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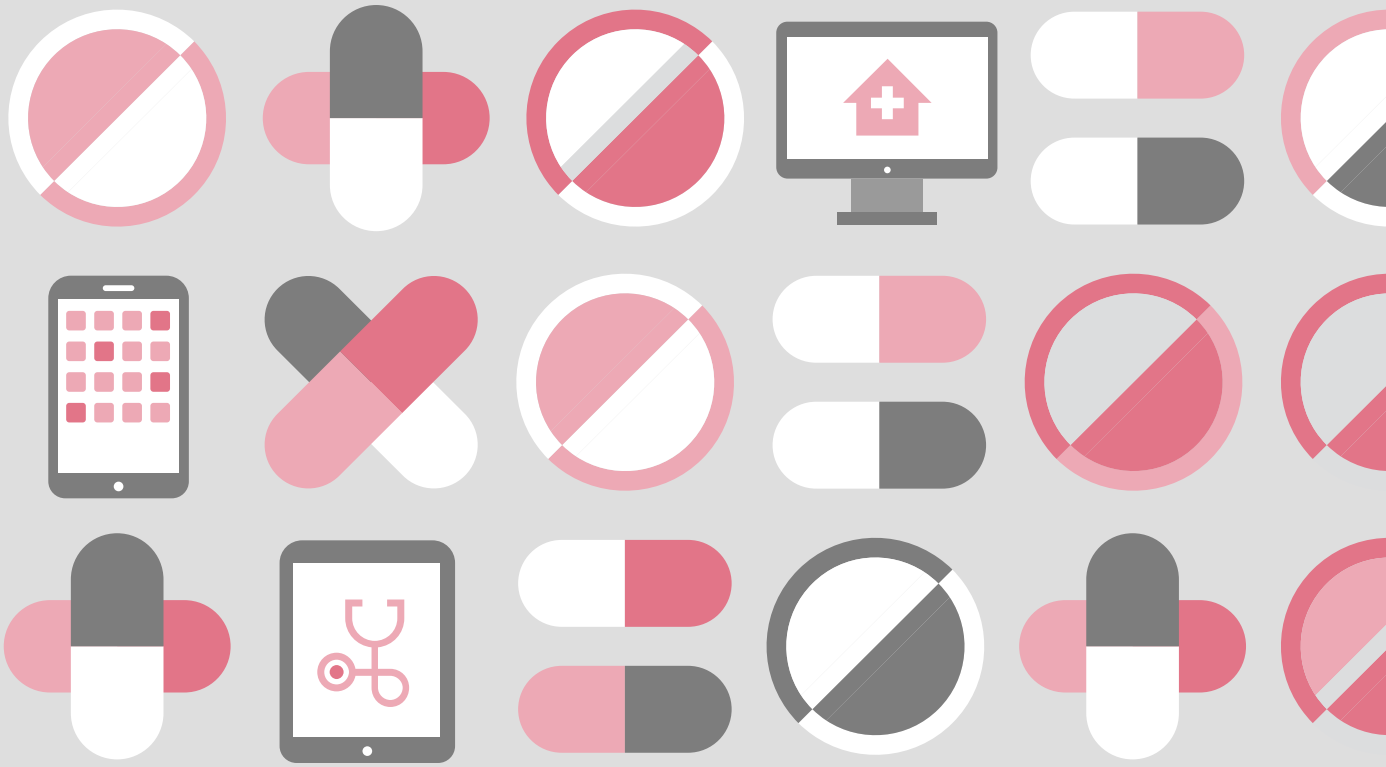
Acceleration by regulation:

Pharma stands to benefit from the FDA's new digital health approach



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Changes at the FDA have cleared the way for digital solutions and therapies to come to market more easily than ever. For the pharmaceutical industry, these changes represent substantial new opportunities to market new products and connect with patients and providers.

Recent changes made by the FDA have made it easier for digital health products to be cleared and approved, offering life sciences companies – and pharmaceutical companies in particular – the opportunity to accelerate approvals and improve provider and patient satisfaction. Companies willing to invest in strengthening or building digital competencies may win market share, while those without sufficient investments may find themselves at a disadvantage.

Companies with prospective over-the-counter drugs may find it easier to obtain approval. Companies with products intended for complex therapeutic areas, chronic conditions or rare diseases likely will find it easier to develop companion applications or delivery devices that support the use of their products. Companies looking to differentiate their products to patients, clinicians and insurers may find new opportunities through digital applications.

