Tec4med

Home-Based Clinical Trials

Table of contents

Key Challenges Facing Clinical Trials

Scientists and physicians are working tirelessly to improve upon the diagnosis and treatment of cancer and other serious illnesses, and to find new ways of preventing them altogether. This research is very costly and time-consuming. It takes ten to fifteen years for a new drug candidate to reach commercialization, while many auspicious treatments do not even reach the approval stage because they do not pass the rigorous testing required.[1]

Despite this, the number of clinical trials being performed worldwide continues to increase at a rate of around 10 to 12 percent each year, while research and development (R&D) spending have been growing at a compounded annual growth rate of 1.76 percent over the past decade.[2]

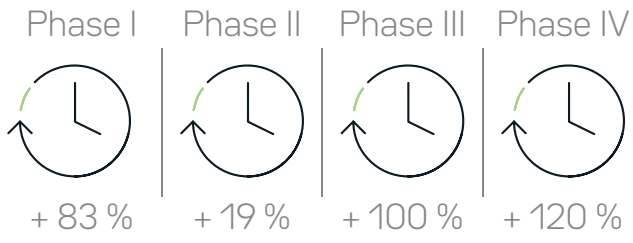
Although many innovations have been brought to the clinical trials market to help improve upon the costs and success rates, overall productivity has remained relatively stagnant. The difference between increased spending and consistent results highlights this significant gap, which is of primary concern for the industry.

Furthermore, from 2002-2014,[3] the duration of the average oncology clinical trial increased by 69 percent or, viewed differently, was extended by an additional 16 months per trial. This increase can be broken down as follows; Phase I: 83 percent increase, Phase II: 19 percent, Phase III: 100 percent, and Phase IV: 120 percent.
More in-depth analysis into the root causes of the increases in study costs and duration leads us to three interrelated factors: the adherence, the enrolment, and the retention rate of patients participating in clinical trials.

These three factors represent challenges that need to be addressed, and it is precisely because of this, that there is a growing movement towards modernizing how clinical trials are conducted altogether. As a result, the traditional clinical trial is slowly shifting from site-based to home-based, all to drive patient-centricity.

1.76 % annual growth

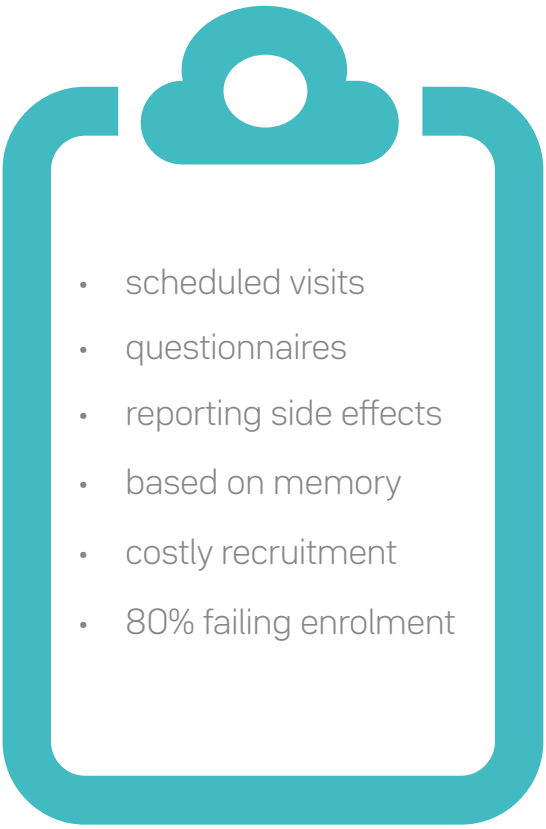
69 % increased duration



„Drugs don't work in patients who don't take them" - C. Everett Koop, M.D. (Former Surgeon General of the United States)

Protocols are becoming more complex with each year, and researchers need more and more data to fulfill all the requirements of each phase of a clinical trial.[4] Yet, at the same time, the adherence of patients is on the decline. Unfortunately, it is only wishful thinking that all patients are adhering to the proper usage of the investigational medical product (IMP) of the clinical trial and its protocol. In fact, studies have shown that only between 43 to 78 percent of patients adhere to the correct use of IMPs.[5]

Tragically, in some cases, misuse can lead to poisoning due to overdose or the ineffectiveness of a treatment altogether, even if skipping just a single dose. At the same time, violating the protocol increases the variability of study results and is corrupting the researchers' study data. Consequently, this has led to an increase in the number of patients that need to be enrolled in a study, in order to ensure an appropriate statistical outcome.



