

Accelerating Precision Health by Applying the Lessons Learned from Direct-to-Consumer Genomics to Digital Health Technologies

Joyce Y. Tung, PhD, ^{23andMe}; **Ryan J. Shaw, PhD, RN**, Duke University School of Nursing; **Jill M. Hagenkord, MD, FACP**, Color Genomics; **Meredith Hackmann**, National Academies of Sciences, Engineering, and Medicine; **Marion Muller**, Emory University; **Sarah H. Beachy, PhD**, National Academies of Sciences, Engineering, and Medicine; **Victoria M. Pratt, PhD**, Indiana University; **Sharon F. Terry, MA**, Genetic Alliance; **Ann K. Cashion, PhD**, National Institute of Nursing Research; **Geoffrey S. Ginsburg, MD, PhD**, Duke University School of Medicine

March 19, 2018

Emerging Opportunities for Digital Health

Digital health technologies have emerged in recent years, providing opportunities for engaging with consumers and integrating with the health care system to realize precision medicine, defined as “an evidence-based approach to the care of people and patients that uses innovative tools and data science to customize disease prevention, detection, and treatment; improve the effectiveness and quality of care; and sustain health” [1]. These technologies—including smartphone applications (apps), wearables (e.g., Fitbit, Apple Watch), and mobile-device-based tools—can make health care and management of health and wellness more efficient for patients and clinicians and can support research. Digital health technologies offer consumers, patients, and clinicians the opportunity to interact with personal health data and the health care system in a way that has not been available previously.

One such tool—the fertility app, Glow—helps users who are trying to conceive track data such as ovulation, physical symptoms, and diet and exercise [2]. The company has amassed a wealth of user-reported data and, in a study, claimed that conception rates are significantly higher in the population that frequently uses the app compared to those who do not [3]. Other health tracking apps increasingly popular among consumers track user-reported food and water intake, as well as steps walked, heart rate, and sleeping patterns by pairing with a wearable device. From 2014 to 2016, wearable use increased by 12 percent, reflecting use by 21 percent of consumers surveyed across seven countries [4]. One wearable company, Fitbit, increased

its active user base from 16.9 million in 2015 to 23.2 million by the end of 2016 [5].

While tracking devices are popular with physically active individuals, they can also be useful for helping consumers with chronic diseases such as chronic heart failure. For example, a wireless scale can be used to track weight and a diet app to record nutritional information—behaviors important for controlling their condition. Other digital health apps have shown potential to improve health care decision making and management, including glucometers that can connect with smartphones to help those with type 1 diabetes and sensors that can attach to inhalers to help those with asthma or chronic obstructive pulmonary disease. According to a 2016 survey, 76 percent of patients who were instructed by a physician to use a wearable to track lifestyle, fitness, or vitals complied with the doctor’s request [4].

In the field of genomics and precision health, digital health apps are also making their way onto the market. For instance, Helix launched a DNA app store in July 2017 that acts as a “one stop shop” for interested individuals to interact with their genomic data [6]. The Scripps Translational Science Institute’s MyGeneRank study is using genetic information received from users of 23andMe, a personal genetics company [7], to assess genetic risk for coronary heart disease and reporting it back through a mobile app [8]. Other research efforts, such as the All of Us Research Program, hope to use wearables and other home-health technologies to gather environmental and personal health measurements to correlate with patient outcomes data [9,10].

Given the short amount of time that mobile health apps have been on the market, and their growth to date, it is not unreasonable to assume that these will continue to be adopted and grow in popularity and use among consumers as other technologies have done. While there is potential for these technologies to improve health, there are still many challenges that must be addressed, including data quality, consumer access to data, others' access to data, data use, and regulatory oversight. The direct-to-consumer (DTC) genomics industry, which has been increasingly moving into the clinical health space over the last 10 years, offers insights for digital health technologies that may help companies navigate integration within health systems. Like digital apps, DTC genomics companies like 23andMe and Helix have become increasingly common, offering consumers the opportunity to gain insights into their genetics. By providing health-related data with potential applications in health care and encouraging patients to take a more active approach in their health decision making, these DTC genomics companies represent a new hybrid business model combining a traditional medical device and consumer product. As DTC genomics has evolved, the industry has had to grapple with many of the same issues now facing the digital health industry. Here we review a number of these key issues and identify recommendations for those working in the digital health space.

Key Challenges

Regulatory Uncertainty

The regulatory uncertainty surrounding laboratory developed tests (LDTs) created a challenge for DTC genomic testing companies from the outset. Although LDTs first came under FDA authority in 1976, the agency had for decades exercised "enforcement discretion," meaning that the laboratories developing and performing the tests were not required to obtain FDA clearance or approval for marketing [20].

