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Single Day Event

Decentralization – Meeting Patients Where They Are …

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Buzzwords !!!

BYOD Devices eConsent Digital

Engagement Tele visit Remote Native Apps

Hybrid Process Efficiency Unified

Biomarkers Inclusion eSource Orchestration

Virtual Siteless eCoA Community

Decentralized Clinical Trial (DCT) - *Definitions*

U.S. Food and Drug Administration (FDA) (Eric Pittman): Defines DCTs as "clinical trials using digital technologies to have remote interactions with real subjects"

FDA (Eric Pittman): Defines virtual trials as "preclinical trials conducted in silico or on models"

Academic Perspective: DCTs are those that use remote technologies (mHealth, sensors, telemedicine, etc.) to interact with subjects away from central research facilities.

Clinical Trials Transformation Initiative (CTTI): DCTs are defined as "those executed through telemedicine and mobile/local healthcare providers, using procedures that vary from the traditional clinical trial model (e.g., a study where investigational medical products are shipped directly to the trial subjects)."

DCTs - *Overview*

- Virtual
- Digital
- Remote
- Site-less
- Direct-to-Patient

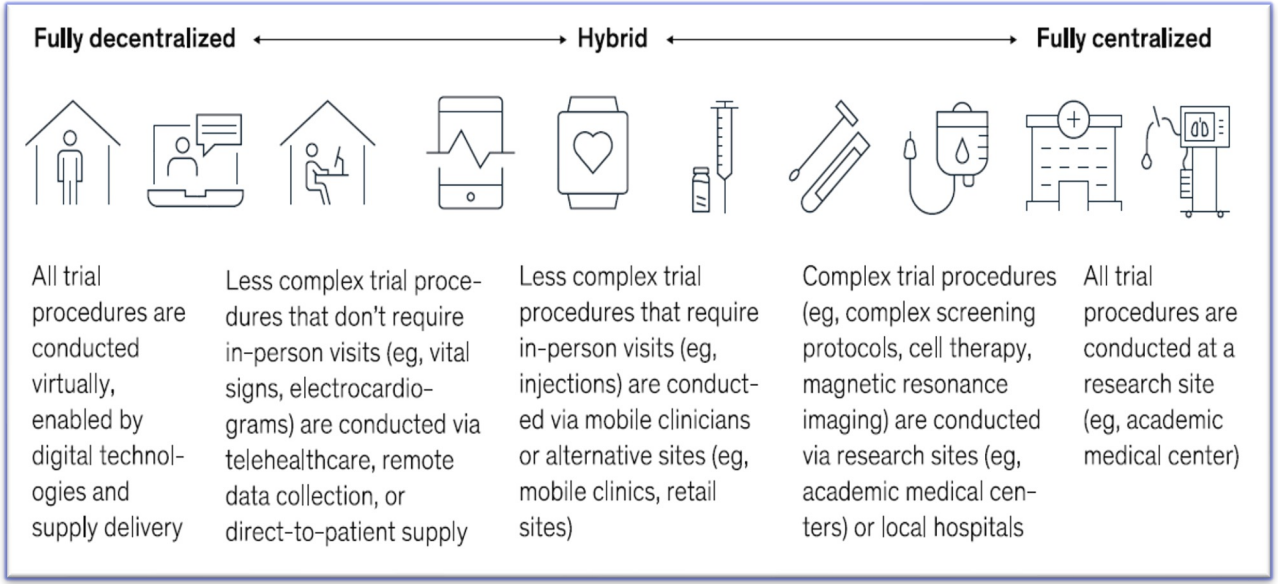
GOAL

Make Clinical Trial Easier for Patients, Caregivers and Industry

- Patient Recruitment
- Population Diversity
- Remote Data Collection
- Reduced SDVs
- Additional Capacity at Site
- Patient Centricity
- Patient Retention

Decentralization is a transformational philosophy for the conduct of clinical trials; fewer in-clinic visits; patient and caregiver burden is reduced; and a wide range of digital technologies deployed

DCTs - *Clinical Trial Designs*



The key feature of a decentralized trial is that most or all study data are collected away from a central research facility. Hybrid DCT trials include a more balanced mix of centralized and decentralized elements. The relevant feature is the location of the subject's interaction.

