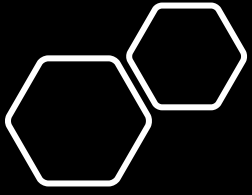


Marc Janssens

Senior Manager Clinical Operations, Benelux

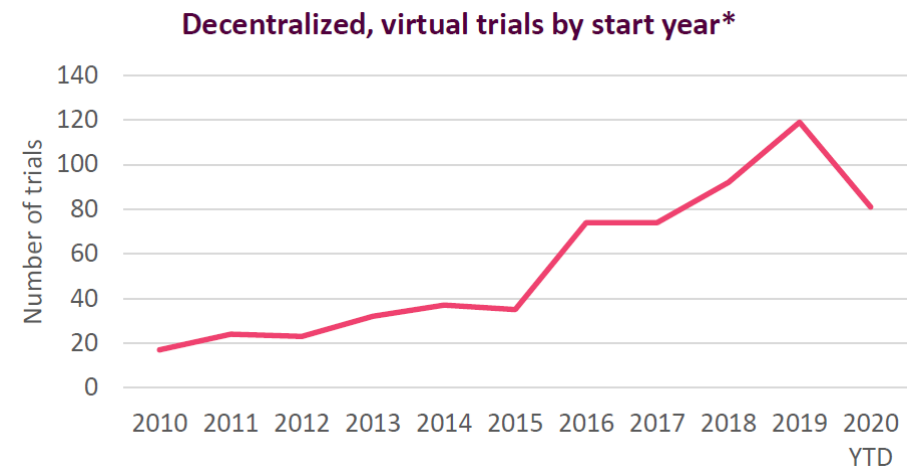
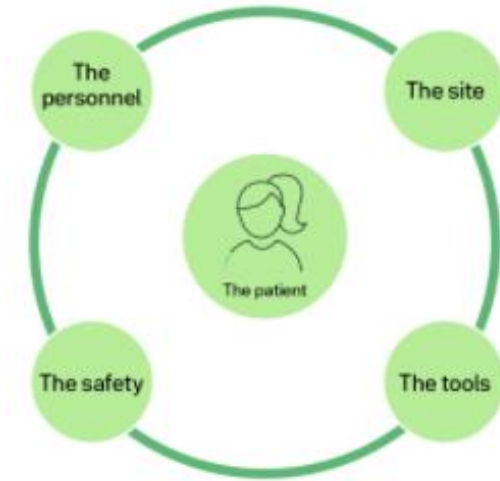
Amgen

Decentralized Clinical Trials | What's the fuzz?

