Defining digital medicine

Eric Elenko, Lindsay Underwood & Daphne Zohar

Digital medicine is poised to transform biomedical research, clinical practice and the commercial sector. Here we introduce a monthly column from R&D/venture creation firm PureTech tracking digital medicine's emergence.

Technology has already transformed the social fabric of life in the twenty-first century. It is now poised to profoundly influence disease management and healthcare. Beyond the hype of the 'mobile health' and 'wearable technology' movement, the ability to monitor our bodies and continuously gather data about human biology suggests new possibilities for both biomedical research and clinical practice. Just as the Human Genome Project ushered in the age of high-throughput genotyping, the ability to automate, continuously record, analyze and share standardized physiological and biological data augurs the beginning of a new era—that of high-throughput human phenotyping.

These advances are prompting new approaches to research and medicine, but they are also raising questions and posing challenges for existing healthcare delivery systems. How will these technologies alter biomedical research approaches, what types of experimental questions will researchers now be able to ask and what types of training will be needed? Will the ability to digitize individual characteristics and communicate by mobile technology empower patients and enable the modification of disease-promoting behaviors; at the same time, will it threaten patient privacy? Will doctors be prescribing US Food and Drug Administration (FDA)-cleared apps on a regular basis, not just to monitor and manage chronic disease but also to preempt acute disease episodes? Will the shift in the balance between disease treatment and early intervention have a broad economic impact on the healthcare system? How will the emergence of these new technologies reshape the healthcare industry and its underlying business models? What will be the defining characteristics of 'winning' products and companies?

These are just some of the questions we plan to ask over the coming months. In the meantime, we introduce here some of the key themes shaping R&D in the digital medicine field and focus on what they might mean for the biopharmaceutical and diagnostic/device industries.

A burgeoning field

Smart devices and apps are now ubiquitous in the digitally connected world. In 2010, 12.5 billion mobile devices were sold; this year, 25 billion phones are projected to be on the market—more than three phones for every person in the world[1].

Once solely the province of social interaction, smartphones and related devices are increasingly viewed as a medium for sharing and gathering personal health and wellness information—an opportunity that is spurring commercial interest. For instance, in 2014, digital companies in the healthcare space garnered over four billion dollars in venture funding, almost as much as in the previous three years. There is an increasing convergence between pharma companies that are starting to play in digital products and tech companies that are increasingly moving into healthcare[2]. Apple (Cupertino, CA, USA), Google (Mountain View, CA, USA), Samsung (Seoul) and dozens of others are entering the space. Likewise, pharmaceutical companies are increasingly expressing a desire to offer digital interventions rather than just drugs as disease solutions. For instance, Joseph Jimenez, the CEO of Novartis Pharmaceuticals (Basel, Switzerland) was quoted in *Forbes* as saying "Beyond-the-pill is a logical and inevitable path forward for all"[3]. An example of this convergence is the $100-million joint investment vehicle set up between Novartis and Qualcomm to invest in digital medicine companies. Another example is the collaboration between Google and Johnson & Johnson's (News Brunswick, NJ) Ethicon to help develop better robotic surgical tools.

Despite the increased interest and investment in this arena, some in the biopharmaceutical and device/diagnostic industries may be inclined to dismiss digital health as a potentially irrelevant or overhyped area that has yielded mostly consumer health–oriented products rather than disease-focused interventions. We propose here and in forthcoming columns in *Nature Biotechnology* that there is an emerging subset of digital health products that are being developed and clinically validated and that ultimately will be applied as legitimate medical modalities—products that the readers of this journal can no longer afford to ignore.

Digital health versus digital medicine

Digital health is a widely used term that encompasses an enormous variety of products from consumer-focused mobile apps with no clinical validation to FDA-approved apps aimed at patients, physicians or clinical pathologists to tools targeted at researchers. It also includes potentially disruptive technologies whose full impact has yet to be understood. In the past five years, a host of wearable sensor technologies—activity trackers, smart watches, smart clothing, jewelry, patches and wearable tattoos—have emerged, aimed at capturing physiological data, such as movement, respiration, hydration, glucose, skin conductivity, heart rate, sleep, temperature, posture, brain activity, oxygen level, muscle activity, blood pressure, eye tracking and ingestion. The emergence of this field places the fast moving, user-centric, focused tech sector on a fascinating collision course with the much slower-moving, diligent and highly regulated world of medicine.

