Step by step: Leveraging wearables in clinical trials

Regardless of geography or therapeutic area, wearables offer an important, exciting opportunity to better understand patients and improve their experience at each stage of their journey. Today, wearables are demonstrating real potential to transform data collection for clinical trials and accelerate the role of technology in clinical development. But to get there, pharmaceutical companies must take a disciplined approach and focus on five critical actions to succeed.

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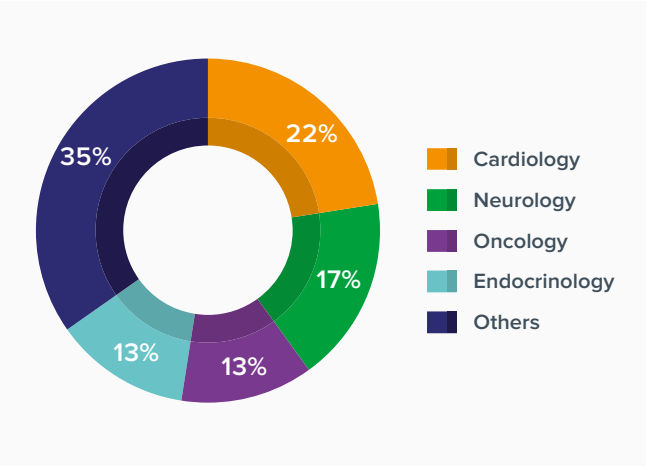
How can pharma confidently generate evidence from wearable technologies?

Wearables (devices that capture continuous health and activity data from individuals) have technically been around for a long time; in 1960, the first continuous ECG data was collected from patients. However, the real watershed moment for wearables came in 2007, when Fitbit® entered the market and the concept of a wearable device to monitor personal health information was introduced to consumers.[1] Since then, the use of wearables has been increasing throughout healthcare, including in clinical trials.

Statistics from the National Institutes of Health (NIH) show that by the end of 2015, approximately 300 clinical trials incorporated some kind of wearable device.[2] Looking at 2016 NIH data,[3] it is also clear that the concept is relevant across therapeutic areas (see Figure 1).

Figure 1: Utilization of wearables in clinical trials by disease area in 2016[3]



That said, a myriad of conflicting studies have been published in the last 24 months that alternately tout the benefits of wearables[4,5,6] or dismiss them as hindrances in the delivery of quality medical care.[7,8,9] Such contradictions have left many in the industry struggling to determine when and how wearables should be used, if at all, in the development of pharmaceutical products.

Closer evaluation shows that even negative studies provide valuable learnings and shine a light on emerging best practice.

Some of the observed pitfalls include

- Insufficiently defined endpoints (e.g., sustained weight loss with limited interventions)
- Multiple influences on patient behavior (e.g., observation, incentives)
- An excess of factors to measure with varying relevance

Despite these challenges, there is growing recognition that wearables and other digital technologies are here to stay. Continuous developments in technologies are helping pharmaceutical companies dive deeper into digital health.[10] Bayer is expanding its incubator Grant4Apps program;[11] EMD Serono is partnering with Big Data firm Palantir across discovery, patient experience and the global supply chain;[12] and Novartis has publicly stated its intention to take "a greater leadership role" in this area.[13] The imperative, then, is for pharma to proactively figure out how to make the best use of these devices in R&D and how to incorporate even negative data.

Outsiders come in

With the increased attention on leveraging new digital health technologies, companies outside of the healthcare space are paying closer attention to the trial setting and trying to help provide the tools necessary for using wearables in trials. Apple, for instance, is continuing to invest in ResearchKit, an open source framework for the creation of mobile applications that support medical researchers by gathering robust and meaningful data.[14] A second example is Qualcomm, which has been selected by Novartis as a global digital health collaborator for its Trials of the Future program. This program will leverage Qualcomm Life's 2net™ Platform to serve as a global connectivity platform for collecting and aggregating medical device data during clinical trials.[15] The type of data collected by each of these platforms is shown in Figure 2.

While Apple and Qualcomm offer very different technologies, both are key tools in incorporating wearables into trials: ResearchKit provides researchers with tools to create apps that enable customer data collection; the 2net™ Platform allows for the secure storage and accessibility of continuously collected data, and it provides a way to connect data from various sensors and link it to a single patient.

