Why innovate and bring clinical trials home?

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The research leading to these results has received support from the EU/EFPIA Innovative Medicines Initiative [2] Joint Undertaking (H2020-JTI-IMI2) Trials@Home grant n° 831458.

Disclosure Mira Zuidgeest

Potentiële belangenverstrengeling	Zie hieronder
Voor bijeenkomst mogelijk relevante relaties met bedrijven	Geen
• Sponsoring of onderzoeksgeld • Honorarium of andere (financiële) vergoeding • Aandeelhouder • Andere relatie, namelijk….	• IMI funding, zie disclaimer hiernaast • geen • N.v.t. • GetReal Institute Board Member

Disclaimer

The research leading to these results was conducted as part of the Trials@Home consortium. This presentation only reflects the personal view of the stated authors and neither IMI nor the European Union, EFPIA, or any Associated Partners are responsible for any use that may be made of the information contained herein.

The Trials@Home project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No 831458. This Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA.

Trials@Home project

The aim

Provide recommendations on Decentralised Clinical Trials (DCT) approaches in Europe

Project start September 1, 2019, due to end November 30, 2025

The consortium

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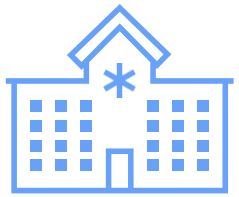
What are Decentralised Clinical Trial (DCT) approaches?

"operational model in which trial activities are designed to take place at or in the vicinity of the participant's home"

"rather than at a traditional clinical site"



"This approach may make use of technologies and other innovative operational approaches to facilitate data collection"

Santa-Ana-Tellez et al. Decentralised, patient-centric, site-less, virtual, and digital clinical trials? From confusion to consensus. https://doi.org/10.1016/j.drudis.2023.103520

- Not a methodology
- Can be fully decentralised or hybrid
- Can be steered towards pragmatic or towards explanatory methodology

- Better recruitment and retention?
- Lower participant and site burden?
- Lower costs?
- RWE opportunities:
  - More representative study population?
  - Less interference with routine clinical practice?

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Recommendations on decentralised elements in CTs

From European Medicines Regulatory Network, Published Dec 14, 2022 on Eudralex Vol. 10

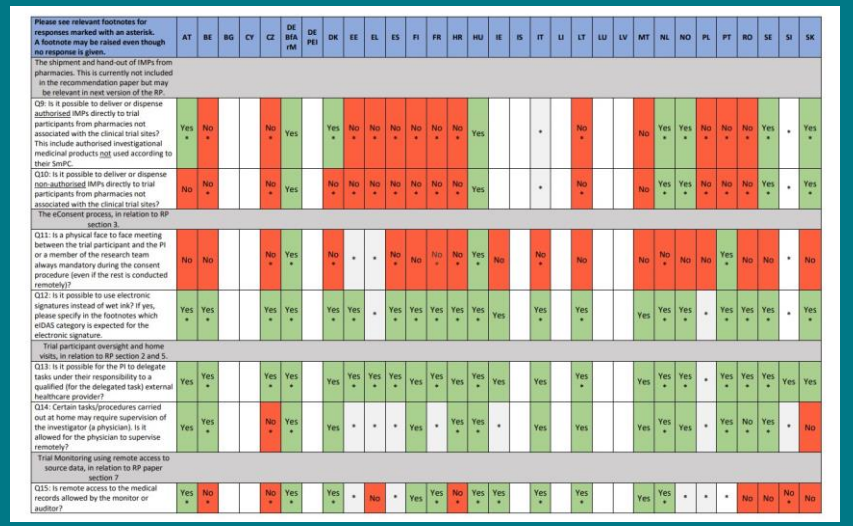
DCT Recommendation paper

Direction of EMRN harmonisation

1. Introduction, scope, general considerations
2. Clinical trial oversight: roles & responsibilities
3. Informed consent process
4. Delivery of medicinal products & administration at home
5. Trial related procedures at home
6. Data collection and management incl. defining & handling source data
7. Trial monitoring

National provisions overview

Member state specific provisions, where national legislation does not currently allow for alignment