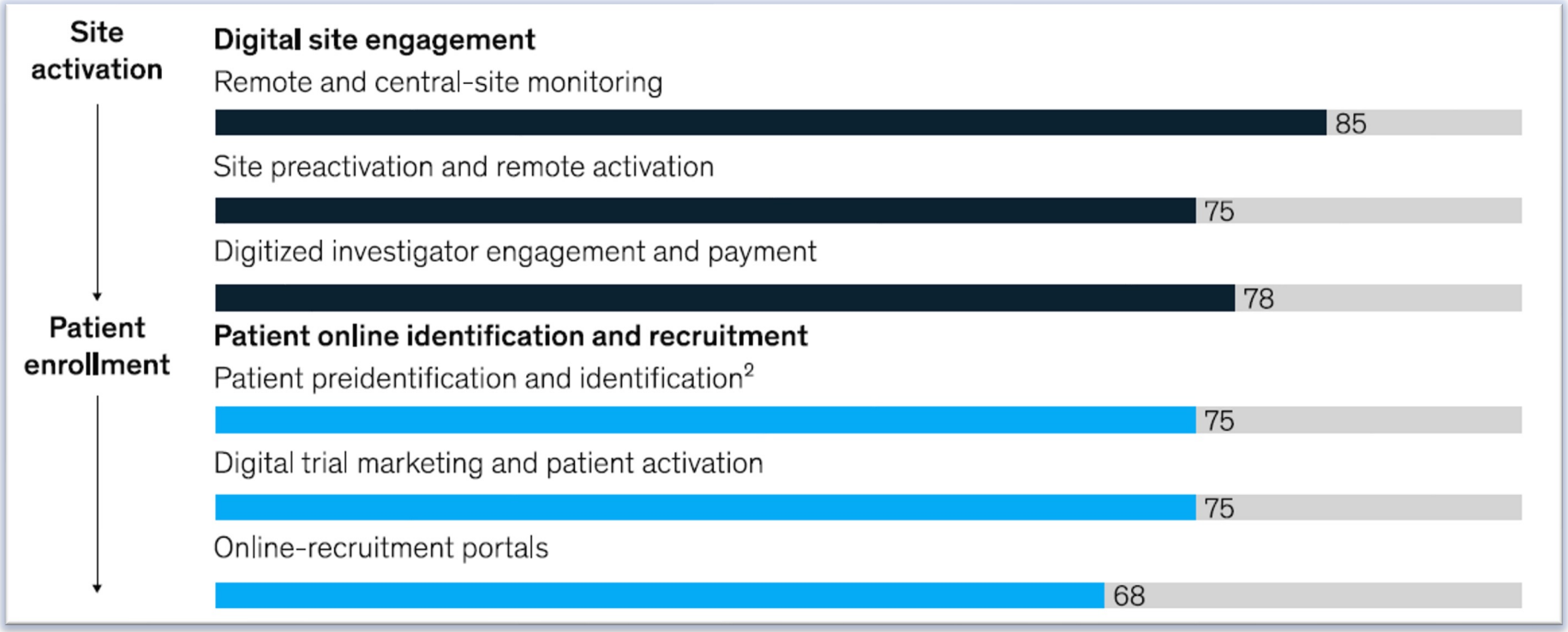
Decentralization broadens trial access to reach larger number and potentially a more diverse pool of patients. The relevant feature is the location of the subject's interaction and / or method of interaction.

Unfit For DCT, Even Hybrid !!!

