



831458 – Trials@Home

Center of Excellence – Remote Decentralised Clinical Trials

WP3 – PILOT

## D3.2 Finalised list of KPI's to be used to qualify and quantify the flow of activities in the pilot

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### Document History

Version	Date	Description
V1.0	27 May 2021	First draft by AS (UMCU)
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## Abstract

The Trials@Home (T@H) consortium aims to explore opportunities to move clinical trials from the traditional clinic setting into the participants' local surroundings or even homes. These so-called Remote Decentralised Clinical Trials (RDCTs) make use of digital technologies and other innovations, which enable participants to visit a clinical trial site less frequently, if at all, potentially making it easier for larger, more diverse and remote populations to participate in clinical trials. These trials are expected to enrol faster, more efficiently, and provide opportunities to collect data that are closer to the daily context of the participant, depending on the aim and design of the trial. However, little evidence exists on how fully remote and hybrid approaches (a model that involves both remote/decentralised and site-based trial elements) compare to traditional site-based approaches regarding scientific and operational quality of the trial. T@H is therefore planning to conduct a pan-European pilot clinical trial to compare fully remote, hybrid and traditional site-based approaches, to help inform future researchers on appropriate use of RDCT methods. Hybrid and RDCT approaches need to meet the same Key Performance Indicators (KPIs) as traditional trial approaches for generating valid and appropriate data to allow drawing correct conclusions from the study results. Therefore, the pan-EU pilot study (RADIAL) will focus on the characterisation and evaluation of recognised KPIs, which reflect scientific and operational quality of clinical trials.

This report describes the final list of KPIs to be used to qualify and quantify the flow of activities in the pan-EU pilot study. This report represents the results of the WP3 PILOT KPI working group, whose objectives were to:

1. Define and operationalise primary endpoint(s), i.e. single or composite KPI, for pan-EU pilot study;
2. Define and operationalise other secondary KPIs for pan-EU pilot study.

Using a modified Delphi study with a panel of 16 experts, a list of 10 main and 12 secondary KPIs to be measured in the pan-EU pilot study were identified.

## Methods

A modified RAND/UCLA Appropriateness Method (RAM) Delphi study was conducted to develop a set of KPIs for the pan-EU pilot study.<sup>[Fitch 2001]</sup> The Delphi method is a widely used systematic approach for the development and prioritization of quality indicators in healthcare, especially where existing evidence is unavailable or insufficient.<sup>[Mellet 2020; Koenders 2019; HIQA 2013; Fernandes 2015; Boulkedid 2011]</sup> It accumulates and synthesizes the knowledge of a group of experts (i.e., an expert panel) in several rounds until consensus is reached.

### *Participants and procedures*

Within the PILOT work package of Trials@Home, a call was made for members with specific expertise relevant to the development and definition of KPIs for clinical trials, to join a working group that was tasked with defining a list of main and secondary KPIs to be measured in the pan-EU pilot study. The expert panel (working group members) of this Delphi study consisted of 16 members from both public (5) and private partners (11) of the Trials@Home consortium that signed up for the working group. Participation in the expert panel was implied by signing up for the working group, and thus no informed consent procedure was applied. The working group met for 15 group discussions from December 11, 2020 (kick-off meeting) through April 29, 2021 (final meeting).

### *Study design*

This Delphi study consisted of several rounds as depicted in the flowchart (Figure 1) and described below.

#### *1. Identification of KPI of interest for the study*

As a starting point of reference, the description of task 3.5 (i.e., “Qualification and quantification of pan-EU pilot”) from the Description of Action (DoA) from the Trials@Home project proposal was used. This task describes a list of KPIs that may be included in the pan-EU pilot to compare the different operational approaches. This list consists of 5 KPI ‘categories’, under which (various) individual KPIs can be grouped, as depicted in Table 1 below. The expert panel was asked to review this list and add any KPIs that were missing and of relevance for the aim of the study, from their perspective. The complete list of KPIs was reviewed and discussed during subsequent group discussions. Any KPI that had been added were assigned to the appropriate category.

