DIGITALISEREN VAN DE ZORG –DE BLIK VAN DE CCMO VANUIT EUROPA

- Digitaliseren van indienen protocollen
- Digitaliseren van het toetsingsproces
- Gebruik van data ipv ongestructureerde informatie
- Digitaliseren van klinisch onderzoek

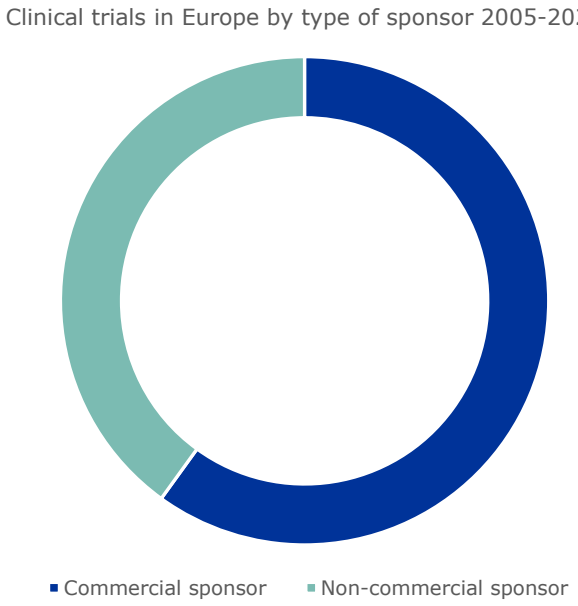
ACRON Najaarssymposium
Digitaliseren in de zorg
1 november 2022

