AFCROs

DECENTRALIZED CLINICAL TRIALS: FROM WORDS TO ACTION

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Preamble

Decentralized clinical trials (DCTs) are trials designed to "bring the trial to the patient by using local healthcare providers, optimizing digital health technologies, and encouraging patient voices to accelerate the availability of new therapies for patients and to create efficiencies across clinical research processes."

Decentralization can be hybrid, meaning that only a portion of the clinical trial is decentralized, while the core of the clinical trial remains at a primary investigation center.

In the context of this work, we were specifically interested in the home as the decentralization modality using the intervention of health professionals to:

- Collect health data via questionnaires completed by patients or health professionals
- Organize samples (blood, urine, DNA, etc.) and subsequent transport
- Take measurements (weight, vital signs, electrocardiogram, etc.)
- Perform screening tests (covid-19, pregnancy, etc.)
- Administering treatment and arranging subsequent transport
- Providing care (e.g., rehabilitation session)
- Informing patients
- Monitoring compliance with treatment

In the majority of cases, the health professionals involved in this context are nurses or physiotherapists who are self-employed.

Based on feedback, interviews with various stakeholders, and the views of different actors in the care of patients, this white paper aims to determine the optimal conditions for carrying out a hybrid decentralized clinical study in the home.

As a new practice, we hope that it will answer the questions of promoters or investigators wishing to embark on this high-impact organizational innovation for the French healthcare system.

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The benefits of decentralizing clinical trials

For patients

- **Improve the patient experience** of clinical research by avoiding hospital visits and the stress associated with these visits
- **Ease the organization and logistics of participating** in a clinical trial by reducing travel and increasing the accuracy of visit times
- **Increase the safety of the patient**, as traveling may present a risk depending on the pathology
- **Avoid indirect costs of travel** to the investigation center by family members, which are not reimbursed, or the repayment of travel expenses for patients
- **Save time** while preforming the protocol and collecting the data by being in a familiar environment (their own home) and developing a relationship with a dedicated health professional
- **Reduce sick leave** due to the absence of patients needing to travel to the hospital and carry out the clinical study visits

70% of patients included in a clinical trial live more than 2 hours away from an investigation center (source: McKinsey Report 2021 *)

Following a survey of patients in the libheros community, out of 383 respondents:

- only 8% of respondents have ever been offered to participate in a clinical trial
- Among the patients who refused to participate in a clinical trial, 1 out of 5 did so because the protocol was too restrictive
- 65% of individuals who have participated in a clinical trial state that they would have preferred that part of the research protocol take place at home, particularly for blood tests

*McKinsey Report 2021 : https://www.mckinsey.com/industries/life-sciences/our-insights/no-place-like-home-stepping-up-the-decentralization-of-clinical-trials

The benefits of decentralizing clinical trials

For investigators and sponsors

- **Improve study recruitment/inclusion** rates
- **Optimize retention/adherence** to protocols
- **Optimize the quality of the data provided,** completed through assistance to the patient by the healthcare professional (or completed directly by the healthcare professional themselves)
- **Guarantee in completing the required scheduled visits detailed in the protocol,** by facilitating the visits at the patient's home
- **Secure compliance** in case of co-medications
- **Reduce hospital overcrowding** by carrying out some study visits in the patient's home, thus freeing up the time of medical teams, allowing them to focus hospital resources on other higher priority tasks
- Facilitate patient access to clinical trials by allowing **people who are more distant** from clinical research to participate

80-90% of trials are delayed due to difficulties in recruiting patients*

*source : Rapport Essais cliniques 2030, LEEM et IQVIA, 2021

The benefits of decentralizing clinical trials

For health professionals

- **To feel valued** for participating in innovation, by integrating them into the research team
- **To develop the skills** of urban caregivers by training them in good clinical practices
- **Strengthen the hospital-community linkage** through an increase in team projects (for example, the private nurses may have all previously worked in hospitals)

A survey conducted by libheros polled 18,000 freelance nurses from the libheros PRO community, confirming the high rate of interest these professionals have in clinical research:

- On a scale of **1 to 5**, their interest in participating in clinical research projects in the home is rated at **4.1/5** on average (834 respondents)
- The following comments were among the feedback expressing their reasons of interest: "To participate in improving patient care", "To develop my know-how", "To work again with hospital teams".
- **107** said that they had already participated in a clinical research project

When questioned, the Conseil de l'Ordre des Masseurs-Kinésithérapeutes (Council of the Order of Masseurs-Physiotherapists) confirmed the interest of the profession in participating in research projects, especially since 87% of the physiotherapist profession works outside the hospital environment (in private practice), thus making physiotherapy therapies more accessible to patients. Today, 300 physiotherapists have completed training in clinical research, which is constantly increasing.