Many companies incorrectly assumed that DTC genetic tests, which often were also LDTs, would fall under this same enforcement discretion and thus were unprepared for the regulatory challenges that followed [13] (see Box 1).

A key lesson for app developers is the importance of understanding the regulatory landscape, the differences in regulatory categories (i.e., drugs, medical

devices, and diagnostics), and their place in it in order to assess what requirements they will need to fulfill to market their products and services. For example, it may be important to understand and plan for what is needed to demonstrate analytical and clinical validity at the beginning of product development. The FDA's 2013 warning letter to 23andMe cited the company's failure to provide sufficient information to support the analytical and clinical validity of the test. This requirement was predicated on the FDA's assessment that the 23andMe product was a medical device and thus required to meet certain standards for that type of regulatory category, which the FDA has subsequently published.

Many parallels can be seen between the regulation of DTC tests and mobile health tools, the latter referred to by the FDA in three categories: mobile platforms, mobile apps, and mobile medical apps. Mobile medical apps meet the definition of a device; mobile platforms are handheld commercial off-the-shelf computing platforms, such as smartphones and tablets; and mobile apps are software applications that are run on mobile platforms. Current FDA regulations explain that the FDA uses a tiered approach to oversight [21]. The agency's focus is on apps and devices that meet the definition of a medical device and that present a significant risk to patients if the apps or devices do not work as intended. The FDA does not apply regulatory requirements to mobile health tools that are not considered mobile medical apps. For example, a mobile app may potentially be used as a tool to help an individual be aware of their risk for skin cancer based on an image provided by the end user; however, the app would have to meet much stricter regulatory requirements if it were to diagnose that individual with skin cancer and/or provide a treatment plan, rather than give general guidance that the user should consult a physician. Regulation of digital health products will necessitate developers being aware of appropriate regulatory pathways, specific regulatory requirements (or lack thereof), and what will be needed to demonstrate performance.

Consumers versus the Health Care System

Analytical Validity, Clinical Validity, and Clinical Utility

Central to the question of how DTC health information should be integrated into health care are issues

Box 1 | The Rise of Direct-to-Consumer Genomics

Companies began offering direct-to-consumer (DTC) genetic testing in or around the early 2000s, primarily focusing on nutrigenetics. This drew the scrutiny of multiple federal agencies, leading to a 2006 US Government Accountability Office (GAO) report that raised serious concerns about the accuracy and interpretation of DTC genetic tests, as well as their lack of regulatory oversight [11]. In an effort to educate consumers about the potential risks and benefits of purchasing at-home genetic tests, the Federal Trade Commission (FTC) published a general guidance, drawing on information from the US Food and Drug Administration (FDA) and Centers for Disease Control and Prevention. The guidance advised consumers to approach these tests with skepticism and encouraged consumers to involve physicians when interpreting their test results [12]. The guidance highlighted some of the potential concerns for consumers engaging with these tests, including analytical and clinical validity and clinical utility. The points on which this guidance touched remain at the forefront of the DTC genomics discussion.

By 2007, companies such as deCODE Genetics and 23andMe began to market more complex DTC genetic tests to the public [13], sparking much interest among consumers and concern among regulators about the potential benefits and harms. Companies provided health reports that linked a participant's genotype results to associations with disease risks, as well as physical and personality traits. In 2008, the DTC genetic testing service from 23andMe was named *Time's* Invention of the Year [14]. The company 23andMe's "\$399 saliva test that estimates your predisposition for more than 90 traits and conditions" was considered a pioneer of retail genetic testing [14]. By late 2009, 23andMe and another company, Pathway Genomics, had increased their offerings by adding information that was considered "actionable" for health care decision making, such as testing for rare variants, drug response based on genetics (pharmacogenetics), and carrier screening [15]. New DTC genetic testing companies continued to join the field, despite ongoing regulatory scrutiny. With minimal federal regulations from the Clinical Laboratory Improvement Amendments (CLIA) of 1988 already in place [16], discussion regarding the best way to proceed quickly gained attention and continued for many years.

At the same time, the clinical genetic testing regulatory system continued to face scrutiny. The Secretary's Advisory Committee on Genetics, Health, and Society at the National Institutes of Health released an extensive report related to clinical genetic testing in 2008 that pointed out major gaps in the current regulations and offered solutions to many of these problems [17]. The GAO issued a second report in 2010. Several professional societies also issued statements in opposition to DTC genetic testing, maintaining that such testing should be performed and interpreted by medical professionals. In 2010, the FDA held a public workshop on DTC genetic testing to gather more feedback to inform developing policy. Some claimed that DTC tests did not fall under the FDA's jurisdiction because they reported educational information, however, the FDA's position was always that DTC tests were medical devices. In 2010, the FDA sent letters to several DTC genomics companies informing them that their tests were medical devices that provided data on "genetic predispositions for important health conditions and medication sensitivities," as well as pharmacogenetics results that might influence drug treatment. The letters also indicated that these tests did not have FDA clearance or approval. In 2013, the FDA issued a warning letter to 23andMe that prevented it from marketing any health-related genetic reports until the FDA authorization was obtained. In the letter, the FDA stated that it had given the company various opportunities to comply with feedback on analytical and clinical validity requirements for its tests and potential regulatory pathways to pursue, but the agency had received little indication that the company was taking the necessary steps toward compliance [18].