Please see relevant footnotes for responses marked with an asterisk. A footnote may be raised even though no response is given.	AT	BE	BG	CY	CZ	DE BfArM	DE PEI	DK	EE	EL	ES	FI	FR	HR	HU	IE	IS	IT	LI	LT	LU	LV	MT	NL	NO	PL	PT	RO	SE	SI	SK
The shipment and hand-out of IMPs from pharmacies. This is currently not included in the recommendation paper but may be relevant in next version of the RP.																															
Q9: Is it possible to deliver or dispense authorised IMPs directly to trial participants from pharmacies not associated with the clinical trial sites? This include authorised investigational medicinal products not used according to their SmPC.	Yes *	No *			No *	Yes		Yes *	No *	No *	No *	No *	No *	No *	Yes			*		No *			No	Yes *	Yes *	No *	No *	No *	Yes *	*	Yes *
Q10: Is it possible to deliver or dispense non-authorised IMPs directly to trial participants from pharmacies not associated with the clinical trial sites?	No	No *			No *	Yes		No *	No *	No *	No *	No *	No *	No *	Yes			*		No *			No	Yes *	Yes *	No *	No *	No *	Yes *	*	Yes *
The eConsent process, in relation to RP section 3.																															
Q11: Is a physical face to face meeting between the trial participant and the PI or a member of the research team always mandatory during the consent procedure (even if the rest is conducted remotely)?	No	No			No *	Yes *		No *	*	*	No *	No	No *	No *	Yes *	No		No *		No			No	No *	No	No	Yes *	No	No	*	No
Q12: Is it possible to use electronic signatures instead of wet ink? If yes, please specify in the footnotes which eIDAS category is expected for the electronic signature.	Yes *	Yes *			Yes *	Yes *		Yes *	Yes *	*	Yes *	Yes *	Yes *	Yes *	Yes *	Yes		Yes *		Yes *			Yes	Yes *	Yes *	*	Yes *	Yes *	Yes *	*	Yes *
Trial participant oversight and home visits, in relation to RP section 2 and 5.																															
Q13: Is it possible for the PI to delegate tasks under their responsibility to a qualified (for the delegated task) external healthcare provider?	Yes	Yes *			Yes *	Yes *		Yes	Yes *	Yes *	Yes *	Yes	Yes *	Yes	Yes *	Yes		Yes		Yes *			Yes	Yes *	Yes *	*	Yes *	Yes *	Yes *	Yes	Yes
Q14: Certain tasks/procedures carried out at home may require supervision of the investigator (a physician). Is it allowed for the physician to supervise remotely?	Yes	Yes *			No *	Yes *		Yes	*	*	*	Yes	*	Yes *	Yes *	*		Yes		Yes			Yes	Yes *	Yes	*	Yes *	No *	Yes *	*	No
Trial Monitoring using remote access to source data, in relation to RP paper section 7																															
Q15: Is remote access to the medical records allowed by the monitor or auditor?	Yes *	No *			No *	Yes *		Yes *	*	No	*	Yes	Yes *	No *	Yes *	Yes *		Yes *		Yes *			Yes	Yes *	*	*	*	No	No	No *	No

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Stakeholder views & preferences

Interviews regulators

de Jong *et al.* Clin Pharma Therapeutics 2022.
doi: 10.1002/cpt.2628

Focus groups ECs/NCAs

- Social value & scientific validity
- Favourable B/R ratio & respect for subjects
- Informed consent
- Fair subject selection

Van Rijssel *et al.* Drug Discov Today 2022.
doi: 10.1016/j.drudis.2022.07.011

Interviews HTA

Key findings

Opportunities	*Challenges*
1 Data collection reflective of the real-world setting	1 Impact of data collection in a less controlled setting
2 Reduced recall bias and Hawthorne effect	2 Change of behavior when outcome data is observable
3 Increased generalizability	3 Limited knowledge of DCTs among HTA assessors

de Jong *et al.* Value in Health 2024.
doi: 10.1016/j.jval.2023.11.006

The research leading to these results has received support from the EU/EFPIA Innovative Medicines Initiative [2] Joint Undertaking (H2020-JTI-IMI2) Trials@Home grant n° 831458.

Do people prefer to participate in a clinical trial from home or not?

Patient preference study

- Step 1: focus groups to identify drivers
- Step 2: Discrete Choice Experiment (DCE) to quantify preferences

Characteristics:
- People with DM2
- DE, AT, NL

Status:
- Focus groups finalised
- DCE recruitment finished ~800 participants, analysis ongoing

