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Agile innovation – an adaptive approach to transformation in Clinical Research Organization

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ABSTRACT

Healthcare organizations today need to be agile in the age of digital transformation. Creativity, innovation, and sustainability are some of the key skills that organizations today need to be continually adaptive.

Healthcare organizations are under mounting pressure to improve quality and reduce expenses. Agile helps the organization to quickly respond and adapt to ever-changing customer needs and evolving research requirements.

Agile relies on iterative improvement, encouraging adaptability and quick responses to validated feedback. This process can help in integrating design with development and adapt continually to reduce the innovation time.

INTRODUCTION

As quoted by Thomas A. Edison, “There’s a way to do it better – find it.” [Ref:1]

Innovation arises when we can see the same set of data in a new way. Clinical research organizations that manage clinical trials are part of an extremely innovative industry and need to constantly adapt in order to stay competitive. Organizations today need to shift their meaning of innovation from the generation of ideas to swift methods of running experiments to test them.

The clinical trials are under continuous pressure to reduce costs, improve quality, comply with regulatory requirements and meet the end-user needs. This type of approach will help clinical organizations to develop a solution, test them, make changes and adjust as needed, and move forward iteratively to achieve the desired planned output.

In the agile innovation process, if the project is accessed based on success or failure rather than learning, then the predominant motivation of people would be to avoid failure. For ideas to be useful, the ideas need to be openly shared, experimented with, and refined.

In a clinical research organization, the need for innovation depends on several factors such as customer needs, creating relational and emotional freedom for people to explore, changing roles, shift in a traditional mindset, advanced data analytics, accelerated automation, etc. as shown in Figure 1 below.

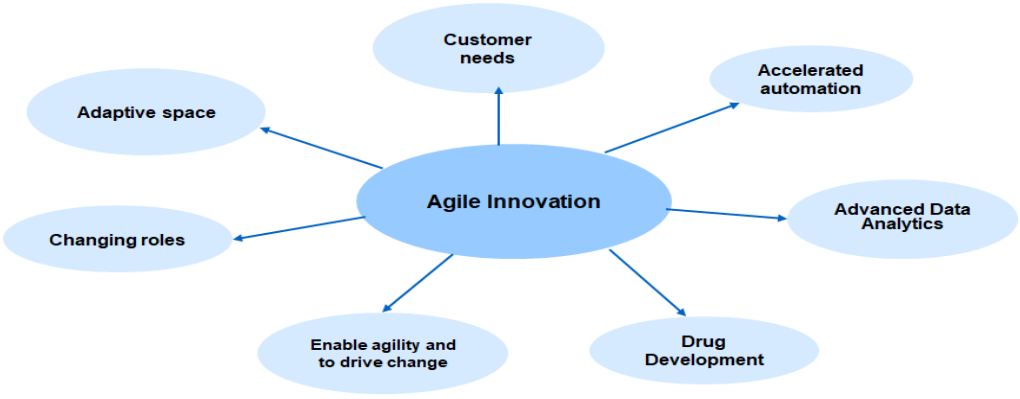

Figure 1: Agile innovation

In this paper, we will be discussing some of the above agile innovation areas where organizations need to focus on in creating an agile and adaptive innovation culture.

ADAPTIVE SPACE

Speed, agility, and responsiveness are essential to success in any organization.

Adaptive space is relational and emotional freedom for people to explore, exchange, and debate ideas on an ongoing basis. It is the space where we create intentional connections for people to be able to discover, develop, or diffuse ideas in a radical manner. Adaptive space is a bridge that connects operational systems and entrepreneurial pockets inside the organization as shown in figure 2 below.

The operational system is the day-to-day operations to scale, formalize and formally endorse ideas and deliver results on an ongoing basis.

Every organization would have entrepreneurial pockets in any hierarchy. These are individuals with novel ideas within the organization.