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> "Companies seeking to maximize the value of digital health and wearables in R&D can gain significant ground through the use of proof of concepts"

Figure 2: Data collected by ResearchKit and 2net™ Platform programs

Platform	Program	Target	Type of Data Collected
ResearchKit (Apple)	mPower	Parkinson's disease	Dexterity, balance, gait, memory
	Autism & Beyond	Autism	Emotional reactions
	EpiWatch	Seizures	Heart rate, movement
	Concussion Tracker	Concussion	Heart rate patterns, physical and cognitive function
	StopCOPD	Chronic Obstructive Pulmonary Disorder (COPD)	Physical activity, heart rate, sleep patterns
	GlucoSuccess	Diabetes	Movement, food intake, medication compliance
	C Tracker	Hepatitis C	Heart rate, activity level
	Mole Mapper	Melanoma	Photography of moles
	PPD ACT	Postpartum depression	Saliva (DNA) sample
	SleepHealth	Sleep health	Daytime alertness, sleep pattern, sleep quality
2net™ Platform (Qualcomm Life)	Breezhaler	Chronic Obstructive Pulmonary Disorder (COPD)	Inhaler usage including the duration of the patient's inhalation

Finding the right path

Direct experience helping pharmaceutical companies navigate this difficult terrain shows that the industry is only starting to understand how and when to test wearable technologies and take advantage of them in the clinical trial setting. Many have yet to learn the art of 'win fast, fail fast' or how to leverage proof of concepts (POCs) vs. larger pilots. A measured, practical approach to adopting new technologies has been proven to yield better ROI, more efficient use of time and resources, and valuable learning opportunities.

Case Example 1: Big hopes. Big disappointments.

Recently, a company new to mobile patient devices incorporated Fitbit® into a trial to explore its potential for a respiratory indication, without sufficiently clear clinical endpoints. The trial encountered various challenges, including a lack of clarity around the desired endpoints for defining success, and did not have the security of running a smaller POC. As a result, the inconsistent frequency and quality of the data being collected led to multiple protocol amendments, increasing the administrative burden. In the end, the trial could no longer be justified from a financial perspective and was canceled.

The reality here was that much of the trial's cost and many of its shortcomings might have been avoided had the company invested in a small POC to quickly gain knowledge of how to use the technology before incorporating it into a larger trial.

Case Example 2: Winning with POCs

Diabetes studies provide a number of early examples of success with wearables. In one case, incorporating a wearable glucose monitor into POCs allowed for both concrete data collection and the establishment of the data infrastructure to support future, larger trials and pilots. The wearable was used not only to measure glucose levels over multiple years but also, importantly, to put in motion the processes, capabilities and systems to

- Determine inter- and intra-patient glucose variation
- Advise on dosing schedules
- Set standards for ongoing surveillance and management
- Identify measures for managing drug adherence in future trials
- Measure the impact of activity and other patient characteristics on overall patient care

As these examples demonstrate, companies seeking to maximize the value of digital health and wearables in R&D can gain significant ground through the use of POCs. This approach will help them better evaluate technologies, identify appropriate opportunities for using wearables, set up the required capabilities and partnerships, and learn what works well and what does not.

Five steps to success

Against this background, companies should focus on five critical components of success.

1. **Embrace 'win fast, fail fast' with POCs.** As indicated, POCs provide a necessary and valuable approach for pharmaceutical companies to test confidently and practically the feasibility of new technologies (see Figure 3). For example, if a company is interested in using telehealth to monitor patients in a clinical trial, POCs can serve to test the prioritized technologies, understand their associated UI/UX (user interface/user experience), and ensure the capabilities required for set-up, partnering, support, etc.

   As a result, companies can save significant time, money and resources by deploying a POC compared to simply selecting one telehealth vendor and implementing a trial. POCs are the best way to learn how to use and maximize value from wearables and other technologies – especially in an industry unaccustomed to such an expedited approach.

   Of course, if a technology is already well understood (in terms of security, user interface, back-end data collection, geographic constraints, etc.) and all the data, systems and procedures are in place (e.g., appropriate platforms with required security for data aggregation, alerts and notification algorithms, pharmacovigilance requirements, etc.), then companies may be well suited for going direct to pilots.

2. **Be clear about who owns the POC and how it will be funded.** Testing the use of a new technology in a clinical trial has multiple implications and uncertainties. It changes the way the protocol should be written, incurs additional cost and may raise unanticipated questions from regulators – hence the hesitancy in assessing wearables or new technologies for use in trials. Best practice companies dedicate funding and an independent team to drive innovation in R&D, with the ability to test technologies quickly and cascade the learning through the broader organization.