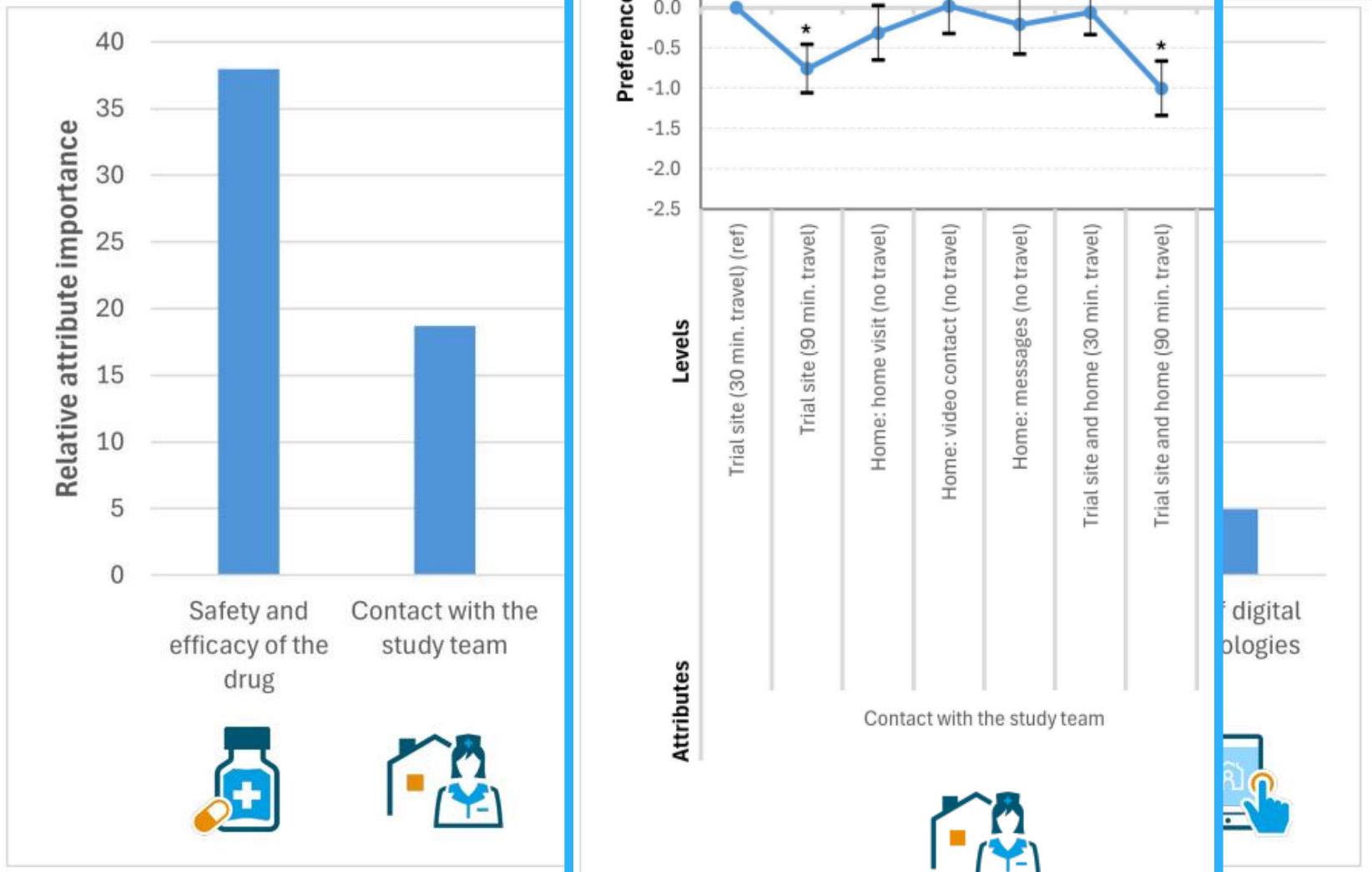
Focus group findings: drivers for participation

Kopanz *et al*. CTS 2024 https://doi.org/10.1111/cts.70070

The research leading to these results has received support from the EU/EFPIA Innovative Medicines Initiative [2] Joint Undertaking (H2020-JTI-IMI2) Trials@Home grant n° 831458.

DCE Interim Results NL

- N = 276
- 39% female
- Median age 66 yrs

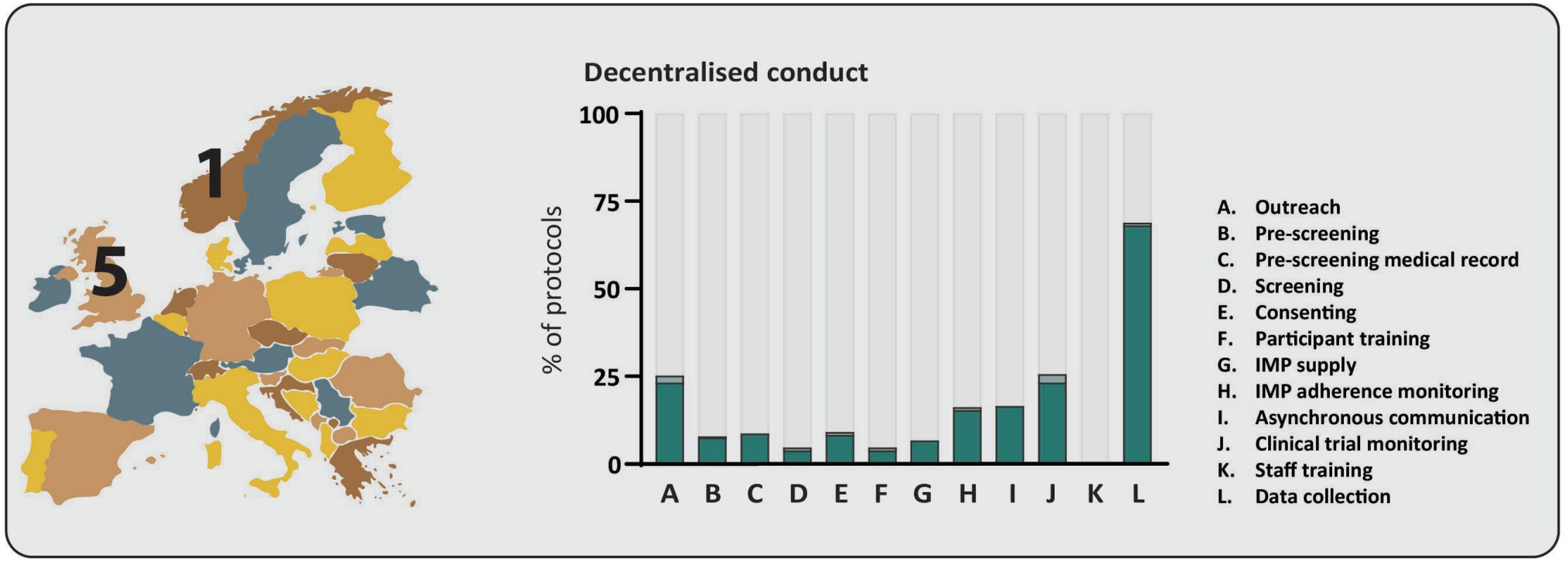


The research leading to these results has received support from the E ant n° 831458.