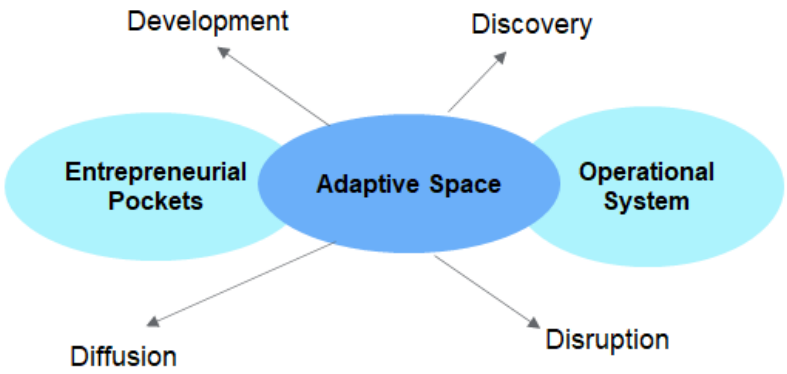

Figure 2: Adaptive space

Discovery connection helps people to have access to new innovative information. It can be through internal/external connections or brainstorming ideas through tools like design thinking. But ideas that aren't implemented are useless so we need small cohesive development teams where people can rapidly iterate tests, experiment, and exhibit them into real solutions and services.

Diffusion connections are needed to diffuse the ideas and solutions from the development team and diffuse them into the organization. Finally, we need disruption to create new normal within the organization with a new set of possibilities and ideas. For more details refer to the book Adaptive Space by Micheal J. Arena.

DESIGN THINKING

Design thinking starts with an intention, need, or a desire towards finding a better innovative solution. We can use creative problem-solving to quickly test ideas with end-users, iterate and move on.

Design thinking is an agile, iterative process for design and innovation that revolve on users' desires and needs and enables an organization to evolve as the industry changes and technology evolves. Design thinking acknowledges that there isn't one way to solve a problem. Instead, the methodology encourages questioning, experimenting, observing, and innovating in an environment that accepts diverse opinions and ideas.

The five steps that make up the design thinking process are empathize, define, ideate, prototype, and test as proposed by the Hasso-Plattner Institute of Design at Stanford (d.school) as shown in Figure 3 below [Ref:2]

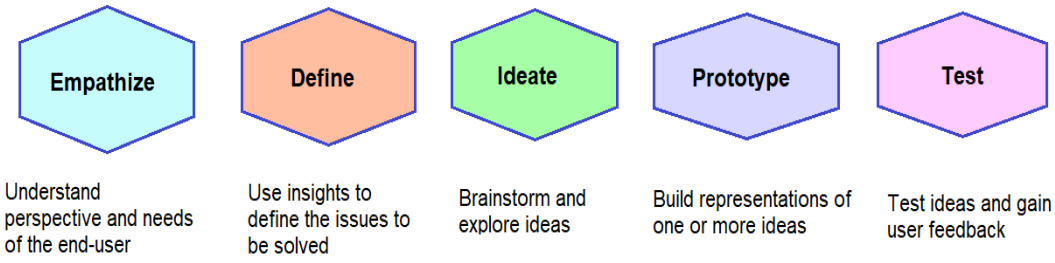

Figure 3: Stages of design thinking process

Design thinking can help in solving complex issues like understanding human needs, redefining the problems, creating several ideas in ideation sessions, adopting a hands-on approach, and developing a testable prototype/solution to the problem.

CUSTOMER NEEDS

Customer-centric organizations can anticipate customers' needs and delight them with innovative solutions and services. In agile methodology, the teams work intensively over short-cycle sprints to create working prototypes, test them with clients and obtain feedback to guide the next sprint.

Agile innovation is strongly focused on customer needs, collecting and quickly responding to customer feedback in sprint cycles, and empowering teams to freely adjust to customer demands.

We can provide useful innovative solutions once we understand the needs of the customer. This process is facilitated using an agile approach of providing several prototype iterations with frequent feedback and revisions. The customer is central throughout the process as shown in Figure 4 below.