In the coming months, we intend to focus mainly on the subset of those products with nearer-term potential in disease management

Eric Elenko, Lindsay Underwood & Daphne Zohar are at PureTech, Boston, Massachusetts, USA.
e-mail: DaphneNB@puretechhealth.com

that could have a significant impact on existing healthcare ecosystems. To differentiate these products from the wider group of digital technologies and products in health, we use the umbrella term 'digital medicine'. The term was first coined in 2002 by Shaffer *et al.*[4] In the context of our discussion, we define digital medicine technology and products as that technology and those products that are undergoing rigorous clinical validation and/or that ultimately will have a direct impact on diagnosing, preventing, monitoring or treating a disease, condition or syndrome. For this reason, we believe there is a high likelihood that digital medicine products will have a great impact on the business of current biopharmaceutical and device/diagnostic companies.

In terms of the commercial sectors, some digital medicine products are an extension of the products manufactured by traditional medical device businesses and instrument manufacturers. On the buyer side, big pharma has already shown interest in exploiting these products as opportunities for increasing patient outreach and communication, among other ideas.

In the following sections, we provide a brief overview of our vision of the digital medicine space. We do so by introducing several themes that we feel illustrate unique characteristics of emerging companies and products in this fast-moving sector.

Continuous and remote monitoring

The ability to continuously monitor human physiology and biology through remote sensor technology is one of the groundbreaking aspects of this field. An individual's immersion in a technological ecosystem that measures millions of physiological and other health-related data points, the data collection, decision support and potential impact, makes this one of the most intriguing areas in digital medicine in its potential to have a transformative effect on research and medicine (**Fig. 1**).

From a research standpoint, tracking and analysis of data gathered in a longitudinal manner may reveal new patterns of markers that are informative of disease severity or progression and open up new lines of investigation for researchers. In the area of infectious disease, for example, monitoring pathogenic agents may help keep track of pandemics and aid in disease surveillance. The potential implications of continuous monitoring for how drugs and devices are tested in humans are discussed below (see "The connected patient").

Under a physician's guidance, continuous monitoring by digital medicine products could complement, and eventually even supersede, the established medical model of periodic testing for certain conditions. In the existing paradigm, patients usually go to the doctor only after they have become symptomatic. A physician makes a diagnosis on the basis of the symptoms, supported by a battery of validated clinical tests, and the patient is then assigned treatment and monitored to see whether therapy ameliorates symptoms. In the coming digital medicine era, for a number of conditions, there is the potential to shift toward earlier intervention using both continuous temporal monitoring of an individual's health status for clinically validated markers and prevention tools mediated through digital devices. These devices may include tools for behavioral modification or mechanisms that offer therapy delivery through devices such as smart pumps. Indeed, several markers of disease can already be tracked remotely using physiological sensors attached directly to a mobile device containing an app (e.g., AliveCor's electrocardiogram (San Francisco), Kinsa's Smart Thermometer (New York) and Sanofi's iBGStar glucose monitor (Paris)).

Control of high blood pressure, for example, is an early intervention that greatly decreases the probability of a vascular event[5]. Most patients, however, only get their blood pressure checked as part of a physical exam; continuous digital monitoring could make earlier intervention possible. One company, iHealth (Louisville, Kentucky), already markets an FDA-cleared[6] wireless blood pressure wrist monitor that uses motion-sensor technology to track blood pressure and synchronizes wirelessly to a smartphone app. For cardiovascular disease, several companies, such as ZOLL Medical (Chelmsford, Massachusetts) are developing wearable defibrillators like the LifeVest that are worn by post-myocardial infarction patients.

In the future, the line between diagnosing and monitoring could start to blur as continual patient monitoring allows diagnosis or predisposition screening on an on-going basis, rather than the current situation where diagnosis is made when the patient turns up sporadically at the doctor's office. Such an approach could allow the detection of flare-ups and acute disease before onset of critical symptoms that require hospitalization, resulting in improved patient outcomes and concomitant savings in critical care. As continual monitoring becomes more of a reality, it will be important to balance the positives of early detection and intervention against the downside of false-positive signals that lead to unnecessary additional invasive testing and/or overtreatment.