Current landscape & DCT elements

- Limited full DCTs have been conducted in Europe
- DCT elements are being used in clinical trials

DCT approaches are a continuum



Rogers *et al.* Br J Clin Pharmacol 2022. doi: 10.1111/bcp.15205

de Jong *et al.* BMJ Open 2022. doi: 10.1136/bmjopen-2022-063236

The research leading to these results has received support from the EU/EFPIA Innovative Medicines Initiative [2] Joint Undertaking (H2020-JTI-IMI2) Trials@Home grant n° 831458.

RADIAL PROOF-OF-CONCEPT STUDY

Aim:
To assess the scientific and operational quality of a fully decentralised and hybrid trial approach compared to a conventional trial approach

Approved proof-of-concept study

Methodological objective: KPIs as main outcomes

Low intervention phase IV trial

Compound® used within market authorization label

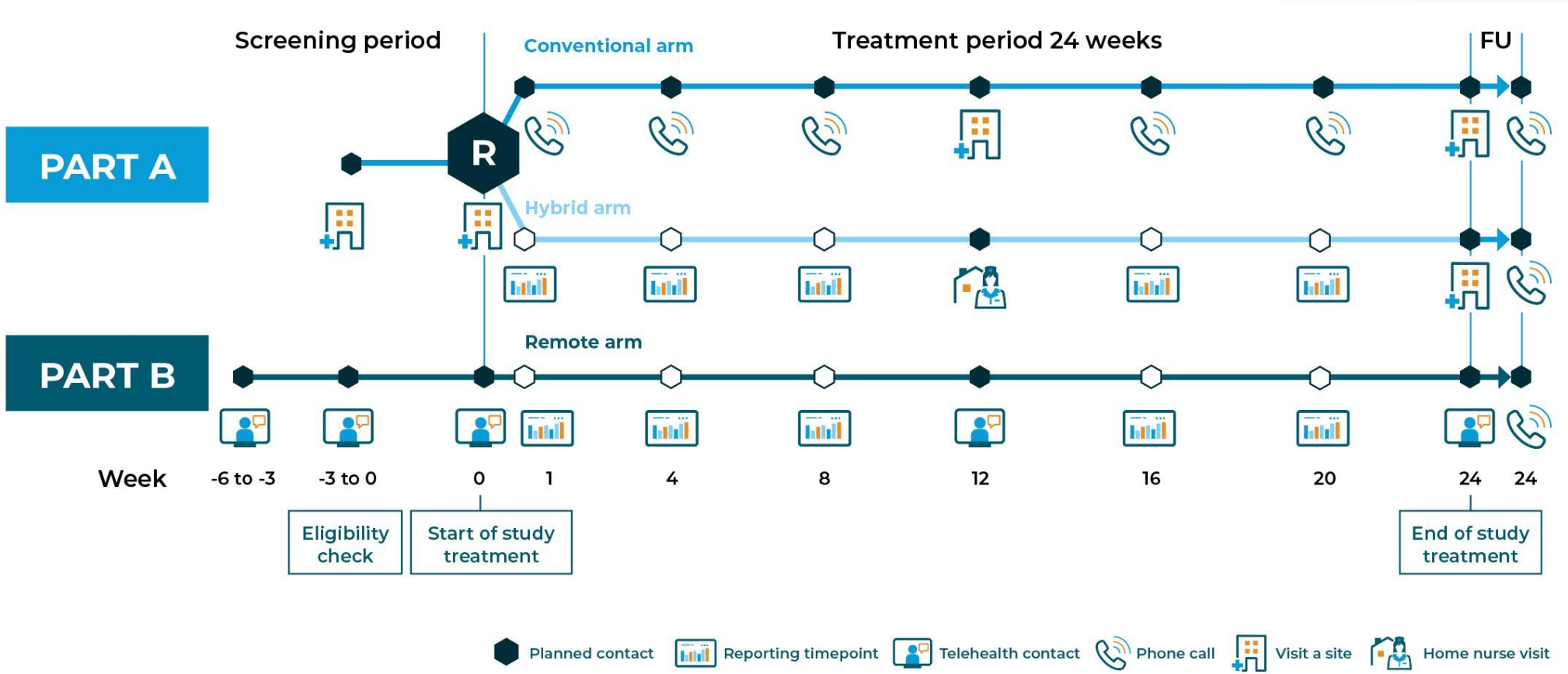
Population familiar with insulin use

People with DM2 treated with basal insulin with HbA1c 7-10%

Explore <u>potential benefits:</u> participant retention, recruitment, diversity, cost, site & patient satisfaction

