THE FUTURE OF CLINICAL TRIALS

From continuous patient data to trials by algorithm
Clinical trials are one of the pharmaceutical industry’s most painful and costly processes. Here’s how technology could shape the future of clinical development and transform the trial process from nine years to a matter of hours.

Órlaith Burke

In September 1928, Alexander Fleming discovered the beneficial effects of penicillin in his lab at St Mary’s Hospital, London, after famously returning from a two-week holiday to find that a mold had grown on a staphylococcus culture plate.

Fleming stopped working on penicillin in 1931 but others continued his research and it wasn’t until 14 years after its initial discovery that this new drug was successfully used as a treatment – in this case for burn victims of the 1942 Cocoanut Grove fire in Boston, US.

Today, more than 90 years since Fleming’s first discovery, a newly discovered drug will take a median of nine years before it is approved for the market at an average cost of $2.6 bn

This modern, rigorous trials process – involving scientists, researchers, pharmaceutical companies, patients, doctors, clinics and regulators – ensures the safety and efficacy of treatments, and helps to avoid events such as the global thalidomide disaster of the 1950s.
The wider healthcare market is transforming, thanks to the introduction of new data sources, the increasing momentum for patient-centricity, and the dawn of new, readily-accessible technologies such as wearables or portable clinical devices.

But the clinical trial process remains riven with pain points for almost every stakeholder.

By taking full advantage of emerging technologies, how might we reimagine the clinical trials process? And in doing so, how could we vitally improve the trial process for patients, companies and clinicians while significantly improving its outcomes?

Researching the future of clinical trials

A team of analytics experts, software engineers and Fjord designers at The Dock – Accenture’s flagship R&D and global innovation center – spent six weeks investigating this topic with our Life Sciences team.

We compiled a study of the current state of clinical trials, from the perspectives of:

- patient and clinician experience
- clinical data collection and management
- state of the art technology.

The findings were tested in a series of innovation sessions with a wide panel of healthcare experts and numerous clients in The Dock, and we presented the work to a series of international pharmaceutical clients during a series of sessions at The Dock in December 2018.

Their feedback was used to validate and refine the findings that are presented in this document.
The three waves of the future

We envisage the future of clinical trials arriving in three, successive waves.

The next wave will take advantage of new technologies and start-up inventions.

The near wave will address the high volume of increasingly complex clinical data sources and connect patients to trials remotely.

The horizon indicates a trajectory towards global clinical trials and a potential promised land of patient-free trials.
NEXT WAVE: The rising tide of change

Our research indicates that there will be a significant increase in the efficiency and effectiveness of the next wave of clinical trials, thanks to the emergence of improved technologies, access to real-time clinical data and new use cases.

This should also increase the industry’s capacity to innovate, and we’ve identified four main ideas in this space:

01 Immersed in treatment
02 Continuous patient data
03 Adaptable trials
04 Next-gen support eco-systems
Next Wave: The rising tide of change

01

Using XR to get immersed in treatment

Immersive technologies are already being used as a controlled distraction from pain with direct therapeutic capabilities. Applied VR uses a virtual reality platform to treat “chronic pain as well as acute pain and anxiety experiences for patients.”

We expect extended reality (XR) technologies to become prevalent in trial operations in this manner. It can also facilitate daily operations, improve compliance and assist in achieving better overall results: a 2017 Cedars-Sinai study showed that VR therapy decreased pain scores in hospitalized patients by 24%.

XR is also an effective tool for patient care. It can help teach patients about their treatment plans, explain a condition’s impact on the human anatomy, or describe an upcoming procedure.

As the cost of XR technologies continues to decrease, and their use increases in people’s everyday lives (e.g. in gaming or work training), we expect a greater XR impact across the medical sector. And we’re not alone: Goldman Sachs predicts that AR/VR use in the medical sector in 2025 will have revenues of $5.1bn.