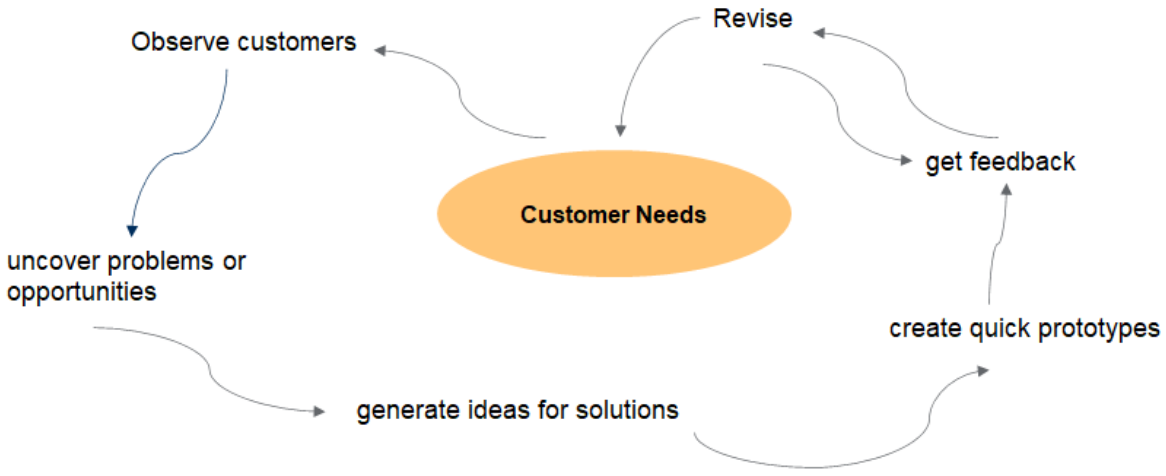

Figure 4: Customer Needs

ENABLE AGILITY AND DRIVE CHANGE

To be successful, an organization requires an agile mindset and drive to constantly rethink, revive, respond, and reinvent based on customer needs.

In today's world, programmers need to be more agile and faster when it specifically comes to understanding data, decision-making, and day-to-day deliverables. In order to build the right mindset, the programmers today need to focus on passion/commitment, curiosity/learning, and a growth mindset as shown in figure 5 below.

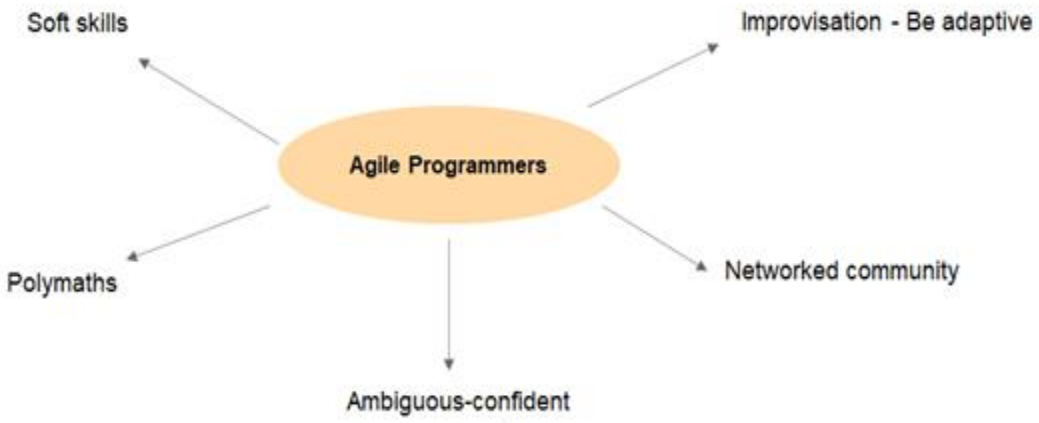

Figure 5: Agile programmers

Soft skills are the most important skill for agile programmers. The programmers are required to have expertise and experience in multiple areas and skillsets and be polymaths. Programmers should also be able to cope with change effectively and be comfortable handling risk and uncertainty.

Diverse thoughts and perspectives are very important in any team environment. Diversity ensures that organizations have different people with varying degrees of skills, expertise, experience, and approaches to problem-solving that will guarantee different innovative solutions. Every member in team brings diverse knowledge, experience, and vision to ensure that the project exceeds the expectations of the customer.

The agile programmers need to be adaptive and ready to provide spontaneous solutions. They also need to be confident in situations where enough background or supporting data for a particular situation is not available.

With the evolution of digital capacity, cloud computing, and handheld devices, more clinical data is available and stored in the digital space. The traditional programmer role may not be enough to handle these needs in the future. So, every function needs to evolve to the next stage to take on new responsibilities with changing roles.