Continuous monitoring combined with smart drug/devices may also enable drug

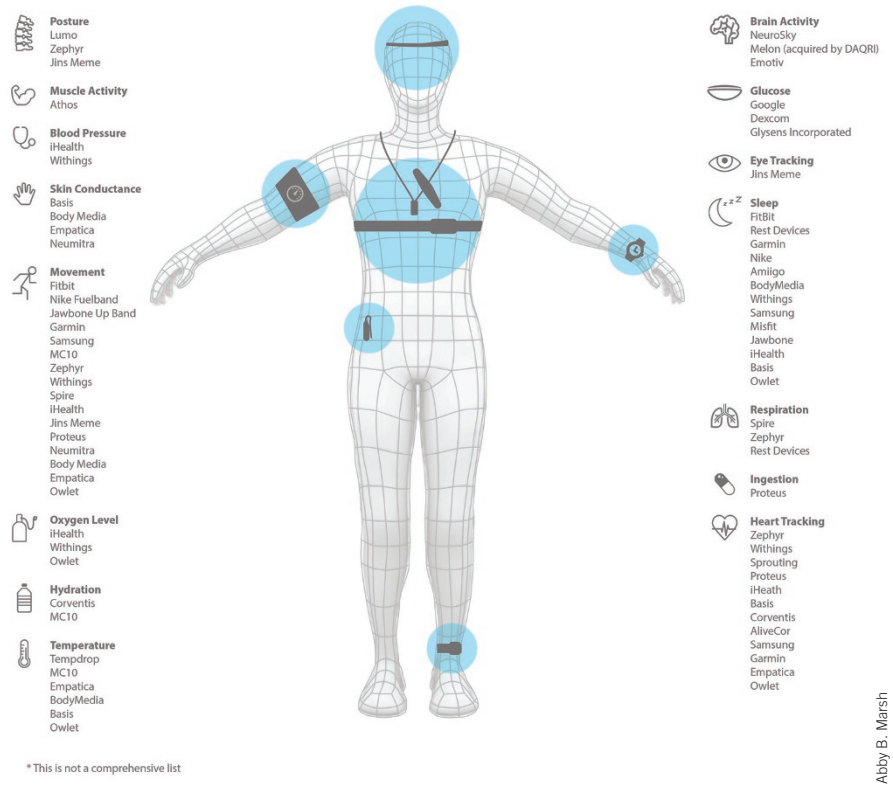

Figure 1 The types of physiological data points and the wearable sensors under development or on the market to monitor them. Illustration by Abby B. Marsh.

makers to design new types of therapies/smart pills. In contrast to current oral dosing regimens (which may or may not be followed by a patient) or injections administered via a weekly/monthly visit to a doctor's office, it is possible that smart pills that respond to patient readouts and deliver drugs continuously, will enable more exquisite control of patient response. Such precise tailoring of therapy promises a number of potential advantages over traditional drug administration and may also give rise to unforeseen disadvantages.

The digital phenotype

Apart from validated markers that have long been used in clinical practice, several digital health ventures are turning their attention to gathering new types of physiological data that, when combined with other information, could prove to be quite powerful.

In 2012, Snyder and colleagues[7] at Stanford University published the first integrative personal omics profile of a single individual that combined genomic, transcriptomic, proteomic, metabolomic and autoantibody profiles gathered over a 14-month period. Their integrated analysis revealed a highly complex and dynamic multidimensional picture of transitions between healthy and diseased states that occurred during viral infection and type 2 diabetes onset.

