

Delight the Customer using Agile Transformation in Clinical Research

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ABSTRACT

In the new era of drug development, the pharmaceutical industry needs new solutions to meet rapidly changing client and patient necessities. The healthcare industry is under increasing pressure to increase the customer experience, improve quality, cost efficiency, and come up with innovative solutions to keep up in rapidly evolving markets.

Applying agile methodologies will allow clinical organizations to collaborate, focus swiftly, and diligently prioritize the innovations and developmental tasks that matter the most, resulting in a shorter developmental timeframe.

Agile methodology was created as a response to the shortcomings of traditional development methods such as the waterfall method that is traditionally used in the drug development process.

In this paper, we will be describing how clinical organizations can benefit by adopting agile, briefly discuss some of the use cases of agile in various areas of clinical research and share some challenges associated with agile implementation.

INTRODUCTION

As quoted by Edward T. Hall, an American anthropologist that “Culture is not made up but something that evolves which is human” [\[Ref:1\]](#)

We all know that about 10% of the iceberg is visible and around 90% is not visible and submerged in the water. What moves the iceberg is not the visible breeze on the surface, but invisible undercurrents in the water. In agile terms, the visible iceberg is about DOING agile and the submerged section is more about BEING agile. The top portion is about the processes, tools, practices, and submerged portion, which is more powerful is all about the mindset and cultural aspects like principles, values, collaboration, and flexibility, etc.

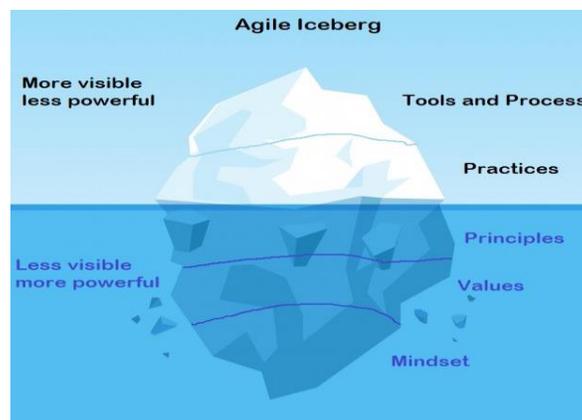


Figure 1

In current circumstances of a global pandemic and new age of urgency, it's time to reconsider the current approach of clinical trials and regulatory approvals. It's more important than before to supplement traditional randomized clinical trials with real-world evidence data so that real-time clinical analysis can be achieved and customized therapies to patients can be accelerated.

Agile processes have already proven their ability to be more efficient in the development of software devices and applications as compared to the traditional waterfall model as it provides an iterative development process. The agile methodology involves user's and stakeholders' feedback at the early stages of development thus helping in incorporating any changes early on.

The traditional waterfall methodology is useful when requirements are not expected to change and expected results including intermediate steps are clear. However, it is generally difficult to define the scope before initiation of the task. In the traditional approach, since user's or stakeholders' involvement is limited, timely feedback is not included during the initial stage. This can lead to a final product that's not in line with customer needs and expectations.

Agile teams are usually small, self-governing, cross-functional teams focused on solving complex problems rapidly. In an agile process, the project progress is monitored in every iteration (sprint) and if the approach is not working then the suitable changes are made swiftly as shown in figure 2 below.

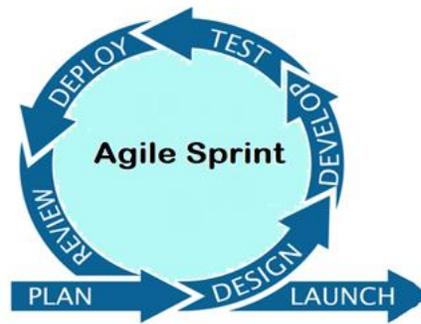


Figure 2

The agile key principles of envisioning, engagement, and empowerment will enable agile transformation within clinical organizations. Agile can be useful in projects where requirements are ambiguous and the user is not sure of their needs beforehand. It is difficult to predict risks during the planning phase but with the agile approach, risk analysis and process assessment are performed in every phase which will help to avoid rework and any additional costs in the later stage.

