

CLINICAL TRIALS

FROM BENCH TO BEDSIDE

CIST



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The Current Clinical Trials Scene

Clinical trials are a complex process that involve recruiting of healthy volunteers (Phase 1) and subsequently patients. Trials are performed to demonstrate the safety and efficacy of new medicines. In short, they measure the performance of new drugs. The clinical trial market is expected to grow at 5.7% per year to an overall value of \$65B by 2025. To put this in perspective, according to clinicaltrials.gov, in the year 2000, there were about 2,100 trials registered, and by 2019 this number had grown to over 280,000 active trials. Recruiting and retaining patients for clinical trials has long been a problem.

The delivery of new medicines to the marketplace is the lifeblood of the pharmaceutical industry and now more than ever requires something new and innovative. The global coronavirus pandemic has brought this into sharp focus and urgent action is required.

Patient-centricity has long been the focus for pharma companies and now decentralized trials is the next natural step. Traditional trial models and practices are unsustainable.

Out with the Old in with the New

Traditional clinical trials require a great deal of investment; the process is costly, inefficient and inconvenient for participants due to the travel and attendance required as well as many other logistical demands. Recently a shift from centralised to decentralised clinical trials (DCT) has gained more interest. Decentralised clinical trials are designed to be more patient-centric than the centralised trial. Fully decentralised clinical trials move the trial process into the patients' home. The use of advanced technologies artificial intelligence, machine learning, cloud computing for a decentralised approach can improve the efficiency of trials. Given the present situation amidst a global pandemic removing the fear of having to attend a medical facility, avoiding the need to travel and collecting data remotely will improve patient compliance and enhance recruitment rates for new trials. Economically, a decentralized approach makes sense due faster recruitment and improved retention which gets you to the results faster.

This shift is affecting health care stakeholders who are now exploring and expanding their technological investments. Patients are valuing support services and self or at-home administered treatments more and more since it offers greater convenience, frequent care, and it's often less costly for them.

Alternatively, a hybrid approach is also available, by mixing on-site patient visits with remote visits--using healthcare facilities closer to the patient's home (e.g. when an MRI scan is necessary). It is claimed that decentralised trials would alleviate some of the bottlenecks that trouble centralised clinical trials.

The Complex Nature of Clinical Trials

Pharma companies aren't well-versed in the patients' complete journey

Pharmaceutical companies do not give sufficient attention to the “customer and patient decision journey” that patients and healthcare providers go through. Nearly 40 percent of pharma companies admit they do not understand these journeys well enough to map the appropriate digital touchpoints. If this remains the position, then the industry will fail with regard to adequately altering the present situation. It is imperative that the clinical trial model from phase 2a through to phase 4 is overhauled to take into account the new normal we now need to accommodate in order not to lose on – going trials as well as encourage new recruitment to ongoing and future trials.

There are a few vendors and early adopters in the space, however in order to imbed decentralized trials as an alternative and eventually the new normal in the industry we need a cross industry collaboration as well as working with regulators to ensure we have standards and interoperability for monitoring devices as well as approval of new operating procedures. Then we can look at the corporate challenge of how to best change from where we are now to our desired future state.

The Process Demands Commitment and Patients are often Unclear in what they are Committing to

Before even starting a trial, there's the arduous consent process which usually involves extensive paperwork that can often be trying and confusing. Streamlining the process of consent and making it more transparent can make it easier for patients. Then there's the lack of patient awareness where only 33% of patients are

aware of trials that they could benefit from. Of those who are aware, many are hesitant to participate due to the amount of travel required and more recently the fear of attending appointments in a healthcare setting where they perceive an increased risk of being infected with coronavirus. Moreover, motivation to seek and adhere to the treatment during the experience of participating in a trial demands resilience. Many physicians have been refractory to demands for a new model, however in the; last 6 months there has been an enormous acceleration in the acceptance of videocall triage across the healthcare industry

Hospitals and Staff have their own Hurdles

Hospitals and their staff are in normal periods are both time and resource constrained and struggle to enroll patients. In today's world this is getting to be an even bigger challenge. Keeping patients for the duration of the protocol and the art of managing them to stay on-board and avoiding poor protocol adherence is another major issue which does affect the conclusiveness of many clinical trials. Depending on the organisation with whom you are working with the motivation of the hospital, the staff and the patients' needs to be fully aligned to be successful. Reducing the nuisance factors and removing hurdles which frighten the patient are key. Remote monitoring and decentralised trial protocols will be important tools to overcome the present situation.

