



Response Evaluation In Neurofibromatosis Schwannomatosis INTERNATIONAL COLLABORATION

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Understanding decentralized trials: benefits and challenges

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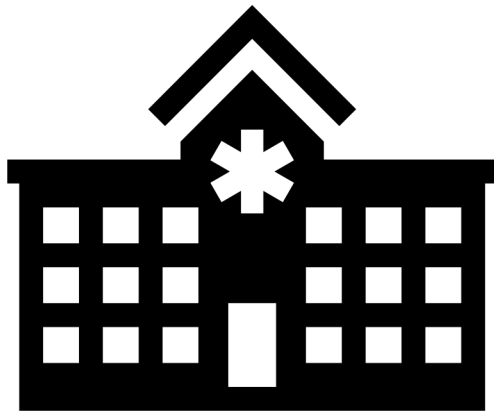
Massachusetts General Hospital

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Response Evaluation In Neurofibromatosis Schwannomatosis
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Decentralized Clinical Trial



A clinical trial where some or all of the trial-related activities occur at locations other than traditional clinical trial sites.

Food and Drug Administration (FDA)

Current State: All activities are centered around the hospital

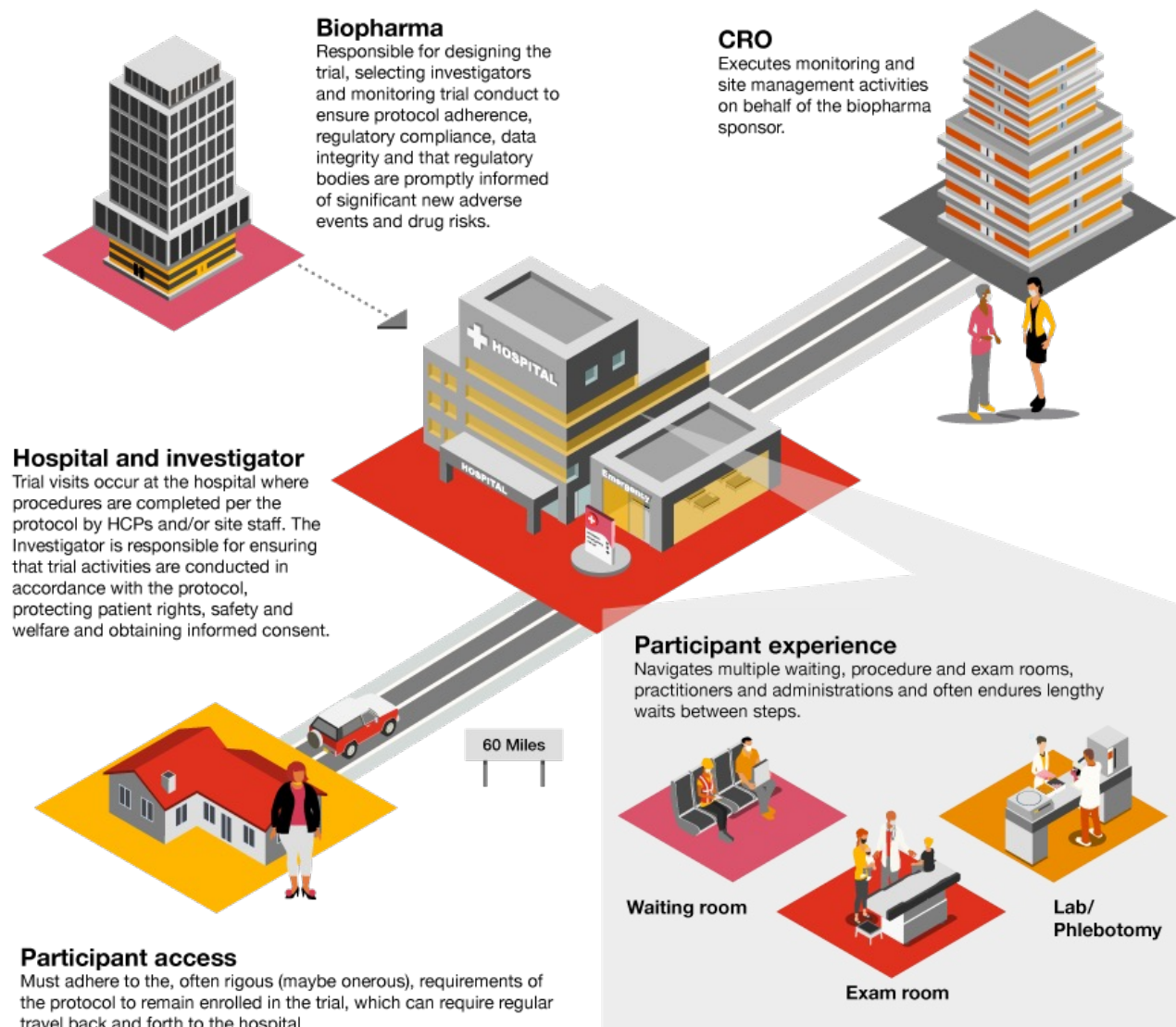


Image credit: PwC

Future State: All activities are centered around the patient

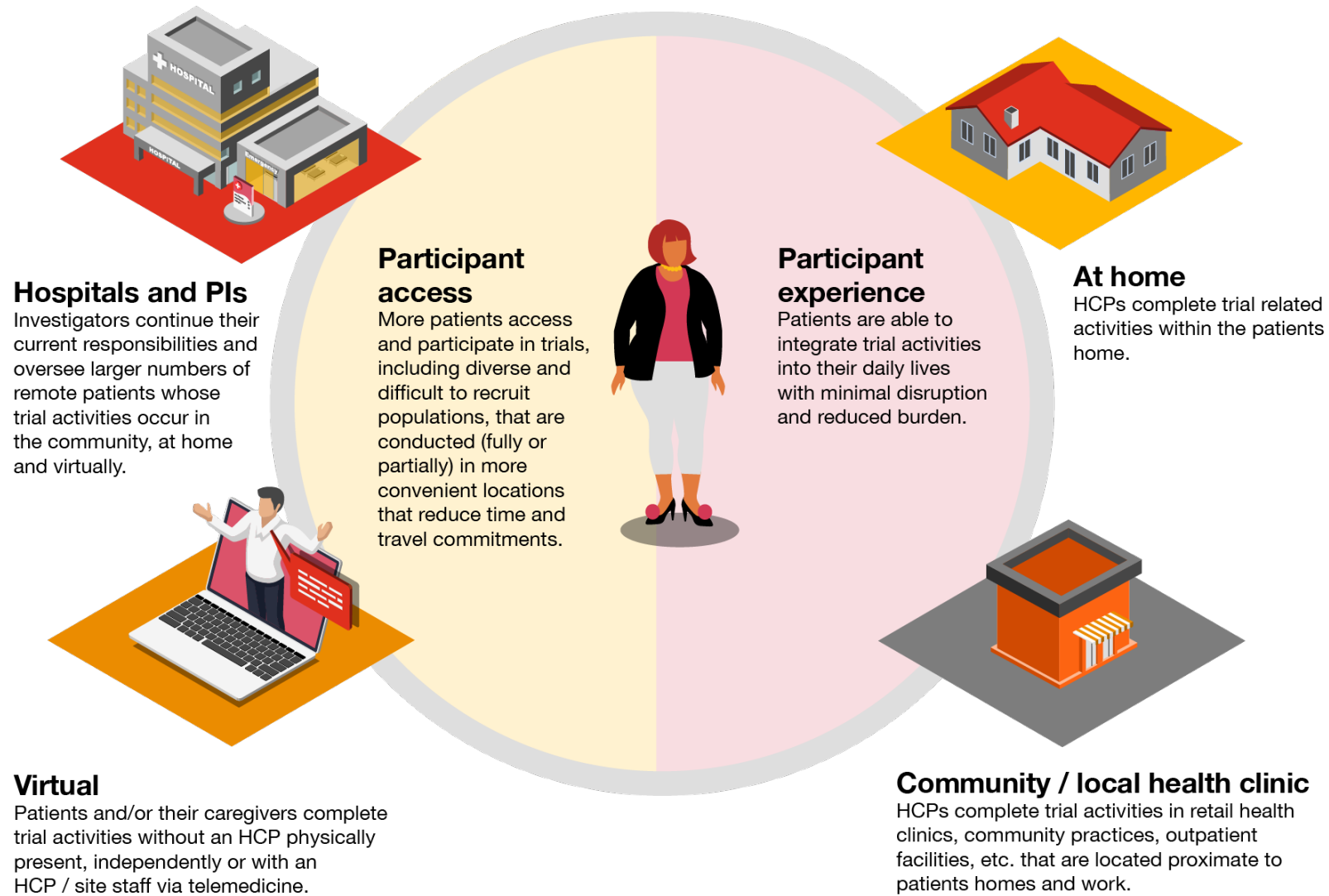


Image credit: PwC

Trials May Be Fully or Partially Decentralized

Clinical-trial designs

Fully decentralized ← Hybrid → Fully centralized



All trial procedures are conducted virtually, enabled by digital technologies and supply delivery