Evaluate <u>acceptability:</u> safety oversight, data quality & treatment adherence

Set-up of RADIAL proof-of-concept study



Countries

- Poland
- Germany
- UK
- Denmark
- Spain
- Italy

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Decentralised elements in RADIAL

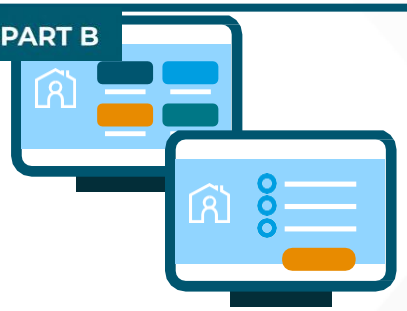
PART B

eConsenting and eSignature

PART B

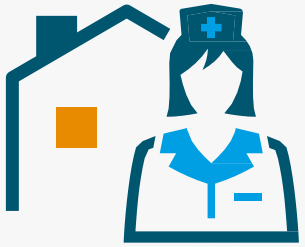
Telemedicine

PART B



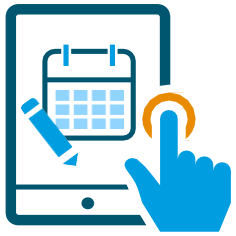
Online recruitment and pre-screening

PART A



Home nurse visits

Remote monitoring IMP adherence



Study app for reporting (S)AEs and ePROs

Direct to patient shipment of IMP

At home sample collection

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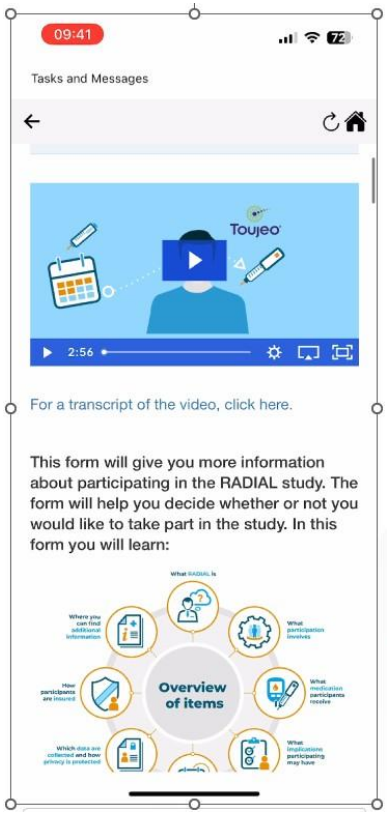
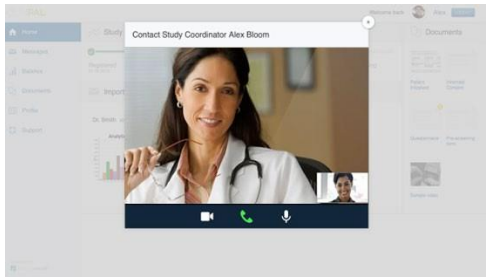
RADIAL part B consent - Participant Experience

Clinpal eConsent solution with Qualified Electronic Signature

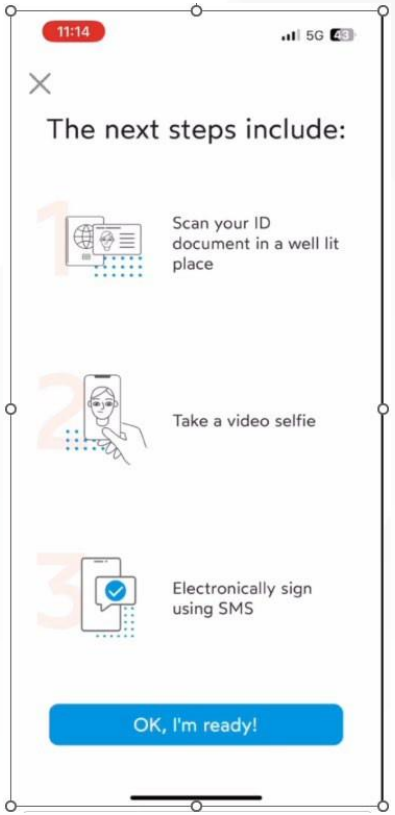
Informing (watch, read, quiz, check willingness to proceed)



Consultation (video call with site)



Signature (opt-ins, identity, signing, download)