One particular area of interest is patient adherence and retention. Non-adherence is a significant problem in clinical trials, with 40 percent of patients become non-adherent to investigational medical products after 150 days. If XR technology can make an impact in this area, its deployment will grow significantly.
People are now using wearable technology in their daily lives to track exercise, heart rates, sleep patterns, and much more. In the medical world, an individual’s health data can now be collected with their consent more easily, passively and “cleanly” than ever before.

Built-in sensors in clothing, phones and household devices can collect data from patients, effortlessly and continuously, 24 hours a day.

Small, wireless, self-powered, passive sensors can be placed in specific parts of the human body to increase the quality of the data captured in a way that is comfortable for the user “wearing” them.

Temporary digital tattoos, for example, are akin to a new generation of skin patches, with capabilities including ECG measurement, fall detection, and even drug release.

This approach can provide trials with a real-time, holistic view of a patient’s health by capturing their exposome, which is a measure of all the exposures of an individual in a lifetime, and how they relate to a person’s health. It can also provide a more accurate picture of the potential impact of a patient’s environment on their treatment. Across the wider patient population, this provides companies with a richer understanding of discrepancies in treatment response.

For example, patients with similar medical history might respond differently to a treatment due to differing levels of air pollution in their home cities.

Current, localized data on pollen count and other air-particle sensors could give clinicians a more detailed picture and pinpoint the reasons for an unexpected variance in their patients’ responses.

Of course, none of this is without significant challenges. A director of early phase clinical trials for one of the world’s largest pharmaceutical companies told our research team that:

“While I wouldn’t say continuous patient data is impossible... it is very difficult.”
There is a booming market in standard (though unregulated) wearables, which means it is increasingly simple for patients to capture and monitor their health-related data. In March 2019, Apple announced a new electrocardiogram app that allowed users to monitor their hearts for irregular rhythms, using its FDA-approved Apple Watch Series 4 product.

As healthcare electronic health record (EHR) integration improves and becomes directly accessible to patients, individuals will be able to access their personal records as and when they choose, and have real “ownership” of them – which creates the first stages of a market for patients who may be willing to share their data for payment.

The handling of data is also particularly sensitive in a healthcare environment. During a 2018 innovation session in The Dock, one of the clearest messages from our multinational clients was that “transparency is key” when it comes to collecting and analyzing continuous patient data.

This transparency for the patient refers not only to the immediate uses of their data but also to their expectations regarding the full spectrum of possible tests provided.

One significant question that has been raised is, are the companies who are using the patient’s data responsible for ensuring that all available tests have been conducted on each individual’s data? And are they subsequently responsible for appropriately communicating all the results to the patient, even if the original use of that data was entirely unrelated?

Imagine, for example, that a company uses an individual’s genetic data with their full consent to test a new product. But during those tests it identifies markers that could indicate that the patient is showing signs of Huntington’s disease. Is the company then obliged to inform the individual – and would the individual want to know in the first place? What if the test turned out to be a false positive?

Our clients questioned whether it would be possible to control such a situation, and it raises a range of ethical considerations that have yet to be fully considered.
Leading-edge trials learn as they progress and allow process and operational updates on an iterative basis, following a pre-set adaptive trial design methodology. Examples of these updates include:

- **updates to the sample** (additional patients may be recruited to ensure statistical power is not lost);

- **a reallocation of patients** (allocation methods are adapted so that patients are assigned to preferable treatments); and

- **new treatments can be added to the process.**

These adaptive trials are well established as having the potential to **improve trial success rates and significantly reduce time and resource costs.**

Right now, adaptive trials are in use in small pockets of research and until recently there was little guidance for their design and implementation.

In a **2018 BMJ article**, the authors outline the best practice for designing the operational protocol for such a trial, and it supports this approach. In addition, electronically captured data provides faster analysis, allowing these iterative changes to be made in a timely manner.