Prerequisites for launching a decentralized clinical research project

1. The patients must **take their role seriously and must be capable** when choosing the decentralization of activities, implying a necessary upstream evaluation of the complexity of the tasks to be carried out and to be formalized in the delegation protocol

2. The guarantee of **equity of access for illiterate patients**

3. Obtaining the **agreement of the Committee for the Protection of People (CPP)** for the organization of part of the protocol at home

4. The **protection of patients' personal data** and the traceability of the data circuit, in particular the respect of the CNIL MR-001 reference methodology

5. The use of **dematerialization tools** (such as ePRO, eCO, eCRF, etc.) adapted to remote data collection

6. Training in **Good Clinical Practice (GCP)** for the healthcare professionals involved

7. Established **communication procedures the medical team must follow in the case of an adverse event**, for an optimized realization of the progress of the clinical study including the occurrence of an adverse event

8. The completion of documentation to the correct governing bodies prior to the response of the health professionals

Current obstacles to the development of decentralized clinical trials

Feedback from decentralized clinical research projects and the interviews conducted have highlighted various obstacles to the implementation of decentralized clinical trials.

Cultural

- Faced with certain obstacles linked to habits, presenting a significant organizational change, **a change management approach** must be taken with all the players

- In addition, health care institutions need to be reassured that the budget allocated to them will **be maintained despite these new practices.**

- Decentralization necessarily entails a **reallocation of these investments** to the home, and in the absence of a medico-economic study to demonstrate the time saved by hospital teams, this reallocation is perceived as a reduction in resources.

- Finally, even if this has not been observed in practice, some actors wonder **whether some patients want to continue to have their protocols carried out in hospital**, either out of habit or out of a desire to keep their care in hospital; we have not been able to measure this point

Current obstacles to the development of decentralized clinical trials

Quality and regulations

- **Training in Good Clinical Practice (GCP) is not included in the training curriculum for health care workers**, and few of them are currently trained and qualified to work on decentralized clinical research protocols, particularly in the home

- **Often considered too late**, requests for authorization can block steps in the decentralization process; in particular, RIPH studies require the home to be declared as a research site to regional health agencies

- As the principal investigator is fully responsible for the delegation of tasks, decentralization can **be a source of reluctance or even refusal on the part of investigators to take responsibility for activities carried out in the home**, and the more risky acts requested (e.g. injection of the study product vs. taking of vitals), the greater the reluctance of the professional investigator

- In the absence of a clearly identified intervention framework, the opinion of the various Personal Protection Committees (PPC) on the framework can vary and is sometimes protocol-dependent. For example, one PPC imposed the presence of a physician during visits organized by a physiotherapist.

- At present, **e-consent is not authorized in France** because of the rules around processing computerized data. Authorizing it would require the modification of the CNIL's (National Commission for Computing and Liberties) reference methodologies. Work is underway on this subject, led by the CNRIPH (National Research Commission Involving the Human Person). Consent must be obtained by the center during the initial visit, which does not pose any obstacle as such during hybrid decentralization projects. On the other hand, the lack of authorization of the e-consent may be an obstacle in the case of a need for re-consent during the study.

Current obstacles to the development of decentralized clinical trials

Operational

- For the investigators, past experiences have highlighted **the difficulties in identifying trained and qualified** carers and in organizing coordination with the existing health care team

- From an organizational point of view, **planning of the logistics is often complex** (especially if there is equipment or analytics to be provided), as is the organization of visits and the involvement of caregivers. These time-consuming steps can be a source of discouragement for hospital healthcare professionals.

- When transporters are integrated into the logistics, constraints on the days and/or times of availability make these organizational schemes even more complicated.

- With regard to the management of the drug dispensation, some of the pharmacists interviewed feared, for example, that the tasks will be "shifted" to the site pharmacy to prepare, send and monitor treatments when they are not sure to be completed by the carrier.

- In some cases, partners were identified but were involved too late in the studies. In the case of poor information or coordination of actors, city health professionals may find themselves isolated.