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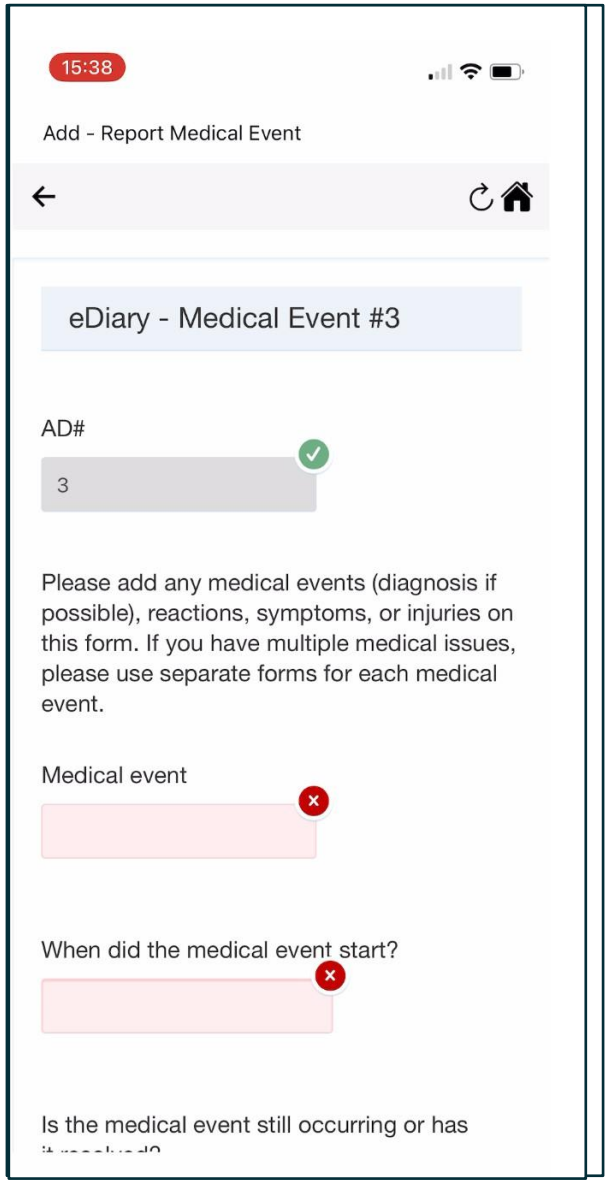

Reporting of Medical events by Participant

- Based on 'The Yellow card' application to report side effects - IMI WEB-RADR

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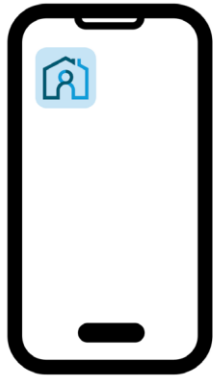
How to maintain oversight when participants are remote?

- In decentralised/hybrid arm, the investigator has access to tools to maintain oversight – even though the participant does not physically visit the site.

Remote

Data collection



Continuous reporting

Remote

monitoring

(Ad hoc)

Telemedicine or phone call

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A remote site, a 24/7 clinical trial site?

- We cannot expect real-time review and follow-up on collected data and reports
- Risk-based approach
- Expectation management (for both site and participant)

Weekly ‘digests’ of dosing data

Automated alerts for possible SAEs

Reporting timepoints

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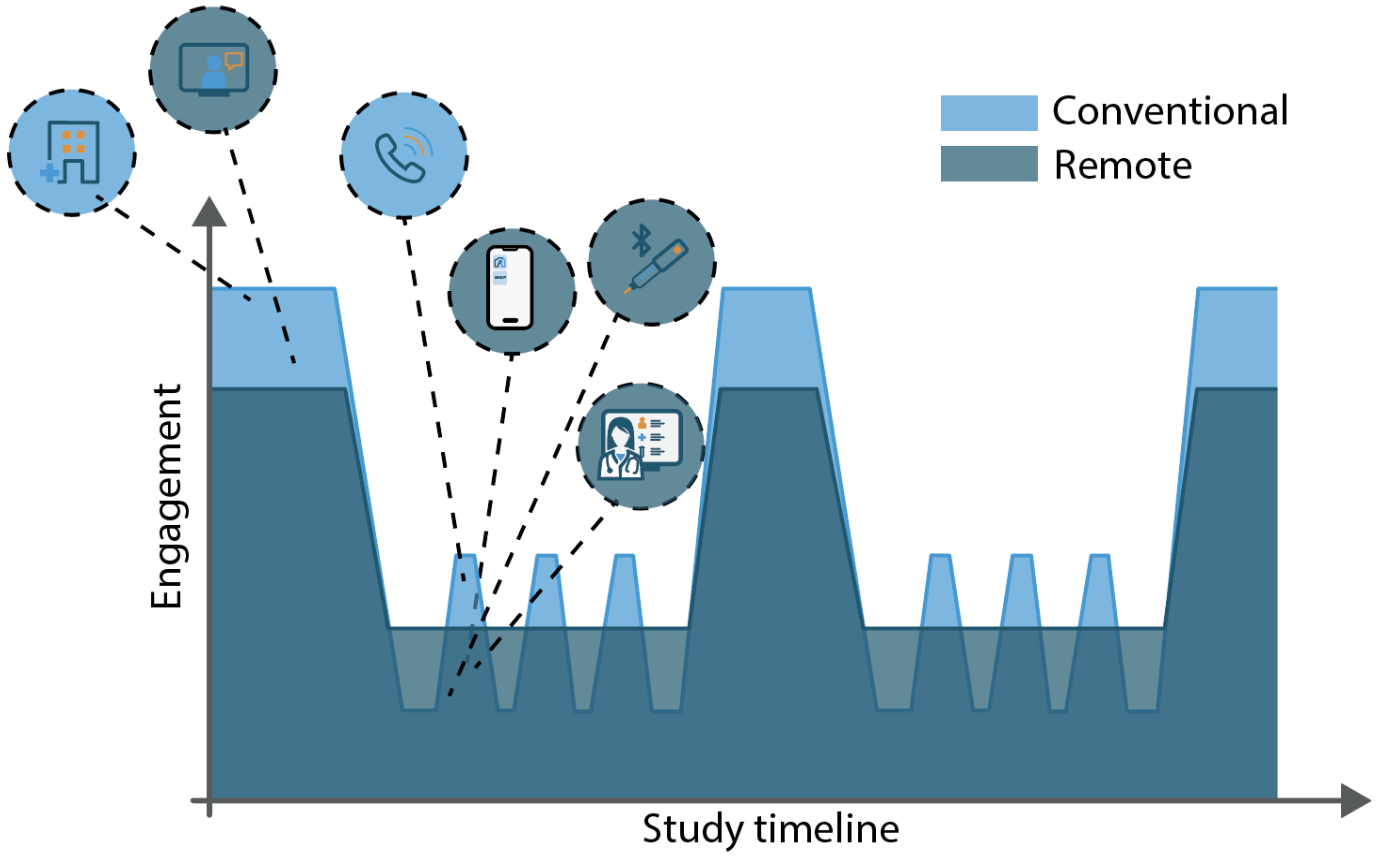
Investigator oversight in a DCT (RADIAL)