This type of approach will help clinical organizations to develop a solution, test them, make changes and make adjustments as needed, and move forward iteratively to achieve the desired output as planned.

In this paper, we will briefly discuss some areas in healthcare (figure 3 below) where the agile methodology is already helping in the transformation.

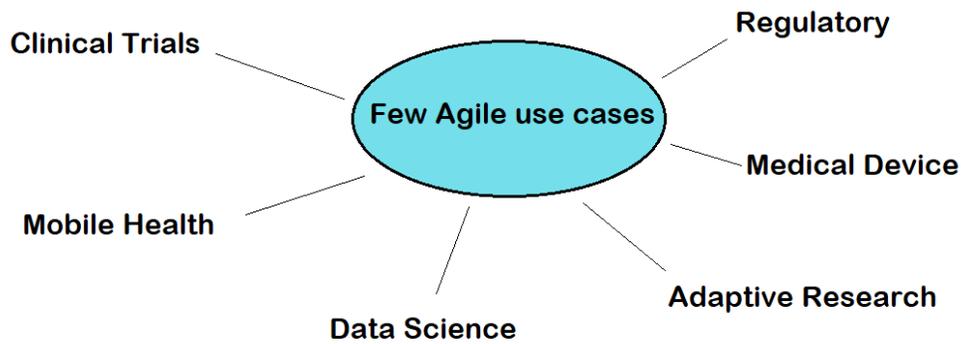


Figure 3

Applying the Agile Mechanism in the Clinical Trials

Nick Kenny, Chief Scientific Officer, Syneos Health, says, “The key is building a flexible and agile trial platform. If you can see, early on, that a protocol isn’t working, the scalable platform design allows you to swap in another, almost the way you would replace a light bulb” [\[Ref:2\]](#)

The clinical trial process has been under constant pressure to reduce costs, improve quality, comply with the regulations and meet end-user needs. Some of the current challenges in clinical trials are trial design, regulations, costs, patient access, and technology.

Figure 4 below mentions some of the areas in the clinical trial process where agile is already helping in resolving some of the above challenges.

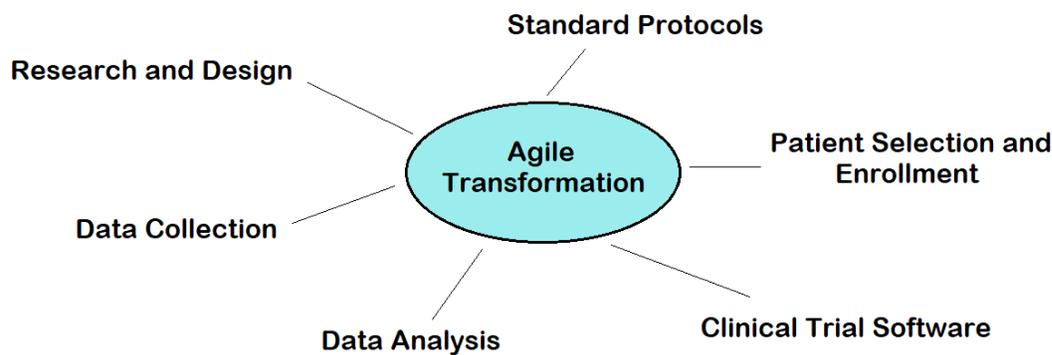


Figure 4

The introduction of the agile methodology has played an essential role in the transformation of cost-effective and efficient clinical trials.

One of the major advantages of agile methodology is the fact that the clinical trial process can be altered during the development phase. It increases flexibility and makes it easy to reassess and make any needed changes at every stage. The feedback at every stage of development helps in achieving the desired output.

In agile methodology, the testing periods are reduced, and the tasks are made to be worked within shorter timeframes which can be easily handled. Agile methodology equally uses the processes of coding, iteration, and testing which are done as the processes are established to create effectiveness in the product quality.