The importance of patient centricity

In the traditional clinical trial model, patients must make scheduled visits to a clinic, to receive their treatment and complete questionnaires about how they feel, including any potential side effects they may have experienced between visits. As much of this information is based on memory, it can lead to highly error-prone information being collected.

Today, only about 5 percent[6] of eligible patients are participating in clinical trials and sponsors face a time-consuming and exceptionally costly recruitment process. In most cases, clinical trials cannot meet their enrolment deadlines, with roughly 80[7] percent of clinical trials and more than 35 percent of research institutions failing to meet their enrolment targets. This problem is heightened when targeting a very particular condition with a smaller patient population.

To make matters worse, the average patient drop-out rate across all clinical trials is roughly 30 percent.[8] While dropping-out is a patient's right, there are arguments as to why a patient tends to end their participation, and it is commonly understood that it is because the study is not flexible enough for their lifestyle and schedule. For example, lengthy travel to a clinical site - routinely during a study's duration - can be extremely burdensome, making the patient much more likely to end their participation.

In an effort to reduce non-adherence, low enrolment, and increasing drop-out rates, research institutes are shifting towards more patient-centric clinical trial models. That is, to organize their studies around the patients' lifestyle and individual needs and to ramp up patient communications.

The latter is an extremely important point for, while it is crucial to understand the daily life and needs of individual participants, the patient must also understand that strict and error-free adherence to the study protocol is necessary to improve their well-being and for the overall success of the treatment; that it can help reduce costs, free-up valuable resources, speed-up the treatment process and impact on their lives and those of countless others.

How Technology Is Impacting Home-Based Clinical Trials Today

Patients' adherence is a critical risk factor in conducting a successful clinical trial. To help improve this, novel wearable devices and companion apps are being developed and introduced to the market. These technological innovations are being used to guide patients and to encourage behavioral changes where it is needed.[9] For instance, the app Medisafe gives patients the ability to track their prescription medications and their adherence to their administration. Currently, Medisafe is being used by over five million patients worldwide with the developer claiming that it increases adherence by 72 percent.[10]

Other apps are enabling the patients to better engage with their illnesses by monitoring their progress and self-diagnosing. For instance, patients suffering from hypertension are now able to monitor their blood pressure using devices like the Apple Watch, ultimately handing over the task of measuring blood pressure from the doctor to the patient. This single capability releases the patient from many lengthy visits to a doctor or clinic and their reliance on a specialized device to measure their blood pressure.

Placing the Patient at the center of their treatment

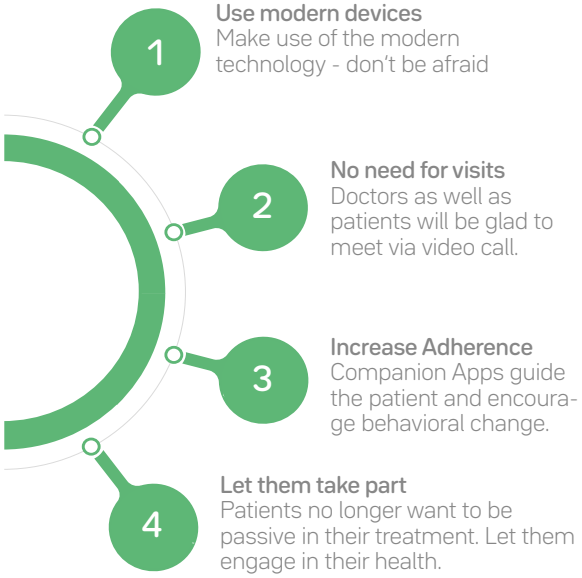
Another wearable device, named Kardia, converts a patient's smartphone into an EKG that can detect Atrial Fibrillation, Bradycardia, Tachycardia, or normal heart rhythm within 30 seconds.[11] This device immediately sends the data of an occurring event to the doctor who can take the necessary steps to intervene. It also allows the patient to send the doctor a voice recording with comments on they feel. A doctor's consultation via video call is becoming more commonplace too, especially for patients living in rural areas or a significant distance away from a study center/clinic. This has made a crucial difference for many.[12]

We are at the cusp of a truly transformational change. The advent of digitization, coupled with the concept of placing the patient at the center of the clinical study, is beginning to gain serious traction.[14]