Digital biomarkers present an additional layer of information that, combined with the types of data above, may enable comprehensive models of disease to be built. For example, Alzheimer's disease prediction and progression monitoring has been an elusive target of the pharmaceutical industry using biological markers alone. Now researchers are turning to digital tools to help broaden the biometric profile and ability to detect disease. Last year, for example, results of a longitudinal study on a cohort of healthy subjects from the Australian Imaging, Biomarkers and Lifestyle Research Group found that high amyloid burden at baseline correlated with a three-year cognitive decline as measured by repeated computerized cognitive tests, suggesting the potential for digital neural correlates of disease progression[8]. Toward the goal of digital correlates that might be used before disease progression is observed, Pfizer (New York), together with Akili Interactive Labs (Boston; author disclosure: Akili was founded by PureTech), recently initiated a study where healthy aging subjects will receive neural imaging, short-term drug dosing, and mobile video game measurements, all in the same study aimed at determining a profile of prodromal (presymptomatic) Alzheimer's disease. The potential for such biological and digital markers in these and other neurological indications is intriguing.

Several companies are also looking beyond neurology. Last year Google, through its research arm Google-X, initiated the ambitious 'Baseline Study', where the tech giant will strive to characterize initially hundreds of healthy subjects over time with biological specimens such as urine, saliva, tears, blood, stool and microbiome swabs (tongue, post-auricular), which will be complemented by monitoring by a Google-X wearable sensor package[9]. Even in settings where researchers are not aiming to be as ambitious as Google, advanced signal-processing techniques are powering healthcare innovations. For example, signal processing and machine learning have been used to explore the potential for predicting apnea events in preterm infants in intensive care units[10]. Other efforts focus on detecting gait asymmetry and early physical distress by means of foot-worn accelerometers—potential applications could include injury reduction during high-intensity training and measurement of rehabilitation progress[11]. In another application, wearable sensors have been used to explore the potential for predictive monitoring of post-operative patients at high risk for complications that could result in readmission to intensive care[12].

In biomedicine, continuous monitoring technologies are collecting a whole raft of new data, with the potential to promote health.This type of data—the so-called digital phenotype (p. 462)—represents a new way to express an individual's state of health. For example, Ginger.io's (San Francisco) products seek to use smartphones to measure and improve mental healthcare. The company's product captures data about a user's activity levels (e.g., level of phone usage) with the goal of discerning changes in the user's health (e.g., detection of depression). An advantage of passive tracking approaches of the type taken by Ginger.io is that they require no effort by the user in contrast with some other approaches that require motivation and therefore pose potential compliance problems. The use of apps that automatically gather information about an individual does raise questions about privacy (see "Security and privacy").

In the consumer sector, the gathering of phenotype data forges ahead. Companies are already producing and marketing sensors that keep track of such physiological data as steps taken, calories burned and sleep patterns, although the sensitivity and accuracy of these gathered data are often not documented in the literature.

Remote disease management

Despite its great potential to transform clinical practice, preventive medicine has taken a backseat to treatment of symptomatic disease for several practical reasons. Primary prevention strategies in healthcare have relied mostly on behavioral intervention with the exception of a few examples like vaccines to prevent microbial infections and interventions like statin therapy for lowering cholesterol.

In this context, behavioral interventions can themselves be effective tools for preventing disease[13,14], and digital medicine approaches provide opportunities to enhance both compliance, and potentially efficacy, of these interventions.

Companies like Omada Health (San Francisco) are creating personalized digital health programs for individuals with conditions like high blood sugar, high blood pressure, dyslipidemia or obesity. The programs are guided by online health coaches, encouraging compliance. Propeller Health's (San Francisco) product is designed for people with asthma or chronic obstructive pulmonary disease and uses a small sensor attached to the top of a person's inhaler to wirelessly keep a record of the time and place in which the inhaler is used. The data collected and feedback given can be used to aid people in the management of their conditions. Similarly, monitoring of brain activity can be used to help epilepsy sufferers better anticipate and improve control of seizures (e.g., Empatica; **Fig. 1**).

The ability to modify behavior may also have implications for chronic disease management. For example, according to the US Centers for Disease Control (Atlanta), there are currently 86 million prediabetic patients in the United States; preventing those individuals from advancing to full-blown diabetes through drug and/or device therapies or behavioral modifications would have a huge impact on morbidity and health economics. Apps that allow early intervention and monitoring of prediabetes could start to shift medical practice from treatment to prevention and early intervention. This past summer, Google announced a partnership with Novartis (Basel) aimed at developing a contact lens that can monitor a person's blood sugar levels, which could be applicable for both diabetics and, more generally, for alerting a user to the presence of a prediabetic state.