In modern clinical trials, we need end-to-end data standardization and integration strategy that considers all the dimensions of clinical data.

CDISC 360 is a new project from Clinical Data Interchange Standards Consortium (CDISC) organization that uses agile scrum methodology to support standards-based, metadata-driven automation across the end-to-end clinical research data lifecycle and substantially improve efficiency, consistency, and re-usability [\[Ref:3\]](#)

Some of the examples of agile use in clinical trials are as follows:

- Beat AML master clinical trial is a novel trial to speed the development of drugs for acute myeloid leukemia (AML) which was designed by the Leukemia & Lymphoma Society (LLS) in partnership with the FDA and a host of oncology companies, and Syneos Health providing contract research services [\[Ref:2\]](#)
- Elligo Health research site-less trial pilot- Elligo's digital system reimagines patient recruitment and helps prepare the new sites to conduct the research, leveraging centralized infrastructure, technology, and expertise that replaces the need for typical on-site clinical research teams [\[Ref:2\]](#)
- ACORN AI intelligent trials solution helps in enabling more agile and make confident decision to optimize clinical trials. It delivers insights to improve the speed and success of trials through better study design, optimized site selection, enrollment and forecasting, and real-time performance monitoring [\[Ref:4\]](#)
- Electronic patient-reported outcomes (ePRO) and Agile methodology- Clinical Ink uses an agile approach focused on improving user experiences for patients, sites, and sponsors/CROs. It provides a more direct pathway to prototype evaluation, reduces testing, and moves scoring and coding earlier in the process to accelerate the deployment process for sponsors and CROs [\[Ref:5\]](#)

Agile and Regulatory Compliance

Clinical agile methodology can easily adapt to the challenges presented by the changing regulations, guidelines, and emerging technologies, thus providing a competitive edge and additional growth opportunities.

FDA and the regulatory bodies mainly focus on the safety of the products being manufactured. They allow the organizations to design and document their development process, their compliance with regulations, and demonstration of the products created by following the prescribed guidelines.

The 21st Century Cures Act provides expedited approval pathways for revolutionary medicines and encouraging the use of real-world evidence to ensure that effective medicines are available to more patients. The law builds on FDA's ongoing work to incorporate the perspectives of patients into the development of drugs, biological products, and devices in the FDA's decision-making process [\[Ref:6\]](#)

In 2012, the Association for the Advancement of Medical Instrumentation (AAMI) released the technical information report (TIR45 guidance document) to steer medical device design and development companies on how to work agile within a regulated process [\[Ref:7\]](#)

US FDA explicitly recognized agile as an acceptable standard in January of 2013, referring to AAMI TIR45 guidance document and added it to its list of the approved standards to be used by the manufacturers [\[Ref:8\]](#)

Agile in Medical Device Development

Medical device companies can incorporate agile methodology to improve the quality of the medical device software and continuously improve their functionality. As agile allows to incorporate feedback during the entire process, it provides an opportunity to check the evolution of the project. Agile focuses on aligning the final product more precisely with the user's needs.

MDevSPICE®, an integrated framework of medical device software development best practices using Agile methodology, has been developed to assist software medical device developers to reach regulatory compliance. It integrates generic software development best practices with requirements from medical device standards enabling robust software process assessments to be performed when preparing for a regulatory audit [\[Ref:9\]](#)

Agile in Digital Health Solutions

The rapid pace of change in mobile technology has led to exploring agile research methods. Agile methods help in ongoing and iterative evolution based on continuous feedback and also help improve the quality and safety of digital health solutions.

Agile development is one of the common approaches to digital product development to provide software at regular short intervals, offer flexibility to respond to changing requirements, and incorporates the ability to adapt to feedback through continuous iteration.

An iterative approach to research that allows additional flexibility, rapid evaluation, and changing specifications as technology changes may encourage additional assessments of digital health products.

