuable, how additional value could have been added, and what could have been improved. For those who ended their participation in the trial early, they were asked why. These results are provided in Annex 2, however, as only a small number of respondents answered these questions, additional analysis was not performed.

➤ Interest in DCTs. All participants were asked to gauge their interest in six different aspects of DCTs on a scale of 1 to 5, with 5 indicating 'Very interested' and 1 indicating 'Not interested at all.' The topic which seemed to garner the most interest was 'Return of clinical trial data to the participant and sharing rights.' Over half of participants (57%) stated they were 'Very interested' in this topic, with an average score of 4.35. The other aspects also garnered strong interest, with the lowest average rating still over 3.5. These topics were 'Use of local language for technical support' (average rating of 4.25) 'Data ownership/rights' (4.15), 'Data security, storage, and backups' (4.11), and 'Emotional care and peer community' (3.92). None of the topics were rated a 1 more than 3.1% of the time, and 5 was the most common rating given for all topics. See Figure 7 for an overview on the average score for each topic.

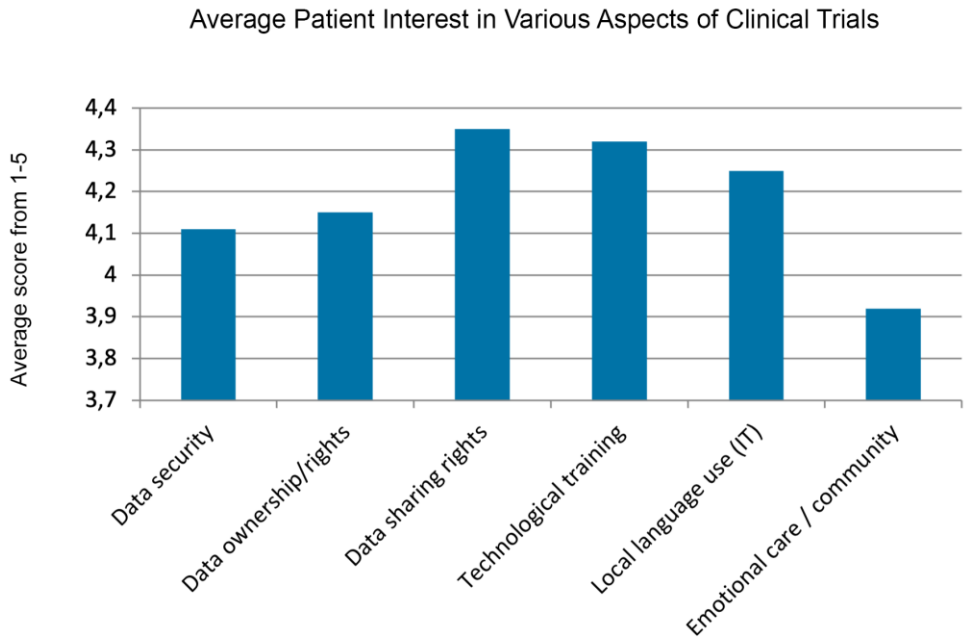

Figure 7 – Weighted average interest score for each aspect of DCTs, with 1 indicating no interest and 5 indicating 'very interested.'

Discussion

Most respondents across both the HCP and the patient survey confirmed significant interest in DCTs. That said, we cannot rule out a bias towards a more favourable opinion about DCTs by responders. People that are not interested in DCTs would be less likely to participate in the surveys. This might also explain the low turnout from GPs. The GP survey was open and extensively spread through consortium networks for nearly two years and received only 28 responses, as opposed to the PI and patient surveys which both received over 400 responses each after less than five months. It is likely that clinical trials are not a top priority for GPs. The COVID-19 pandemic may have also led to excessive work for GPs, which would not have affected patients and PIs quite as much. This would give them less time to devote to taking a survey. A significant portion of study staff might also be GPs. As such, their responses may have already been captured in the PI survey. Future researchers might consider a dedicated study on this group with more robust recruitment methods.

Only a small number of HCPs were aware of DCTs and even fewer had experience with them, however they seemed to agree that DCT elements and hybrid trials in particularly would become more common in the future. Interestingly, informed HCPs were significantly more interested than uninformed respondents. This suggests that education and exposure might increase HCP interest, although we cannot conclude a causal relationship from this data. Many HCPs did report experience with specific DCT elements, mainly online patient diaries, IMP self-administration and telemedicine visits. Note that this survey was active between October 2020 and February 2021, meaning there was some overlap with the COVID-19 lockdown measures, where many healthcare offices were practicing partially or even fully remotely. We expect that the number of providers with experience in DCT elements would be lower if this survey had taken place before these lockdown measures.