One company in the space is Akili Interactive Labs, which is developing a video game platform for remote management of cognitive disorders, such as attention deficit hyperactivity disorder, autism-spectrum disorders and Alzheimer's disease. The firm's software measures a proxy of executive functions in the brain by quantifying an individual's cognitive interference processing abilities in a consumer-grade video game environment[15]. The product

can then remotely deploy a module aimed at improving a user's cognitive function, using those same game mechanics. In addition to being a potentially new type of digital medicine that could be prescribed in a doctor's office, this type of technology opens up the possibility of entirely remote medical intervention where patients could receive treatment without seeing a doctor, a concept that is currently being tested in the Bridging Research and Innovation for Greater Health in Technology, Emotion and Neuroscience (BRIGHTEN; http://www.brightenstudy.com/index.html) study.

The connected patient

With a myriad of sensors and passive monitoring tools capturing an unprecedented amount of data about patients and treatments, such as drug efficacy and interactions, as well as effects of non-drug factors, such as nutrition and environmental conditions, from entire populations, digital medicine is also changing the way we think about clinical studies.

Digital medicine platforms empower patients in several ways. They allow communities of engaged patients to monitor their own symptoms and proactively submit data on their experiences associated with conditions and various treatments in a clinically relevant manner. They also enable patients to share this information and connect with other individuals who may be suffering similar symptoms or are at a similar stage of disease progression. Data gathered on such platforms provide both breadth across many individuals, as well as depth in measuring the health state of one individual over time (through the ability to monitor numerous markers of disease continuously and plot disease progression temporally). Apple's recent launch of ResearchKit (http://apple.co/1zg4l1l), which will host apps that gather data from the general public, has the potential to further accelerate the involvement of not only patient communities but also researchers. If successful, ResearchKit could start to transform every iPhone user into a potential research subject. This raises questions related to consent and privacy which we discuss below (see "Security and privacy").

In addition to the information gathered by sensors, communities of engaged patients are proactively submitting data on their own experiences with conditions and various treatments. These include offerings from companies, such as PatientsLikeMe (Cambridge, MA, USA), Alliance Health's (Salt Lake City, UT, USA) social health communities and the CureTogether.com of genetic testing company 23andMe (Mountain View, CA, USA), which has now extended its business to use its genetic data to conduct drug discovery. Some of these data sets are now being analyzed to assess the quality and validity of data collected online[16]. Online patient platforms have the potential to generate clinical data about approved drugs that patients are taking off label[17] as well as the effects of other interventions in which patients might be engaged.

Of course, patient-reported data has drawbacks, including biases arising from variable and inconsistent data sampling schedules, lack of objective validation of reported data, missing data and incomplete participation. But this new paradigm for clinical studies could begin to enable an '*n* of 1 million' where we have millions of data points from millions of people available to us versus the established paradigm of perfectly controlled clinical studies and limited post-market surveillance. These data sets could also open up new possibilities as we learn how treatments are faring in both controlled traditional clinical trials and real-life settings.

Interpreting the coming data torrent

The utility of data is constrained by the ability to interpret it and draw conclusions from it. As the number of mobile devices and digital sensors mushrooms, torrents of data are going to be generated. There is a question about how well prepared both the medical and research communities are for the onslaught. Integrating heterogeneous and large data sets into current medical decision-making processes not only presents conceptual challenges but also likely practical and economic challenges to healthcare agencies and providers. Ensuring that the fire hose of data generated can be extracted, stored and shared securely, annotated, harmonized to relevant standards, analyzed and interpreted to yield clinically actionable information and insights into research questions will be challenging. Building mathematical and relational models that can describe mechanistically the relationships between multiple data types (e.g., genomic, sensor data, environmental data and past health history) is not trivial. Innovative new tools and technologies for scalable (and flexible) integration of multiple types will be developed and represents an opportunity.