Some examples of agile use in digital health solutions are as follows:

- Iora Health built its electronic health records to respond to its agile and team-based approach to coordinate care [\[Ref:10\]](#)
- mHealthDroid is an open-source android implementation of a mHealth Framework designed to facilitate the rapid and easy development of biomedical apps. The framework is devised to leverage the potential of mobile devices like smartphones or tablets, wearable sensors, and portable biomedical devices [\[Ref:11\]](#)
- The NeoTree is a fully integrated digital health intervention that combines immediate data capture, entered by healthcare workers (HCW) on admission, while simultaneously providing them with evidence-based clinical decision support and newborn care education [\[Ref:12\]](#)
- MindClimb - A mobile phone-based application for use during cognitive behavioral therapy for adolescents with anxiety [\[Ref:13\]](#)

Using Agile Methodology in Data Science

Figure 5 below describes the Agile iterative process in Data science.

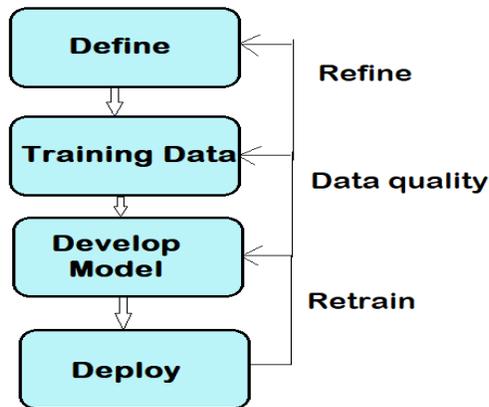


Figure 5

Christos Hadjinikolis, Data Scientist at Mcubed London 2018, says, “If practicing Agile Software Development produces value from learning through failing fast and safe... then a Data Scientist’s role in an Agile team is to help the team to fail faster!” [\[Ref:14\]](#)

The agile framework prescribes a rapid, continuous-improvement process that enables healthcare practitioners to provide regular feedback to data scientists and evaluate the predictive model to make the model robust. In the traditional approach, the data scientists worked on the tasks in isolation and didn’t deploy the models in real-time and healthcare practitioners were not involved.

The goals and requirements for the predictive models may change by the time the model is deployed which may make the model outdated.

There may also be a scenario that the predictive model performs well only in certain patient populations across a certain time period. In such a case, the model is modified before the next sprint cycle. The agile approach can shorten the time of final models with collaboration and constant iteration compared to the traditional approach.

Some examples of agile use in data science are as follows:

- The Team Data Science Process (TDSP) is an agile, iterative data science methodology to deliver predictive analytics solutions and intelligent applications efficiently. TDSP includes best practices and structures from Microsoft and other industry leaders to help toward the successful implementation of data science initiatives [\[Ref:15\]](#)
- DataOps is an agile methodology for developing and deploying data-intensive applications, including data science and machine learning. A DataOps workflow supports cross-functional collaboration and fast time to value. With an emphasis on both people and process, as well as the empowering platform technologies that underlie it, a DataOps process allows each collaborating group to increase productivity by focusing on their core competencies while enabling an agile, iterative workflow [\[Ref:16\]](#)

The Agile Approach to Adaptive Research

The use of adaptive design has been shown to shorten product development time and is therefore very cost-effective for clinical organizations.

The role of adaptive design is to make clinical trials more flexible, efficient, and faster and these trial designs are also known as flexible designs.

The 21st Century Cures Act instructs the Food and Drug Administration (FDA) to update its guidance on adaptive designs for sponsors of investigational drugs and biological products. The legislation refers to adaptive designs as modern and novel methods [\[Ref:17\]](#)

The agile approach to adaptive clinical trials will bring many advantages such as bringing new drugs and vaccines to patients faster, cost reduction, improvement in patient selection, and making the whole clinical trial process more flexible, adaptable, and being able to respond to change.