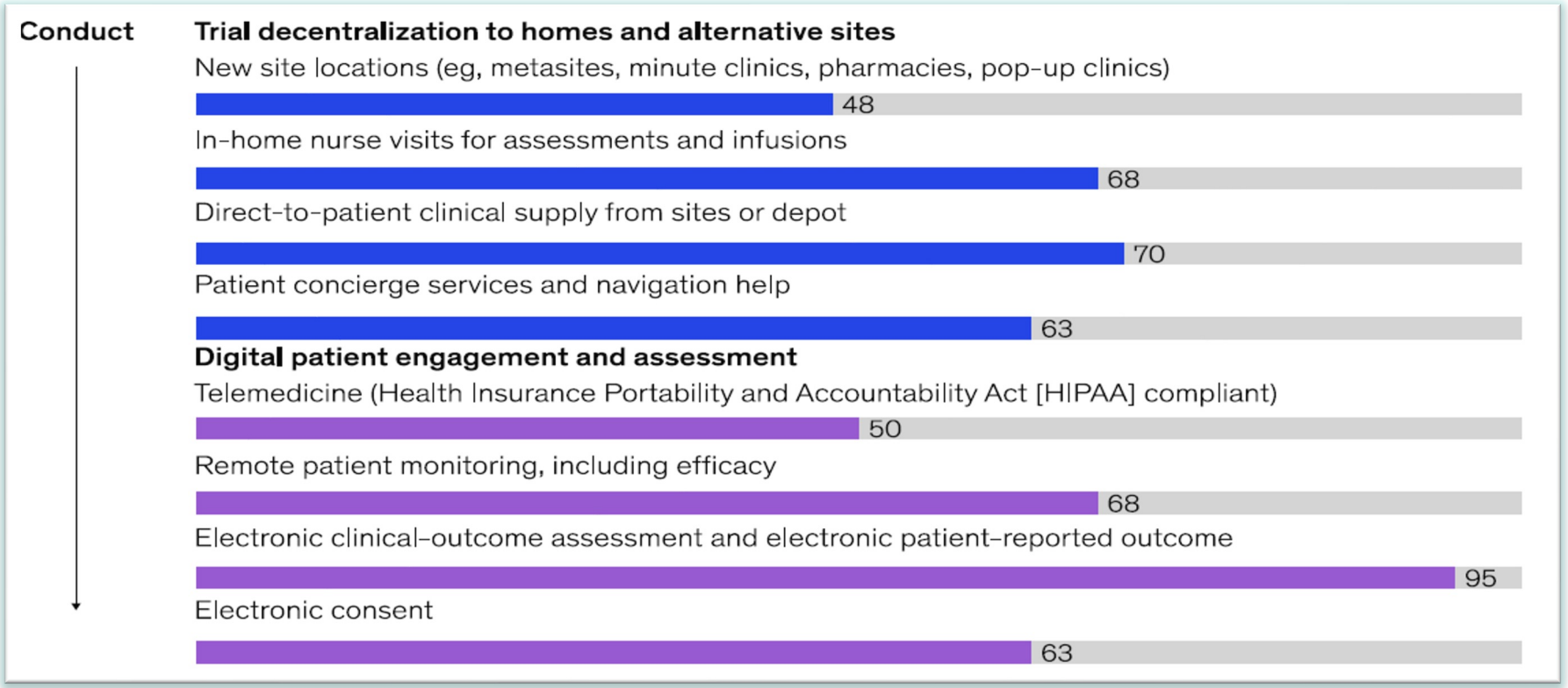
	Screening	Treatment period													Protocol section
Visit Week[1]	1 -4 to -2	2 0	3 1	4 2	5 4	6 6	7 8	9 12	10 14	11[14] 14PK	12[14] 15PK	13 16	15 20	17 24	
Day	-28 to -14	1	8	15	29	43	57	85	99	V10+3	V10+7	113	141	169	
Visit window (days)[2]	NA	NA	±1	±1	±3	±3	±3	±3	±3	±1	±1	±3	±3	±3	
Investigator assessments of efficacy															
PASI	X	X	X	X	X	X	X	X	X			X	X	X	11.3.1
BSA	X	X	X	X	X	X	X	X	X			X	X	X	11.3.2
sPGA	X	X	X	X	X	X	X	X	X			X	X	X	11.3.3.1
sPGA-G[7]		X	X	X	X	X	X	X	X			X	X	X	11.3.3.2
Substudy assessments at selected sites – Pharmacodynamics															
Skin and SAT biopsy[8]		X										X			11.6.2.1
RH-PAT[8]		X										X			11.6.2.2
Suture removal[8]				X[3]									X[3]		11.6.2.1
Investigator assessments of safety and PK and pharmacogenomics sampling															
AEs and SAEs	X	X	X	X	X	X	X	X	X			X	X	X	13
Vital signs	X	X	X	X	X	X	X	X	X			X	X	X	11.4.1
Physical examination	X	X						X						X	11.4.2
Body measurements[9]	X	X						X						X	11.4.3
ECG	X	X												X	11.4.4
Biochemistry[10], haematology[11], urinalysis[12]	X[10,11,12]	X			X		X	X				X	X	X	11.4.5
Pregnancy test[13]	X	X			X		X	X				X	X	X	11.4.5
Anti-drug antibodies		X										X			11.4.6
PK blood sample[14]		X							X	X[14]	X[14]	X			11.5.1
Blood biomarkers		X										X			11.6.1
Pharmacogenomics[15]		X													11.6.3
QuantiFERON® or PPD test	X														11.4.5
HIV, HBV, HCV test	X														11.4.5
Patient-reported outcomes – Safety															
C-SSRS[16]	X	X	X	X	X	X	X	X	X			X	X	X	11.7.1.1
PHQ-8[16]	X	X	X	X	X	X	X	X	X			X	X	X	11.7.1.2

- Technology should enhance the patient's journey, not complicate it.
- It is a flexible continuum
- Start with a minimum and build to a full-fledged virtual trial
- Create an innovative solution to fit the study population and, produce effective outcomes

Activities Enabling Decentralization - *Views* (1/2)



Activities Enabling Decentralization - *Views* (2/2)



A Menu – *Choice Of Services & Technology*

Visit	Assessment	Setting	Patient miles traveled
1	● Physical exam ● Neurological exam ● ECG[1] ● Lab and drug tests	Clinical-trial site	89
2	● Vital signs ● Height and weight ● Pregnancy test	Virtual	0
3	● Vital signs ● Height and weight	Virtual	0
4	● Vital signs ● Physical exam ● Neurological exam ● ECG ● Lab and drug tests	Patient home	0
5	● Delivery training ● Vital signs ● Height and weight ● ECG	Virtual	0
6	● Vital signs ● Height and weight	Virtual	0
7	● Vital signs ● Height and weight	Virtual	0
8	● Vital signs ● Physical exam ● ECG	Virtual	0
9	● Vital signs ● Height and weight ● Pregnancy test	Virtual	0
10	● Vital signs ● Height and weight	Virtual	0
11	● Physical exam ● Neurological exam ● ECG ● Lab and drug tests	Mobile clinic	23

- Remote monitoring of visits, mobile clinics, home visits are of choice for hybrid designs
- Traditional site visits will still be needed for complex procedures and specialized assessments (screening, magnetic imaging etc.)
- Smart hybrid designs will use other touch points – virtual or closer to patients' homes (mobile clinics, primary care physician etc.)