A growing number of companies are focused on providing solutions for analyzing genomic information to provide clinically relevant knowledge to guide disease risk assessment, diagnosis or therapeutic targeting and to integrate multiple streams of data. Genomics represents an area where progress has been made in practically analyzing large data sets. Companies are starting to streamline reporting of genetic analysis within the context of specific diseases and are also setting up tools for collaborators to analyze the same data set from different physical locations. Examples in this category include Foundation Medicine (in which Roche (Basel) has a majority interest), DNANexus (Mountain View, CA, USA), Invitae (San Francisco), Knome (Waltham, MA, USA) and Personalis (Menlo Park, CA, USA), 23andMe as part of its overall efforts, Genospace (Cambridge, MA, USA) and Human Longevity (San Diego). Cloud-based solutions of the type being pursued by DNANexus and Genospace have the potential advantage of simplifying secure data sharing.

Security and privacy

Notwithstanding the opportunities described above, the ubiquity of smart devices and the slew of highly personal data they can generate about health status, mood, diet, lifestyle, location and environment raises privacy and security concerns. Although smartphones and online platforms monitor vast amounts of personal information, all too often users are only partly aware of the types of information being collected about them, let alone how it may be used by others in the public and private sectors.

A key consideration for all digital medicine applications is obtaining an appropriate form of consent from users and knowing what that consent means for how data can be released, accessed and reused. In contrast to traditional healthcare, where a patient's signature on a consent form obtained after an 'informing' conversation creates a legal agreement allowing research (or medical procedures) to go ahead, most applications in today's online world collect personal data with only perfunctory consent—and sometimes with no consent at all. Often users must sign boilerplate legal agreements to access an application, but the legalese is so prolific that users may not fully comprehend what they are agreeing to. Although anonymization can provide some protection for individual confidentiality and privacy, computational analysis and a combination of different data sets have in some cases enabled the identification of individuals or the tracking of individual behavior.

In a related, but separate category, efforts like the Blue Button Initiative focus (http://www.va.gov/bluebutton/) on making a patient's own health data available to him or her as a primary owner of the data. There are also opportunities for patients to donate their data to organizations for research purposes with the patient's consent including Reg4All (Genetic Alliance), DonateData, HealthBank, Kaiser Permanente Research Program on Genes, Environment, and Health and Data Bank and BioRepository at Roswell Park Cancer Institute (Buffalo NY, USA).

In the world of healthcare, patient health records are protected by the Health Information Portability and Accountability Act (HIPAA), a law passed nearly two decades ago when the internet was in its infancy. It remains unclear how digital medicine models that stream patient information from devices to doctors (and potentially other intermediaries) and back again will be hindered by privacy and confidentiality restrictions in HIPAA. On the flip side, the increasing ability of patients to share data and connect online may also undermine existing clinical practices. For example, it has been suggested that the use of social media by patients could potentially lead to the premature unblinding of data in a traditional clinical trial.

And quite apart from privacy, there is also the issue of data security breaches—an increasing general concern for online consumers. In the case of digital medicine, the stakes are even higher. For smart devices, such as insulin pumps, pacemakers or defibrillators, which perform life-saving functions, the possibility that a hacker could take over control has serious consequences—it was the reason the wireless function was disabled on the pacemaker of the former US vice president Dick Cheney.

A plethora of questions is starting to arise around privacy and safety concerns that we will explore in future pieces. How should consent be obtained for sharing data in a clinical context or in a research context? What can be shared with public health agencies? When does the interest of the greater public trump those of private individuals (e.g., in the case of a pandemic or a food poisoning outbreak)? How will companies contend with these issues in designing products?

Opportunities and challenges

We believe emerging diagnostic and therapeutic digital health interventions have the potential to alter the way medicine is practiced and experienced. However, like any other emerging technology area, the companies and products in this space face several fundamental challenges.

The existence of large numbers of digital health companies with unsubstantiated claims whose medical value is untested has muddied the waters, and key opinion leaders in certain areas have publicly expressed their skepticism *vis-à-vis* the space. The US Federal Trade Commission (FTC) has cracked down on apps that have made false claims, such as those that claimed to detect melanoma (http://1.usa.gov/1FQQcj4).

The flip side of this increased focus on scientific evidence and validation, however, is a heightened expectation for digital medicine approaches with true clinical value and with seals of approval from agencies, such as the FDA, which should help identify real winners in the space faster.