The use of **synthetic control arms** is particularly beneficial to reduce risk in vulnerable patient populations (such as geriatric or pediatric populations).

Flexible trial design will decrease the overall clinical trial cycle time by accelerating the go/no go decision process and allowing for more relevant analysis timepoints.

In addition, it should minimize patients’ exposure to side effects. Studies show that **29% of all patients drop out after consenting to trials due to their fears about side-effects**. Fully flexible trials will help alleviate this and improve patient retention.
Participating in a clinical trial might feel like an isolating experience for patients, something which was identified by several global clients during our research.

By appropriately connecting patients to each other and to the researchers, there should be more meaningful communication across the process. This will develop greater trust and transparency throughout the trial, which should improve patient engagement and retention.

The prevalent use of social media platforms, with more than 2 billion users on Facebook alone, provides a huge opportunity for pharma companies to support these types of connections.

Although it is currently not permitted within the industry – as ethically a pharmaceutical company cannot contact a clinical trial patient directly – the possibilities that social media presents are intriguing to those who participated in this research and something that pharma companies are beginning to come to terms with as they pivot to increased patient-centricity.

As a trial progresses, patients need, demand and get access to more contextual information. Privacy is clearly a challenge with direct engagement between pharma and patients. But the industry recognizes that there is a strong need to get involved in patient support. To not do so is equivalent to “an ostrich’s head in the sand”, according to the director of one multi-national pharma client interviewed during our research.

They suggested that third-party companies could perhaps be the key to owning this market. By facilitating this community, companies could increase their brand value and reputation among investigators and patient advocacy groups.
Our research indicates that in the near future, fully virtual trials could become standard.

In this wave, doctors, patients, and their families will be directed to suitable, available trials, checked for eligibility, and fully informed and onboarded using intelligent digital agents. Decentralized data repositories will manage data, largely in response to heightened standards and awareness on security and ownership, which will improve the overall management of clinical data. In this scenario, patients will actively own their data and may be able to provide it to researchers and clinics to further the research agenda, on their terms.

The ideas for this wave that we have collated focus on patient experience and the rapid influx of vast volumes of data. In our research, one Accenture managing director commented that this future is not “that far away” but further noted that “the future can be quite overwhelming” for what is traditionally a conservative industry. A cautious approach from the industry would of course slow down the trajectory of these developments.
An intelligent approach to onboarding

Before a patient can be enrolled on a trial, they must be able to find it. And **86% of clinical trials do not meet enrolment timelines** due to issues with recruitment.

In the Near wave, to create an improved patient experience from the beginning of the trial, we predict that doctors, patients, and their families will have access to intelligent digital agents to direct them to existing, appropriate trials based on their data.

The agent will then check whether the patient is eligible for any of the suggested trials and provide supplementary information.

Once a patient gives their informed consent, the agent can complete the administrative onboarding process.

For this to work, all parties (e.g. trial sponsors, pharma, clinical research organisations, and hospitals) need to be using paperless management systems.

These support the accurate collection of trial information, inclusion/exclusion criteria, and collecting the patient’s EHR data. For such a system to apply across all known clinical trials, all administrative data must be collected and represented in a consistent, standardised, unified form.

Artificial intelligence and machine learning will power the intelligent digital agent. As these technologies mature, agents will be trained to conduct complex cognitive tasks, such as determining the eligibility...
of patients for a trial in the context of the various clinical trials’ requirements and the individual health status of each patient.

By facilitating fast, efficient trial discovery and on-boarding, these digital agents should be able to recruit patients quickly and easily.

Eighty percent of trials are delayed due to recruitment problems, according to a study by the Center for Information and Study on Clinical Research Participation.

From the patient’s perspective, Intelligent Trial Onboarding provides a more fully supported experience by guiding them directly to suitable trials and education materials.

However, the efficiency of the system may have a deleterious effect on the patient’s confidence in the system. Consider the social responsibilities and ethics related to such a system.