Life sciences companies may find new regulatory strategies for developing products as well. “Compared with traditional medical products, some digital health products can be used by much larger populations of people,” Bakul Patel, associate center director for digital health at the FDA, told HRI. “There’s an opportunity for digital health products to learn in real-world settings how the product is being used in these populations, and that perspective and input can influence the entire development strategy used by the company that makes the product.”

Companies’ competitors, established and emerging, also could leverage digital technologies to unseat established market leaders. Medical device manufacturers, already adept at creating traditional devices and software, also could benefit.

New regulatory pathways could accelerate digital health

Four regulatory changes, as well as a host of smaller changes, are creating new opportunities for the pharmaceutical sector (see Figure 1).

Figure 1: Four major regulatory changes to digital health are driving new opportunities for pharma

Digital health precertification

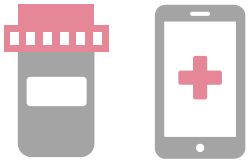
Companies with high degrees of regulatory quality are eligible for shorter reviews and ONC certification

Multiple function devices

The FDA will treat as separate the various functions of a digital health device, making it easier to have full-function products

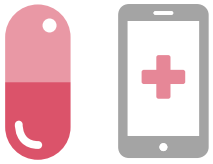
Companion applications

The FDA will allow digital apps intended to supplement prescription drugs to be regulated as labeling and not require approval



OTC drug digital labeling

OTC drugs may be approved based on evidence that consumers can use digital labeling to select a drug for treatment



Source: PwC Health Research Institute analysis

Digital health precertification: The FDA is advancing a new regulatory approach to digital health called the Digital Health Precertification (Pre-Cert) program. Now in pilot-phase testing with nine companies, the approach aims to make reviews of digital health products more efficient by rewarding companies assessed and evaluated by the FDA as having a "robust" culture of quality and organizational excellence for the purposes of developing digital health products.

Those companies will be permitted to have their products reviewed in a streamlined way, which would reduce the review time for the product by focusing on what the product is rather than what it does. This would then be paired with real-world health analytics, product performance analytics and user experience components, requiring the company to track how the product is being used and quickly address issues.

The FDA plans to begin expanding the program to additional participants in 2019, and the model could eventually become the way in which many digital health products come to market.

Critically, the Office of the National Coordinator for Health Information Technology (ONC) has said that companies participating in the Pre-Cert program will be exempt from some elements of its Health IT Certification program's requirements for testing and certification of health IT.

Devices with multiple functions: The FDA has published draft guidance that would make it easier for companies to include multiple functions in their mobile applications. Some devices, for example, may include a complex prescription function intended to help diagnose disease, like an algorithm that detects signs of cancer from a photo, as well as some unregulated functions intended to benefit the end user like a step counter or diet tracker.

Rather than treating all of the functions of the device as a single, combined entity, the FDA will instead treat them as separate. This will permit a regulated device to include otherwise unregulated or minimally regulated functions without subjecting them to rigorous oversight by the FDA. This could help companies to develop, upgrade and update more full-service applications without having to worry that each added function would trigger new regulatory requirements. It could also help companies to develop products in an iterative manner, allowing them to incorporate patient feedback into developing more useful products.

Companion applications as labeling: The FDA has proposed a substantial change in the manner in which it will subject pharmaceutical companies' drug-use-related software to regulatory oversight. Such applications include companion mobile applications that help consumers to use a company's prescription drug products in accordance with the FDA-approved labeling.

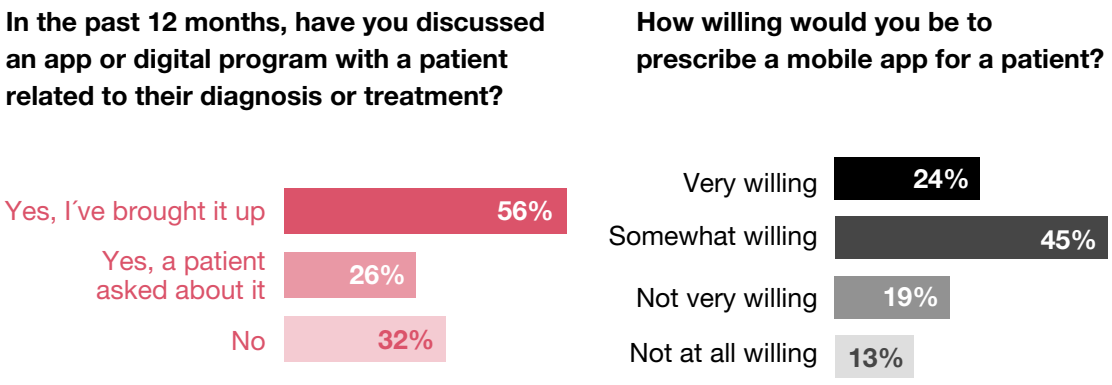
Previously, companies could be required to submit these applications for approval under the premarket notification pathway, also known as the 510(k) pathway, if they were not exempted. Under the new proposed change, the FDA would instead treat such applications as promotional labeling, a much lower standard of review that does not require FDA approval prior to dissemination.