An important part of the regulatory framework started to emerge for digital products when the FDA released a guidance document for mobile medical apps[18], which places apps under the purview of the US Centers for Devices and Radiological Health. Apps, therefore, are currently regulated in the same manner as medical devices. The dividing line between when a digital product is likely to be FDA regulated rests mainly in the claims a company makes for the product. If claims for a product relate to diagnosing or treating a disease, the FDA could regulate the product, but a nondisease claim (e.g., promotes relaxation) is much less likely to result in regulation. The framework is analogous to the dividing line between a food supplement, which cannot make direct disease claims, and a drug, which can. Adding to the complexity, as described above, the FTC has jumped into the fray and has selectively cracked down on what it deems to be apps making misleading claims. The debate about how to balance protecting the public from snake oil and not hindering innovation is ongoing with members of the US Congress expressing an interest in participating in the discussion. Products in the digital space pose unique challenges for regulators, such as how does one run a placebo-controlled study for software? As unique products come into existence that even a few years earlier would have sounded like science fiction, older regulatory frameworks may not fit. We will be exploring the complex and important topic of regulation in a future column.

Dennis Ausiello, a former Chief of Medicine at Massachusetts General Hospital in Boston and a member of Pfizer's board of directors, says "The patient is an enormous repository of information that needs to be harvested as a partnership not only in clinical care but in discovery. It is the only way we will define wellness and its progression to disease, rather than traditional medicine that defines disease and its progression to death. The ability to stratify the phenotypic expression of wellness and disease will ultimately lead to better validation of human therapeutic targets for drug discovery."

Reimbursement has historically been both a driver and a limitation to market uptake of new medical products, and digital medicine will likely be no exception. Patients may be willing to pay out of pocket for certain types of digital medicine products, particularly therapeutics that represent a safe, nonpharmacological alternative. However, the ability of digital health products to secure premium pricing compared to consumer apps may be limited without reimbursement. There are examples of digital health products that have started to get reimbursement (e.g., Baltimore-based Welldoc's BlueStar). Some US employers have started to give wearables to their employees as part of encouraging overall health and have sometimes offered incentives associated with achieving certain levels of physical activity, which constitutes a form of reimbursement. According to consulting firm Endeavor Partners (Cambridge, MA, USA), ~6% of people in the US who own a wearable that tracks activity received it from their employer.

A new field of research is poised to emerge as wearables become more prolific and as digital medicine moves increasingly into the mainstream. A host of techniques, terminology and specialized knowledge could start to develop just as it has in areas like genomics. Given that digital medicine represents the convergence of multiple fields, researchers doing digital medicine typically identify with an existing discipline (e.g., being a biostatistician). Researchers will likely start to appear who consider themselves 'digital medicine' experts. It is not unrealistic to expect that students may eventually be able to get PhDs in this discipline, and that academic institutions may even create digital medicine departments.

As digital tools emerge that provide patients with ever-increasing amounts of information and as those patients find social networks to share information, there is the potential to alter the fabric of the doctor-patient interaction. Some leaders in the medical community already understand the tectonic changes underway with the advent of digital medicine. For example, Dennis Ausiello, a former Chief of Medicine at Massachusetts General Hospital in Boston and a member of Pfizer's board of directors, says "The patient is an enormous repository of information that needs to be harvested as a partnership not only in clinical care but in

discovery. It is the only way we will define wellness and its progression to disease, rather than traditional medicine that defines disease and its progression to death. The ability to stratify the phenotypic expression of wellness and disease will ultimately lead to better validation of human therapeutic targets for drug discovery." But many doctors can find it irksome when patients come in with self-diagnoses or second guess a physician based on information found online. The amount of time that physicians have to spend with patients is already limited, and the necessity of integrating greater amounts of patient-specific data will be a challenge to physicians. As recordkeeping goes from paper to electronic health records (EHRs), there are both opportunities and challenges in integrating digital medicine data (e.g., problems with the lack of interoperability of EHRs). Physician acceptance is going to be an important part of driving digital medicine into the mainstream. The timing and drivers of that acceptance could prove to be critical for the field.