The move towards technology introduces inherent bias and risk due to its focus on a specific population. Low and middle-income countries, or factors relating to social class, could generate bias in these systems.

In order to have access to these systems, patients probably need broadband access or an accessible EHR. Even that can unfairly skew the eligible pool towards a specific demographic.

However, pharmaceutical clients in our innovation sessions recognized that there is already a “market in this” that is being captured in the start-up space, by companies such as Medable, Deep 6 AI, and Antidote.

The rest of the industry will have to catch up.
In data we trust

Data ownership, security, and privacy are among the most prevalent topics in technology today. As data collection in healthcare increases in complexity, the importance of these topics and the sensitivities around them become amplified. Our research suggests that we can overcome the fragmented nature of healthcare systems and the related lack of transparency by distributing clinical trials data across all actors in a system.

Using a decentralised data repository will improve data security, ensure appropriate data ownership and privacy, and maintain the veracity of clinical trial data. This in turn lays a solid foundation for online regulatory validation of clinical trial outcomes.

The replication of trial analysis is important in clinical trial regulation and blockchain technologies could ensure that a trial’s full history is immutable and traceable.

Patients, doctors, devices, and clinical systems will be able to push and read data to and from the network through the use of decentralized applications (DApps), which are run by many users on a blockchain network.

Actual ownership of healthcare data should be more clearly in the hands of the patient and this should give individuals more direct control over their information. Blockchain and cryptocurrency will also make it easier for patients and researchers to exchange health data for payment, as in the case of current start-up Health Wizz.

A scenario of continuous patient data, as outlined above, will mean an increase in the burden of responsibility around data security for pharma, biotech and healthcare companies. However, a system built to “in data we trust” standards could offset these increased demands. Trusted and secure data that is visible by all the necessary actors in a clinical trial could also make regulatory audits quicker and easier. Its benefits would also extend to other parts of the drug lifecycle.
To efficiently process a large, continuous stream of patient data, clinical trial organizations will need an equally swift system to clean, aggregate, code, store and manage it. Our research indicates that further improvements in technology will make this a quick, seamless, and dynamic process.

Improved electronic data capture should reduce the impact of human error in data collection and enable seamless, instantaneous integration with various databases.

The maturity and pace of developments in artificial intelligence will also enable real-time data capture and processing for autonomous agents and connected devices.

Seamless data management should reduce the increasing amount of time and manual effort being poured into clinical data management processes.

Our research indicates that this could be one of the most valuable improvements in the clinical trials process.

Pivoting to data direct from source and merging integrated data systems with AI would reduce the overall burden of clinical data management, through query generation, and reducing unnecessary and low-impact queries. This would give researchers more time to concentrate on higher-value clinical tasks. The context of this data would also allow researchers to make observations on patients’ behavioral health as well as allowing companies to consider the effect of both therapeutics and lifestyle factors on treatment outcomes.

During our innovation sessions, clients homed in on seamless data management as a much-needed and overdue improvement to current data-management processes. This has led to two new workstreams related to clinical data management. Accenture Life Sciences is now coordinating a collaboration to develop these ideas with The Dock and multiple clients.
Frequent clinic visits will soon be a thing of the past for patients on some clinical trials.

Connected devices, advances in home delivery, and improved virtual communication will mean that clinic visits can be conducted at a time and location more convenient for the patient. A great example here is the AOBiome Trial.

This Phase 2b acne study screened more than 8,000 candidates and enrolled 372 patients for a 12-week study with no site visits. It also experienced increased inclusivity in recruitment (specifically an increase in non-white participants) compared to traditional trials.

Patient-centered connected devices will be key here. Connected devices (e.g. wearables, nanotech, XR, virtual assistants, bots and more) can be used to accurately and efficiently capture measurements during virtual appointments. The wide-spread adoption and use of virtual communication is already facilitating remote interactions between clinicians and their patients (e.g. the GP-at-hand service offered by the NHS in the UK).