Governing Bodies have to Make Sense of the Complex Nature of Trials

The vast number of trials and their complex nature and design make it difficult for regulatory and governing bodies (RGB) to have accurate, real-time information on safety and efficacy for all trials. The decentralised trial and remote monitoring lends itself to real time data collection and monitoring. Algorithms can be constructed to

PHARMA ECOSYSTEM



Data and Security

Clinical trial success is dependent on capturing interoperable quality data in order to apply the findings of all stages of medical research (Discovery and Development) and provide evidence of benefit to patients. Terabytes (or more) of data including the number of patient dropouts, adverse reactions, frequency of data collection, pre and post-dosing of therapeutic, and nature of data collection, hours traveled to site, etc. are just some of the complex data that need to be tracked, logged, and analyzed. The entire process requires Herculean coordination of the pharma industry, physicians and patients to generate valid evidence, which can later be submitted to regulatory

agencies. Much of this work has been outsourced by large pharmaceutical organisations to CRO's clinical research organisations who provide this service. Historically, pharma companies have built digital solutions that best suit their purpose and that don't necessarily work with already established systems within healthcare system. The present model used by the industry is over-complex and beset with organisation specific dogma alongside a geographically non-uniform set of regulatory guidelines. It is essential to ensure data is secure and regulations are met. One challenge today is to effectively manage the plethora of different platforms and data sources as well as ensure the patient data is high quality as well as safe and secure.

Data collection will be key. A significant incentive for DCTs post approval is the collection of real-world data (RWD) and real-world evidence (RWE). RWD and RWE provide an assessment over the lifetime of a trial and beyond. As technology continues to advance there continues to be increased exploration of decentralized clinical trials and remote models, where patient data can be partially or completely collected remotely. Additionally, there is now a trend to look for data to allow a synthetic arm to be added to a clinical trial and in time this might well be a source of reliable data that will both speed up and reduce the costs of clinical trials. Regulators are looking at this area and are keen to encourage organisations to further investigate the area. Synthetic data is the next big hurdle which when proven to be reliable will significantly reduce time and costs of new drug development.

The Bottom Line: How DCTs Can Help Solve All of the Above

Patient Centricity

DCTs have the ability to accelerate the trial site initiation, patient recruitment, and lower the rate of dropouts with better patient engagement, and reduction in travel time to the trial site. By requiring fewer site visits, DCTs decrease the challenge for patients contributing to patient retention. (remote monitoring, safety alerts etc.)

Recruiting with a more Diverse Pool

Trial sponsors may gain access to a more diverse patient population by gaining a more geographical footprint. The ethnic, racial, and gender diversity within clinical trials is an ongoing issue which requires urgent attention. Diversification is critical to the success of clinical trials and the development of effective and safe drugs. It is no longer morally acceptable to test a drug in one particular population and then treat another without first ensuring both safety and efficacy remains equivalent across the population.

Collecting More Data and Reducing Data Collection Costs

With the use of various different technologies [see picture below], DCTs can collect more data from patients than at traditional site-based clinical studies. The availability quality and applicability of numerous specialist resources is greater than ever, however in some larger Pharma organisations this has added to a further layer of complexity. Overall, we are looking at a reduction in Source Data Verification: Additionally, these technologies/platforms deliver data straight from the source, thereby reducing the need for additional data verification.