Illustrative protocol for neuroscience-related Phase III trial (simplified and anonymized)

● In-person visit required
● Possible through digital/remote assessment

DCTs – *Enabling Technologies* *(Illustrative)*

Consent	*eConsent*
IMP	*Direct To Patient IMP*
Follow-up Visits	*Text / Video Chats / Tele-visits*
Vital Signs	*Devices / Wearables*
Paper Questionnaire	*ePRO / eCOA*
Sample Collection	*Home Health Nurse*
Adverse Events	*eAdverse Events Reporting*

Accelerate Enrolment | **Increase Comprehension** | **Influence Behaviour** | **Remote, Real-time, Accurate Data**

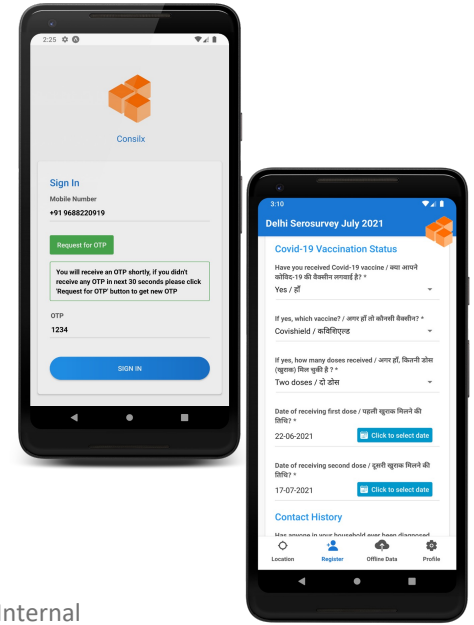
DCTs - *Experience Gained* *(During COVID-19 Pandemic)*

Pharma and CRO's response on the following questions	Industry Standard Research Survey (December 2019)	McKinsey's Clinical Operations Roundtable (December 2020)
Virtual trials and remote components as major part of portfolios	38%	100%
Expected to run trials with most activities done at patients' home	48%	89%

eConsent - *In COVID-19 Studies* *(Aug 2020 – Oct 2021)*

COVID-19 Sero-prevalence community-based studies in multiple Indian cities

50,000+ subjects successfully eConsented on a mobile App



eConsent App

- Multiple devices
- Unique KYC
- Online verification
- Multiple languages
- Multi-media support
- LAR option
- Questionnaire
- Off-line data capture
- Data sharing
- KPI dashboard
- Geo location

Mumbai
August 2020
12,613 subjects
Aged 8+ years

Mumbai
September 2021
8,644 subjects
Aged 18+ years

Delhi
August 2021
28,645 subjects
Aged 5+ years

Thane
October 2021
1,573 subjects
Aged 8+ years

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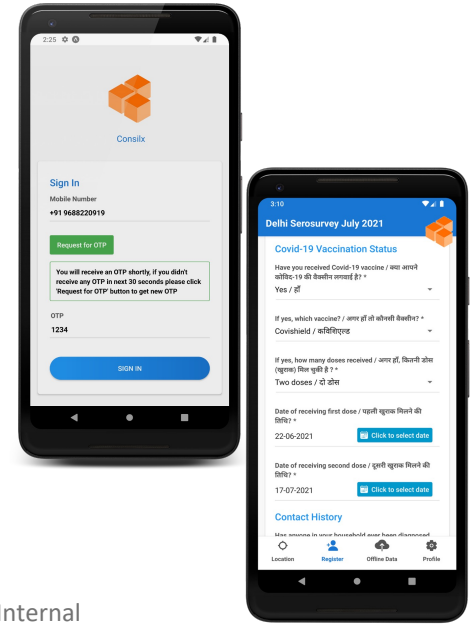


Outcomes Delivered

- Digital process delivering operational efficiency in large scale community-based surveys
- Real-time sharing of signed informed forms (pdf) with subjects through whatsapp / email
- Real-time SMS notification on subjects mobile phones about their consenting status
- Daily reconciliation between eConsent and lab database
- Geo location maps to check sampling plan adherence by field teams
- Performance reports within an hour post completion of survey for management review daily
- Test results shared with subjects within 3 days post sample collection
- Targets achieved in significantly lesser duration (40% time saved) compared with previous rounds using paper-based consenting process