Less complex trial procedures that don't require in-person visits (eg, vital signs, electrocardiograms) are conducted via telehealthcare, remote data collection, or direct-to-patient supply

Less complex trial procedures that require in-person visits (eg, injections) are conducted via mobile clinicians or alternative sites (eg, mobile clinics, retail sites)

Complex trial procedures (eg, complex screening protocols, cell therapy, magnetic resonance imaging) are conducted via research sites (eg, academic medical centers) or local hospitals

All trial procedures are conducted at a research site (eg, academic medical center)

McKinsey
& Company

A Menu of Decentralization Options

	Traditional Site-Based	Virtual
Recruitment	Hospital-based recruitment	Targeted digital recruitment
Enrollment	In-person consent	eConsent and multifactor identity verification
Product Distribution / Intervention Delivery	Medication dispensed and reconciled by study staff at in-person appointments	<ul style="list-style-type: none"> • Medications shipped directly to patient • Psychological, cognitive, and other interventions delivered virtually
Safety Assessment	Hospital-based assessments	<ul style="list-style-type: none"> • Monitoring at local outpatient facilities, labs, and imaging centers; • Digital platforms for adverse event self-reporting
Outcomes Assessment	<ul style="list-style-type: none"> • In-person COA assessments • Paper PROs and diaries 	<ul style="list-style-type: none"> • Electronic PROs via web/mobile app • Remote monitoring via wearables and connected health devices

A Brief History of Decentralized Trials

- When did the first decentralized trial conducted under an IND in the United States start?

Pfizer Conducts First “Virtual” Clinical Trial Allowing Patients to Participate Regardless Of Geography

Tuesday, June 07, 2011 - 05:30am



Research on Electronic Monitoring of Overactive Bladder Treatment Experience (REMOTE) trial

- Phase 4 RCT of tolterodine ER vs. placebo for treatment of overactive bladder symptoms in women aged ≥ 21 years

Participant:

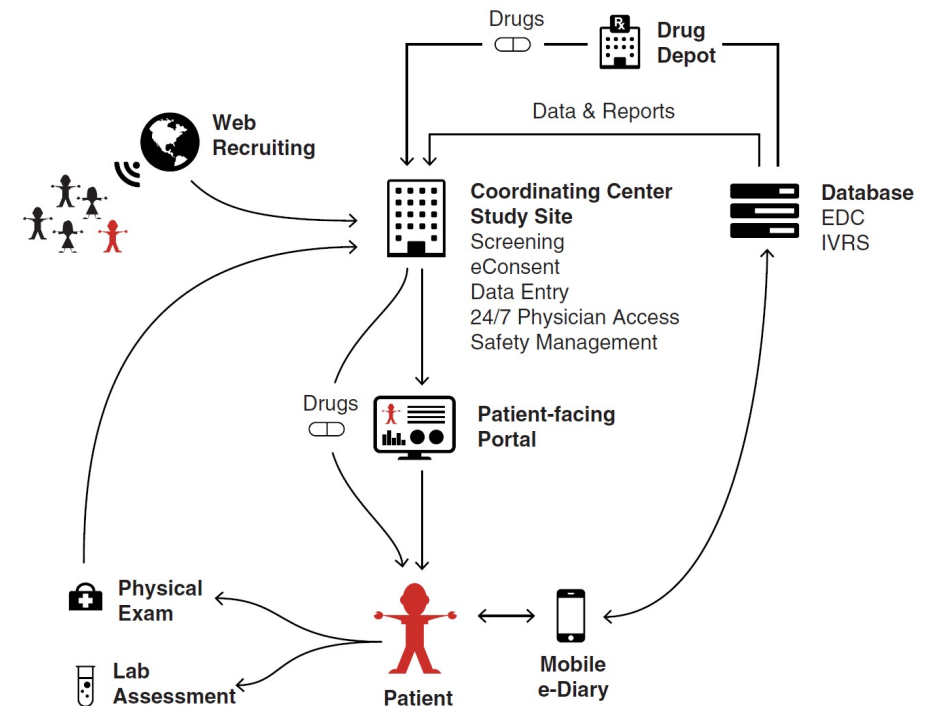
- Web-based recruitment
- Web-based multi-media informed consent process
- Web-based screening