Though these DTC companies have faced some practical hurdles in recent years, the field continues to learn from early challenges and evolve. For example, 23andMe's Bloom syndrome carrier test report was authorized in 2015, and the FDA exempted this kind of device from premarket review moving forward. Alberto Gutierrez, then director of the Office of In Vitro Diagnostics and Radiological Health at the FDA said, "The FDA believes that in many circumstances it is not necessary for consumers to go through a licensed practitioner to have direct access to their personal genetic information." This was followed, in April 2017, by the FDA's decision to authorize 23andMe to market DTC tests that provide information on an individual's genetic predisposition to certain medical diseases or conditions, such as Parkinson's disease and late-onset Alzheimer's disease [19]. While 23andMe currently has the only DTC genetic test to receive FDA authorization, these recent innovative regulatory decisions define a clear path to market for additional DTC genetic tests and are likely to pave the way for expansion of the DTC genetic test industry.

SOURCE: Tung et al., "Accelerating precision health by applying the lessons learned from direct-to-consumer genomics to digital health technologies," National Academy of Medicine.

concerning the analytical validity, clinical validity, and clinical utility of the information. Briefly, an assay is analytically valid if it accurately and reproducibly measures what it intends to. A test is clinically valid if what it measures is clinically meaningful [22]. Clinical utility describes the ability of a test to lead to a clinical decision with evidence of improved outcomes, and for a digital device that is manufactured to replace an existing device, this is usually measured by direct comparison to the current standard of care (e.g., a device that attaches to a smartphone to measure blood oxygen saturation versus a battery-operated pulse oximeter). For genetic tests, which may assay up to millions of endpoints, identifying the right studies to demonstrate analytical and clinical validity has been challenging [23], and showing clinical utility is an even higher bar that generally requires more complex clinical studies. Studies of health care professionals show that they consistently have concerns about the quality, reliability, and clinical utility of information from DTC genetic testing [24].

Consumers, and oftentimes their clinicians, are generally not able to assess analytic validity and clinical validity. Consumers might misunderstand clinical utility for usefulness in a real-world context. Thus, a key challenge for the DTC genomics and digital health industries will be navigating these differences in understanding of definitions around validity and utility.

Physicians use health information to help diagnose disease and guide treatment, and generally require the accuracy demonstrated by medical-grade devices, which have strong analytical and clinical validity. For example, mobile medical apps that require FDA approval, such as a Bluetooth-enabled glucometer, may be viewed by physicians as valid tools. Consumers, on the other hand, may see the apps as helpful to maintain or improve their health, manage a condition, or gain insights into their personal habits. For these purposes, their standards for the validity of the information they receive may be less stringent. In addition, a consumer may see personal utility in information that has little clinical utility. For instance, a survey by Rock Health found that 47 percent of consumers were willing to pay \$50 for a test to identify a predisposition for Alzheimer's disease, which has no cure and for which there are early clinical interventions only in clinical trials, whereas only 28 percent were willing to pay the same amount for a genetic test of metabolism [25].

This gap in clinical utility and consumer expectations can create challenges when consumers bring information from DTC devices and apps to their physicians. Many consumer devices, including many wearables, are not intended for clinical use and thus may have performance that is not validated. For example, a study by Wang et al. found that wrist-based wearable devices used for heart rate monitoring varied widely in terms of accuracy compared to the standard chest strap electrode-based monitors prescribed by many physicians for their cardiac patients [26]. Similarly, while accelerometers such as those found in smartphones may be useful to understand a "gestalt" view of activity and serve as motivational tools for health behavior change when coupled with apps, their accuracy as a clinical-grade tool has not been well described. These distinctions may not be clear to many consumers. In addition, many providers, health systems, and electronic health records are not adequately prepared to handle the large amounts of data from DTC genetic testing or digital health apps. When patients bring this information to their providers, they may expect answers or guidance on how it should influence their health behaviors, even though in many cases evidence-backed clinical guidelines do not exist for this type of information. If, instead, providers are not able to respond to the data in a way that consumers expect, they may become frustrated or disappointed, which may lessen the value of the device or app to the consumer.