> *Since its launch in 2015, the mPower app for research on Parkinson's disease has enrolled over 10,000 participants, making it the largest Parkinson's study in history — with 93 percent of participants having never taken part in any kind of research before.*[13]
>
> - Apple

However, there is considerable potential for much more efficient, reliable, and less costly solutions. The majority of studies still rely on old-fashioned methods to conduct i.e., the use of patient diaries, done with a paper notebook, entirely relying on the patient's memory and the many visits to the clinic that require the patients to travel countless miles every month.[15]

While wearables are getting more and more popular in trials, they are still not accepted in everyone's mind. Despite that, the number of wearable devices are increasing. Matthew Bonam (AstraZeneca – Pharmaceutical Project Manager) believes that by 2020, nearly 70-80 percent of healthcare data will be collected by the patient in their own home. This leads to a new understanding of the truly patient-centric approach, which combines all aspects of a study's coordination.

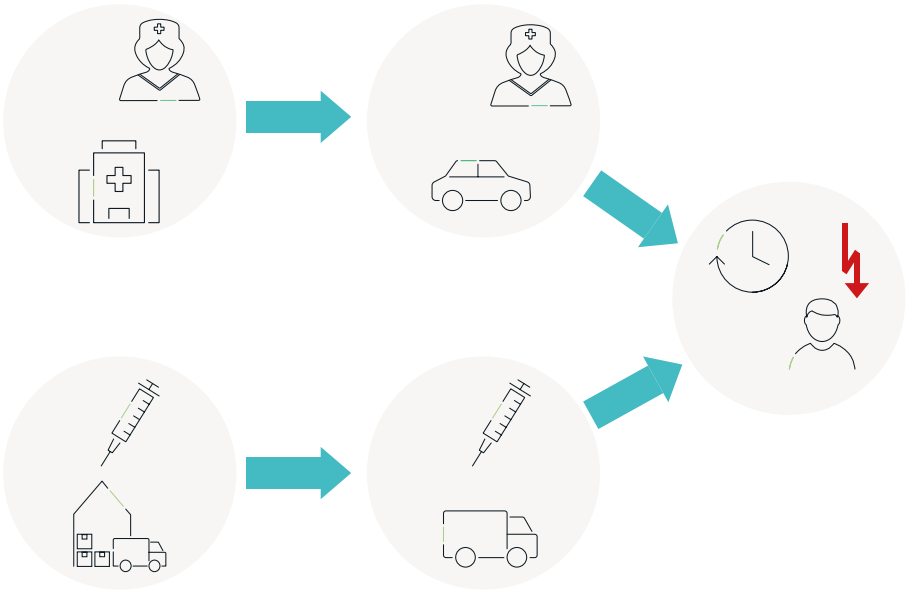


Truly Patient-Centric Home-Based Clinical Trials

> *Patients increasingly act like consumers, expecting to control decisions about their care and to receive individualized products and services.*[16]
>
> - Vicki Anastasi, Vice President and Global Head of Medical Device and Diagnostics Research

For a truly patient-centric approach, the participant must be able to complete nearly the entire study at the comfort of their own home, with their participation integrated into their own lifestyle and at their own schedule. For this reason, it is believed that the Direct to Patient (DTP) model is the way to go. As the logistics provider Marken explains, the DTP approach has a positive effect on the commitment of patients.[17]

One major challenge that is often overlooked is the distribution and administration of the IMPs. Today, in most cases, specialty logistic providers play an integral part in the process; picking up the pharmaceuticals from a pharmacy or distribution center and delivering individual shipments in a tightly-defined time frame to the patient's home. For this process to work effectively, many things need to align. The logistics provider, home trial nurse, and patient all need to be at the patient's home at a specific time in order to receive and administer the medication. Matters can become complicated when the IMP is temperature sensitive, and the necessary verification to its integrity must be made before administration.



> *Managing such a decentralized process requires precision in coordinating clinical staff, clinical trial product, and the patient. From ensuring the product integrity away from a clinical site, to scheduling delivery of the product during a time that a nurse can be available to administer it, to capturing the right data at the right time during the patient's course of treatment.*[18]
>
> - Sam Herbert, President at World Courier

With the home-based approach, new challenges arise. The difficulties seem to be endless as Sam Herbert describes it.

28 out of 57 new approved drugs were bound to the cold chain in 2017 and with the continued rise in biological candidates[19]; this ratio is only set to increase. Such medicines need a verifiable, unbroken cold chain, so the success of the delivery depends on multiple factors, particulary the punctuality of each party in the delivery chain. Product security and the privacy of the patient are also of paramount concern.