This could greatly increase incentives for companies to develop digital companions for their products by lowering the regulatory hurdles for entry.

It may also find a ready audience with clinicians. Forty-five percent of clinicians responding to a 2017 survey by HRI reported being somewhat willing to prescribe mobile apps to patients, and another 24 percent said they were very willing to do so. Responses varied significantly, however, depending on practice type. For example, 17 percent of medical specialists said they would be very willing to prescribe a mobile app, while 43 percent of those working in community health would. Twelve percent of those working in an urgent care center would be very comfortable prescribing, while 45 percent working in a federally-qualified health facility would.

Fifty-six percent of physicians surveyed in 2018 said they have discussed an app or digital program with their patients in the last 12 months (see Figure 2). However, just 14 percent of consumers said they had ever been prescribed a mobile health app, of which 50 percent could be categorized as frail, elderly patients.

Figure 2: The majority of physicians say they're willing to prescribe digital health apps and programs



Source: PwC Health Research Institute provider surveys, 2018 and 2017

New OTC drug approvals: In July 2018, the FDA released draft guidance saying the agency is willing to allow the approval of over-the-counter drugs that it would otherwise not approve – as long as they have the right type of product labeling, which could include digital labeling on smartphone apps accompanying the drug. Under the FDA's approach, these digital tools – primarily mobile applications – would help consumers choose OTC drugs that would be best for them and avoid drugs that could harm them. Companies would be required to conduct studies of the application to ensure it correctly steers consumers to or away from its product.

The FDA said it believes the new approach could support the approval of a "wider range" of nonprescription drug products than is on the market, which could benefit pharmaceutical companies with long-marketed, generally safe products with minor safety concerns that have prevented them from obtaining OTC approval.

The use of digital labeling is likely to have an impact on some, but not all, consumers. Thirty-two percent of consumers surveyed by HRI in 2018 reported having used a mobile device to look up information about symptoms, conditions, diseases and treatments. This type of activity could expand with the support of the FDA and industry, however.

Separately, both the House and Senate are considering legislation that would overhaul the manner in which OTC drugs are approved in the U.S., shifting to a system in which products would be approved based on administrative orders instead of through a notice-and-comment rulemaking process. This could potentially shave months and even years off of the regulatory review process, and, paired with the digital health component, create new opportunities for companies to get new OTC drugs to market more quickly. The FDA said it plans to hire significant numbers of new staff to review products, and that products will be reviewed within 17.5 months of the date of submission. Versions of the bill have previously passed the House and Senate.

Shorter risks, exempt devices: The FDA has asked for public input on an early-stage proposal to shorten the amount of risks that must be presented in direct-to-consumer pharmaceutical advertising, which could increase the need for companion mobile applications with good explanations of a drug's risks and benefits.

The 21st Century Cures Act required the FDA to exempt certain software functions from regulatory oversight, including products serving as electronic patient records,

general wellness products, devices that store or display medical data, and certain software that helps providers and patients make more informed decisions about treatments. Paired with the FDA's decision to treat as separate the various functions of a device, this change could lead to more devices having functions that are helpful to clinicians, such as electronic patient data and records. Regulators are also selectively exempting some digital health devices from requiring oversight, including those intended to guide contraception.

Overall, these changes – though individually small – are resulting in a significant change that will allow many high-value digital health products supporting pharmaceutical approvals and products to come to market more easily (see Figure 3).