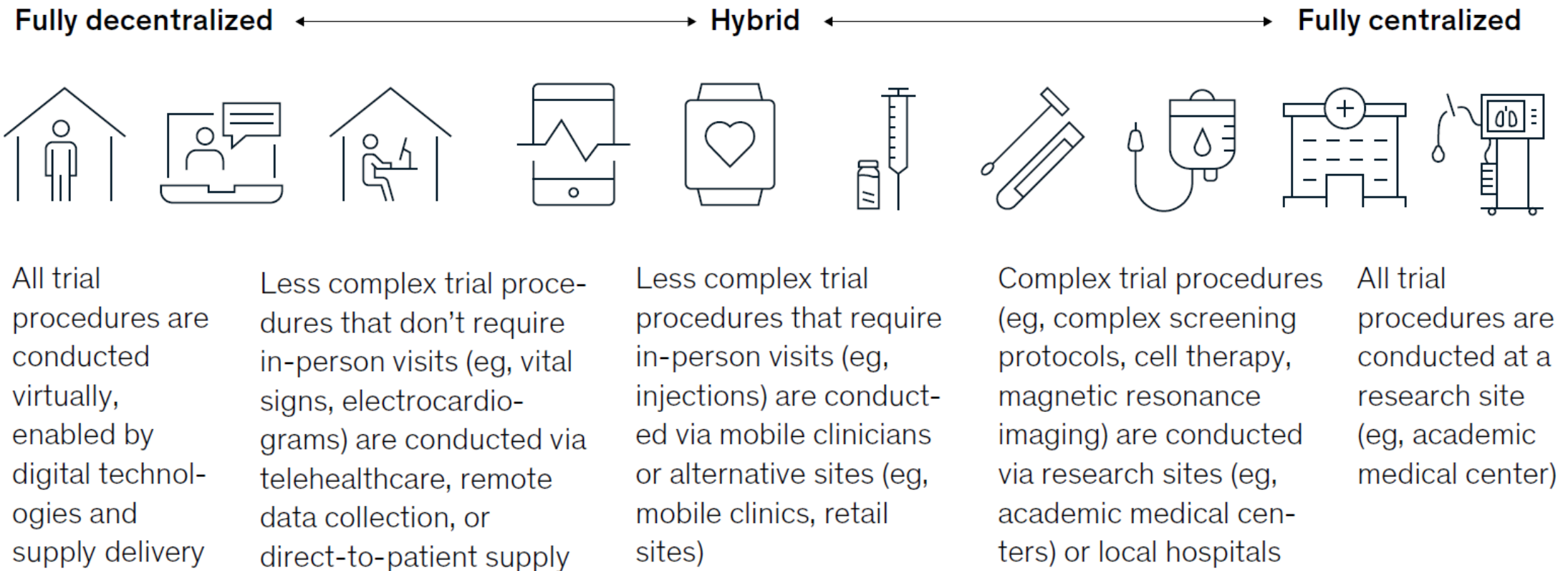


The case for change

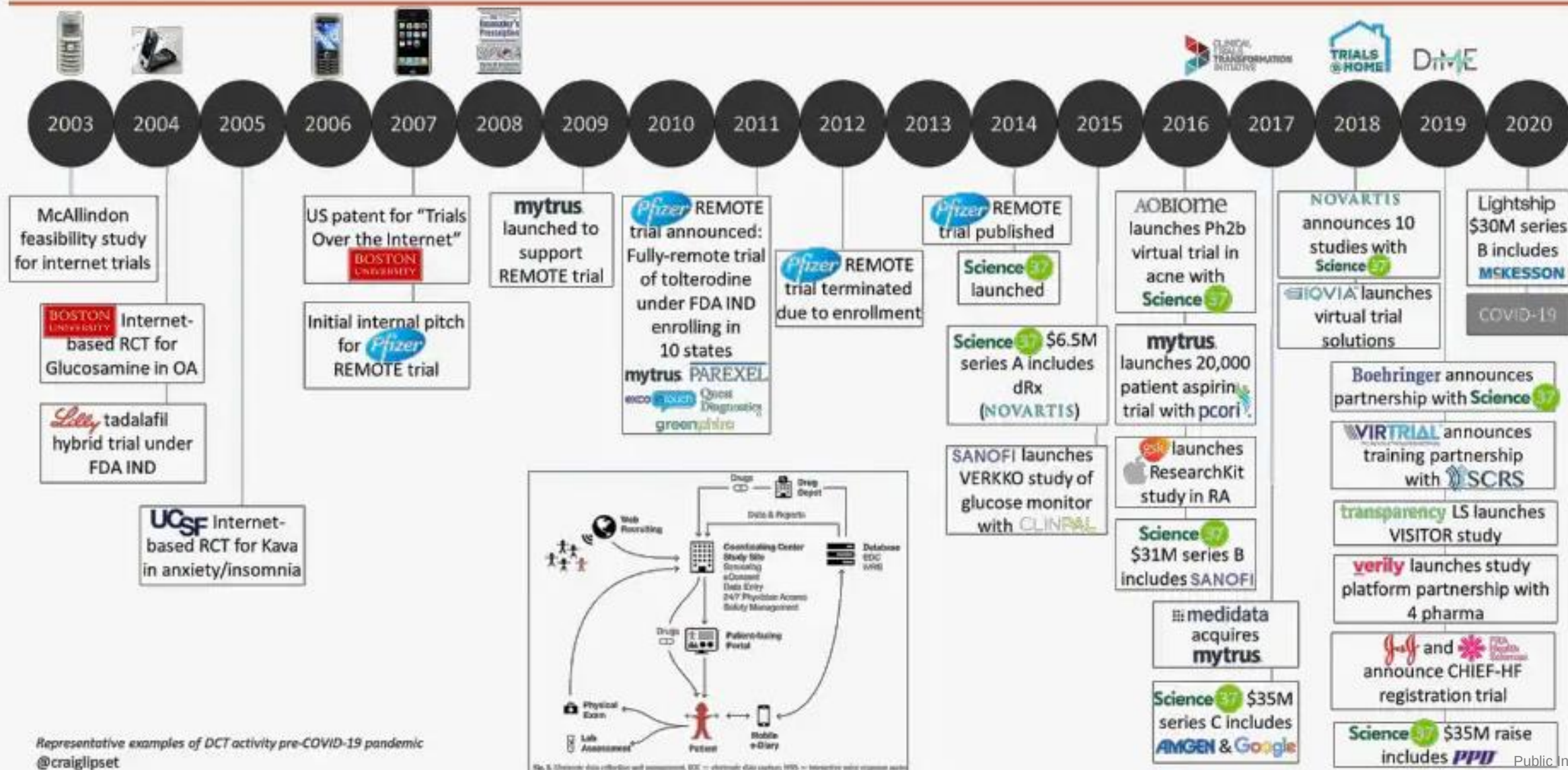
- 50 – 60% of RCTs do not meet original recruitment target or face significant delay's
- Complexity of clinical trial designs and increased number of participant visits and procedures
 - Negative impact on willingness to participate
 - Distance to trial site is a major barrier for participation
- Increasing importance of patient centricity and RWD (real world data)
- Bussiness continuity during Covid-19 pandemic required major changes in clinical trial conduct