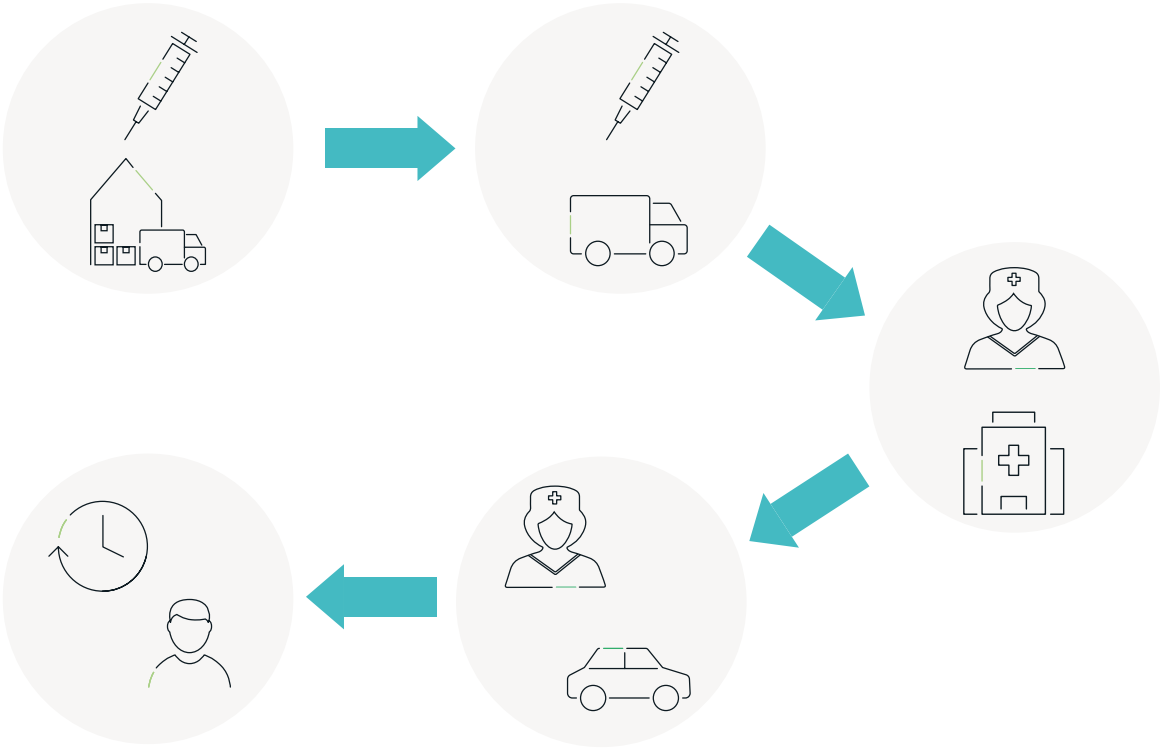
The storage and transport of IMPs can be a daunting and extremely complex process when it comes to DTP clinical trials and must comply with GDP (Good Distribution Practice) standards. Highly trained staff is required to handle the product throughout the transportation cycle.

They must adhere to strict controls and be able to verify the product is delivered in perfect clinical condition. Failure to do so can cause severe setbacks for the patient, the sponsor, and the general progress of the study.

The major pain-point in this process remains the coordination of the three key parties (home nurse – transport provider – patient). It's a highly inflexible process that can negatively impact the patient experience, especially when delays occur. In such cases, the home nurse's schedule becomes stressed; the patient is confined to their home until the product arrives or worse, misses their scheduled dosing altogether. Such instances risk the integrity of the trial and can increase the likelihood of patient non-adherence or dropping-out.

Addressing The Key Logistics Challenge

The first step to finding a solution to the challenges surrounding the coordination between home nurse, logistics provider, and patient is to ask; is it really necessary to have the most critical and challenging part of the supply chain - the coordination of logistics provider and home nurse - take place at the patients' home? The answer should be no.



The risk of this crucial meeting point puts a lot at stake, but in order to change, all parties have to come together to redefine the process. It would be far more comfortable, safer, and less costly if the logistics provider could deliver the drug product to the home nurse's local study center/pharmacy. The nurse could then bring the medication to the patients with him/her directly. However, in order for such a shift in the supply chain to be feasible, an innovative cooling device with smart tracking capabilities would be required.