Figure 3: Digital health products likely to benefit from changes in the FDA's approach

Type of product	Example	Regulatory approach
Digital companion apps for prescription drugs	Software designed by a drug sponsor that allows patients to track their use of a drug and share that data with their provider.	Treated as labeling, not subject to review prior to release.
Self-selection mobile application	An application that prospective consumers download and helps them to determine if a drug is right for them.	Treated as labeling, but will require studies in support of label's effectiveness at promoting self-selection.
Multiple function device product	A software-enabled device that allows patients to test if they need a drug, and also contains information to help them track their adherence to a drug and general wellness.	FDA will treat as separate the various functions of the device as the functions don't interact in a way that would compromise the overall function of the device.
General wellness devices	An application that tracks a user's step-counts throughout the day.	Exempt from FDA oversight unless it makes specific medical claims.
Clinical and patient decision software	An application that tracks levels of a drug in patients' blood using a corresponding device and recommends changes to dosing levels to their physician.	Generally subject to FDA oversight, but functions to support or provide recommendations to health care professionals are exempt.

Source: PwC Health Research Institute analysis

Implications

Digital health products need evidence and buy-in to succeed. New regulatory pathways will simplify market access and product development cycles, but companies will still need to take stock of how they can best leverage digital health with their new or existing product portfolios, and the data that will be necessary to support these products.

"The opportunities of digital health are limitless. All of big pharma is aware they can accelerate their drug development or improve their new drug uptake with digital technologies," Dr. Eric Topol, executive vice president of the Scripps Research Translational Institute, told HRI. "But it's all about the research. Pharmaceutical companies need their digital health products to be supported by published evidence so that physicians and patients can look at it and be confident that the application or sensor works in the real world."

According to research published in the journal Health Affairs, even well-funded companies often lack clinical evidence supporting the use of their products. Of the top 20 digital health companies by funding, nine companies lacked any peer-reviewed evidence, and 28 percent of the studies conducted on the companies' products looked at high-risk or high-cost patients.

"Physicians have key requirements for adopting digital health products," said Meg Barron, director of digital health strategy at the American Medical Association. "These requirements fall into four key buckets: Does it work and can you prove that there's evidence to support it? Will I receive proper payment or reimbursement for this product if I use it? Would using it expose me to legal liability, and does it treat data safely and securely? Will it work in my practice environment and with my electronic health records?"

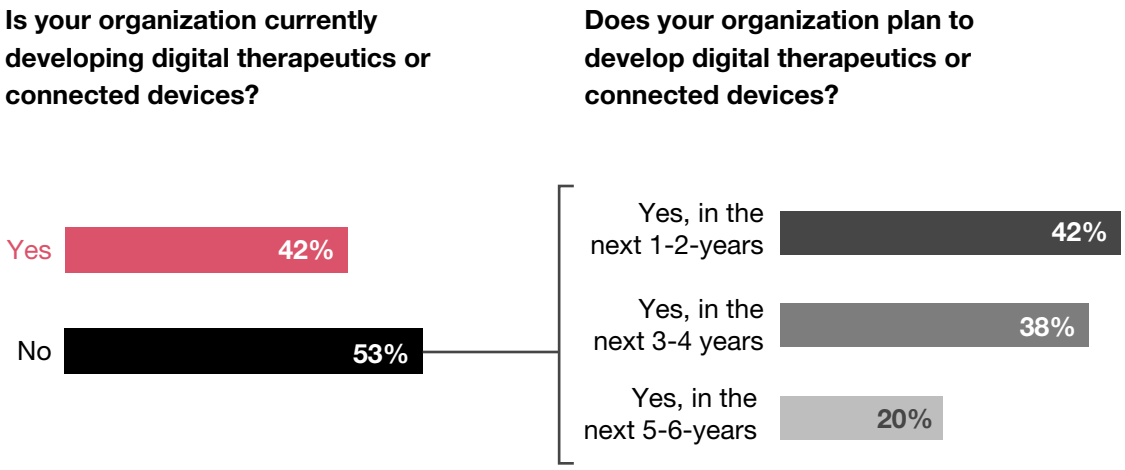
"Physicians are ready to embrace technology, especially if it's going to help them manage their patients and chronic disease," Barron said. "But first they need to be able to answer those questions around safety, efficacy, security and interoperability."

Companies may also find it beneficial to work together on common approaches to data. In comments to the FDA, the American Pharmacists Association suggested that when it comes to prescription drug-use-related software, "processes and systems must be standardized and interoperable" to ensure the use of the software doesn't "disrupt or disjoint" care.