Accessibility and Reimbursement

When DTC genomics companies first appeared on the market, the cost of some full screening tests ran upwards of \$2,000. Thus, the price point was well out of range for the average consumer [15]. As technological improvements were made, these tests decreased in price, allowing more consumers into the market. While the question of whether these technologies will exacerbate health disparities is still being debated, the need for people of all backgrounds to have access to DTC genomics is important [27]. While much genetic variation is shared among all people, there are important differences across populations, and having greater diversity among consumers of genetic testing will help the industry improve the services it provides to everyone. Digital health technology may offer a significant opportunity to reduce health disparities by affordably increasing access to care. According to the Pew Research Center, 77 percent of Americans own

smartphones [28], creating a potential outlet to reach a majority of consumers across socioeconomic and urban and rural divides.

A secondary concern in this area is whether and how these technologies may be reimbursed by third-party payers. While strictly DTC genetic tests have generally stayed out of the reimbursement space, there are physician-prescribed genetic test providers that have taken a hybrid approach by helping people seek reimbursement but limiting an individual's out-of-pocket expense to a certain amount [29]. In addition, as McGuire et al. discussed, in the early stages of DTC genetic testing, reimbursement systems were not ready to handle the challenges of DTC genomics, both in terms of covering the time spent by health care providers reviewing DTC genetic test results, and additional testing prompted by the DTC reported results [30]. Engaging with payers and health care providers may be of value for digital health stakeholders, as it will set expectations for requirements to fully realize the technology in a clinical setting.

Recommendations and Guidelines from Professional Societies

Early on, DTC genetic testing companies were met with caution from professional societies and agencies, including the American Society of Human Genetics (ASHG). ASHG recognized the potential for increased access to testing and greater consumer awareness, but also recommended actions around transparency, provider education, and test and laboratory quality if the field wanted to move forward [31]. For their part, several DTC companies indicated a willingness to work with stakeholder groups to define a set of standards that could help companies in the field self-regulate [13]. As consumers increasingly showed interest in these tests and the evidence base grew, some groups updated their position statements in support of tests that provided meaningful information to patients and proper education to act on the results [32,33].

Because digital health is a relatively young field that is rapidly evolving, gaps exist in guidance and recommendations from professional societies, but key leaders can be engaged to offer direction and encourage innovation. Some groups have sought to help lead the way by creating frameworks and resources for the field, among them the Health App Decision Tree from the Children's Health Fund and an interactive tool created by the FTC. The Health App Decision Tree starts

with the question "Is the app selling a product or therapy?" and then goes through a detailed decision-making process of yes-or-no questions until an app developer either gets to an inappropriate app or appropriate app end point [34]. The questions pertain to privacy issues, data settings, and the type of information provided in the app, among others. Another tool created for app developers is the FTC's Mobile Health Apps Interactive Tool, which helps determine which federal laws apply to the app [35]. Based on 10 yes-or-no questions, the tool provides information on the Health Insurance Portability and Accountability Act (HIPAA), and FDA and FTC laws that may or may not apply based on whether the tool is considered a medical device and who the intended user is. For those areas where HIPAA does not apply, Dzau et al. recommend industry implementation of a "digital Hippocratic oath" to help strengthen data security and privacy for consumers using digital health apps [9].

Data Privacy and Data Accessibility

Many digital health apps collect a large amount of private data about their users, which presents issues of data privacy and security. In the DTC genetics world, the Genetic Information Nondiscrimination Act (GINA) and HIPAA both provide privacy protections to patients. Despite these important pieces of legislation, there are still gaps—HIPAA may not apply to all players in the DTC genetic testing or digital health space [35,36], and GINA protects against discrimination in health insurance and employment, but not life insurance. Being the steward of users' personal data may also have other legal ramifications. In 2015, a man named Michael Usry was taken into questioning for an open murder case from 1996, based on a familial DNA search in a publicly searchable database owned by the company Ancestry, which provides customers with genealogical information. When police found similarities between the DNA found at the crime scene and Usry's father, Ancestry was compelled by a court order to provide the name of Usry's father [37].

In addition, as it is not always easy to understand what data are being used by apps and devices, consumers may not be aware of how their information is being used. For example, GPS information could be continuously collected in the background of the app without a consumer realizing or remembering that it is still happening. Even if this information on data collection was given to a consumer when downloading the

app or activating it at baseline, the consumer still may not understand what is being presented to them due to digital literacy challenges [38,39]. Furthermore, data collected from sensors connected to mobile devices (e.g., wearables) could be analyzed to predict certain health behaviors such as dental or smoking habits, highlighting potential privacy and insurance implications [40].

Having access to their own data is also important for consumers. A 2016 survey of consumers and physicians showed that 92 percent of patients believe that they should have full access to their health records, while only 18 percent of physicians agree [4]. Similarly, a study by Kaufman et al. showed that the top incentives for people to get involved in a large cohort study included receiving their own lab results, genetic results, and medical records [41]. Government regulations are starting to favor consumers in this regard. The US Department of Health and Human Services states that an individual has the right to access his or her lab results, including the underlying data. This includes, for example, the full underlying gene variant data generated by a lab test that uses next generation sequencing [42]. Increasingly, consumers expect to control their own data [43].