#### *2. Deduction of KPIs through review for uniqueness and measurability*

In the next round, the expert panel reviewed the KPI to confirm that each KPI were unique and could be measured effectively as part of the pan-EU pilot. Consideration was given to the data points needed and whether they were routinely measures in clinical trials, based on external benchmark data. If not, through group discussion it was determined whether, in principle, the KPI could be measured. Any KPI that were not unique or could not be measured were removed to give a final table of relevant KPI for ranking (see Table 2).

#### *3. Prioritisation of KPIs through ranking procedure*

The expert panel were then asked to prioritize the KPIs by importance by giving them a rank between 1 (most important) and 15 (least important). The prioritisation was anonymous and discussed during subsequent group discussions.

#### *4. Classification of KPIs through operationalisation and measurement effort*

In the next round, the expert panel was asked to comment on the data needed to operationalise the KPI and the effort that would be needed to measure each KPI on the

list, i.e., if data for a KPI are collected through routine processes, if some additional effort is required to collect the data for a KPI, or if a lot of effort is required to collect the right data for a KPI. This classification was done through group discussions and the KPI colour coded red, amber or green to reflect extreme effort to measure, requiring some effort or additional data collection, and routinely captured and measured data points as part of the clinical trial management systems respectively.

### 5. Final list of KPIs

In this next and final round, both the prioritization from step 3 and the classification from step 4 were shown in one overview (Figure 2). A final group discussion took place, to reach consensus on the final list of main and secondary KPIs to be included in the pan-EU pilot study. An effort was made to include at least one KPI from each of the 5 KPI categories in the final list.

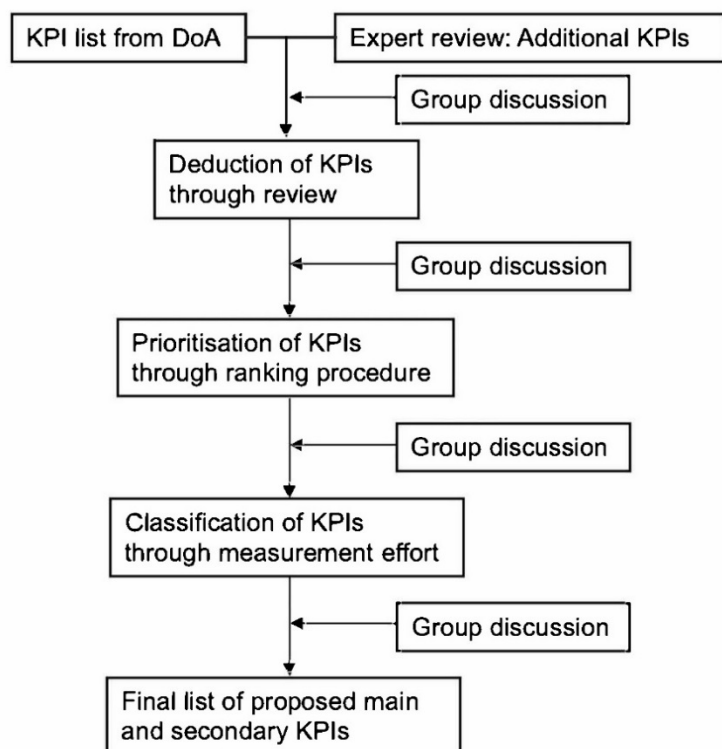


Figure 1. Flowchart of Delphi study

*KPI = Key Performance Indicator, DoA = Description of Action*

### Data analysis

After step 2, the expectation was that there would be more than 15 KPI left for ranking in step 3 (see Table 2). As such, during the ranking, the reviewers had to decide on two levels: “A. For which KPI will I provide a ranking?” and “B. What rank value do I attribute to a selected KPI?”. For this reason, two statistics were derived for each KPI item: “The number of votes (i.e. selections) for the given KPI item” and “The average of the ranks for the given KPI item”. Between those two statistics, one is able to discern between “vocalized and preferred” and “vocalized and not preferred” cases. The most direct method to explore the relationship between number of vote and average rank is via a basic scatter plot. This allows for easy

exploration of potential clusters and separation of clearly preferred (and vocalized) versus those, which were not preferred (or not vocalized).