Companies face a choice of where to invest, balancing the costs of development with returns from their customers.

In a 2018 survey of pharmaceutical executives by HRI, just 42 percent said they were actively developing digital therapeutics or connected devices. Of those executives whose companies were not actively developing these products, 42 percent said they planned to begin doing so in the next 1-2 years, and 58 percent said they planned to do so in the next 3-6 years (see Figure 4).

Figure 4: The FDA's new regulatory opportunities for pharma come just as the sector is beginning to invest in digital health



Source: PwC Health Research Institute pharmaceutical executive survey, 2018

The FDA's new and emerging regulatory changes may make it easier for these products to get to market, especially if they have invested in analytical capabilities.

"Companies don't have to start off with the biggest claim possible," Bakul Patel said, referring to the digital health pre-certification program. "They can instead focus on small, distinct claims, and then slowly – using real-world evidence – build up the product and add claims to it over time. The Pre-Cert program is intended to provide a glide path for products to enhance their performance over time. The goal is to achieve the same standard for safety and efficacy as other products, but to make the regulatory process more efficient."

There are challenges ahead. Pharmaceutical companies have cultures of manufacturing quality, but relatively little experience developing digital health products or apps, both of which are traditionally the purview of medical device and technology companies. Creating a culture of coding quality and software quality will therefore require a new investment.

Beyond culture, creating competencies in analytics, machine learning, user design, usability engineering, risk management, cybersecurity and user experience will also be needed to excel in digital health and create tools that are useful for both the end user and physicians.

Companies' focus should be on the quality of their applications and use cases rather than quantity. Providers and patients don't necessarily want a digital health product or application that does the bare minimum, but instead are seeking ones that will make an impact on patient care.

To succeed, pharmaceutical companies should focus on the needs of patients and providers.

Digital health products must ultimately be designed with their users and their unique needs in mind. A product that is not useful to, or usable by, a patient will not be effective no matter how good the product is otherwise. A product that does not integrate into physician workflows in a straightforward way may not be prescribed.

For companies developing digital health applications and products, their focus should be on how to treat patients in ways that go beyond a single dimension of health.

"We're at an inflection point when it comes to technology that's being developed and how it's being applied to healthcare," Michael Senical, Digital Health Incubator lead at Astellas Pharma US, told HRI. "Ultimately, pharmaceutical companies may become more disease treatment companies where a pharmaceutical is still going to be at the core of that treatment, with a suite of technology solutions surrounding it to support better outcomes and experience. Not every patient will need all of those solutions, but some patients might need a mix of pharmaceuticals and digital health tools supplementing them."

For companies, the focus should be on the type of digital health product to develop, and whether they are developing solutions or therapies (see Figure 5).

Figure 5: Solutions or therapies: Companies face a choice of where to invest, balancing costs and returns

Features	Digital solution	Digital therapy
Generally require prescription to use	No	Yes
Supported by clinical trial data	No	Yes
Require FDA approval or clearance	No	Yes
Generally reimbursable by payers	No	Yes
Cost to develop	Low	High
Examples	• Fitness trackers • Adherence programs • Direct refill services • Companion labeling app	• Software-enabled hardware • Algorithms intended to diagnose • Behavior modification programs • Software intended to treat a condition

Note: Some applications will blend aspects of both solutions and therapies to meet patient needs, such as an over-the-counter applications supported by clinical data and cleared by the FDA.

Source: PwC Health Research Institute analysis

Solutions can be thought of as nonprescription applications that don't require FDA approval but add value for patients, while therapies are physician-prescribed products supported by clinical data and reviewed by the FDA that may also be reimbursed by an insurer. While the former are easier to get to market, digital therapies may ultimately offer more value to companies and their customers.