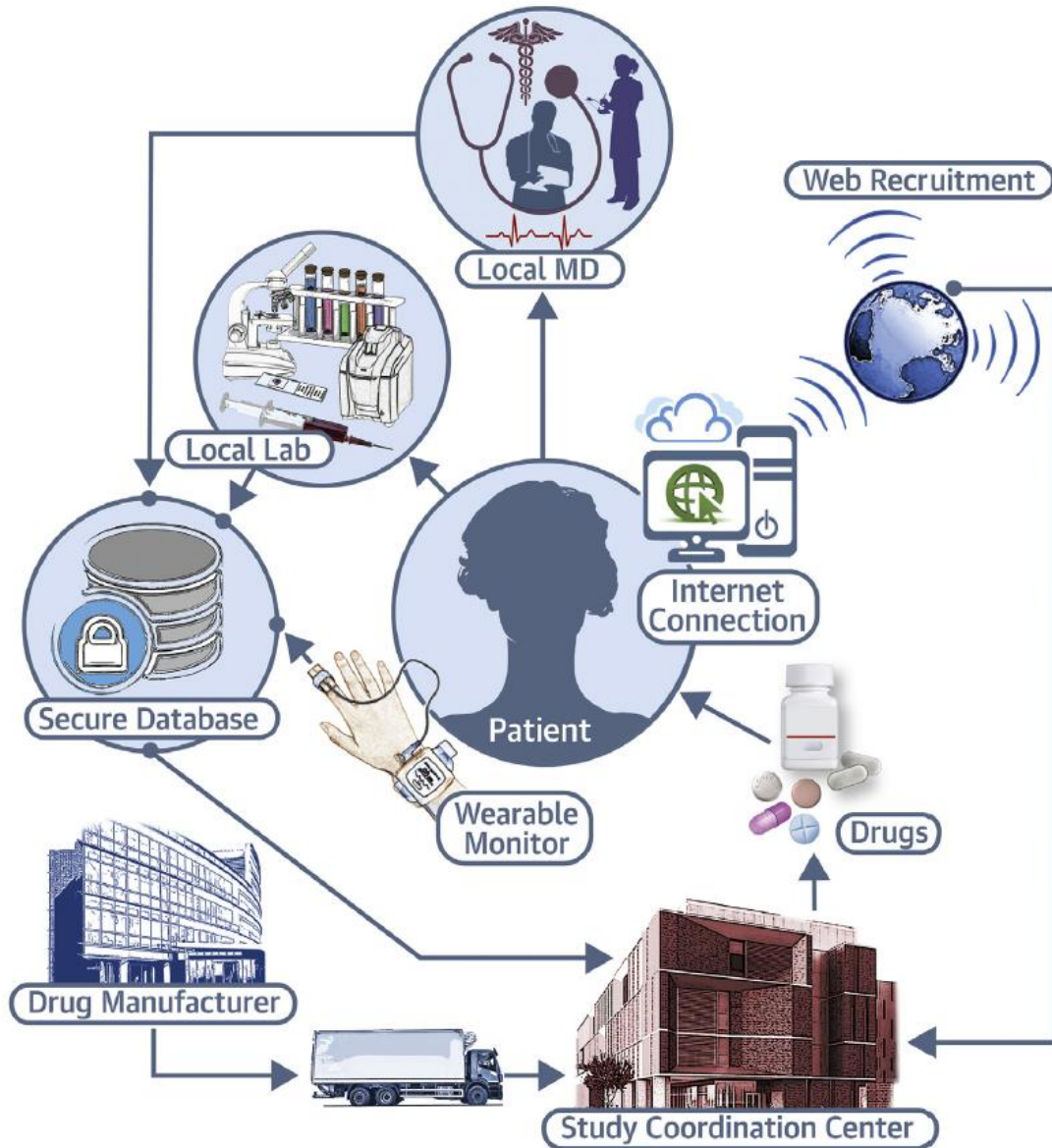


DCT = decoupling clinical research activities from the physical site location



Pre-Pandemic DCT: 17-year History Prior to COVID-19





Digital evolution drives innovation

- Datacollection - eg. wearables, direct data capture, blockchain technology...
- Recruitment and retention through AI, machine learning
- Telemedicine and the use of mobile apps for disease assessments (eg. dermatology assessments,...)

Reaching underserved patient populations more easily – increased diversity in participants leading to increased external validity of the data

Real world examples

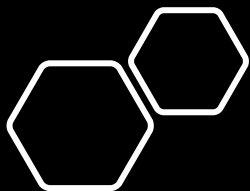
Sponsor	Year	Phase	VCT/hybrid	Detail	Enrolled
Duke University [19]	2016–2020 (estimated)	NA	VCT	Compare the effectiveness of two doses of aspirin to identify the optimal dose for secondary prevention in patients with atherosclerotic cardiovascular disease	15,000 (estimated)
Hoffmann-La Roche and Genentech [30]	2015–2019 (estimated)	Phase 3	Hybrid	Evaluate the efficacy and safety of rituximab compared with mycophenolate mofetil in participants with pemphigus vulgaris	135
Eli Lilly [20]	2017–2018	Phase 4	Hybrid	Estimate missed bolus insulin doses in diabetics	79
AOBiome [25]	2017	Phase 2b	Hybrid	Topical probiotic spray for mild-to-moderate acne	372
PellePharm [26]	2016–2017	Phase 2	Hybrid	Topical patidegib for basal cell carcinomas (Gorlin syndrome)	36
Sanofi [17]	2014–2015	Phase 4	VCT	Remote system to diabetes management	60
Pfizer [15]	2011–2012	Phase 4	VCT	Efficacy and safety of tolterodine ER 4 mg in participants with overactive bladder	18

- Initial results have shown that decentralization works in comparison with the traditional model:
 - Several studies ongoing comparing the traditional approach in multiple physical centers with 1 virtual site
 - VERKKO study vs traditional design – increase in patient compliance, faster recruitment and less study coordination activities
 - REMOTE study in overactive bladder, confirmed results of traditional clinical study
 - Several fully decentralized studies in Covid-19 patient population have been reported