- In terms of tools, the **collection and transmission of data and/or the use of unsuitable paper notebooks is still prevalent.** There is an increased risk of them being forgotten or lost and are more problematic in the context of off-site clinical trials. Digitization is even more important in an environment where there are many documents and not all are digitized yet; often, the investigating centers are not prepared for the digitization of the data collected, nor are they equipped with secure messaging

- On the other hand, the **multiplicity of digital tools** can be detrimental to efficiency and require specific training (e.g. projects involving the use of a platform for collecting patient consent and another platform for collecting study data)

Use cases conducive to decentralization

Decentralization of a clinical trial is of greater interest when:

- **The frequency of visits** to be planned is high (for example: blood samples to be taken every day over a certain period to evaluate the pharmacokinetics of a drug)
- The procedures and protocols to be performed are not **very complex** (e.g., taking of vitals, simple blood samples, subcutaneous medications in injectable form)
- **The distance to be traveled by the patients is high** (for example: blood samples, vital signs measurements and a pregnancy test to be performed for patients with soft tissue and cartilage calcification, coming from France and Spain)
- The patients have **mobility issues or are frail** (e.g. Parkinson's, multiple sclerosis, Alzheimer's patients)
- **The monitoring methods and times are short** (as such, some treatment administrations are not necessary)

Key factors to success

Before the decision to decentralize

- Anticipate decentralization at the protocol design stage
- Conduct an upstream risk analysis on the decentralization of the protocol, limiting it to interventions with lower risk or complexity
- Involve the investigators so that they are convinced of the relevance of decentralization

When selecting partners

- Seek expertise in the organization and management of caregivers when necessary
- Use a network of qualified and trained caregivers, covering the entire country at the national level if the project is multicentric or in remote areas
- Anticipate the use of service providers early on, and invite them to participate in the implementation of the protocol and in the co-construction of essential documents (delegation of tasks, training manual)
- Ensure that the proposed tools comply with the Ma Santé (My Health) 2022 core reference frameworks
- When it comes to drug administration, rely on the institution's in-house pharmacies or pharmacies to anticipate any stock management issues

Key factors to success

During the preparation of the research project

- Digitizing the process and data collection via secure HdS tools, guaranteeing the confidentiality of information (e.g.: digital transmission book used in a clinical trial at the AP-HP)
- Use tools that are integrated into the practices of health professionals, that run autonomously, and can reduce their number of interactions
- Ensure that the protocol is accessible to all types of patients (access to digital technology, understanding of the involvement of decentralization, etc.); in some cases, give the patient the choice of carrying out his or her protocol in the hospital
- In terms of transporting the drug doses, pay particular attention to storage and transport conditions, their traceability and monitoring (e.g., under controlled temperature).
- Ensure that the healthcare professional has dedicated his or her schedule to clinical research, to avoid mixing or prioritizing routine care above the trial.
- Value the time spent by the freelance professional by integrating them in training and administrative aspects.

During the project

- Develop strong coordination between the investigating teams (hospital, CRA, TEC) and the private healthcare professionals working in the home; in particular, identify a contact person who can be reached at all times.
- Rapidly create a close relationship between the CRAs and homecare professionals
- Organize regular, ongoing training for the teams

Our recommendations

1. **Financially encourage decentralization**: through the allocation of dedicated subsidies or incentives for those who commit themselves to it, without depriving public hospitals of the means granted to research.

2. **Reassess the scope of responsibility of the hospital actors**: keep the supervision of the study to the investigator, but limit the responsibility of the activity carried out in the home to the private health professionals involved and not to the hospital professionals

3. **Conduct a medico-economic study** to demonstrate the impact of decentralizing clinical trials

4. **Evolve MR-001,** which today does not allow one actor to coordinate the decentralized component in the most fluid way, "the processing of Personal Identifying Information (PII) and health data by the same subcontractor [remains] excluded from the reference methodology."

5. **Officially recognize the home as a place of research**: if today, as specified in the minutes of the 2021 Giens workshops, there is nothing legally preventing the organization of some clinical research in the home, formally incorporating it into the law would be easier

6. **Encourage the use of e-consent** to facilitate the renewal of consent (re-consent).

7. **Facilitate the evaluation of PPCs** of projects with a decentralized component by harmonizing the project review criteria

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https://www.afcros.com/groupes-de-travail/essais-cliniques-decentralises/

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