The nurse can arrive at the study center/pharmacy, take secure, temperature-controlled possession of the patients' medications for the day, and leave for their scheduled appointments. Such an approach would require no unnecessary waiting time for the home nurse and patient, no coordination struggle between the parties, better overall service, and experience for the patient, and is less error-prone.

The Quest For A Fully Integrated Solution

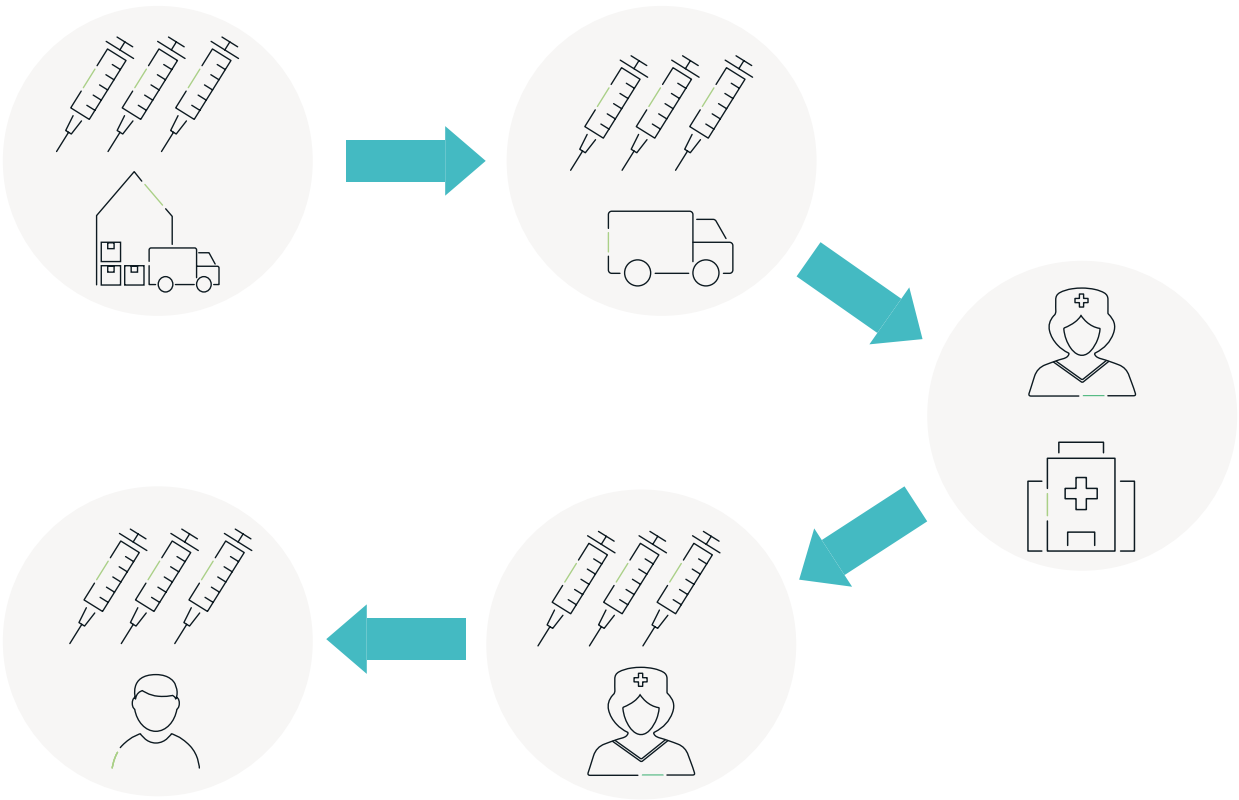
With wearable devices and healthcare apps on the rise, the opportunity exists to combine the usage of such gadgets and smart IoT devices to create a private healthcare hub directly at the patients' home.

A fully-integrated solution has the ability to increase trial participation, retention rates, and overall adherenc. Also, with home nursing not bound to non-core activities such as those presented by the current logistical challenges, the nurse can spend more time with patients, creating closer relationships and providing enhanced care.

To improve on this solution further, one can look to the secure, temperature-controlled storage of medications at the patients' home.

This would further reduce the burden on the home nurse by requiring fewer medication drops, if any, by effectively extending secure GMP storage to the patients' home. As a result, the home nurse has less to carry, and the study center/ pharmacy would have more storage space at their facility.

In this scenario, the logistics provider would transport larger batches of product to the study center/ pharmacy, and the home nurse would then deliver set quantities, which may last several weeks, for the patient to store at their home.



