The use of data to find efficiencies in Drug Development - Getting the Most out of Wearable Technology in Clinical Research

Supriya Deshmukh

Sr. Manager, Statistical Programming, Syneos Health

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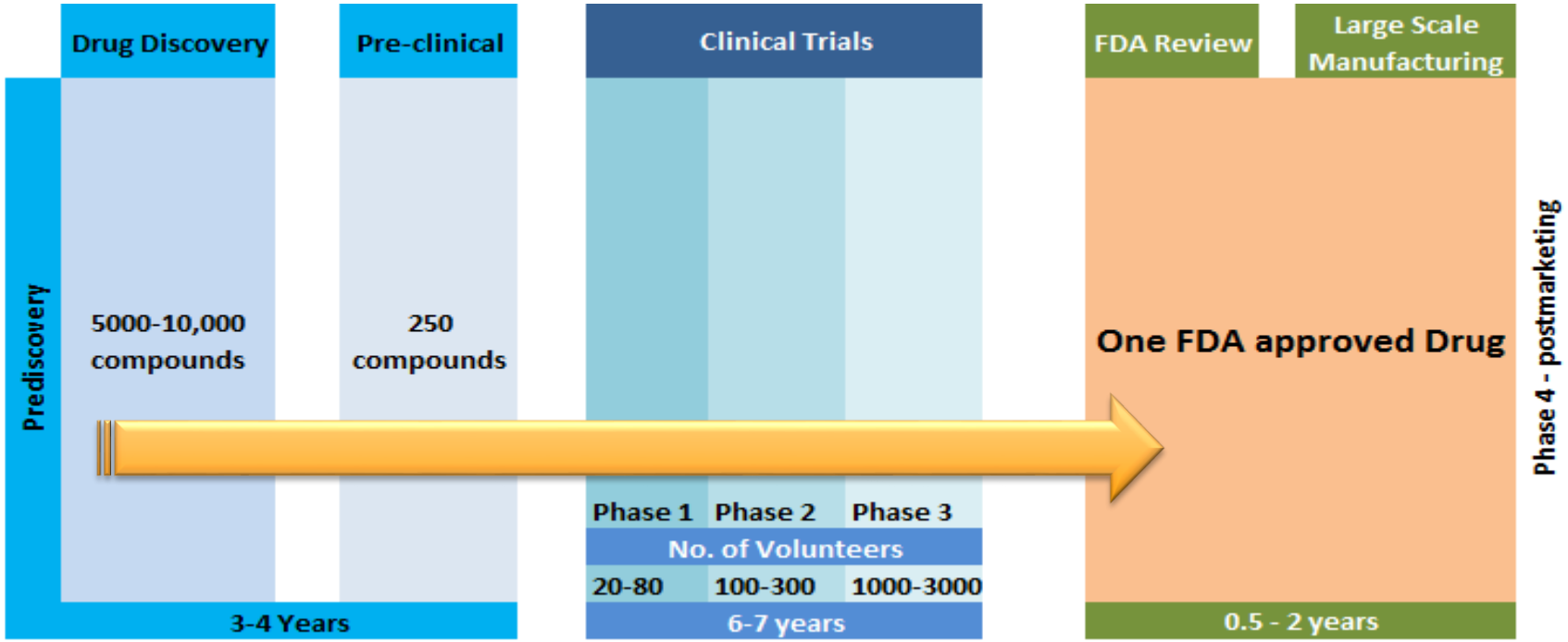
Drug Discovery and Development

A concatenation of many smaller stages –



Statistics about Drug Approvals

Preclinical testing
5000 drugs

Human Testing
5 drugs/10%

Approved for Human Use
1 Drug

Average investment of 10 years

Costly efforts and high risk undertaking

~10 years investment ~ USD 2.5 billion

Post-approval R & D ~ USD 300 million

Business Challenge

Factors contributing to high costs :

- Broad range of technologies and models used for capturing patient data.
- Drugs are increasingly being designed for patients meeting very specific criteria leading to involvement of various sites in different countries, each having its own regulatory requirements.
- The inability to recruit, enroll, and randomize sufficient numbers of patients incurs delays and increased costs.
- Another big challenge is to retain the patients and a timely & accurate data collection from them.