Technology:

- Mobile communication device-based efficacy assessments (eg, e-diary)
- Interactive remote data capture via secure participant portal
- Real-time data access for site, monitors, and auditors

Investigator site:

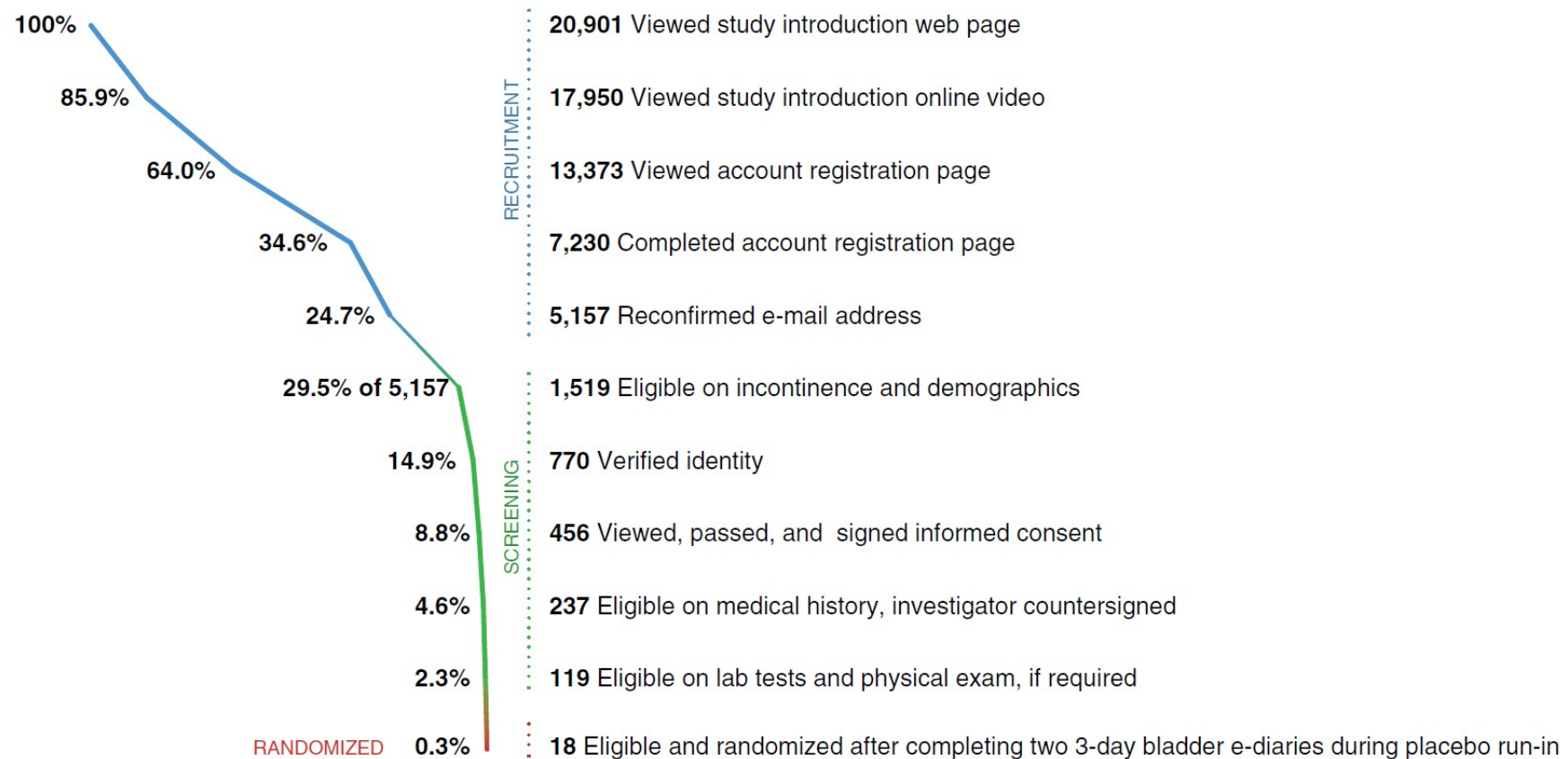
- Coordinating function for virtual assessments: participant does not attend investigator site
- Study drug delivery to participants by overnight courier
- Study physician/call center available 24/7 by e-mail and phone
- Real-time processing of safety data
- Individual study data to each participant