HCPs predicted that providers themselves would be more likely to conduct a DCT trial and that DCTs would positively affect their study teams. Later, when asked about opportunities, a common response was that DCTs would be more efficient and that there would be more research opportunities as a result. However, most HCPs perceived a neutral impact on their business model and operations, suggesting that they don't expect these opportunities to change how they conduct business nor its financial viability. HCPs did state that they thought significant changes would be required within their own teams and offices if there were to be a shift towards DCTs. They seemed to mostly agree that education would be needed in the office for DCT

technologies. A modest number of providers also thought education in regulatory and legal issues as well as communication might be helpful. The other topics were also selected, albeit less frequently.

Patients were interested in a variety of subtopics within clinical trials, with particular interest in the return of clinical trial data and sharing rights. As very few patients in the sample had experiences with clinical trials, and even fewer with DCTs, it was not possible to draw any conclusions about their perception of them beyond this initial strong interest. Only about one-quarter of participants had even heard of DCTs. HCPs thought that patients would be more likely to join a trial if there was a widespread shift towards DCTs in clinical trial models. Later, when asked about perceived opportunities they foresee with DCTs, many HCPs indicated they thought that patient burden would be decreased, and that recruitment would improve with a move towards DCTs. HCPs also agreed that greater understanding from the patient perspective would be required to prompt a paradigm shift towards DCTs. This suggests that, from the perspective of a HCP, decreasing participant burden might make patients more likely to participate, however greater education efforts would be required to expose patients to DCTs. Future researchers might consider targeting specifically the population of patients who have participated in DCTs to glean more about the patient perspective.

Among HCPs who reported having any sort of concern over DCT adoption, a reduction in patient trust was a common response. Closely related to the concept of trust is that of the doctor-patient relationship. Interestingly, the scores for how much the doctor-patient relationship would be impacted by a shift towards DCTs were normally distributed, suggesting a lack of consensus among HCPs surrounding how they believe DCTs will impact their relationships with their patients. It is important to note that most HCPs did not identify any concerns at all. It is possible those were the same HCPs who rated the impact on doctor-patient relationship to be neutral or positive.

Commitment to traditional methods of healthcare delivery was also a commonly cited concern. HCPs did overwhelmingly believe that DCTs would increase patient willingness to join a trial, however. It is possible that participants who don't trust DCT models or who are more comfortable with a traditional trial approach are not perceived as part of this group who would be more willing. HCPs also perceived that hybrid models would become more prominent in the short term. It is not clear whether the concern of reduced trust would apply to partially remote and/or hybrid approaches. Patient safety and compliance was expected to be more relevant, but it was only mentioned in 16% of responses. Patient safety highly depends on the protocol and the specific DCT elements that will be used, and their technical realisation. As such, it is highly case-specific. The present survey asked for only overall concerns, which may account for a lack of interest in this patient safety.

Conclusion

Both patients and PIs/clinic staff have strong interest in DCTs, but very little knowledge or experience with them. Unfortunately, it was not possible to conclude anything concrete about GPs, as there were very few responses to this survey. Similarly, although the sample of patients who completed the survey was adequate, most of them had no experience with clinical trials or DCTs, making it difficult to obtain an accurate picture of their perspective and experience. As a result, PI and study team perspectives were mainly taken into account in this report. This group seemed to agree that DCTs and hybrid models are likely to replace traditional trials to some extent in the future, and that recruitment and other opportunities will increase along with this change. Most HCPs did see the need for education for themselves, their teams and for patients. Additionally, respondents seemed to be conscious of the fact that to perform DCTs, significant changes would be needed such as site staff education on DCTs and appropriate technical equipment.

After a thorough analysis and many discussions, the team has proposed to the Trials@Home Executive Board to start creating a general DCT awareness campaign, starting with a series of videos including an explanation of IMI, the project in general and a topline overview of trials and DCTs. This campaign is expected to be useful for both site staff and patients, given the general lack of knowledge on DCTs in both groups. Further details on the creation and delivery of these materials will be provided in the report for D5.5.

Annexes

ANNEX 1 – Detailed results of the PI survey
ANNEX 2 – Detailed results of the patient survey
ANNEX 3 – Detailed results of the GP survey