DCT Components - *Increased Adoption*

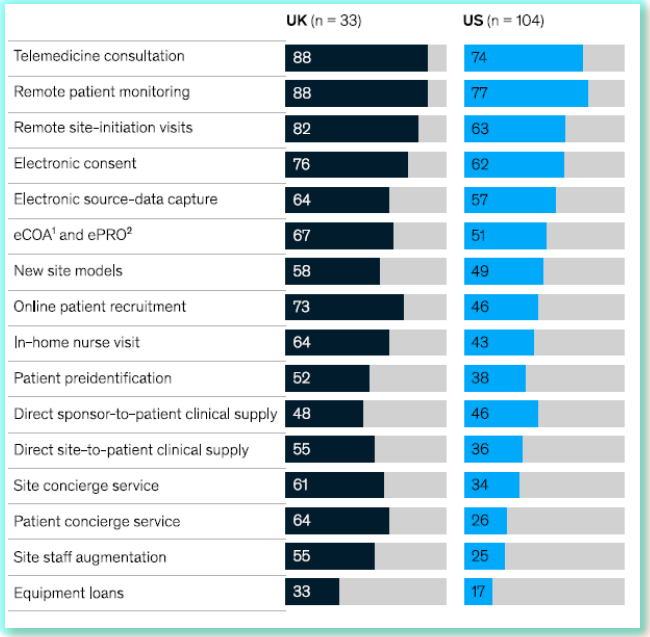
India

DCT Component	Allowance status	Source
E - consent		Source 1
E - signature		Source 1
e PRO		
IP supply		Source 2
Telemedicine		Source 2
Home nursing		
Wearables		
Home sampling		

RED:	YELLOW:	GREEN:
Regulation found, and activity not allowed.	Specific regulations not found. Conditioned acceptance	Regulation found, and activity is allowed

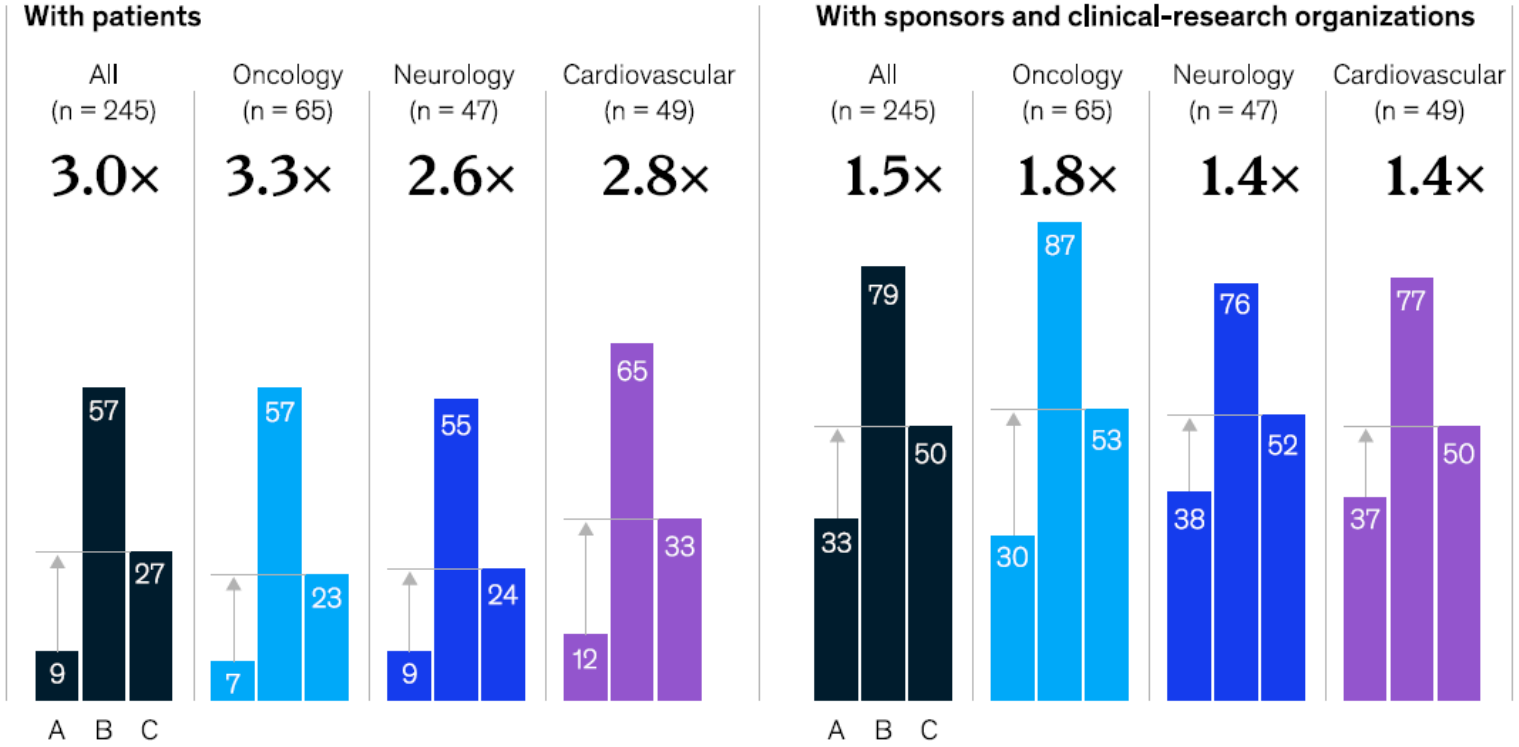
Sources:

1. National Guidelines For Ethical Committees Reviewing Biomedical And Healthcare Research During COVID-19 Pandemic (Indian Council of Medical Research, Apr. 2020)
2. Guidance for the Management of Clinical Trial Activitiesin response to COVID-19 Pandemic (ISCR, 2020)



Investigators in many countries have predicted an increase in patient-centric trial features following the COVID-19 pandemic

Investigator's Interactions - *More Virtual*



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

DCT – *A Medical Device Phase I Trial* *(Feb – May 2022)*

	Visit #1	Visit #2	Visit #3	Visit #4	Visit #5
Protocol-defined Location	**In-Clinic** 	**In-Clinic** 	**At-Home** 	**At-Home** 	**At-Home** 
Procedures	Consent Screening	Enrolment Baseline assessments IP administration Pain assessment Acceptability questionnaire AE assessment	Follow-up visit Pain assessment AE assessment	Follow-up visit Pain assessment AE assessment	Follow-up visit Pain assessment AE assessment
Solution / platform used	**eConsent** **eSource**	**eSource** **Direct data collection tools**	**Tele-visit** **Text & Video chat** **eSource** **eQuestionaire**	**Tele-visit** **Text & Video chat** **eSource** **eQuestionaire**	**Tele-visit** **Text & Video chat** **eSource** **eQuestionaire**

Outcomes

- Digitized all components involved in the conduct of the hybrid study (consent, data collection, acceptability, safety & pain assessments)
- Seamless experience in onboarding volunteers, executing consent at site, sharing the signed consent form with the volunteers on email
- Online data collection using eSource modules and real-time insights on missed data or if there were any issues
- Subjects completed pain assessment electronically – VAS; all data points related to timing of administration & measurements are tracked
- Tele-visit was successfully used to contact the subject for visits #3, #4, & #5 and AE assessments
- Effective coordination of multiple In-clinic and Tele-visits; real-time data visibility was well received by the study team and sponsor

DCTs – *Cumulative Experience*

S. No.	Phase	Area	Sites	Geography	No. of subjects	eConsent	Languages	eSource	Patient App
1	PoC		4	US, EU	40	Yes	1		
2	PoC	Cardiovascular	1	US	30	Yes	1	Yes	Yes
3		COVID-19	4	India	50,000+	Yes	3		
4	I	Medical Device	1	India	30	Yes	3	Yes	Yes
5	II	Nutraceuticals	6	India	200	Yes	3	Yes	Yes
6	II	COVID-19 Rx	8	India	200	Yes	4	Yes	Yes
7		Oncology	10	India	3000	Yes	8	Yes	
8	II	COVID-19 Rx	20	India	300	Yes	8	Yes	Yes
9	II	Diagnostic Kit	2	India	200	Yes	4	Yes	Yes
10	II	Probiotics Use	Nil	US	200	Yes	2	Yes	Yes

DCTs – *Voice Of Stakeholders*

HITLAB, A Digital Health Research Lab (Nov 2008)

Patients

In numbers

- **75%** participants needed no support to setup
- **87%** patients completed consent remotely
- **86%** compliance to completing questionnaires
- **75%** medication adherence reporting

What worked?

- Usability: navigation, understanding, layout
- Perform trial activities remotely
- In-app activities, reminders promoted adherence
- AE reporting feature preferred over other methods
- Viewing own data drives engagement & retention: one place, immediate access, share with care providers
- Security element of blockchain made users feel more comfortable and secure

Recommendations

- 100% interested in owning their medical records
- 86% interested in sharing data with other trials
- Additional features: Payment, site travel logistics

87% participants would recommend LifeLedger™ for future clinical trials

Investigators

What worked?

- Usability: dashboards, navigation. Even for less technically-savvy
- eConsent and re-consent feature. Blockchain expected to address security concerns.
- Expect patient adherence and retention to improve
- AE alert feature and timestamping helps track timely responsiveness
- Real time data hit all the right points
- Record events electronically (including visits), connect with other devices enhances overall PX
- Reduces paper storage
- Real time research allows changes in protocol as needed

Recommendations

- Tailoring dashboard, data collection fields and app for specific populations will improve adoption
- Timestamping when data is submitted would be useful information

Expressed desire to extend the app to their clinical trials

Sponsors

What worked?

- Delivers value to clinical trial sponsorship
- Blockchain helpful to solve known impediments to data-driven clinical trials.
- Reporting AE is an important tool and will help sponsors to understand safety issues quickly
- With blockchain, one can verify the sources of the data and where its coming from including reproducibility
- Data immutability and provenance are important to the sponsor
- The big benefit is the regulatory authorities could take the audit from this product at face value
- LifeLedger™ could potentially save significant money in streamlining the auditing process

LifeLedger™ can help make trial auditing faster with significant savings

DCTs – *Overcome Your Doubts !!!*

Literacy

- Unable to read. Hence, the imperativeness to ensure that the patient / LAR have understood all information presented
- Features of videos, graphics, audio ensure patient / LARs have comprehended the requirements to make an “informed consent”
- Mimic current process for signatures – LAR, Impartial Witness