The high costs involved in the research & development contribute to :

- Higher drug prices , pushing Pharmaceutical Companies to focus on most common diseases only.
- Slowdowns the flow of groundbreaking medications , reducing treatment choices for patients with rare diseases.

Patient data collection – Challenges

Getting **Timely** Data from the participants .

- Patients need to report on their symptoms, medication regimen and observations at the time of the clinical visit or record them on their paper diaries. These approaches can burden them, leading to untimely reporting or even dropouts.

Getting **Accurate** Data from the participants .

- Evidence given by the patients for symptoms, medication regiments etc. can be subjective, especially for lengthy trials it can be of varying accuracies.

The above issue in data collection leads to limited basis for analytics and decision making. It may inadvertently also produce biased results.

Why Data Sciences?

There is a high pressure to Improve overall productivity and reduce development time.

Data science techniques dealing with large volumes of structured and unstructured data (collectively known as ‘Big Data’) offer prescriptive clues to solve patient recruitment and retention issues.

A data science approach generates insights by harvesting the data with sophisticated algorithms.

With this approach, we can better understand why timely enrollment isn’t happening, and ultimately what needs to happen to improve success for clinical trials.

The Wearable Technology Bandwagon and Clinical Research

The wearable technology market is rapidly growing, and impacting many different areas of our culture such as social interaction, environment, self-awareness, and healthcare.

As more money is spent on wearable devices, innovation expands, which in turn increases the many facets of our lives that these devices can be incorporated into.

The development of innovative wearable technologies has raised great interest in new means of data collection in healthcare and biopharmaceutical research and development.

What are Wearable Technologies?

Wearable technologies as sensors and/or software applications (apps) on smartphones and tablets that can collect health-related data remotely, i.e., outside of the healthcare provider's office.

The data can be collected passively or may require a user's input. An accelerometer embedded in a wristband or a cell phone is an example of a sensor passively collecting data about a person's physical activity and movement.

Software (e.g., ePRO (electronic Patient Reported Outcome)) can output a patient's report capturing health-related information, collected by means of a cell phone app or a web-based interface.

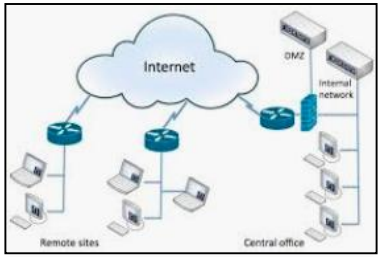
Additionally, some technologies, such as smart-cap bottles designed to monitor medication adherence, can use a combination of a sensor and app-based data collection.

The event recording is triggered by a user action (opening the bottle), but the data are transmitted from a sensor to a server passively via Bluetooth. The transmission is mediated by a cell phone app.

Examples of wearable sensors

Device type	Data collected
Wrist worn	Actigraphy, HR (Heart Rate), BP (Blood Pressure), EDA (Electrodermal activity)
Skin patch	ECG (Electrocardiography), actigraphy, skin temperature
Cuffs	BP, HR
Finger worn	HR, SpO2
Clothing embedded sensors	HR, HRV (Heart Rate Variability), ECG, Breathing Rate, actigraphy
Headbands	EEG (Electroencephalogram), EMG (Electromyography)