INNOVATION IN DRUG DEVELOPMENT

Accelerating new drug discovery is critical, especially in addressing the spread of new diseases and preventing a pandemic. If we can use advanced digital technologies, to guide more judicious use of our resources, we can make many more drugs and bring them into market more effectively and quickly to patients.

Some of the areas of innovation that can help in improving the drug development process are shown in figure 6 below.

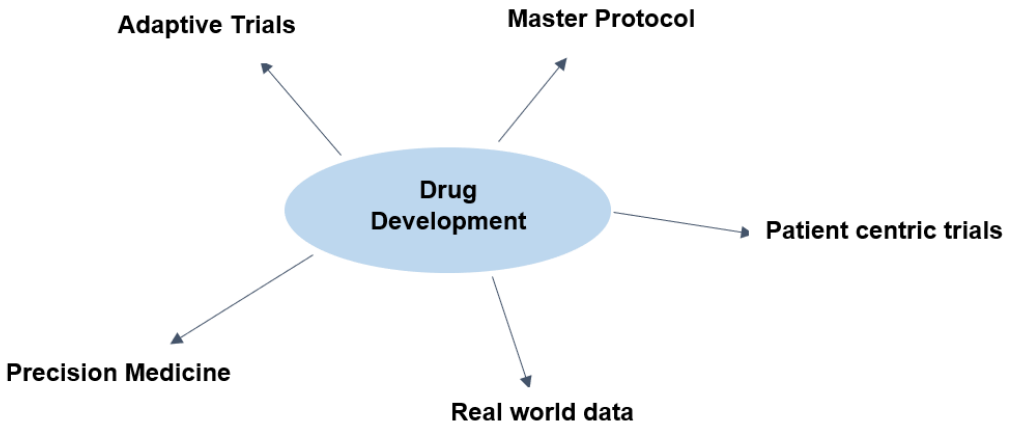

Figure 6: Drug Development

The innovations in drug development can help with efficient trials, accelerating patient recruitment, quicker drug launch, and market access.

Artificial intelligence has potential to transform many of the key areas in clinical trials, from protocol design to study execution, thus improving trial success rates and reducing the research and development burden.

Clinical trials using innovations offer greater opportunities to produce drugs that meet patient, regulator, and consumer needs.

ADAPTIVE TRIALS

An adaptive design is defined as a clinical trial design that allows for eventual planned revisions to one or more aspects of the design based on data collected from subjects in the trial. They allow the trial to adjust to information that was not available when the trial began. The adaptive design has several advantages including statistical efficiency and improved understanding of drug effects. [Ref:3]

The ability to stop a trial early if it becomes clear that the trial is unlikely to demonstrate effectiveness can reduce the number of patients exposed to the unnecessary risk of ineffective investigational treatment and allow subjects the opportunity to explore more promising therapeutic alternatives.

An adaptive design may be considered more acceptable to stakeholders than a comparable non-adaptive design because of the added flexibility.

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 GBM AGILE (Adaptive Global Innovative Learning Environment) [Ref:4]

MASTER PROTOCOL

The innovative regulatory approaches resulting from the 21st century Cures act [Ref:12] are modernizing new drug development. The use of clinical trials with a master protocol design is one example of a modern approach to expedite the development of oncology drugs. Because of the complexity of trials and the potential regulatory impact, trials must be well designed and well-conducted to ensure patient safety and to obtain quality data that may support drug approval.

Master protocols are used to simultaneously evaluate more than one investigational drug within the same overall trial structure.

A master protocol is defined as a protocol designed with multiple sub-studies, which may have different objectives and involve coordinated efforts to evaluate one or more investigational drugs in one or more disease subtypes within the overall trial structure.

Efficient clinical trial design strategies to expedite development of cancer drugs and biologics guidance document from FDA [Ref:5] provides recommendations on the design and conduct of clinical trials using master protocol.

The potential advantage of a master protocol is flexibility and efficiency in drug development, consistent with FDA's goal of helping to make safe and effective drugs and drug combination treatments available to the public. A master protocol provides an opportunity to incorporate efficient approaches, such as a shared control arm and/or the use of centralized data capture systems to enhance efficiency.

Master Protocols are often classified as basket trials, umbrella trials, and adaptive platform trials.