Recommendations and Opportunities

Based on the issues outlined above, we offer the following recommendations for groups developing digital health apps and technologies:

1. Engage early with regulators and professional societies about product development.
2. Identify and articulate well the intended use and audience.
3. Proactively address issues of data privacy and data accessibility.

Engage Early with Regulators and Professional Societies about Product Development

As described above, there remains uncertainty around regulation of apps and services in the digital health space. It is thus valuable to engage with potential regulators early and often in the product development process to determine the appropriate regulatory path, particularly as it relates to generating data to demonstrate the performance of the product. Furthermore, companies may find value in aggregating evidence to substantiate prior claims. Interestingly, in July 2017, the FDA announced new steps to empower

consumers and advance digital health care [44]. As part of the Medical Innovation Access Plan, the agency created a new component focused on digital health innovation that included a pre-certification for a software pilot program. The pre-certification would allow companies to submit less information than currently required before marketing new digital health tools.

Still, digital health that goes beyond the FDA classification of a mobile medical app is considered the “wild west” [45]. There is an absence of peer review of apps in health care, which makes ascertaining the quality of an app and verifying its claims challenging for both consumers and health care providers. There is a need for a peer review body or a set of guidelines that clinicians and consumers can look to for guidance. Peer review of apps may also be needed during the peer review process of manuscripts that focus on digital health tools used in studies. Engaging with professional societies can help drive the development of consensus guidelines that will make it easier to develop products and drive the industry forward more quickly.

Identify and Articulate Well the Intended Use and Audience

As consumers and health care providers have different requirements and expectations for digital health products, developers should identify the intended use and audience for their products. A product that is aimed at clinicians, or is intended to produce information a consumer would share with a clinician, may need to demonstrate a certain level of analytical validity, clinical validity, and/or clinical utility before a clinician would find the information valuable. A product that is intended for a consumer’s educational or personal use, however, may not need the same level of validation. Identifying who will use the product and how will help define what types of studies need to be conducted to support the product’s intended uses.

In addition, identifying who will use the product can help define who should pay for the product and, as appropriate, how it can be integrated in the health system. A product aimed at consumers will involve considerations of cost in terms of accessibility to many consumers. There may be different considerations if a developer wants to seek reimbursement from third-party payers, so engagement with those groups during the development of the product can provide guidance. Given the already limited time and capacity of health care providers, a new model for incorporating data from digital health technologies into health care

may be needed, both in terms of clinical workflow and reimbursement models, which, again, may require a multistakeholder approach from those involved in the industry.

Proactively Address Issues of Data Privacy and Data Accessibility

The privacy of their personal health information is important to many consumers, even early adopters [46]. Digital health app developers should proactively address privacy challenges by evaluating potential privacy issues and creating a consumer-centric privacy policy that describes how customer data are used. Some companies even publish a transparency report describing government requests for data [47,48], which many see as a welcome additional step.

To encourage open data-sharing policies and allow consumers to be stewards of their own data, digital health technology developers should build application programming interfaces to make it easier for users to access and share their data with other services. Developers should also consider working together to come up with data standards that will make it easier to share, exchange, and understand the data. Making the data more portable will support the growth of the industry as a whole. Giving consumers dynamic and granular data-sharing, access, and privacy preference tools could accelerate knowledge gain and benefits for health. With the larger amount of personal health data that will be stored, we also note that certain security issues will need to be addressed. In the health care setting, recent data breaches have highlighted some of the vulnerabilities in data security, which may have serious consequences for patients and consumers. Health care organizations have indicated that they lack the infrastructure and expertise to ensure necessary data protections for patients [40]. As new technologies come to the market, it will be important for developers to build security protections within their devices to thwart potential cyberattacks aimed at disabling or manipulating devices.

Future Potential

When the internet was in its infancy, many people believed it would serve as a tool for basic education and research — or, in other words, be a simpler way to communicate. User growth of more than 500 percent between 2000 and 2012 has led to the evolution of an incomprehensibly influential tool that has molded the

world — and will continue to do so [49]. Many people believe that precision health has the potential to follow a similar trajectory of growth, and if used effectively, the field of digital health could be a catalyst for accelerating its rise. Similar in complexity to the genome, the internet and smartphones feature a majority of users who are not familiar with how they work. As knowledge and technology advance to widen the range of people participating in genetic testing, an extremely large and influential dataset could be created, providing new opportunities to accelerate research, drug development, and precision health. The DTC genomics industry has had to navigate the challenges of regulatory issues, health care provider and consumer expectations, and privacy issues. Digital health, by learning from some of the lessons learned by DTC genomics, may be able to more efficiently integrate with the health care system and, in turn, help realize the full potential of precision health for the larger population.