3. **Start outlining a foundational data strategy.** Particularly in the case of wearables, the amount of collectable data can often be overwhelming and not always necessary. Take this simple example: a company wishing to use total sleep time as an indirect indicator of activity decides to use a validated actigraph (wearable). Theoretically, collecting sleep time should be easy. In reality, there is much to consider, including

   - How is sleep defined?
   - How is the sleep data displayed?
   - How will physicians see the data?
   - What will they do with the data?
   - Is there a requirement for thresholds to trigger medical visits or calls?
   - Who will triage the data?

   There is also a wide range of additional (but likely irrelevant) data that the wearable will collect (e.g., number of steps). Having a clear data strategy upfront is essential, impacting everything from informed consent to protocols and data security.

4. **Go outside your firm – involve key stakeholders, including patients and physicians, early and often.** Clinical trial protocols cannot be developed in isolation, especially when it comes to incorporating wearables or other digital health innovations. Viewing patients as technology *consumers* rather than as *patients* is critical. For example, understanding how patients will interact with the technology on a daily basis, how often they are likely to wear it, in what conditions (e.g., exercising, sleeping, showering, etc.), and what they consider to be incovenient, is extremely important when designing a trial protocol that incorporates wearables. Failure to consider these factors runs the risk of poor data and lack of compliance.

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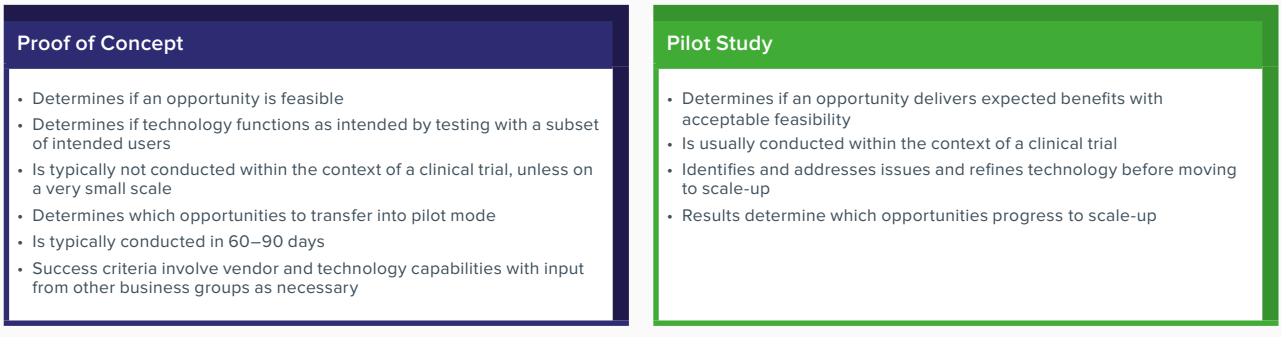
Figure 3: Key attributes of POCs vs. pilot studies



5. **Ensure that stakeholder-specific KPIs and learning goals are incorporated.** When considering incorporating wearables into a clinical trial, it is important to know exactly what endpoints are needed, how they will be analyzed and who will use them (e.g., payers, regulators, physicians, others).

Figure 4: POC learning goals should have broader application to other opportunities

Evaluation Questions	Success Factors
Was the vendor suitable?	Selected vendor was identified as a good partner and met timelines, milestones and service agreements
Did the technology work?	Technology was available, performed for a specific use/function, and was validated (if validation was required)
Were risks proactively identified and addressed?	Risks were identified during the course of the POC and mitigation tactics were developed
Were the scope and goals clear?	Key endpoints were captured and POC was completed in a timely manner
Are learnings (good and bad) useful and replicable?	POC learnings can be applied to other opportunities across the organization

Clear KPIs can include

- Time for technology installation
- Frequency of user errors
- Number of customer support calls

Most companies have now become adept in this area. However, just as important is having a clear idea of learning goals from a trial or POC. Even if trials or POCs fail to demonstrate usability of a technology, the learnings can and should serve to inform other opportunities (see Figure 4).

Moving forward

As the development of digital health technologies continues to accelerate, so do the opportunities to enrich R&D programs with patient wearables. To capitalize on this potential, there are certain key steps pharmaceutical companies can take to evaluate the relevance of technologies to their trials and build the competencies required to leverage them to best effect. First and foremost is a pivot to a 'win fast, fail fast' model that embraces POC as a catalyst for better learnings and more deliberate progress.

Ensuring dedicated funding and an independent team, defining a clear data strategy upfront, engaging early with key stakeholders, and establishing specific KPIs and learning goals are also fundamental to success. Certainly, companies that can bring together clinical trial and digital technology expertise will be the ones to confidently and sustainably plan, scale and implement wearables in R&D.

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