The convergence between traditional and nontraditional players in the digital medicine era opens up new opportunities for existing drug, device and diagnostic companies as well as new entrants. The winners in the emerging space will be those companies that can successfully blend both technology and medical expertise. Well-designed and easy-to-use products that have no clinically validated effect on health will likely have less economic potential, and, conversely, a product with great data that nobody wants to use will have challenges in the market. Being successful will require traditional players to establish new sets of internal competencies. It will also require the ability to bring together teams that typically have different cultures, jargon and ways of looking at the world. We will be exploring more deeply what the success factors will be as this new industry emerges in future columns, including interviews with leaders in technology and pharma providing intriguing perspectives on this question.

There are many opportunities and challenges that will be clarified as this exciting new field emerges and over the coming year; this column will dig deeper into topics, such as the complexities of data sharing, interpreting data for real decision support, the shifting regulatory landscape, new company opportunities and emerging business models.

COMPETING FINANCIAL INTERESTS
The authors declare competing financial interests: details are available in the online version of the paper (doi:10.1038/nbt.3222).

1. Topol, E.J., Steinbuhl, S.R. & Torkmani, A. *J. Am. Med. Assoc.* **313**, 353–354 (2015).
2. Kocher, B. & Roberts, B. *Harvard Bus. Rev.* https://hbr.org/2014/12/why-so-many-tech-companies-are-getting-into-health-care (8 December 2014).
3. Bloomberg, J. Digital transformation moves pharma 'beyond the pill'. *Forbes* (15 August 2014).
4. Shaffer, D.W., Kigin, C.M., Kaput, J.J. & Gazelle, G.S. *Stud. Health Technol. Inform.* **80**, 195–204 (2002).
5. El-Khatib, F.H., Russell, S.J., Nathan, D.M., Sutherlin, R.G. & Damiano, E.R. *Sci. Transl. Med.* **2**, 27ra27 (2010).
6. Food and Drug Administration. 510(k) summary—KD-7964 fully automatic electronic blood pressure monitor. (FDA, 2012). http://www.accessdata.fda.gov/cdrh_docs/pdf12/K121470.pdf
7. Chen, R. *et al. Cell* **148**, 1293–1307 (2012).
8. Lim, Y.Y. *et al. Alzheimers Dement.* **10**, 743–751.e1 (2014)
9. Barr, A. Google's new moonshot project: the human body. *The Wall Street Journal* (27 July 2014).
10. Williamson, J.R., Bliss, D.W., Paydarfar, D. *Respir. Physiol. Neurobiol.* doi:10.1016/j.resp.2013.05.034 (2 June 2013).
11. Williamson, J.R. *et al.* in *Body Sensor Networks*, 1–6 (IEEE International Conference, 2013).
12. Clifton, L., Clifton, D.A., Pimentel, M.A.F., Watkinson, P.J. & Tarassenko, L. *IEEE J. Biomed. Health Inform.* **18**, 722–730 (2014).
13. Avery, L., Flynn, D., van Wersch, A., Sniehotta, F.F. & Trenell, M.I. *Diabetes Care* **35**, 2681–2689.
14. Lin, J.S. *et al. Ann. Intern. Med.* **161**, 568–578.
15. Anguera, J.A. *et al. Nature* **501**, 97–101 (2014).
16. Hafen, E., Kossman, D. & Brand, A. *Methods Inf. Med.* **53**, 82–86 (2014)
17. Wicks, P., Vaughan, T.E., Massagli, M.P. & Heywood, J. *Nat. Biotechnol.* **29**, 411–414 (2011).
18. US Food and Drug Administration. *Mobile Medical Applications. Guidance for Industry and Food and Drug Administration Staff.* http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM263366.pdf (FDA; 9 February 2015).

Corrected after print 13 October 2016.

Erratum: Defining digital medicine

Eric Elenko, Lindsay Underwood & Daphne Zohar

***Nat. Biotechnol.* 33, 456–461 (2015); published online 12 May 2015; corrected after print 13 October 2016.**

In the version of this article initially published, PureTech was incorrectly credited for the illustration on p. 457. The Biosensing Body Image illustration is by Abby B. Marsh. The error has been corrected in the HTML and PDF versions of the article.