Improved home-delivery technologies – such as advances in cold chain, 3D printing for medical devices and medicines (as outlined in this Forbes article), and the use of delivery drones – will allow direct-to-patient distribution of trial materials that would previously have been given to patients during traditional clinic visits.

The shift from clinic to patients’ homes should increase patient adherence and minimize patient drop-out, partly thanks to the fact that patients will no longer have to travel frequently to take part in clinics. Stay-at-home trials should also provide financial savings for pharmaceutical companies, as it costs $9.7M on average to set-up and manage each external trial site.

The potential downside is that with interactions increasingly taking place via technology there is an increased risk of depersonalization. Technology cannot entirely replace the human interaction, support, trust, and care provided by visiting a clinician’s office.

Human connections become so important as we become increasingly dependent on technology, and developments such as stay-at-home trials will need to take this into consideration.
What if clinical trials could be conducted without any risk to patients?

Our research points towards a future in which algorithms will model a patient’s journey through trials to predict clinical outcomes.

Our research on the Horizon wave of clinical trials generated three far-reaching ideas:

09 Declaration of data standards for global clinical trials
10 Personalized trials
11 Trial by algorithm

The challenges for these leaps into the future are immense – but the potential benefits to the healthcare industry are almost boundless.

Innovative companies need to imagine their approach in the context of scenarios such as these to ensure they are moving in the right direction.
The standardization of all data collection and management is a well-known pain point for anyone using healthcare or clinical data across multiple systems.

To date, the hope is that global regulation will provide a single standard, with standards bodies such as the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), industry bodies such as CDISC, and pre-competitive collaborations like TransCelerate and Pistoia Alliance all working together to address this area of opportunity.

A global, standardized, secure database of this kind has unchartered potential for new research discoveries. However, to date the industry has struggled to advance this vision. The idea of a universal declaration of data standards is a hot topic among clients. During our innovation sessions, some recognized that “it’s a big pain point” without being enthusiastic about its feasibility. To quote one executive:

“Every time I hear ‘global’ or ‘one universal standard’, the thought in my head is ‘It’s never going to happen.’

The challenge to create trustworthy, immutable data accessible to all parties is essential for global standardization to work. Regulations focusing on the consistency of all AI-platforms used in data management would be crucial to enabling ubiquitous standardization.

Many clients have attempted this in isolation but recognize that they need to collaborate for it to really work. According to one executive:

“[We] have to depend on ‘real’ standards, not our own, if we want to move forward.”
A universal declaration such as this removes the current pain in pooling clinical trial data sets for the secondary and/or meta-analyses of trials. It would also allow for the creation of a single, global, clinical trial data lake.

It may be an ideal solution to a number of problems (with solutions such as Datacelerate working on use cases in this area), but it’s important to be realistic about the challenges involved.

During our innovation sessions, the CEO of one start-up noted that “it would require immense political will” and, according to the vice-president of a global pharmaceutical client, achieving it might require “an alien attack” to wipe out the status quo and start afresh.

Would we stay ‘special’ or simply adopt healthcare standards?

Imagine a world in which regulatory applications for new medicines could be approved worldwide by satisfying a single universal regulatory standard and one set of internationally accepted ethical standards. Global data allows for globally applicable clinical trial outcomes.

• Consider also the impact of the ability to generate trial data from real world data.

• This would allow global participation in a trial without needing to rely on traditional electronic data collection solutions.

• For a global clinical trial to be effective, it would need to be underpinned by a universal declaration of data standards, and data that is reliable and trustworthy.

• For trial outcomes to be universally accepted, the patient sample must be generalizable to the global patient populations of interest.

• Stay-at-home trials and intelligent trial onboarding would help this significantly as they remove geographical barriers and provide access to a global pool of patients.
Personalized (or precision) medicine is top of the agenda for omics research, with *Nature* publishing several, significant papers on the topic in 2018 alone.