Orri et al. (2014). Contemporary Clinical Trials, 38(2), 190–197.

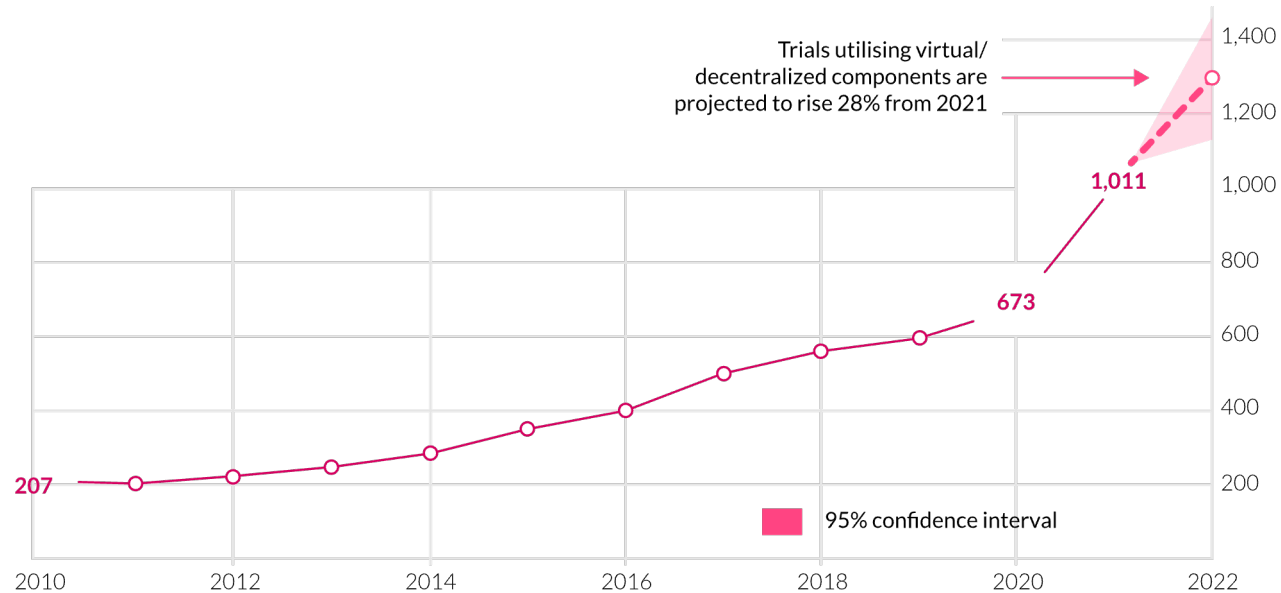
REMOTE trial terminated early due to lack of recruitment

M. Orri et al. / Contemporary Clinical Trials 38 (2014) 190–197



Where Have Decentralized Trials Gone Since 2011?