References

1. National Academies of Sciences, Engineering, and Medicine. 2015. *Roundtable on Translating Genomic-Based Research for Health: 2015 annual report*. Washington, DC: The National Academies Press.
2. Glow. 2017. *Modern care for your fertility*. <https://glowing.com> (accessed December 13, 2017).
3. Hartz, A., P. Chenette, E. Scott, and R. Ye. 2015. *Monthly fecundity and the benefits of ovulation tracking in the United States*. What big data tells us about the true nature of fertility. <https://assets.documentcloud.org/documents/2488193/asrm-benefit-of-ovulation-tracking-amp-big-data.pdf> (accessed October 24, 2016).
4. Safavi, K., and R. Ratliff. 2016. *Patients want a heavy dose of digital*. https://www.accenture.com/t20160629T045303_w_/us-en/_acnmedia/PDF-6/Accenture-Patients-Want-A-Heavy-Dose-of-Digital-In-fographic.pdf#zoom=50 (accessed October 24, 2016).
5. FitBit reports \$574m Q416 and \$2.17b FY16 revenue, sells 6.5m devices in Q416 and 22.3m devices in FY16. 2017. *BusinessWire*, February 22, <http://www.businesswire.com/news/home/20170222006497/en/Fitbit-Reports-574M-Q416-2.17B-FY16-Revenue> (accessed August 17, 2017).
6. Helix. 2017. *Discover your DNA story*. <https://www.helix.com> (accessed December 13, 2017).

7. National Institutes of Health (NIH). 2017. Mygenerank: A digital platform for next-generation genetic studies. In: ClinicalTrials.gov. Bethesda, MD: National Library of Medicine. Available from: <https://clinicaltrials.gov/ct2/show/NCT03277365> (accessed December 13, 2017).
8. Muse, E. D., N. E. Wineinger, B. Schrader, B. Molparia, E. G. Spencer, D. L. Bodian, A. Torkamani, and E. J. Topol. 2017. Moving beyond clinical risk scores with a mobile app for the genomic risk of coronary artery disease. *bioRxiv*, <https://doi.org/10.1101/101519> (accessed August 17, 2017).
9. Dzau, V. J., G. Ginsburg, A. Chopra, D. Goldman, E. D. Green, D. G. B. Leonard, M. McClellan, A. Plump, S. F. Terry, and K. Yamamoto. 2016. Realizing the full potential of precision medicine in health and health care. *NAM Perspectives*. Discussion Paper, National Academy of Medicine, Washington, DC. <https://nam.edu/wp-content/uploads/2016/09/Realizing-the-Full-Potential-of-Precision-Medicine-in-Health-and-Health-Care.pdf> (accessed July 12, 2017).
10. NIH. 2017. *The Dish: Lifestyle data: Fitbit pilot*. <https://allofus.nih.gov/news-events-and-media/videos/dish-lifestyle-data-fitbit-pilot> (accessed November 9, 2017).
11. *Nutrigenetic testing—tests purchased from four web sites mislead consumers*. 2006. Washington, DC: Government Accountability Office.
12. Federal Trade Commission (FTC). 2006. *At-home genetic tests: A healthy dose of skepticism may be the best prescription*. https://osp.od.nih.gov/wp-content/uploads/2013/11/DTC_Consumer_Alert_Jul06.pdf (accessed September 7, 2017).
13. Vorhaus, D. 2010. The past, present and future of dtc genetic testing regulation. *Genomics Law Report*, <http://www.genomicslawreport.com/index.php/2010/08/05/the-past-present-and-future-of-dtc-genetic-testing-regulation/#2007> (accessed October 17, 2016).
14. Hamilton, A. 2008. Best inventions of 2008. *Time*, October 29, http://content.time.com/time/specials/packages/article/0,28804,1852747_1854493,00.html (accessed October 17, 2016).
15. Pollack, A. 2010. Consumers slow to embrace the age of genomics. *The New York Times*, March 19, <http://www.nytimes.com/2010/03/20/business/20consumergene.html?action=click&contentCollection=Business%20Data&module=RelatedCoverage®ion=Marginalia&pgtype=article&r=1> (accessed October 24).
16. Centers for Disease Control and Prevention. 2016. *Clinical Laboratory Improvement Amendments*. <http://www.cdc.gov/clia> (accessed October 17, 2016).
17. Ferreira-Gonzalez, A., S. Teutsch, M. S. Williams, S. M. Au, K. T. Fitzgerald, P. S. Miller, and C. Fomous. 2008. US system of oversight for genetic testing: A report from the Secretary's Advisory Committee on Genetics, Health and Society. *Personalized Medicine* 5(5):521-528.
18. US Food and Drug Administration (FDA). 2013. *Warning letter to 23andMe*. <http://www.fda.gov/iceci/enforcementactions/warningletters/2013/ucm376296.htm> (accessed April 5, 2017).
19. FDA. 2017. *FDA allows marketing of first direct-to-consumer tests that provide genetic risk information for certain conditions*. <https://www.fda.gov/newsevents/newsroom/pressannouncements/ucm551185.htm> (accessed December 13, 2017).
20. Centers for Medicare and Medicaid Services. 2013. *CLIA overview*. https://www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/Downloads/LDT-and-CLIA_FAQs.pdf (accessed October 24, 2016).
21. FDA. 2015. *Mobile medical applications*. <https://www.fda.gov/MedicalDevices/DigitalHealth/Mobile-MedicalApplications/default.htm> (accessed October 2, 2017).
22. Teutsch, S. M., L. A. Bradley, G. E. Palomaki, J. E. Haddow, M. Piper, N. Calonge, W. D. Dotson, M. P. Douglas, and A. O. Berg. 2009. The Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Initiative: Methods of the EGAPP working group. *Genetics in Medicine* 11(1):3-14.
23. Madsen, J. 2015. FDA regulation catches up to next-gen gene sequencing. *Law360*, <http://www.law360.com/articles/705682/fda-regulation-catches-up-to-next-gen-gene-sequencing> (accessed September 29, 2016).
24. Goldsmith, L., L. Jackson, A. O'Connor, and H. Skirton. 2013. Direct-to-consumer genomic testing from the perspective of the health professional: A systematic review of the literature. *Journal of Community Genetics* 4(2):169-180.
25. Devos, L., T. Wang, and S. Iyer. 2016. *The genomics inflection point: Implications for healthcare*. <https://rockhealth.com/reports/the-genomics-inflection-point-implications-for-healthcare> (accessed September 30, 2016).