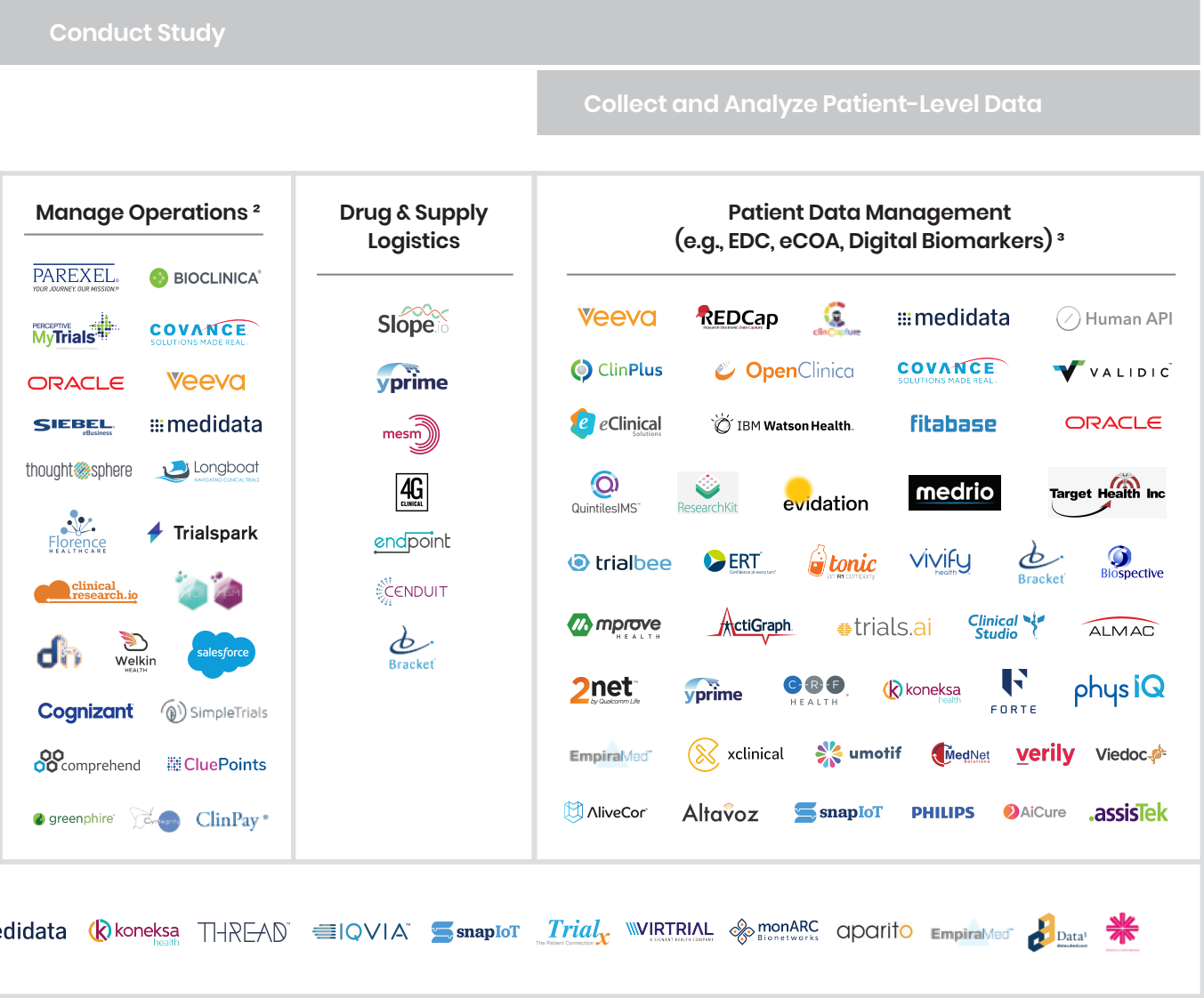
There's Already Support from Some Regulatory Agencies

Regulatory and governing bodies could/should benefit from decentralised trials supported by novel technologies to maintain quality control, storage requirements, and up-to-date standard operating procedures (SOP) amongst others. Several companies are addressing specific pain points in DTC, but no one is addressing it from bench to bedside. This has ended up in a hugely complex ecosystem as it can be seen in the chart below:

Many companies offer products that span across categories.

To keep the map simple, the logo is in the “primary” product.