- In a conventional trial, the participant is most of the time 'remote' (not at the clinical trial site).
- Using (novel) technology the remote participant can be brought 'closer' to the investigator



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DtP IMP delivery in RADIAL

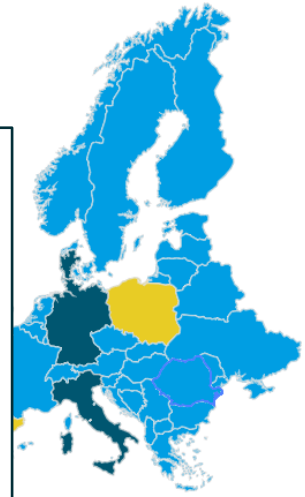
Br J Clin Pharmacol. 2023 Dec;89(12):3512-3522. doi: 10.1111/bcp.15850. Epub 2023 Jul 29.

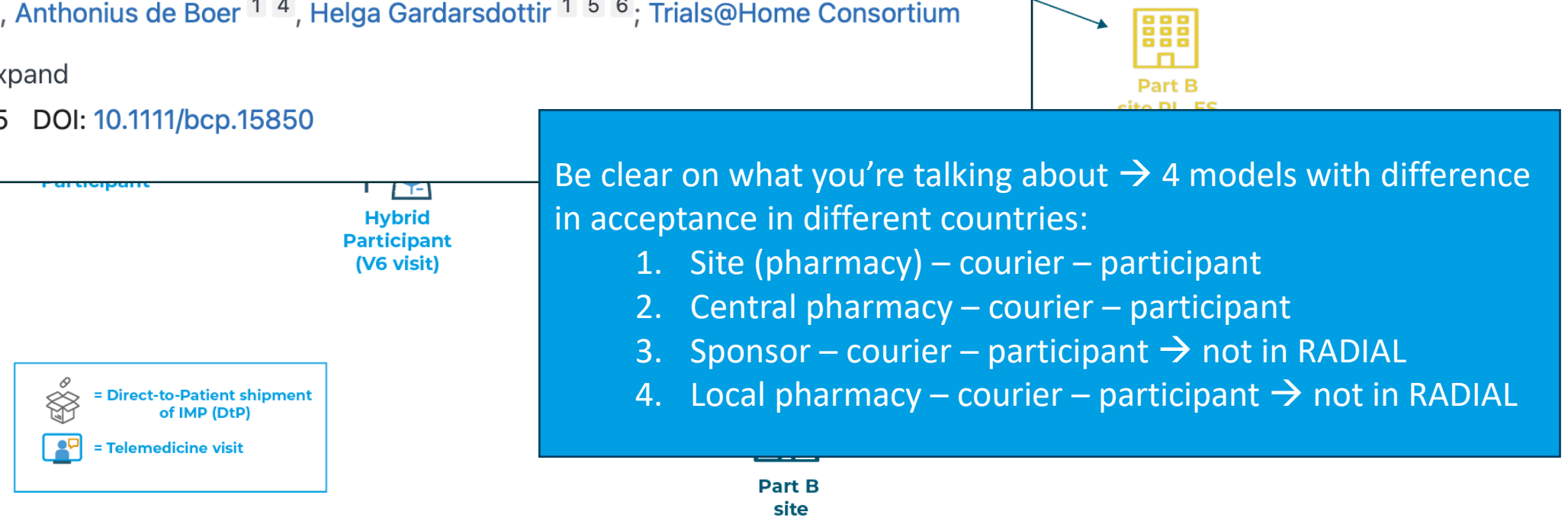
Direct-to-participant investigational medicinal product supply in clinical trials in Europe: Exploring the experiences of sponsors, site staff and couriers