Stan van Belkum
CCMO, The Netherlands

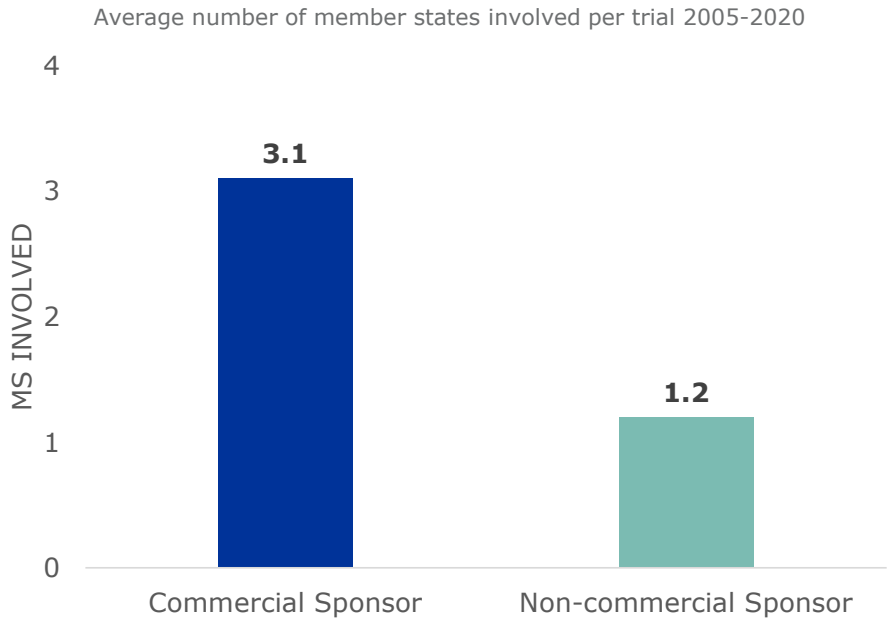
De Europese context

The climate for clinical trials in the EU

40% of clinical trials are non-commercial



Non-commercial CTs are predominantly mono-national

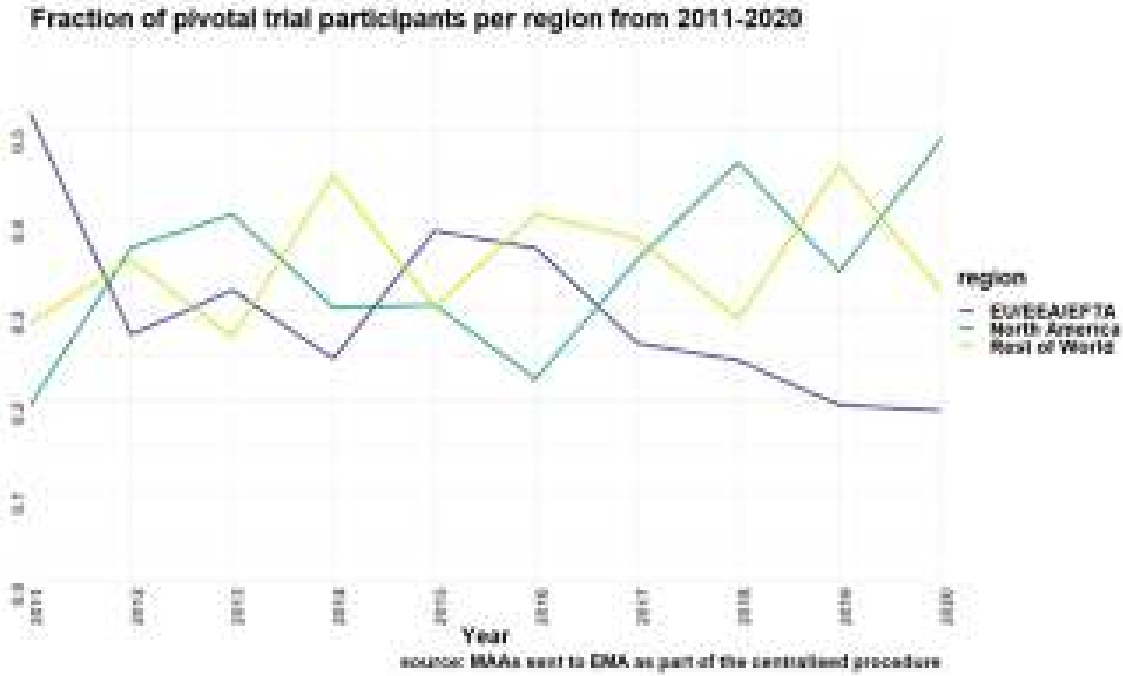


The fraction of EEA trial participants is trending downwards

European trial participants in centralised procedure MAAs:

- Constituted only **19%** in 2020
- Has been **trending downwards** since 2015

Points towards the absence of impactful COVID-19 multi-state trials



- *Vaccines & therapeutics*
- *UK included as Rest of World*

Accelerating Clinical Trials in the EU (ACT EU)

ACT EU is an initiative to **transform the EU clinical research environment** in support of medical innovation and better patient outcomes.

- **Builds on the momentum** of the Clinical Trials Regulation and CTIS
- **Driven by** the Network Strategy to 2025 and the EU Pharmaceutical Strategy
- Launched 13 January 2022
- Read the press release and paper

ACT EU objectives

Support the conduct of **large, multinational trials** with specific support for:

- SME, academia and Health Technology Assessment bodies (HTAs); and
- Trials which address unmet needs, rare diseases & medicines for public health crises

Facilitate **coordinated scientific advice** to support trial authorisation, marketing authorisation & the medicine lifecycle

Ensure **a unified European approach** for trial processes and strategic matters at the international level

Engage all stakeholders to deliver inclusive patient-oriented medicines development and delivery across populations

ACT EU Priority actions and domains 2022-2023

Governance & Integration

1. Develop a **governance rationalisation strategy** (aligning different expert groups and working parties)

7. Reinforce the **coordination** between **scientific advice on CT approval and CT design** and link to the methodologies working party domain.

9. Successfully establish **CT safety monitoring** and bridge to the EU4Health Joint Action and start its integration into a pre- and post-marketing safety monitoring framework.

Engagement

3. Establish a **multi-stakeholder platform**, including patients, after stakeholder analysis.

6. Plan and launch a targeted **communication campaign** to engage all enablers.

10. Deliver a clinical trials **training curriculum** on drug development and regulatory science with links to SMEs & academia.

Methods & Practice

4. Implementing the **GCP modernisation** informed by the development of guidance at ICH.

8. Develop and publish key **methodologies guidance** e.g. on AI/ML impacted CTs, complex trials, decentralised CTs and IVDR/CTR interface (to strengthen links between innovation and scientific advice fora).

Impact

2. The successful and timely **implementation of the CTR** and its implementing acts.

- **KPIs** to track performance of the European CT environment.
- **Promote larger, multinational trials** specifically in academia

5. **Analyse data about clinical trials** leveraging academic, non-profit, European, and international initiatives, improving the impact of policymaking and funding to support evidence-based decision making.

Steering Group highlights for 2022

28 Oct 22

- Monkeypox lessons learned (PA2)
- Simultaneous national scientific advice pilot (PA7)

25 Nov 22

- CTIS planning 2023/2024
- Process to prioritise and resolve CTR blocking issues (PA2)
- DCT recommendation paper (PA8)

20 Dec 22

- Training strategy concept paper (PA10)
- Multi-stakeholder platform concept paper (PA3)
- Steer on governance rationalisation criteria of core network groups (PA1)

EEN ONDERZOEK

Decentralized clinical trials

"The focal point of all study activities is no longer the research site, technology has enabled research to migrate toward participants, and participants should have a greater voice in how and where research assessments are conducted."