Basket designs are intended to study a single investigational regimen in several different diseases or disease subtypes as shown in figure 6 below.

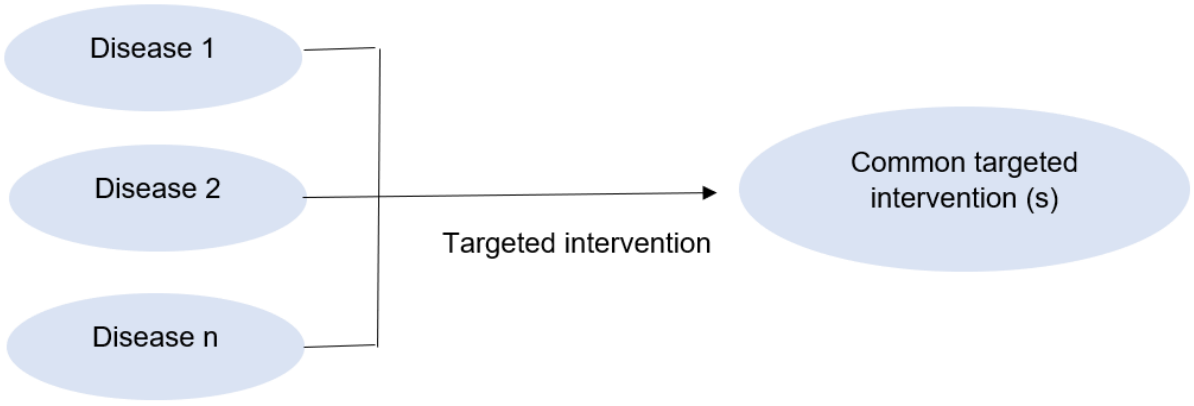

Figure 6: Basket trial

The first drug to receive approval from the U.S. Food and Drug Administration (FDA) for a "tissue-agnostic" indication was pembrolizumab, for the treatment of specific patients with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors, in 2018.[Ref:6]

FDA also approved Larotrectinib for the treatment of solid tumors with a NTRK fusion mutation later that year.[Ref:7]

Umbrella trial looks at multiple targeted therapies against the same disease as subgroups of one overall study population as shown in figure 7 below.

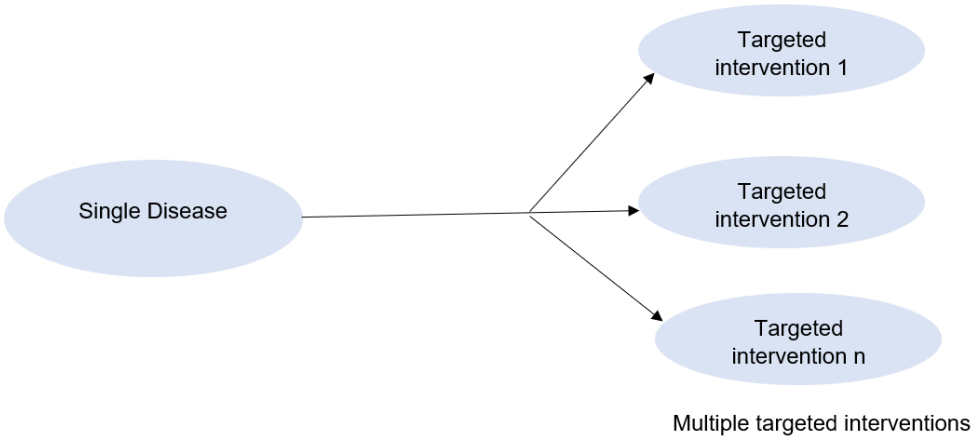

Figure 7: Umbrella trial

In Platform trials, studies are designed to assess multiple targeted therapies in the same study population, amending the protocol design when the ongoing data interpretation indicates that either an ineffective or efficacy threshold is reached

Few examples of the master trial protocol in oncology can be found at the following site [Ref:8].

The number of master protocols, especially in the last few years, has increased dramatically and this trend will continue to rise over the coming years. Master protocols, particularly platform trials, have the potential to improve efficiency across the broad spectrum of clinical trial research.