Tech Savviness

- Today's world many are smart phone users; Simple guidance can overcome this challenge
- Sites have adequate infrastructure *(eConsent is not only for remote consenting; but, at site as well)*
- Survey shows elderly patients also willing to use technology

Confidentiality, Integrity

- Technology architecture with adequate encryption protocol ensures security & confidentiality
- Platforms have to comply to standard regulatory guidelines like HIPAA, 21 CFR Part 11 etc.
- Data visibility is role and permissions based

Cost Effectiveness

- Yes, there is an upfront implementation cost, but it is offset against
  - Process compliance (signatures, ICF versions, protocol deviations/violations)
  - Overcoming the encumbrance of paper process (missing signed consent forms, storage cost)
  - Reduced patient dropouts affecting timelines and associated costs
  - Reduced monitoring cost

DCTs – *To Make It Happen*

In addition to protocol-specific changes, it may be necessary for sponsors to modify general SOPs, impacting many individuals across their organizations.

Sponsor SOPs, general and study-specific training plans, site SOPs, protocol-specific training and technology must be evaluated to assess the impact of increased DCT elements on each study.

All procedures that typically occur at study sites have the potential to be significantly impacted by the increase in DCT elements.

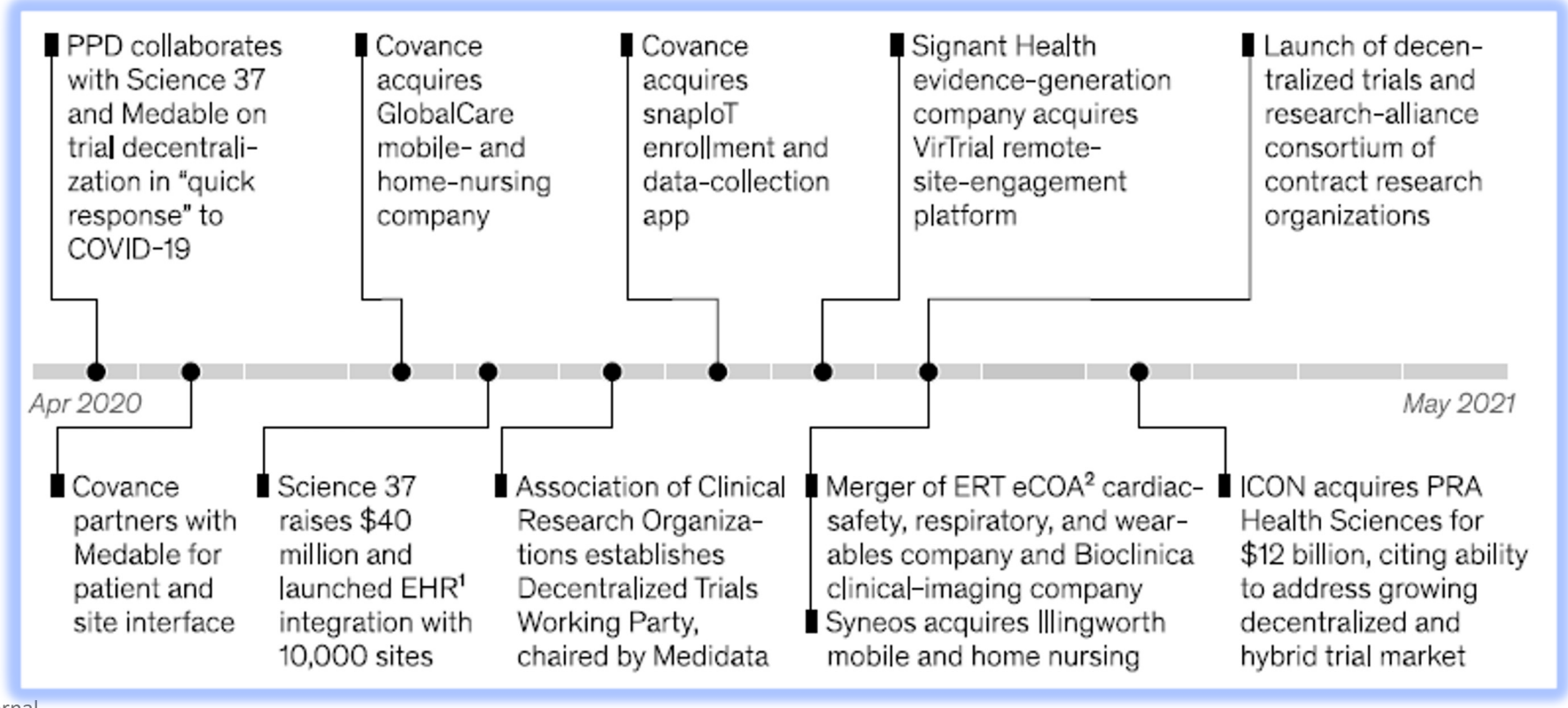
To ensure data quality and integrity in DCTs, it is important that study sponsors and sites focus on building quality into the entire process through proactive compliance rather than being reactive or expecting quality improvements at later stages.