The Wearable Technology and Clinical Research



Remote monitoring of patients in trials

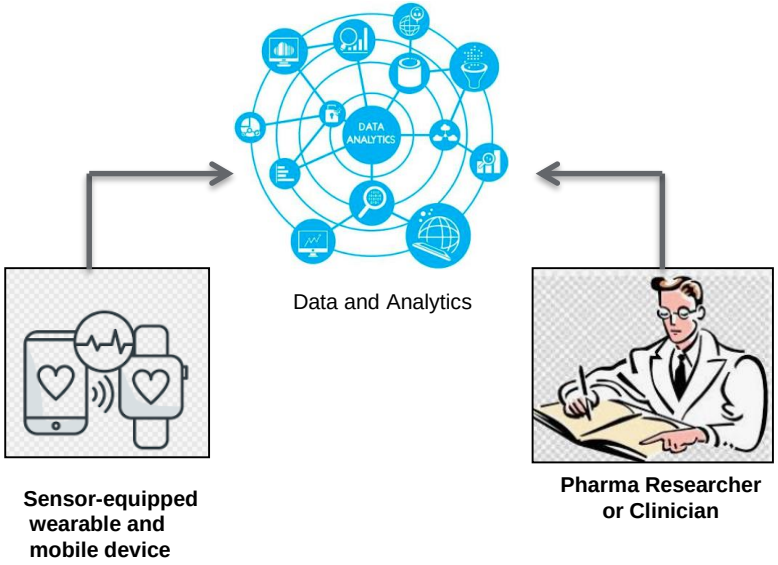
Expensive tests done in a clinic/hospital can now be completed with a mobile device.

Increased patient recruitment

Reduced Cost

Increased Savings

Wearable Devices and Data collection



24 x 7 data collection +
Subjectivity removed

With the help of remote monitoring and continuous capture of clinical data from study subjects using sensors and wearable devices , data scientists can apply machine learning techniques to objectively measure symptoms and quantify the impact of therapies.

By collecting data such as patients movement activity , heart rate, and glucose levels these devices can produce consistent , objective evidence of actual disease state and a treatment's impact.

Capabilities

- Capture de-identified, objective, high-quality, rich sensory data via sensors and wearable devices.
- Get real-time information about protocol adherence while helping patients manage medication, perform structured tests and report symptoms.
- Utilize smartphone applications to collect electronic diaries and patient reported outcomes (PROs).
- Transmit the de-identified data to a secured cloud infrastructure for storage and analysis.
- Apply machine learning and other AI methods to objectively assess and quantify the severity of symptoms, quantify the impact of therapies such as medication efficacy or dose response.

How the capabilities can revolutionize clinical trials

Objective, high-quality data

Collect different type of data both during day or while sleeping in real time as patients live their lives.

Improved Patient Engagement

Easy data collection through electronic diaries,

Feedback on symptoms,

Manage medication

intake with reminders ,

Stay engaged and motivated.

Trials management

Track adherence to protocol in real time , intervene to encourage compliance with protocol .

Monitor patients for adverse events and intervene to improve care and reduce dropouts.

Analytics Insight

Data scientists, researchers can query the data , run machine learning algorithms securely and provide analytical insights to the researchers about the data collected.

Challenges

- The promising potential of wearable devices has attracted enormous attention, including the start of experiments, and a number of deals between biopharmaceutical, contract research organization (CRO), and device companies have been announced.

- Nevertheless, the major impact expected from digital technologies on biopharmaceutical R&D has not yet materialized.

The reasons behind the lack of major transformation include scientific, regulatory, ethical, legal, data management, infrastructure, analysis, and security challenges.

Challenges

Scientific –

- Drug development and device engineering are separate scientific fields.
- Biopharmaceutical R&D scientists are generally not familiar with devices, which creates a barrier for adoption of wearable technologies in drug development clinical trials.
- On the other hand, device engineers are not conversant with the drug development process and regulatory requirements for drug approvals.

The solution would be to bring device engineers into drug development to educate biopharmaceutical R&D and enable adoption of device technologies.

Challenges

Regulatory–

- In the US, the drug and device marketing approval paths are separate and the oversight is done by different divisions of the FDA.
- The approval requirement doesn't include establishing an association with a clinical outcome such as a disease condition.

- Solution –
- A device under consideration needs to be tested in a specific population relevant to the device label claims in order to establish an association with a disease condition.