Note that the reviewers could observe not only the items, but also the categories to which each item belonged. This may induce a behaviour in which the reviewers attempt to select at least one item from each KPI category. This might bias the survey away from purely ranking items regardless of category. This is seen as a minor limitation in our setting as a representation from each category was desired and was a planned approach for the final step of the process, which involved a review of the categories to ensure at least one item representation from each category.

## Results

The adjusted Delphi process resulted in an overview of prioritised and classified KPIs

The colour classification of the KPI dots being:

- Green: Data required for these KPIs are collected through routine processes;
- Amber: Data collection for these KPIs requiring some effort to measure;
- Red: Data collection for KPIs requiring extreme effort to measure.

Subsequently, clusters of KPI have been identified, based on the combined ranking (Average rank & Number of votes) and visualised by the red, white and green area in the below plot.

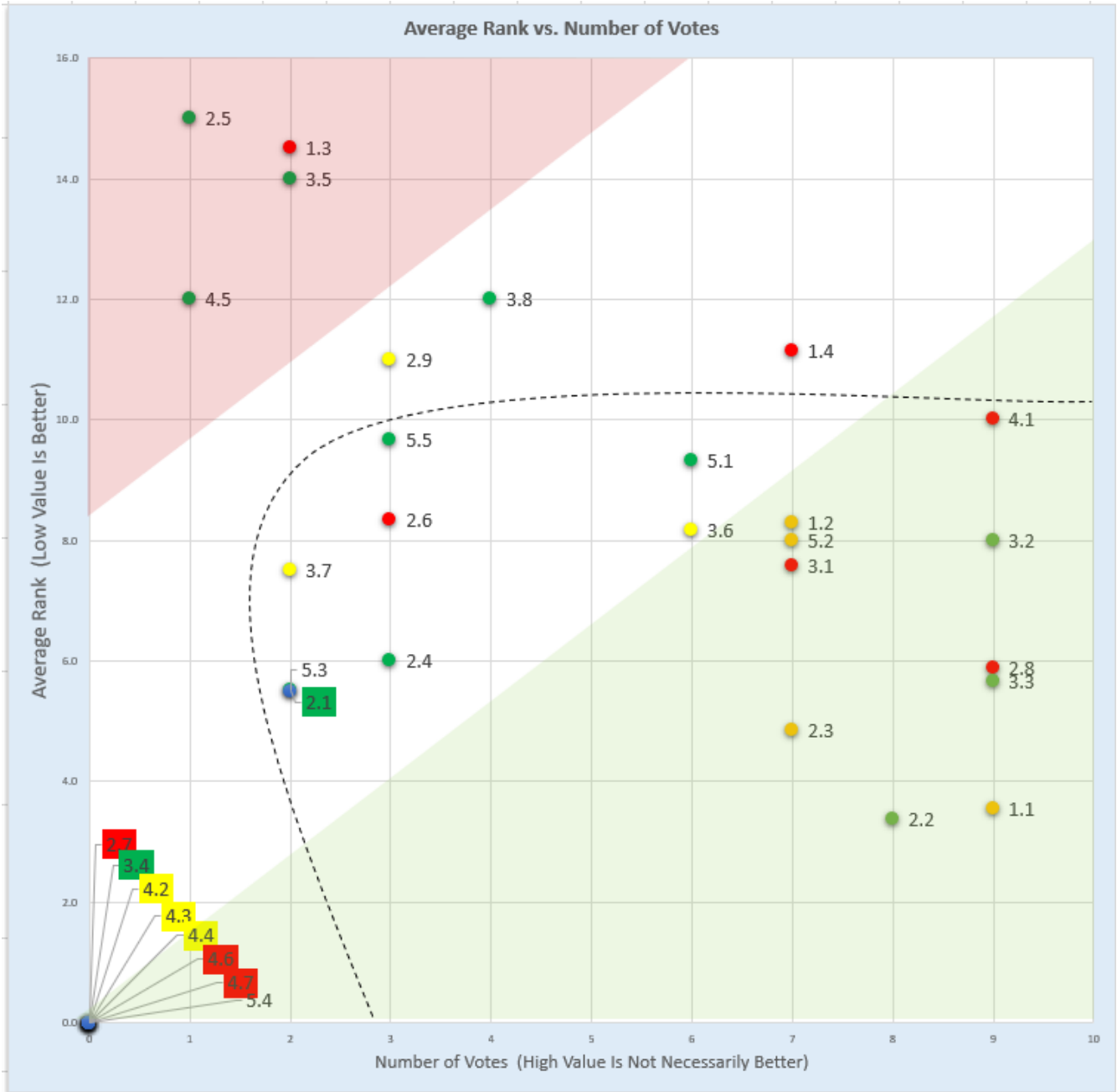


Figure 2 Overview of KPI prioritization and classification

Please refer to Table 3 +4 for the KPI definition by reference number

This process resulted in the selection of two sets of KPIs to be measured in the study:

- **Prioritized KPIs for the pilot study**  
This is the cluster of KPIs that were ranked high in the prioritization process (Average rank  $\leq 10$  and Number of votes  $\geq 7$ , green area in the plot). It was agreed that these KPI are important to include in the pilot study, regardless of the required effort to measure them (classification codes green, orange, and red included). These KPIs are shown in Table 3.
- **Secondary KPIs for the pilot study**  
These are KPIs that are either/and: data collected through standard processes already (colour code green), or require some additional effort to be measured, but are still considered important to include (colour code amber & Average rank  $\leq 10$  and Number of votes  $\geq 2$ ). These KPIs are shown in Table 4.