Traditional expectations and procedures based on use of a central research clinic can no longer be the default model and customization will be required for each new study.

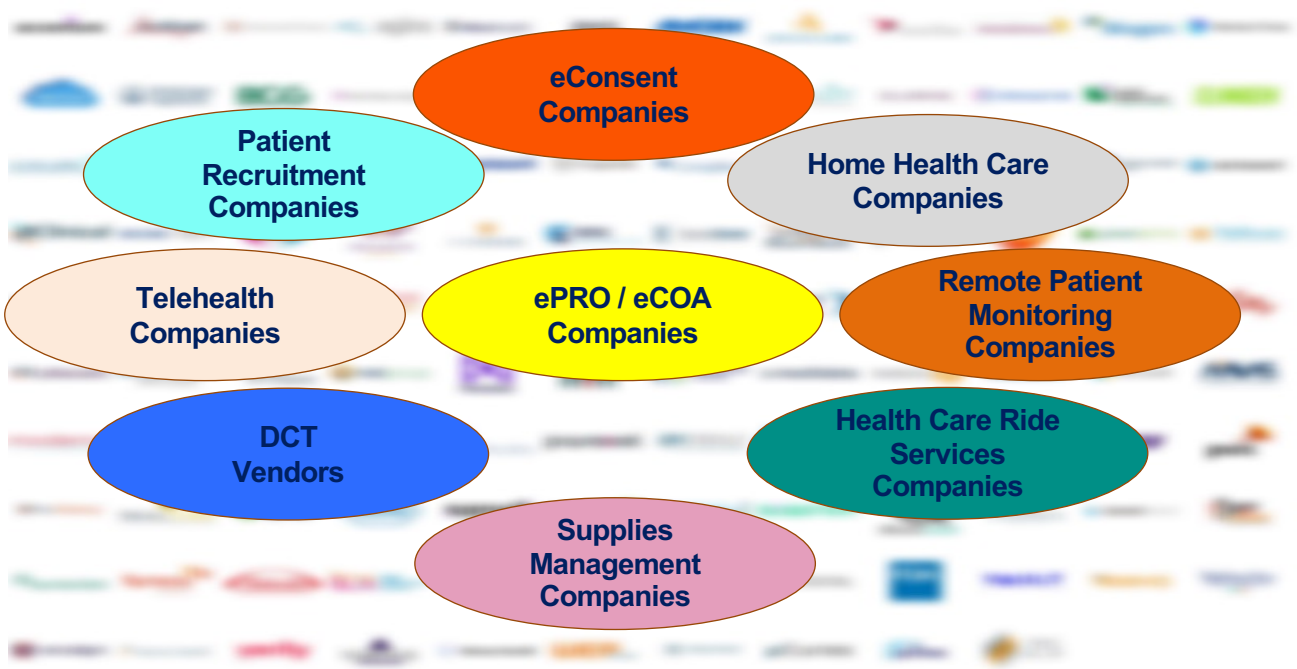
It is clear that the increased demand for DCT elements is changing clinical research from the old paper-based data collection methods to cutting edge eSolutions, requiring study teams to collaborate with multiple functional groups that have informatics expertise to innovatively address these new requests.

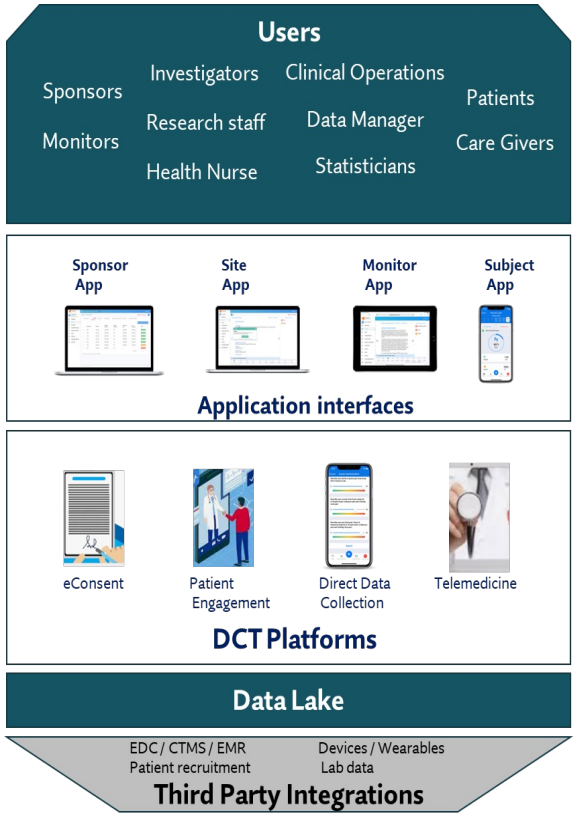
ACRP White Paper: DCTs – Perspectives For Clinical Research Professionals (2021)

DCTs – *Industry Movements*



DCTs – *Ecosystem – 102 Organisations !*





Together We Achieve !

Patient-centric Principles !

The Global Healthcare Data Science Community

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