Real world examples

Summary: Visits & Procedure	Traditional Trial (Current Method)	DCT (Future Method)
Subject Identification	Totally based on the clinical practice of the investigator's site	Mapping of trial information with the potential subject pool (subject data pool to be created based on social media listening, data from healthcare, payers, legacy information, patient registries .etc.)
No. of visits to site	More	No visit needed
Informed Consent	Traditional Approach	eConsent remote
Blood Glucose Levels	Info provided at visits to site	Data transmitted remotely
ECG	During visits schedule as per protocol	Data transmission through connected wearable devices
Labs	Clinic visits & home pick up	Data transmission through connected wearable devices
Concomitant meds	During visits schedule as per protocol	Remote/ eDiaries
Adverse events	During visits schedule as per protocol	Remote/eDiaries
Physical exam (Temperature, Blood pressure, Pulse, Respiratory Rate)	During visits schedule as per protocol	Data transmission through connected wearable devices
Study Medicine (IP)	Dispensed as per visits schedule in protocol	Sent through courier or information collected through payers
Instruction to use IP	Clinical visits, instructions given by site staff to the subject	Telemedicine , 24/7 access to valuable online tools and resources
Review by physician	During visits schedule in protocol	Remote
QoL questionnaires	Clinical visits, data collected by site staff by asking questions to patient	Remote/ eDiaries
Monitoring	SDV done at site, as per monitoring plan	Exhaustive remote monitoring
Diary card	Paper based	eDiaries

Protocol development done based on available technologies and not on traditional knowledge
Wearables need to be Qc-ed and validated throughout the project
Decision and oversight documentation is crucial



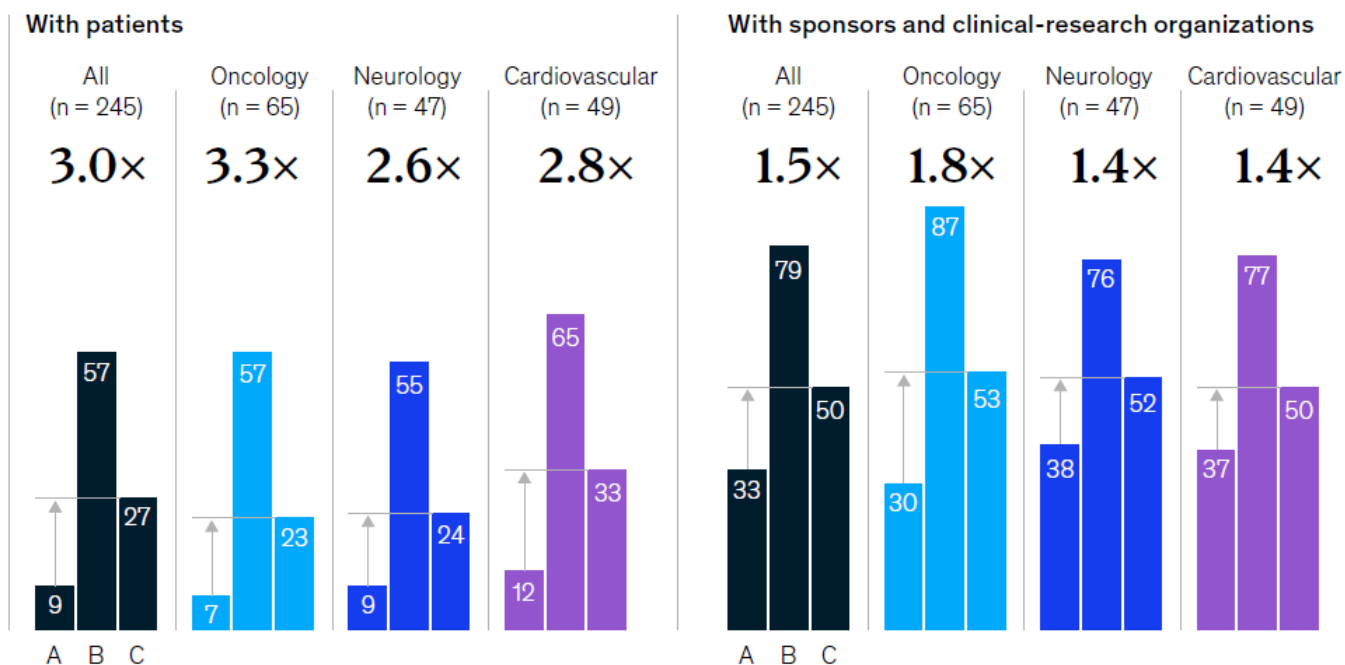
Physicians comfort with remote technologies has increased as a result of the Covid-19 pandemic