The Prioritized KPIs (Table 3) will support the study objectives and cover all categories detailed in the DoA (Subject perception / burden, Protocol and GCP compliance, Productivity, Costing and value aspects, Quality and compliance of data). The secondary KPIs will not be described in the protocol, but will be addressed in the Scientific Analysis Plan.

**Table 1. Identification of KPI of Interest for the study**

*\*KPI added by the working group members following initial review of the DoA*

<b>KPI categories</b>				
<b>1. Subject perception / burden</b>	<b>2. Protocol and GCP compliance</b>	<b>3. Productivity</b>	<b>4. Costing and value aspects</b>	<b>5. Quality and compliance of data</b>
Reason for non-consent	Recruitment rates and timelines	Timelines per study phase	Amount of FTE (on site) for conduct for set-up, oversight and management	Data quality (e.g. query rates, data corrections, # queries/data corrections, completeness)
Participant satisfaction	Percentage of subject visits out of window	Time to data entry	Cost per subject (incl. training and travel)	Missing critical source data
Time spent on study by participant	Missing data including reasons (e.g. technical issues vs. compliance issues patient or staff)	Quality of data	Tracking metrics for vendor helpdesk	Data storage and transmission
Availability and understandability of trial information	Treatment compliance	Number of patients per site*	Cost of external data load	Richness of data captured
Accessibility of study staff	(S)AE reporting rate	Number of sites with zero patients*	Reduced or increased cost by delivery model	Quality of study performance (deviations)
Response time to questions	Data quality	Volumetry*	Costs for quality and compliance (e.g. site monitoring, source data verification).	Confidentiality
Site Staff Satisfaction*	Hypoglycaemia reporting compliance*	Access to broader patient's pool*	Value associated with better/lower patient retention	Lost Data*
All Study Devices (Measure of errors and problems)*	Time to reporting (S)AE*		Value of being able to access a broader patient pool	
	Informed Consent compliance*		Total costs of the study arms from a healthcare or societal perspective.*	

	PI Oversight*		Site staff to subject ratio	
	Involvement of PIs in the operational approaches and number of (social) media interactions		Handling time per activity/subject	
	Correct use of technology*		Cost reduction*	
	Retention rates		Total cost per recruited patient from a healthcare or societal perspective.*	