26. Wang, R., G. Blackburn, M. Desai, D. Phelan, L. Gillinov, P. Houghtaling, and M. Gillinov. 2017. Accuracy of wrist-worn heart rate monitors. *JAMA Cardiology* 2(1):104-106, <https://jamanetwork.com/journals/jamacardiology/article-abstract/2566167> (accessed April 4, 2017).
27. Smith, C. E., S. M. Fullerton, K. A. Dookeran, H. Hampel, A. Tin, N. M. Maruthur, J. C. Schisler, J. A. Henderson, K. L. Tucker, and J. M. Ordovas. 2016. Using genetic technologies to reduce, rather than widen, health disparities. *Health Affairs* 35(8):1367-1373.
28. Pew Research Center. 2017. *Mobile fact sheet*. <http://www.pewinternet.org/fact-sheet/mobile> (accessed July 12, 2017).
29. Farr, C. 2016. Why patients are getting hit with surprise bills after genetic testing. *Fast Company*, April 20, <https://www.fastcompany.com/3059072/why-patients-are-getting-hit-with-surprise-bills-after-genetic-testing> (accessed October 23, 2017).
30. McGuire, A. L., C. M. Diaz, T. Wang, and S. G. Hilsenbeck. 2009. Social networkers' attitudes toward direct-to-consumer personal genome testing. *American Journal of Bioethics* 9(6-7):3-10.
31. ASHG statement on direct-to-consumer genetic testing in the United States. 2007. *American Journal of Human Genetics* 81:635-637, http://www.ashg.org/pdf/dtc_statement.pdf (accessed July 13, 2017).
32. Association for Molecular Pathology. 2015. *Association for molecular pathology position statement: Direct access genetic testing (direct to consumer genetic testing)—February 2015*. http://old.amp.org/publications_resources/position_statements_letters/documents/AMPpositionstatementDTCtesting-FINAL_002.pdf (accessed July 12, 2017).
33. National Society of Genetic Counselors. 2015. *Direct access to genetic testing*. <http://www.nsgc.org/pbl/et/blogaid=370> (accessed July 12, 2017).
34. Children's Health Fund. 2015 (unpublished). *Health app decision tree*.
35. FTC. 2016. *Mobile health apps interactive tool*. <https://www.ftc.gov/tips-advice/business-center/guidance/mobile-health-apps-interactive-tool#which> (accessed October 24, 2016).
36. Institute of Medicine and National Research Council. 2011. *Direct-to-consumer genetic testing: Summary of a workshop*. Washington, DC: The National Academies Press, <https://doi.org/10.17226/13021>.
37. Koerner, B. 2015. Your relative's DNA could turn you into a suspect. *Wired*, October 13, <https://www.wired.com/2015/10/familial-dna-evidence-turns-innocent-people-into-crime-suspects> (accessed October 23, 2017).
38. Mackert, M., A. Mabry-Flynn, S. Champlin, E. E. Donovan, and K. Pounders. 2016. Health literacy and health information technology adoption: The potential for a new digital divide. *Journal of Medical Internet Research* 18(10):e264.
39. Tennant, B., M. Stellefson, V. Dodd, B. Chaney, D. Chaney, S. Paige, and J. Alber. 2015. Ehealth literacy and web 2.0 health information seeking behaviors among baby boomers and older adults. *Journal of Medical Internet Research* 17(3):e70.
40. Kotz, D., C. A. Gunter, S. Kumar, and J. P. Weiner. 2016. Privacy and security in mobile health: A research agenda. *Computer* 49(6):22-30.
41. Kaufman, D., J. Murphy, J. Scott, and K. Hudson. 2008. Subjects matter: A survey of public opinions about a large genetic cohort study. *Genetics in Medicine* 10(11):831-839.
42. US Department of Health and Human Services. 2016. *Health information privacy*. <https://www.hhs.gov/hipaa/for-professionals/faq/2048/does-an-individual-have-a-right-under-hipaa/index.html> (accessed October 23, 2017).
43. Adams, A., M. Shankar, and H. Tecco. 2017. *50 things we now know about digital health consumers*. <https://rockhealth.com/reports/digital-health-consumer-adoption-2016> (accessed October 25, 2017).
44. Gottlieb, S. 2017. *FDA announces new steps to empower consumers and advance digital healthcare*. <https://blogs.fda.gov/fdavoices/index.php/2017/07/fda-announces-new-steps-to-empower-consumers-and-advance-digital-healthcare> (accessed September 20, 2017).
45. Gagnon, L. 2014. Time to rein in the "wild west" of medical apps. *Canadian Medical Association Journal* 186(8):e247.
46. Cheung, C., M. J. Bietz, K. Patrick, and C. S. Bloss. 2016. Privacy attitudes among early adopters of emerging health technologies. *PLOS One* 11(11):e0166389.
47. 23andMe. 2017. *Transparency report*. <https://www.23andme.com/transparency-report> (accessed December 13, 2017).