Beloften van DCTs

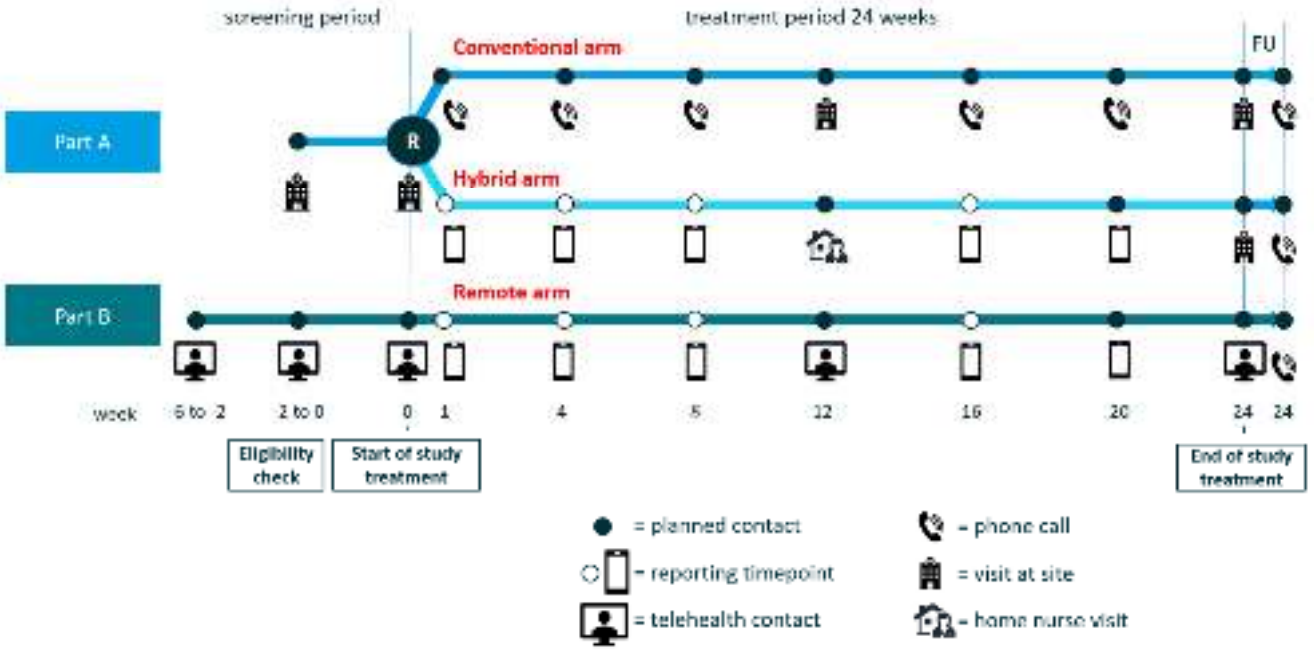
- Lagere belasting voor deelnemers
- Includeren van grotere en diversere populaties
- Verbeteren recruitment en retention
- Efficiëntie
- Betere data-kwaliteit en veiligheidsmonitoring
- Vergroten autonomie van deelnemers
- Frequenter contact mogelijk tijdens en na trial

UMC Utrecht

A Phase IV randomised, open label, multinational Decentralized Clinical Trial (DCT) to determine the real world effectiveness of Insulin Glargine 300 U/mL vs standard basal insulin with continuous glucose monitoring (CGM) in patients with Type 2 diabetes mellitus (T2DM)

Note: Not Final Protocol Content

Overview of the Trial Design



R = Randomisation / FU = Follow Up

"Mock ethics review": Beoordeling van voorbeeld protocol door leden van Europese ethische commissies

The research leading to these results has received support from the EU/EFPIA Innovative Medicines Initiative [2] Joint Undertaking (n°853988-JTI-IMI2) Trials@Home grant n° 831458.