PRECISION MEDICINE

Precision medicine, sometimes known as "personalized medicine" is an innovative approach to tailoring disease prevention and treatment that considers differences in people's genes, environments, and lifestyles. The goal of precision medicine is to target the right treatments to the right patients at the right time. [Ref:9]

Advances in precision medicine have already led to powerful new discoveries and FDA-approved treatments that are tailored to specific characteristics of individuals, such as a person's genetic makeup, or the genetic profile of an individual's tumor.

Next-Generation Sequencing (NGS) tests are capable of rapidly identifying or sequencing large sections of a person's genome and are important advances in the clinical applications of precision medicine. Patients, physicians, and researchers can use these tests to find genetic variants that help them diagnose, treat, and understand more about human disease.

PATIENT CENTRIC TRIALS

Patient-centric trials offer more relevant benefits to patients than those developed in a less patient-centric manner. The patients today are more aware, making use of latest technologies and informed which has led to the way clinical trials are being approached and conducted.

‘Patient centricity’ means designing a treatment, clinical trial, or other health solution centered around the patient. Creating a patient-centric solution involves getting feedback from real patients and their loved ones and making decisions based on their needs and perspectives. [Ref:10]

REAL WORLD DATA

Real-world data is the data related to patient health status and/or the delivery of health care routinely collected from a variety of sources. RWD can come from several sources like electronic health records (EHRs), claims data, registries, mobile/sensor devices, etc. [Ref:11]

Although randomized control trials (RCTs) are ideal for deciding the efficacy and safety of new treatments, they are sometimes inadequate to address the evidence requirements of regulators and payers, which may prefer real-world data. Such data can be incorporated into clinical trials through hybrid trials.

Real-world data can also be used as an addition to the randomized clinical trial data to support drug approval. It can help in expediting the process of patient's access to treatments they need and also timing.

The combined data can help in quicker adoption of new innovations and technologies in drug development and market access.

The 21st Century Cures Act provides expedited approval pathways for revolutionary drugs and encourages the use of real-world evidence to ensure that effective drugs 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:12]

SOME AGILE INNOVATION EXAMPLES

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) [Ref:13]
- Elligo Health research site-less trial pilot [Ref:13]
- ACORN AI intelligent trials solution [Ref:14]

Some of the 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 coordinating care [Ref:15]
- mHealthDroid is an open-source android implementation of a mHealth Framework designed to facilitate the rapid and easy development of biomedical apps. [Ref:16]
- 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:17]

Few examples of agile use in data science are:

- The Team Data Science Process (TDSP) [Ref:18]
- DataOps is an agile methodology for developing and deploying data-intensive applications, including data science and machine learning. [Ref:19]

CHALLENGES AND SOLUTIONS

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.

One of the major challenges faced by pharmaceutical companies today is that the research and development process has become more expensive over time with increasingly complex trials and regulatory approval processes as described in Eroom’s Law. [Ref:20]

Recent years have seen exponential growth in both amount of data and the types of data used in healthcare research and drug development. Old ways of collecting data such as radiology images and personal medical records have been joined by newer methods, ranging from biometric sensors and genomics to social media

The regulatory and patient privacy policies that are region specific make data utilization a challenge in commercial drug development, since the data cannot be fully utilized till the data silos are further reduced.

Some of the other challenges to innovation in drug development are patients' perceptions of innovation, cultural barriers, and lack of understanding of the disease.

Some of the above challenges can be overcome with a skilled workforce, connecting data and people silos, collaborative partnerships, early patient and regulatory engagement, and advanced analytics.

To foster agile innovations, the organizations must foster an environment that encourages new ways of thinking which can sometimes be challenging.

Some of the actions that clinical research organizations can take are to encourage innovation within the organization, invest in people to update skills required to deliver innovative solutions, collaborate, and support diverse thoughts and perspectives along with a focus on learning. Organizations need to involve various stakeholders early in the initiatives and take feedback and make iterations to the solutions as needed.

CONCLUSION

As quoted by Georg Cantor, that "Great innovation only happens when people aren't afraid to do things differently."

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.

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

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.

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RECOMMENDED READING

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https://www.adaptivespace.net/

Delight the Customer using Agile Transformation in Clinical Research
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Next evolution step(s) for statistical Programmers
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