48. Apple. 2017. *Report on government and private party requests for customer information*. <https://images.apple.com/legal/privacy/transparency/requests-2017-H1-en.pdf> (accessed December 13, 2017).
49. Ray, T. 2013. GenomeWeb feature: Will the future of genomics be consumer driven? *GenomeWeb News*, <https://www.genomeweb.com/clinical-genomics/genomeweb-feature-will-future-genomics-be-consumer-driven/genomeweb-feature-will> (accessed October 18, 2016).

Suggested Citation

Tung, J. Y., R. J. Shaw, J. M. Hagenkord, M. Hackmann, M. Muller, S. H. Beachy, V. M. Pratt, S. F. Terry, A. K. Cashion, and G. S. Ginsburg. 2018. Accelerating precision health by applying the lessons learned from direct-to-consumer genomics to digital health technologies. *NAM Perspectives*. Discussion Paper, National Academy of Medicine, Washington, DC. <https://nam.edu/accelerating-precision-health-by-applying-the-lessons-learned-from-direct-to-consumer-genomics-to-digital-health-technologies>.

Author Information

The authors are participants in the Roundtable on Genomics and Precision Health at the National Academies of Sciences, Engineering, and Medicine. **Joyce Y. Tung, PhD**, is vice president, research, 23andMe. **Ryan J. Shaw, PhD, RN**, is associate professor, Duke University School of Nursing. **Jill M. Hagenkord, MD, FACP**, is chief medical officer, Color Genomics. **Meredith Hackmann** is research associate, National Academies of Sciences, Engineering, and Medicine. **Marion Muller** is a student at Emory University. **Sarah H. Beachy, PhD**, is senior program officer, National Academies of Sciences, Engineering, and Medicine. **Victoria M. Pratt, PhD**, is director, pharmacogenomics, Department of Medical and Molecular Genetics, Indiana University. **Sharon F. Terry, MA**, is president and chief executive officer, Genetic Alliance. **Ann K. Cashion, PhD**, is scientific director, National Institute of Nursing Research, National Institutes of Health. **Geoffrey S. Ginsburg, MD, PhD**, is director, Duke Center for Applied Genomics and Precision Medicine, Duke University School of Medicine.

Conflict-of-Interest Disclosures

Tung is employed by and owns equity in 23andMe. No other authors reported disclosures.

Disclaimer

The views expressed in this paper are those of the authors and not necessarily of the authors' organizations, the National Academy of Medicine (NAM), or the National Academies of Sciences, Engineering, and Medicine (the National Academies). The paper is intended to help inform and stimulate discussion. It is not a report of the NAM or the National Academies. Copyright by the National Academy of Sciences. All rights reserved.