- 250 studies in 2012 to an estimated 1,425 studies in 2022¹



*Majority of components are technology based

Interventional drug trials worldwide which mentioned decentralized/virtual components in clinical registry protocols

¹GlobalData's Clinical Trial Database

Have Decentralized Trials Been Successful?

- Trials with decentralized elements have led to FDA approval (e.g. daily e-Diaries)
 - BNT162b2 COVID-19 vaccine (Polack et al. 2020)
 - Ztalmy (ganaxolone) to treat seizures associated with cyclin-dependent kinase-like 5 deficiency disorder (Knight et al. 2022)
- But this is difficult to track
 - No routine tracking of DCT modifications during COVID-19 pandemic within registrational trials
 - No standard DCT reporting requirements for publications

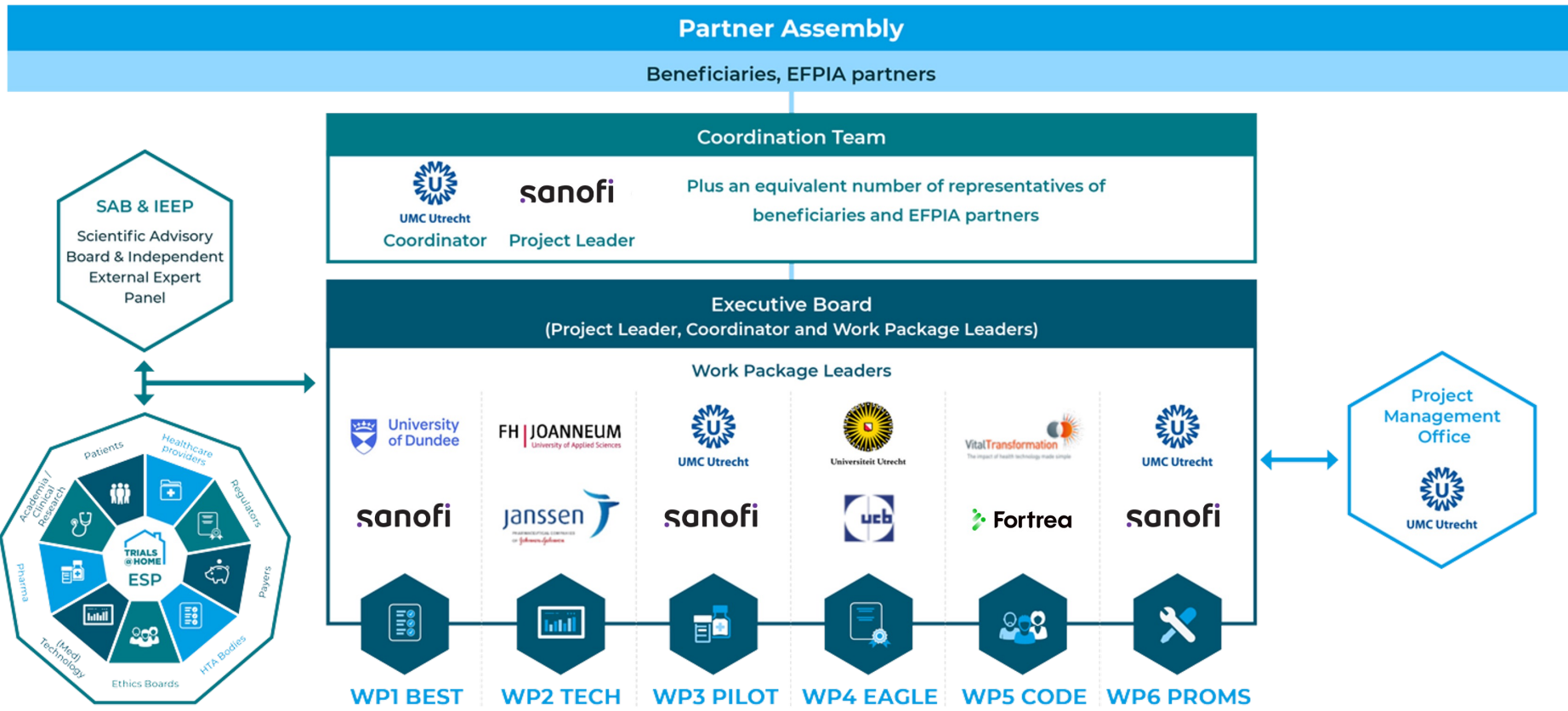
Decentralized Trials and Research Alliance