In combination with novel IoT devices and apps, the patient can be granted access to their health data and be empowered to actively participate in their particular treatment. They can act upon their healthcare.

With the use of RFID technology, devices in which the medication is stored can provide transparency over home inventories and notify authorized coordinators when supplies are running low. Before the medication is stored, the RFID code of the drug is simply scanned over the sensor of the device to log that a full batch is stored. When part of the batch is taken out, a separate RFID code on the product is scanned, which gets logged as taken out and used. Through this process, the device can know when medication is used up and can even place an order for replenishment at the study center automatically. All the while, the patient will have full visibility into their inventory.

When connected to a central record system, the patient, as well as the involved doctors, can begin working closer together. The devices dashboard not only shows temperature but humidity but can highlight any risk of degradation or deterioration. Doctors can see whether the patient takes their medication regularly, and the patient can have insights, giving a participatory feeling, positively impacting their experience in the study.

By adding these very personalized details, patients can have a more inclusive experience, leading to an increase in retention and adherence. The enrolment process will benefit from this innovative approach, as well. If patients know from the beginning of the study, that they will gain control, be afforded flexibility and mainly treated at home, they are more likely to participate in the research and will be less likely to drop out.

The Future Of Home-Based Clinical Trials

Patient centricity, where participants become an active part of their treatment and do not just remain the subject of a study, is increasing. Major pharmaceutical corporations like Bayer and GSK are feverishly promoting a more patient-centric approach to clinical trials and are continuously trying to find new ways to engage with patients.[20] Still, the pressure to reduce costs in the enrolment process remains.

Patient engagement evolves into personalized profiling in search of the perfect participants and tends to adapt to modern social standards like an increase in the diversity of patients and a better online presence. However, by collecting more data from people, another challenge is growing: Getting in charge of the data to arrange it and use it meaningfully.[21]

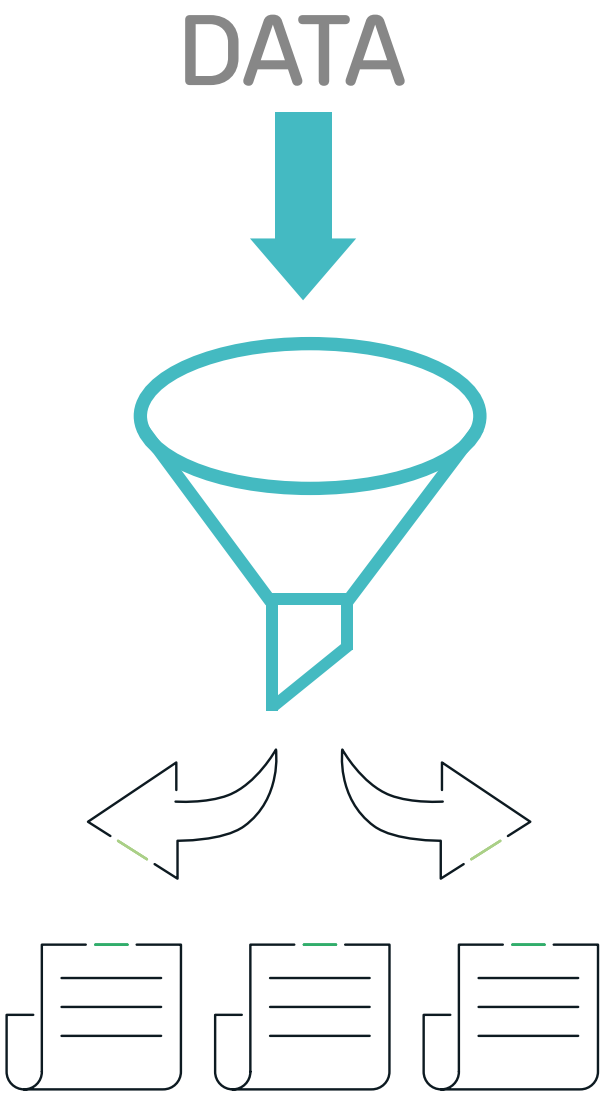
Working together for everybody's advantage

Big Data in healthcare is a double-edged sword. The considerable amount of data offers opportunities for advancements to researchers and physicians, who were not able to access such troves of data in the past. However, to improve the R&D process, it is essential to be prepared to use the data in a standardized format.[22]

Since its inception, each pharmaceutical company and institution has been collecting massive quantities of data. Furthermore, each field of expertise has developed its own way to store and receive the data. It is urgently necessary for companies and research institutions to work closer together to create standardized methods. Such collaboration will make it possible to compare data derived from patients' devices with the data of patients visiting the hospital or study center for consistency.