This research and advances in the accuracy of predictive modelling with healthcare data are expected to drive the extensive use of personalized medicine in the future.

Access to vast, patient-specific information will provide in-depth, accurate knowledge of a patient’s history and environment. This will allow individualized modifications to treatments based on well-informed predictive models. One Accenture MD told our team:

“Genetically-driven trials are going to be the way forward.”

As such, traditional trial risk-benefit analyses must be reconsidered to allow for the trialing of a process (e.g. a cell gene therapy such as CAR T-cell therapy) rather than a product.

Large amounts of accurate data are needed to train these predictive models. To make the process efficient, and to provide useful outputs, patients’ medical data must be represented using standard formats. Assuming these supports are in place, deep learning methods and advances in predictive modelling will be in a position to make use of huge databases to derive insights and generate predictions for individuals participating in trials.

Trials tailored to each individual patient should minimize, and even completely avoid, negative side effects and improve outcomes for each patient. They should also provide insights on the patient-specific variability of treatments during trials, which could lead to further treatment/condition research.
Horizon: Reaching into the future

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Trial by algorithm

We can further reduce the risk to trial participants by replacing the traditional clinical trial with trials by algorithm. In this scenario, data from a global, standardized, secure clinical database will be used to estimate the journeys of simulated patients through the trial, and accurately predict the trial outcomes.

This is not as far-fetched as it may seem. Simulations are currently in the early stages of use for clinical trial design. An interesting example is the HumMod physiological model and the use of real-world evidence from companies such as Flatiron and Medidata as “synthetic control arms”.

Further research and development in the theory and application of these methodologies will lead to more robust, advanced simulation methods for data-only clinical trials. During our research, clients and Accenture colleagues commented that while all ideas in this wave are “definitely achievable”, trial by algorithm is “probably the most likely” and “probably the most fun”.

Fun is one thing: but a disruption to the clinical-trial process of this nature could dramatically reduce the average trial cycle-time from nine years to mere hours. The latter seems particularly achievable in the context of the ongoing, rapid development of quantum computing.

In this environment, trial costs and patient risk will plummet. Furthermore, by combining trials by algorithm with developments in drug discovery, every drug approved and manufactured is essentially guaranteed to be an effective, marketable drug.
Conclusion

New continuous patient data sources, and the accessibility of technology, will have immense impact for everyone involved in the clinical trials process. Yet the overall clinical environment needs to change to allow this innovation. Ethical and regulatory considerations and further debates continue throughout this nuanced, traditional-yet-forward-thinking industry. The proximity of the next wave, near wave, and horizon of clinical trials depends on industry leaders who clearly recognize the importance and advantages of pivoting to this exciting future.

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Órlaith leads the Future of Life Sciences portfolio at The Dock, directing innovation projects across R&D, Clinical, Manufacturing, Regulatory, and Patient Safety for Accenture’s global Life Sciences clients. Órlaith is also a Senior Principal on our Advanced Analytics and AI team. She joined The Dock in 2016 from the University of Oxford, where she worked in the Department of Statistics and the Nuffield Department of Population Health. Her work as a lecturer and researcher during her six years at Oxford focused heavily on advanced analytics in the field of maternal healthcare and clinical trials in geriatric care. Órlaith completed her PhD in Statistics at University College Dublin and Columbia University, New York. She remains a Fellow of Kellogg College, Oxford.

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The Dock is Accenture’s flagship R&D and global innovation centre. It is a diverse team of creative problem-solvers within Accenture – where design, business and technology meet under one roof. We’re a meeting place where Accenture, clients and partners connect to pioneer new ways to fulfil human needs using emerging technology.

We believe future commercial success will come from businesses that are conscious of the intended and unintended consequences of their work. That’s why we’re passionate that true innovation must deliver value for Accenture, our clients and society.

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