One of the examples of agile use in adaptive research is as follows:

The Global Coalition for Adaptive Research (GCAR) is a non-profit established in 2017 to speed the discovery and development of cures for patients with deadly diseases. GBM AGILE (Adaptive Global Innovative Learning Environment), sponsored and managed by CGAR, represents a novel clinical trial system for evaluating and potentially approving multiple treatments for glioblastoma. It is the world's first global adaptive clinical trial for brain cancer [\[Ref:18\]](#)

Challenges of Adopting Agile

Agile development methods are designed to produce smaller quicker deliverables but are typically less formal in the documentation produced that can be a challenge when working in a regulated environment.

Every new methodology brings uncertainty, but without uncertainty, there is no innovation. Clinical organizations need to change their mindset and culture to embrace change and uncertainty.

For the clinical industry to excel, an agile and efficient integrated platform needs to be developed. Even though the new technology won't be adopted overnight and the shift to virtual trials won't be entirely straightforward, clinical research organizations must be agile to keep up with the ever-changing demands in this new era.

CONCLUSION

Per Pearl Zhu (Author, Digitizing Boardroom: The Multifaceted Aspects of Digital Ready Boards), Agile is more a "Direction," than an "End," a philosophy and mindset at board level [\[Ref:19\]](#)

Coming from software development agile transformation is not just about technology. It is about a new way of thinking. It is more collaborative, more creative, and much more effective than other methodology. Agile innovations can target patients, health care practitioners, and healthcare providers and can help in transforming services, customer experiences, and internal practices within the organization.

Agile transformation will help in enhancing the patient experience and will also help in optimizing overall clinical trial and key areas such as patient enrollment, monitoring, and site management. It will also enhance creativity and help in finding better and innovative solutions and redesign patient care.

REFERENCES:

[1] https://www.brainyquote.com/quotes/edward_t_hall_201512

[2] <https://www.syneoshealth.com/sites/default/files/thought-leadership-articles/pdf/Biopharma-Embraces-Life-Fast-Lane.pdf>

[3] <https://www.cdisc.org/cdisc-360>

[4] <https://www.medidata.com/wp-content/uploads/2020/10/Acorn-AI-Intelligent-Trials-FAQ.pdf>

- [5] <https://www.clinicalleader.com/doc/epro-and-agile-methodology-a-winning-end-to-end-solution-for-oncology-studies-0001>
- [6] <https://www.fda.gov/regulatory-information/selected-amendments-fdc-act/21st-century-cures-act>
- [7] https://my.aami.org/aamiresources/previewfiles/TIR45_1208_PREVIEW.PDF
- [8] https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfstandards/detail.cfm?standard_identification_no=30575
- [9] <https://publications.waset.org/10006565/supporting-embedded-medical-software-development-with-mdevspice-and-agile-practices>
- [10] <https://pubmed.ncbi.nlm.nih.gov/26250083/>
- [11] <https://pubmed.ncbi.nlm.nih.gov/26329639/>
- [12] <https://gh.bmj.com/content/bmjgh/4/1/e000860.full.pdf>
- [13] <https://mhealth.jmir.org/2020/12/e18439>
- [14] <https://2018.mcubed.london/sessions/data-science-agile-way/>
- [15] <https://docs.microsoft.com/en-us/azure/machine-learning/team-data-science-process/overview>
- [16] <https://www.oracle.com/a/ocom/docs/oracle-ds-data-ops-map-r.pdf>
- [17] <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5829673/#:~:text=In%20late%202016%2C%20the%20US,%20and%20'novel'%20methods>
- [18] <https://www.gcaresearch.org/>
- [19] <https://www.goodreads.com/quotes/7883455-agile-is-more-a-direction-than-an-end-a-philosophy>

RECOMMENDED READING:

Applying the Agile Mechanism in the Clinical Trails Domain for Drug Development

https://digitalcommons.harrisburqu.edu/cgi/viewcontent.cgi?article=1047&context=pmgt_dandt

Agile in an FDA Regulated Environment

<https://orthogonal.io/insights/ebook-agile-in-an-fda-regulated-environment/>

Agile Manifesto

<https://agilemanifesto.org/>

Mobile Health

<https://www.nature.com/articles/s41746-018-0053-1>

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4547155/>

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