Covid-19 has served as a catalyst as business continuity and patient safety were crucial

- Many sponsors are adapting DCT elements as a standard

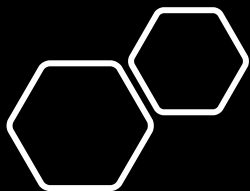
Clinical-trial investigators' share of virtual interactions, % of respondents¹

A. Pre-COVID-19 crisis B. At crisis peak C. 6 months postcrisis



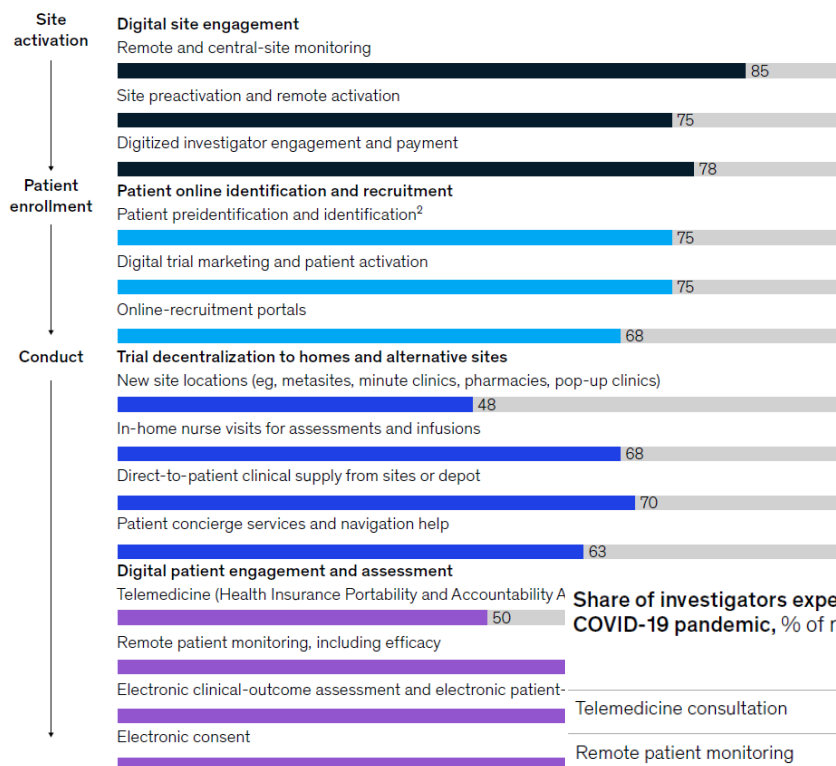
¹Average reported by investigators. Questions: Within your clinical trials, what share of patient interactions do you conduct remotely? How do you expect this to change in future?

Source: John Z. Xue et al., "Clinical trial recovery from COVID-19 disruption," *Nature Reviews Drug Discovery*, September 2020, Volume 19, pp. 662–3, nature.com; McKinsey Global Survey of Clinical Trial Investigators, May 8–18, 2020