<https://www.dtra.org/>



Trials@Home: An Innovative Medicines Initiative project



1. Define best practices for DCTs
2. Identify appropriate technology
3. Run pilot DCT
4. Map ethical, legal, regulatory issues
5. Communication, dissemination, stakeholder engagement
6. Project management

€40 million over 5 years



Trials@Home Pan-EU Proof of Concept Trial

The RADIAL Trial

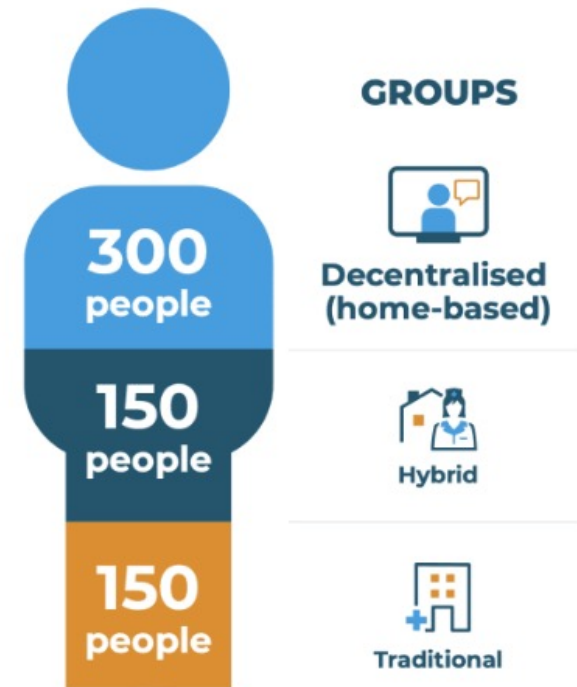
For people living with type 2 diabetes + taking long-acting basal insulin whose blood glucose management is not currently optimal.

All participants will be switched from their current long-acting basal insulin to once-daily Toujeo® (insulin glargine 300 u/ml) and will carefully monitor their blood glucose throughout the 6-month trial.

All other medications and medical care will remain unchanged.

Data quality/completeness, trial completion rate and satisfaction of enrolled participants and trial results will be assessed to judge whether the decentralised (home-based) approach is truly a reliable and dependable way to conduct trials.

- First remote patient enrolled on Nov. 3, 2023



Changing Landscape for Decentralized Trials

Prior Barriers to DCTs

- Requirement to receive investigational products from trial sites (e.g., 21 CFR 312.61)
- Requirement to document all subinvestigators + ensure their training (e.g., Form 1572)
- Technology limitations

Current Facilitators of DCTs

- COVID-19
- Increasing comfort with digital health technology
- Growing focus on patient-centered trials to achieve recruitment, retention, and diversity goals
- Shifting regulatory environment

New Regulatory Guidance on Decentralized Trials



- Decentralized Clinical Trials for Drugs, Biological Products, and Devices **(May 2023)**
- Digital Health Technologies for Remote Data Acquisition in Clinical Investigations **(Dec 2021)**
- Recommendation paper on decentralized elements in clinical trials **(Dec 2022)**
- Guidance on the implementation of decentralized elements in clinical trial with medicinal products **(Sept 2021)**



Potential Benefits and Challenges of Decentralized Trials

	Potential Benefits	Potential Challenges
Patient Access to Trials	More equitable geographic and economic access	Excluding non-tech-savvy; people without smartphones/high speed internet

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Costs	Reduced costs for site activation/monitoring	Increased costs for digital health technology

Imagining the Future for NF/SWN Decentralized Trials

“The question is no longer *whether* we can conduct aspects of cancer trials in a decentralized fashion, but *how* we can best prioritize the most useful DCT methods moving forward, and prospectively design DCT studies in oncology that maintain patient safety and data integrity.”

(Rivera et al, 2022)