Table 2. Relevant KPI for ranking

KPI categories				
1. Subject perception / burden	2. Protocol and GCP compliance	3. Productivity	4. Costing and value aspects	5. Quality and compliance of data
Participant satisfaction	Recruitment rates and timelines	Timelines per study phase	Amount of FTE (on site) for conduct for set-up, oversight and management	Data quality (e.g. query rates, data corrections, # queries/data corrections, completeness)
Site Staff Satisfaction	Percentage of subject visits out of window	Time to data entry	Tracking metrics for vendor helpdesk	Missing critical source data
Time spent on study by participant	Missing data including reasons (e.g. technical issues vs. compliance issues patient or staff)	Number of patients per site	Cost of external data load	Data storage and transmission
All Study Devices (Measure of errors and problems)	Treatment compliance	Number of sites with zero patients	Value associated with better/lower patient retention	Quality of study performance (deviations)
	(S)AE reporting rate	Volumetry	Total costs of the study arms from a healthcare or societal perspective.	Confidentiality & GDPR compliance

	Hypoglycaemia reporting compliance		Site staff to subject ratio	
	Time to reporting (S)AE		Handling time per activity/subject	
	Informed Consent compliance			
	PI Oversight			
	Involvement of PIs in the operational approaches and number of (social) media interactions			
	Correct use of technology			
	Retention rates			

Table 3. Final list of main KPIs to be included in pilot study\*

KPI number	KPI category (DoA)	KPI	Operationalisation
1.1	Subject perception/burden	Participant satisfaction	Measure patient satisfaction with their experience as participant in the pilot study
1.2	Subject perception/burden	Site staff satisfaction	Measure site staff satisfaction with their experience as site in the pilot study
2.2	Protocol and GCP compliance	AE/SAE reporting rate	Rates of AE/SAE reporting
2.3	Protocol and GCP compliance	AE/SAE time to reporting	Time to reporting AE/SAE
2.8	Protocol and GCP compliance	Missing data including reasons (e.g. technical issues vs. compliance issues patient or staff)	
3.1	Productivity	Treatment compliance	
3.2	Productivity	Recruitment rates and timelines	# of patients screened, treated, per month delay between SIV to start of screening etc.
3.3	Productivity	Retention rate	# of pts completed, early treatment discontinuation, withdrawals
4.1	Costing and value aspects	Total cost of the study arms from a healthcare or societal perspective	
5.2	Quality and compliance of data	Data quality (e.g. query rates, data corrections, # queries/data corrections,	

		completeness)	
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\* Colour coding: Green: data required for these KPI are collected through routine processes; Yellow: data collection for the KPI requiring some effort to measure; Red: data collection for KPI requiring extreme effort to measure.

Table 4. List of secondary KPIs to be included in pilot study\*

KPI number	KPI category (DoA)	KPI	Operationalisation
2.1	Protocol and GCP compliance	Hypoglycaemia reporting compliance	
2.4	Protocol and GCP compliance	Informed consent compliance	
2.5	Protocol and GCP compliance	Percentage of visits out of window	
3.4	Productivity	# of sites with 0 patients	
3.5	Productivity	# of patients per site	
3.6	Productivity	Volumetry	
3.7	Productivity	Time to data entry	
3.8	Productivity	Timelines per study phase	
4.5	Costing and value aspects	Site staff to subject ratio	
5.1	Quality and compliance of data	Quality of study performance (deviations)	
5.3	Quality and compliance of data	Missing critical source data	
5.5	Quality and compliance of data	Confidentiality & GDPR compliance	

\* Colour coding: Green: data required for these KPI are collected through routine processes; Yellow: data collection for the KPI requiring some effort to measure.

## Discussion

Given that the pan-EU pilot study aims to compare three operational approaches (i.e., conventional, hybrid, and fully remote) for their scientific and operational quality, the main endpoints for the pilot study are KPIs rather than clinical endpoints. The selected KPIs will reflect the scientific and operational quality of the pilot study.

The Delphi process identified 10 primary KPI and an additional 12 secondary KPI considered important for the analysis of different operational models (conventional, hybrid, and remote) in the clinical trial ecosystem of the future.

Now that the KPIs have been selected, these will be further operationalised through the following steps:

Determine exactly what will be measured per KPI (more precise definition).

Determine what the source of the data is (system or e.g. to be developed questionnaire), how to obtain the data point, whether the data point needs viewing by investigator, whether and

when transformations are required (if so predefine), at what times the data point needs to be collected and when the data point is transferred to the study database.

For those KPI measures that require substantial development (e.g. site/patient satisfaction questionnaire) a subsequent step is to develop the required materials.

## References

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