For example, in France, four Parisian hospitals combined their patient data from the last ten years.[23] Their goal: creating a statistical value regarding patients coming to the hospitals. This data was then used to calculate how many employees should work on specific days. This method not only saved the hospitals money on less busy days but also improved medical services on more stressful days.

The result of such an exercise is the clean and homogenous use of data, which can be used to improve adherence of patients and speed up treatment.

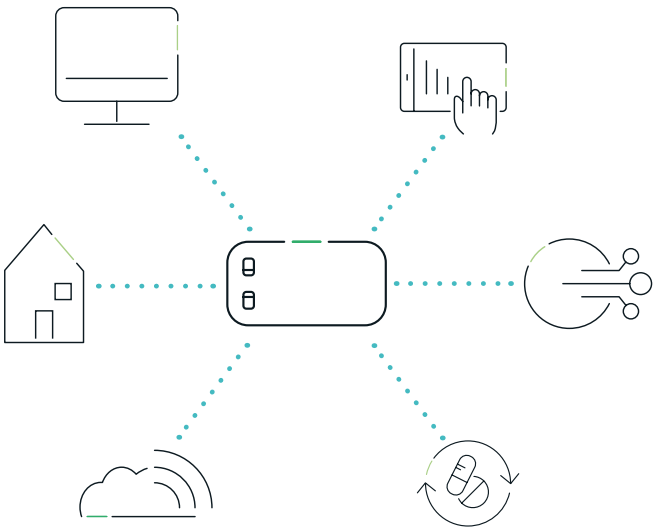


Using the Data

With the right use of Big Data comes the relevance of Artificial Intelligence. Without machine learning, it is impossible to get a complete dataset out of the massive amount of information.

An app called "Autism & Beyond" shows what is possible in diagnostics and research in the future. With the use of the front camera and face recognition, AI can analyze the emotional reactions of the user.[24] The app was developed for children over the age of 18 months, to help diagnose autism as early and as easily as possible. Within the first months, this app has had more participants than a nine-month ongoing trial.

The logistics portion of clinical trials can also use Artificial Intelligence to its benefit. By analysing the data of routes, traffic, time of arrival, or delays, it is possible to optimize deliveries and avoid late arrival. It can also identify potential risk factors to be avoided, like traffic jams or accident routes.



Central record systems and data security

Machine Learning can help increase the enrolment rate by extracting the patient's medical records out of a central system; a task that would take seconds for a computer but weeks or months for humans. This alone highlights the need for a central electronic patient record system. Such a system could help predict potential issues associated with the care of patients, prevent illnesses from spreading and enhance their experience.

However, still one of the greatest concerns with Big Data is data security. When it comes to confidential data, such as a patient file, cybersecurity must be guaranteed. The emerging use of blockchain technology will secure patient's and researchers' data and remain compliant to CFR Part 11 and GDPR, as well as assuring that the study is correctly blinded.

Conclusion

All these facts point to a new era of clinical trials where the patient will no longer be a passive subject in the process. On the contrary, the patient will be the most crucial element of the whole study. After all, it is the patient who is the one that makes a study, affordable or too costly, reliable or not, success or failure.

Only a truly patient-centered clinical trial, with the comforts of home and supported by the latest technologies, can bring healthcare and R&D into the future.

Sources

[1] Science Direct. (2016, April). Retrieved from Drugs, Devices, and the FDA: Part 1: An Overview of Approval Processes for Drugs: https://www.sciencedirect.com/science/article/pii/S2452302X1600036X

[2] Clinical Leader, (2018, August 02), https://www.clinicalleader.com/doc/major-challenges-with-global-clinical-trials-and-how-to-overcome-them-0001

[3] Moe Alsumidaie, P. S. (2015, August 31). Why Are Cancer Clinical Trials Increasing in Duration? Retrieved from http://www.appliedclinicaltrialsonline.com: http://www.appliedclinicaltrialsonline.com/why-are-cancer-clinical-trials-increasing-duration

[4] Commerce, P. (2016, April 04). Advances in clinical trial logistics. Retrieved from pharmaceuticalcommerce.com: https://pharmaceuticalcommerce.com/clinical-operations/advances-in-clinical-trial-logistics/