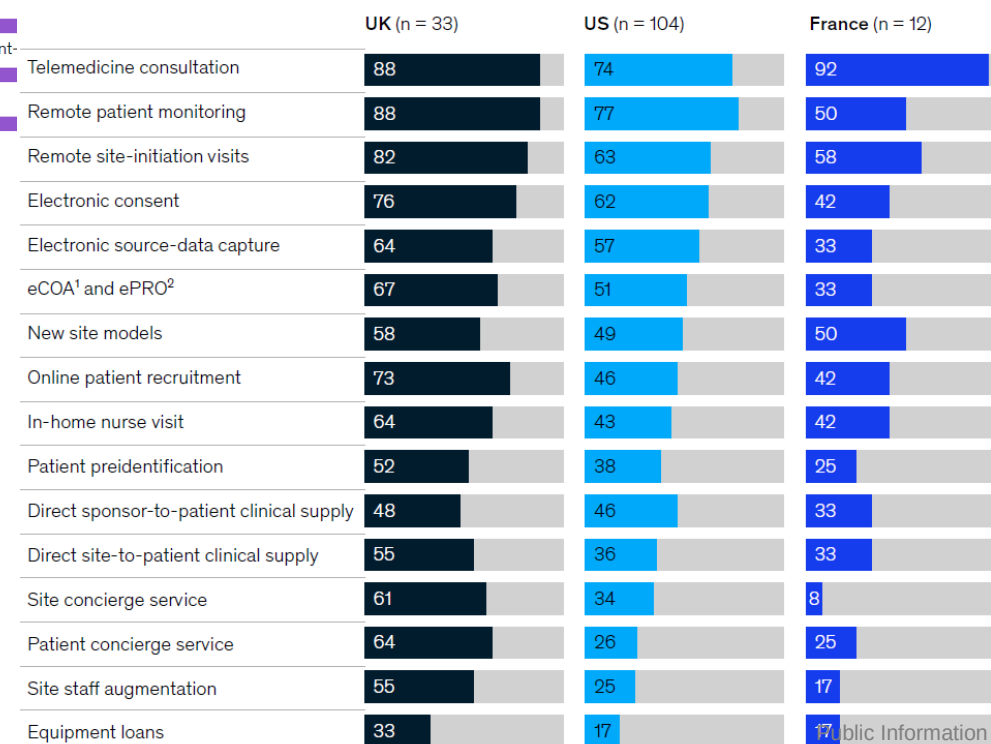


Activities that enable decentralised trial conduct

- Amgen decentralized activities :
- Remote site initiations/evaluations
- Risk based monitoring including central monitors
- Automated payment systems
 - Based on entries in clinical trial database
- Patient pre-identification based on automated searches in EMR
 - Through specialized software like CTCue
- Patient recruitment based on google searches
- Home nursing (selected trials only) including concierge service
- DTP supply (site to patient)
 - Currently restricted as Covid-19 urgent measure
- Telemedicine solutions
- Remote monitoring of end-points based on wearables
 - iPhone activity tracker to track length of migraine attacks
- eCOA via tablets/mobile devices
- eConsent (pilots)



Share of investigators expecting increase in use of decentralized clinical-trial procedures after COVID-19 pandemic, % of respondents (n = 245)



¹Electronic clinical-outcome assessment.

Benefits of Decentralized Clinical Trials

- There is general recognition that DCTs benefit the industry, patients, and caregivers in many ways:
 - Patient Centricity
 - Population Diversity
 - Patient Recruitment
 - Patient Retention
 - Collection of Additional Data
 - Reduction in Source Data Verification
 - Additional Capacity at the Site
 - Pathway to Virtual Clinical Trials

Challenges for decentralization

Not suitable for all RCT's (dose finding, biopsy guided treatment decisions, imaging, ...) and all indications (eg. elderly,...)

Guidelines on compliance expectations for DCTs are lacking.

- Oversight of different parties including mobile HCPs

The need to adapt internal quality management systems (e.g., policies, SOPs, training) driving consistency in approach

The learning curve for project teams, sites, patients, and caregivers.

Differences in telemedicine laws that may preclude some site-to-patient interactions, GDPR and IS security challenges protecting subjects privacy and informed consent procedures

- Especially challenging in Europe

The difficulty of harmonizing the aggregation of large amounts of data when using mobile sensor devices.

The chain of custody of the investigational product if sent directly to patients.

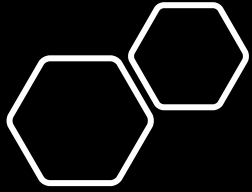
The investment in regulatory compliant technologies that are easy to use.

Qualifying technologies prior to their use, to ensure safety, quality, and compliance.

- Heavily reliant on technological advances

Some clinical trial participants see the F2F interaction with clinical trial personnel as a benefit

Safety follow-up of trial participants through telephone or telemedicine



What does the future hold?

- Will we ever need placebo?
- Will AI design our trials?
- Will “Big Data” become bigger?
- How vulnerable is our technology?
- When will Meta and Google start with clinical trials
- Will we ever need patients?
- What about privacy, data ownership and transparency?
- What’s the role for adaptive trial designs?
- Will technological advances introduce a new bias in clinical trial?