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Patient Technology Interactions

Study Webpage
(Landing page for outreach campaigns, provides Introduction to the trial)

Study Nurse / Study Coordinators
(Acting as first level contact & tech support to participants)

MEMS app
(Provides feedback to the participant about their medication adherence and connects with the injector pen cap and acts as conduit to forward the pen data)

Clinpal/RADIAL Study app & electronic portal
(Provides pre-screening questionnaire, screening support, learning management, informed consent, eCRF and via the app access to eDiary, ePROs and connects to the Glucometer. Also includes reminders, engagement communication messages, and the ability to contact the site via the app)

Smart Insulin Injector Pen
(Used to automatically track intake of treatment)

Virtrial app and portal
(Provides Video Conferencing capabilities to participants)

Signant Randomization and Trial Supply Management (RTSM)
(Used for the management of study kits shipped to patients)

Marken Logistics and label printing system
(Used to ship study kits to the Patient's home)

Blood Pressure Monitor
(Used by participants to check their blood pressure and heart rate)

DCT elementen in voorbeeld protocol

Recruitment and enrollment	Via Social media and patientenorganizaties Online pre-screening vragenlijst Telefonisch contact
Informed Consent	Informatie verstrekking via studie app eConsent in videogesprek
Screening	Maakt gebruik van elektronisch patientendossier
Identificatie van participant	eIDAS gecertificeerde identificatie methode
Drug dispensation	IMP direct-to-patient (DTP) shipping vanuit centrale apotheek
Training participanten	Videogesprek met onderzoeksmedewerkers Web-based Studie Platform
Data collection	ePROs in the studie app Continuous glucose monitoring device Electronische insuline pen adaptor dop meet insuline dosering en injectie data
AE/SAE identification	Videogesprekl gebaseerd op zelf-rapportage ePROs and reviewen van gegevens uit de studie app
Engagement/encouragement	Digital/app engagement strategieen

Resultaten van mock ethics review

- Terughoudendheid ten opzichte van DCT
- Extra veiligheidsrisico's en belasting voor participanten geanticipeerd
- Inclusie bias geanticipeerd
- Impact van gebrek face-to-face contact op vertrouwen en motivatie
- Onduidelijke verdeling verantwoordelijkheden
- Weinig aandacht voor mogelijke voordelen

- Toename regulering door het stellen van extra eisen of vragen om rechtvaardiging (handtekening is altijd een mooi voorbeeld)
- Meer empirisch bewijs en ethische reflectie nodig over risico's en voordelen van DCTs voor evidence-based beoordeling

Enkele voorzichtige conclusies

- Als je kijkt vanuit bestaande kaders (Informed consent, veiligheid en privacy & wetenschappelijke validiteit en data kwaliteit), mis je de impact van digitalisering op de praktijk en beoordeling
- Kijk ook naar het bredere perspectief:
  - Relationele aspecten, vertrouwen
  - Vrijheid en autonomie
  - Rechtvaardigheid, bias, en generaliseerbaarheid
  - Privacy is meer dan dataprotectie
  - Verantwoordelijkheid
- Richtlijn is nodig, maar niet alleen

DE CONCEPT ‘RECOMMENDATION’

Facts and figures

- Al veel activiteiten op dit onderwerp
- Nu: ACT-EU → CTCG + GCP/IWG + CTEG (+WP's) → groot projectteam
- Projectlead: DK en SE
- Doel: uniformering en harmonisering in de EU
- Opdracht: "Recommendation paper on the implementation and conduct of decentralized elements in clinical trials with investigational medicinal products in the European Union"
- NL is schrijver (Monique Al, Solange Levison)
- Eerste versie Q4 2022 publicatie
- Attentiepunten:
  - Volgt EU wetgeving & al bestaande richtlijnen
  - Focus is op decentrale elementen in de uitvoering van onderzoek
  - Volledige DCT en virtuele onderzoeken buiten de scope
  - principes en regels van traditioneel onderzoek niet herhalen
  - Geen definities
  - Betrek patiënten en onderzoekers
  - Zorg voor robuuste gegevensAdequate technologie

Belangrijke elelementen in de aanbeveling:

- **Rollen en verantwoordelijkheden;** hoe hou je goed overzicht, meer partijen, heldere communicatie, meer data: sponsor en onderzoeker
- **Informed consent:** hybride vormen, interview, PIF en tekenen
- **Versturen en toedienen onderzoeksmedicijn:** patiëntgegevens, verantwoordelijkheden, gebruik, bewaarcondities
- **Onderzoeksprocedures thuis:** situatie, wat kan wel/wat niet, hulp
- **Onderzoeksdata:** meer gegevens verzameld, bewustzijn
- **Monitoring onderzoek:** op afstand toegang tot data; wel/niet onderdeel receommendation

Consulatie in het EU regulatoire network, publicatie eind 2022

Thank You!

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