[5] Lars Osterberg, M. T. (2005, August 04). Adherence to Medication. Retrieved from http://www.ub.edu: http://www.ub.edu/farmaciaclinica/projectes/webquest/WQ1/docs/osterberg.pdf

[6] CB Insight (2018, August 07). The Future Of Clinical Trials. Retrieved from https://www.cbinsights.com: https://www.cbinsights.com/research/clinical-trials-ai-tech-disruption/

[7] Clinical Research News. (2015, June 15). Retrieved from http://www.clinicalinformaticsnews.com/eCliniqua_content.aspx?id=151076

[8] Tointon, A. (2016, Juni 27). The issue of patient retention in clinical trials. Retrieved from https://www.centerwatch.com: https://www.centerwatch.com/news-online/2016/06/27/issue-patient-retention-clinical-trials/

[9] The Future Of Clinical Trials. (2018, August 07). Retrieved from https://www.cbinsights.com: https://www.cbinsights.com/research/clinical-trials-ai-tech-disruption/

[10] Medisafe. (2019, Juli 22). Patient engagement platform. Retrieved from www.medisafe.com: https://www.medisafe.com/?lang=de

[11] AliveCore. (2019, Juli 22). AliveCor. Retrieved from https://www.alivecor.com/: https://www.alivecor.com/

[12] Health. (2017, January 30). Retrieved from You Can Video Call a Doctor Now, But Should You?: https://www.health.com/mind-body/you-can-video-call-a-doctor-now-but-should-you

[13] Apple. (2019, Juli 22). ResearchKit and CareKit. Retrieved from www.apple.com: https://www.apple.com/researchkit/

[14] Hebenstreit, C. (2019, March 29). The role of new technologies in creating a patient-centric future. Retrieved from healtheuropa.eu: https://www.healtheuropa.eu/new-technologies-patient-centric-future/91035/

[15] Academy, E. P. (2016, November 18). Assessing participant adherence during clinical trials. Retrieved from www.eupati.eu: https://www.eupati.eu/clinical-development-and-trials/assessing-participant-adherence-during-clinical-trials/

[16] Anastasi, V. (2016, May 25). Applications for Wearables and Apps in Precision Medicine. Retrieved from www.iconplc.com: https://www.iconplc.com/insights/blog/2018/04/18/wearables-and-apps-in-precision-medicine/index.xml

[17] Putwain, A. (2016). Clinical Trials Insight. Retrieved from viewer.zmags.com: http://viewer.zmags.com/publication/ad20d93c#/ad20d93c/1

[18] Commerce, P. (2016, April 04). Advances in clinical trial logistics. Retrieved from pharmaceuticalcommerce.com: https://pharmaceuticalcommerce.com/clinical-operations/advances-in-clinical-trial-logistics/

[19] Commerce, P. (2018, January 17). Half of 2017 FDA drug approvals are cold-chain products. Retrieved from pharmaceuticalcommerce.com: https://pharmaceuticalcommerce.com/clinical-operations/half-2017-fda-drug-approvals-cold-chain-products/

[20] MESM. (2019, July 29). Clinical Trials Innovation: What's on the horizon? Retrieved from https://www.mesm.com: https://www.mesm.com/blog/clinical-trials-innovation-what-s-on-the-horizon/

[21] The Future Of Clinical Trials. (2018, August 07). Retrieved from https://www.cbinsights.com: https://www.cbinsights.com/research/clinical-trials-ai-tech-disruption/

[22] Hebenstreit, C. (2019, March 29). The role of new technologies in creating a patient-centric future. Retrieved from healtheuropa.eu: https://www.healtheuropa.eu/new-technologies-patient-centric-future/91035/

[23] Marr, B. (2016, December 13). Forbes. Retrieved from Big Data In Healthcare: Paris Hospitals Predict Admission Rates Using Machine Learning: https://www.forbes.com/sites/bernardmarr/2016/12/13/big-data-in-healthcare-paris-hospitals-predict-admission-rates-using-machine-learning/

[24] Apple. (2019, Juli 22). ResearchKit and CareKit. Retrieved from www.apple.com: https://www.apple.com/researchkit/

Tec4med

TEC4MED LifeScience GmbH
Otto-Hesse-Str. 19 Block T9
64293 Darmstadt

Contact:
Telephone: +49(0)6151-360 37 00
Email: info@tec4med.com

Responsible for contents and design:
Raphael Warnke, Pascal Hoffmann