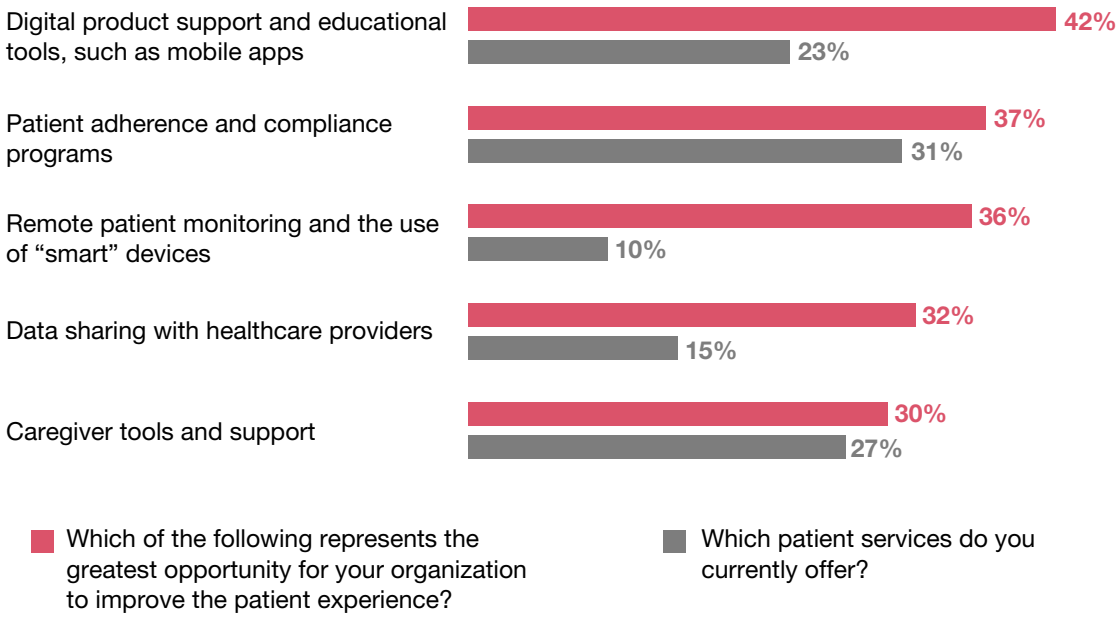
High degrees of competence can help companies get products to market more quickly, increase market share and help companies create ties to physicians and patients that go beyond the pill. These ties can become integrated into clinical practice, making it less likely that doctors or patients will want to switch to market competitors when generic or other competition comes onto the market. Thirty-one percent of patients surveyed by HRI in 2017 said they wanted medication with proof of good outcomes and few side effects and rated it as a "most important" part of their care, and another 22 percent said they wanted help managing their medications.

Digital health applications and tools can help providers to meet these consumer goals, but first companies will have to identify those needs and then create the tools with which to meet them.

"The pharmaceutical industry often doesn't design things to be simple. The minute you start developing a digital health product, and involving more people, including medical, legal and regulatory staff, things frequently get more complex," Melinda Decker, most recently the head of digital health and digital therapeutics for AstraZeneca's oncology division, told HRI. "As an industry, we sometimes forget the perspective of patients, who may be taking several different drugs, or read at a 6th-grade level or many not be super tech savvy. We as an industry need to focus on user-centric design and make sure the digital health product we're developing is a right fit for patients."

Pharmaceutical executives told HRI they believe they know which elements will be important, but many companies have not yet met those needs (see Figure 6).

Figure 6: Most pharmaceutical companies see opportunities for digital health, but fewer have present offerings



Source: PwC Health Research Institute pharmaceutical executive survey, 2017

Similarly, generic companies or competition can use digital health tools to make inroads into therapeutic areas for which good digital health tools are lacking. The ONC's certification stance means companies who are willing to put in the work on digital health certification can find it easier to get their products integrated into provider workflows and clinical trials.

Good digital health tools can also be critical for payers, and in particular those engaged with value-based contracting. If companies are able to generate evidence about their product, improve rates of adherence or improve outcomes for a patient using digital health applications, that could improve its value and help drive more favorable reimbursement rates for the product.

"Whether it's a reduction in HbA1c levels, improvement in overall survival, or a reduction in the frequency or severity of adverse events, digital health has the potential to tremendously improve patient outcomes," Decker told HRI. "As more data is collected remotely, it reduces the burden on patients and should also improve the way clinical trials are run and the speed of those drugs to market."

About this research

PwC's Health Research Institute conducted interviews with industry and regulatory leaders in digital health and analyzed PwC data, including 2017, 2018 and 2019 surveys of pharmaceutical industry executives, providers and consumers.

About the PwC Health Research Institute

PwC's HRI provides new intelligence, perspectives and analysis on trends affecting all health-related industries. HRI helps executive decision-makers navigate change through primary research and collaborative exchange. Our views are shaped by a network of professionals with executive and day-to-day experience in the health industry. HRI research is independent and not sponsored by businesses, government or other institutions.

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