Amos J de Jong [1], Yared Santa-Ana-Tellez [1], Mira G P Zuidgeest [2], Renske J Grupstra [1], Fatemeh Jami [3], Anthonius de Boer [1 4], Helga Gardarsdottir [1 5 6]; Trials@Home Consortium

Affiliations + expand

PMID: 37438875 DOI: 10.1111/bcp.15850





Be clear on what you're talking about → 4 models with difference in acceptance in different countries:

1. Site (pharmacy) – courier – participant
2. Central pharmacy – courier – participant
3. Sponsor – courier – participant → not in RADIAL
4. Local pharmacy – courier – participant → not in RADIAL

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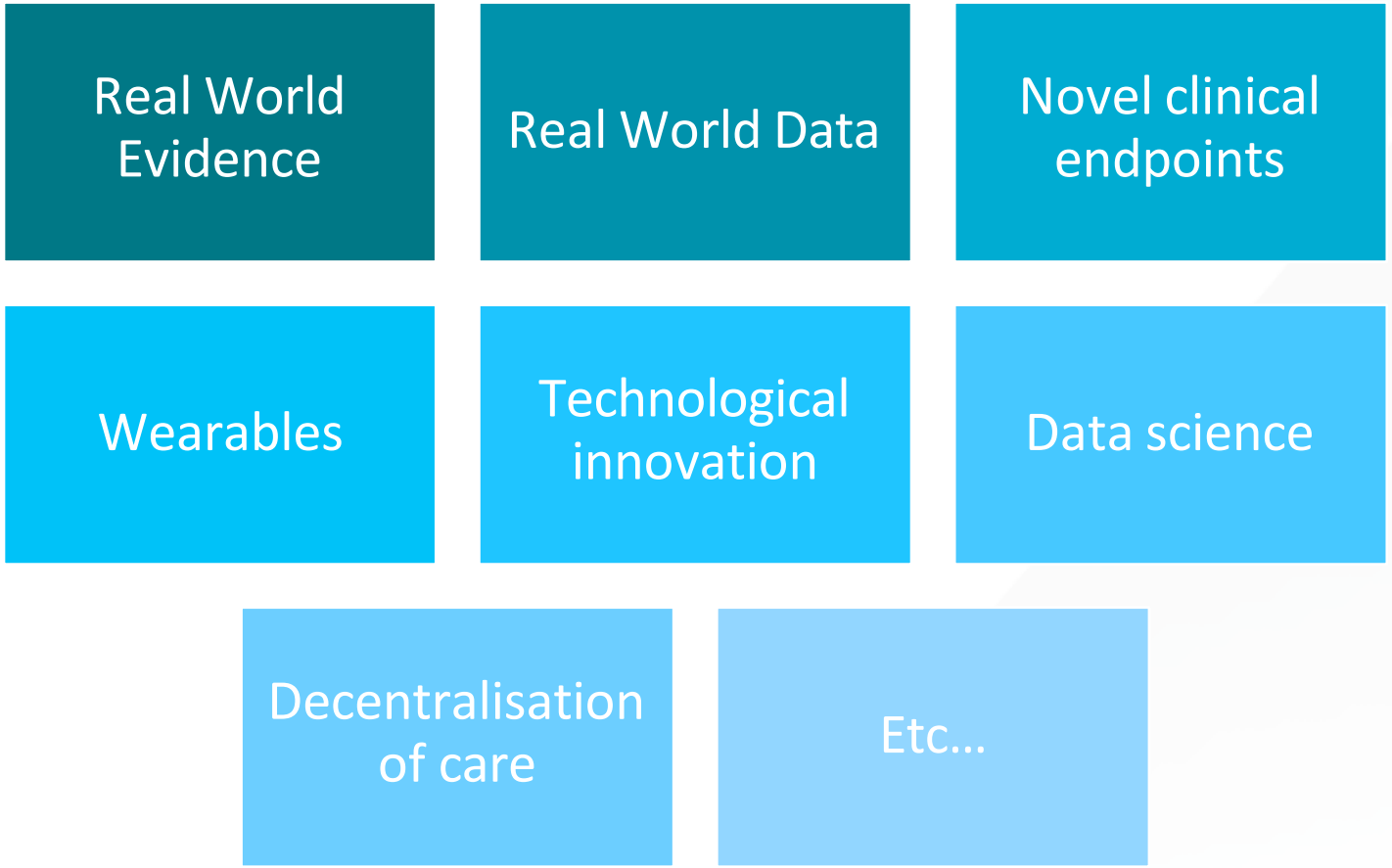
Linking DCT approaches to other innovations



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Should we move trial activities to participants homes?

Share learnings

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Thank you!

Further information on T@H and RADIAL:

Project website www.trialsathome.com
Contact us at trialsathome@umcutrecht.nl
Mira Zuidgeest m.g.p.zuidgeest@umcutrecht.nl

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