Challenges

Data infrastructure, processing, analysis, and interpretation –

- Drug development clinical teams are not familiar with the massive amounts of 24/7 data to be processed and integrated with the rest of study data.
- The sensor data structure is very different compared to traditional data collected at predefined time points by clinical sites and consists of multiple layers: raw unfiltered/ filtered data.
- No well-developed standards that would help to organize, annotate, and standardize the data and provide data mapping tools to electronic data capture (EDC) databases.
- Solution –
- Industry-wide standards for data and terminology, processing principles for similar sets of data, and transparency requirements around data processing algorithms.

Challenges

Ethical and legal –

- Challenges related to Data ownership and sharing, consent requirements, privacy, security, and substantial geographical differences in approaches to addressing these challenges.
- Patient consent for data collection and sharing is taken at some places.
- Legitimate health information such as disease condition, lifestyle, biometric, mobility, and behavioral patterns though shared after de-identifying the patients, does not mentioned explicitly to whom the data will be shared.
- Some countries requires clearly defined purposes for data use, consent for data reuse and sharing, and allows patients to withdraw their consent at any time.

Challenges

Data security –

- Device security of any mobile devices, tablets, and cell phones .
- The potential complications of blending study sponsor-collected personal health information on the personally owned device of a research study participant
- Secure data transmission and receipt, secure account management
- Data encryption; data blinding; and data backup and device fidelity.

Making Sense of Wearable Technology

The emergence of wearables provides clinical trial sponsors with the means to generate unprecedented amounts of data on the lives of patients between site visits.

This should be a boon for clinical trials, but it also creates new challenges that can be easily overcome when sponsors consider the implications of the data they hope to leverage from these innovations.

When supporting endpoints, data from Wearables need to:

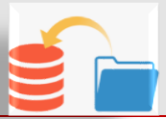
- ✓ Be fit for purpose
- ✓ Capture real-life context
- ✓ Be accurate and validated

Should be driven by ability to support trial endpoints . The technology used should not drive scientific questions of the trial

Data collected can only meaningful if the context in which the data collected is known.

Wearables created for commercial use may not be Validated as per FDA guidelines

Operational Considerations of Wearable Technology

Study Goals 	What data they want to collect and for how long they want to collect it.
	Narrow the scope by knowing exactly what data to collect and for how long to collect it.
	If the data will be submitted to regulatory agencies, and if any regulatory precedent has been established for their use in clinical research.
Wearable Selection 	When people refer to wearables they often mean activity meters, but the wave of innovation in wearables means there are options beyond just activity, including many that have multiple sensors. For example, Vital Connect has a wearable patch that collects single lead ECG, heart rate, RR interval, respiratory rate, temperature, body posture, fall detection and activity including steps. Next generation wearables are likely to include connected clothing and true wearables such as tattoo-like health monitors.
Patient Experience 	To be successful, wearables must be simple to use and integrate seamlessly into everyday life.
	Part of the patient-centric movement in clinical trials is to understand the impact that trial requirements have on a participant's life. This is especially important for wearable technology, as an uncomfortable device or one that requires extensive setup can lead to loss of data and non-compliance.
Data Retrieval 	Data from some wearables can be quite extensive, so it's important to understand the level of data required, and define useful collection intervals.
	Collecting a data point for every step may be more than needed; an alternative might be steps per minute or per day, so a consumer device may be sufficient.

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CONCLUSION

By capturing continuous data from patients via mobile wearable technology, clinical trial sponsors may be able to reduce the burden of frequent site visits, which could improve patient dropout rates and overall clinical trial efficiencies.

Currently, the field is full of enthusiasm, but more data are needed from rigorously designed studies to displace the hype and adopt scientific methodologies to generate and test scientific hypotheses. Further dialog between the biopharmaceutical industry and device manufacturers to develop methodological approaches and shared understanding of the experiments is required to fulfill the requirements of analytical and clinical validation. This conversation would constitute a major step forward facilitating the adoption of wearable technologies in clinical trials.

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