Have an update? Share via www.elektralabs.org/decentralized-trials



0 – Unlike the other for-profit ventures on this map, CTTI is a Public-Private partnership & AllTrials is a registered charity

1 – Includes startup tools like eConsent and site training

2 – Includes clinical trial management systems, risk-based monitoring, site monitoring, payment automation

3 – Includes EDC (electronic data capture), informed consent, Imaging, Lab Data, Digital Biomarker Data and Validation, eCOA (Electronic Clinical Outcomes Assessment)

Our Solution | Recommendations – Ideals & Concepts

With the objective to reduce time as well as costs, pharmaceutical companies are partnering with technology companies to accelerate the clinical trial process. (Financial Times, 2019) They use innovative solutions such as blockchain to minimize distance between doctors and patients by the improving safety of data capture and organization. Not only do distributed ledger technologies play an important role. The application of artificial intelligence, machine learning, cloud computing, gamification, social networks and crowdsourcing are equally important and can help in getting patients more involved in the care and services they receive. (Christensen, 2009)

There are many start-ups and technology firms active in the industry that all work on a tiny part of the solution. In order to improve the execution of clinical trials, by making them decentralised for starters, you would need to integrate the different IT and MedTech solutions available. In this complex industry it will be difficult if not impossible for one company to come up with an overall one-stop-shop solution.

Development of in-house solutions for decentralized clinical trials may represent a significant deviation from the resources and capabilities, and expertise presently available within a large pharmaceutical industry player. Managing different speeds and ways of working (start-ups/tech versus large pharmaceutical) has been proven

difficult in the past. It is also a large challenge for pharmaceutical companies to coordinate and integrate these agile organisations into their own company ways of working and preserve the creative and innovative cultures they hold.

Each clinical trial will need different solutions applied and a one-size fits all solution will not exist. Some trials can be fully virtual, others would need some fixed trial sites (e.g. to perform diagnostic tests), and there might be trials that transition from one form to the other when migrating from phase II to III to IV (e.g. need for diagnostic tests in phases II and III to fully virtual and observational in phase IV).

Pharma companies need to approach automating digital clinical trials in a more cohesive way. (THIS NOT RCT or DCT but beyond. At best it is Phase 4) A way to do this is to work with an ecosystem orchestrator, a company that is a service provider to the life sciences and healthcare provider companies. The latter will (hire the solution and fund the trial and this system orchestrator is the one in charge to manage a customized process from bench to bedside with start-ups and other solution providers. The orchestrator will connect and provide the most appropriate turn-key solution to each stakeholder.

Below we can find our future vision of decentralized clinical trials ecosystem.

Reimagining Clinical Trials

Profiling through her physician	Mobile nurse, remote HCP and chat bot support onboarding	Dealing w/ side effects + routine Device / App autodata collection + patient chat (AI)	Social network + remote HCP: hopes, fears, relationships & unmet needs
Awareness of the and reference to the trial (GP notes w/nlp)	Access to data of the patient	Chat bot for standard Q&A + AI for managing patient	System provides feedback on how patient is performing in clinical trial. EMR updates.
Designing and recruiting for the trial	Profiling of the patients by AI	Controlling KPI's remotely received by device	System alerts for timelines and monitor risks. EMR updates.
Engagement of local physicians	Onboarding of the patient + delivery of first dose and device	Visits patients, gets needed data and redirect to local lab and imaging centre	Supports patient to adhere to the program with digital services.
Pre-clinical trial	Early days of the trial	On-going of the trial	Adherence and end of the study
< Blockchain enabled platform >			

The Big Shift

Building the future-ready capabilities

- Patchwork of providers — **Insourcing & ownership of digital**
- Know-it-all arrogance — **Learn-it-all mindset**
- No mistakes, bullet-proof — **Experiment & reduce uncertainties**
- Programs, years — **Hypotheses, weeks**
- Navel-gazing organization — **Customers' pains-obsessed**
- Collection of digital projects — **Integrated omnichannel experience**
- Fighting technology debt — **Technology at the core**
- Reinventing the wheel — **Search & re-apply for flywheel**
- One "global-flavor" fits all — **Innovate with a local "touch"**

Decentralised trial design is about to disrupt this legacy industry and could improve a drug's journey from bench to bedside. Improving this journey would ideally result in faster, cheaper, and more effective drug development, which in the end should benefit society overall.

Adoption of DCTs has been slow paced. In a risk-averse, highly regulated environment, change is often difficult, but the evidence suggests that governing bodies as well as many pharmaceutical companies support decentralized trials. The next steps require collaboration between the pharmaceutical industry, the medical devices and technology industry as well as the physicians, patients and the regulators.



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