Direct-to-consumer personal genomic tests need better regulation

Increasingly, data are collected by companies that provide direct-to-consumer personal genomic tests, yet the existing health legislation covering the use of these data is lagging far behind in the USA.

Osman Moneer, Jennifer E. Miller, Nilay D. Shah and Joseph S. Ross

In February 2021, 23andMe announced that it would go public through a deal with Virgin Group, at a valuation of $3.5 billion[1]. In similar news, private-equity giant Blackstone reached a deal in August 2020 to acquire Ancestry, a direct-to-consumer (DTC) personal genomic testing (PGT) company, for $4.7 billion[2]. For context, in 2020, biotechnology companies in the USA were valued at $782 million, on average, after their initial public offerings[3]. DTC PGT companies market themselves as providing easy-to-use at-home genetic tests that provide information to customers about their ancestry and disease susceptibility. Although they were initially very popular, DTC PGT companies such as Ancestry and 23andMe have seen decreasing sales over the past few years[1]. So why did both 23andMe and Ancestry still receive such high valuations?

The answer comes down in part to their unique business model, which relies on collecting and aggregating genetic and health data from consumers through their test kits[4], and then marketing these data to other institutions and industries, such as biopharmaceutical companies. In 2018, for example, 23andMe signed an agreement that allowed GlaxoSmithKline to use its genomic database in exchange for an equity stake of $300 million[5]. The databases owned by four leading DTC PGT companies (23andMe, Ancestry, Gene by Gene, and MyHeritage) contain DNA from over 26 million consumers, with 23andMe and Ancestry contributing the most data[6].

In this Comment, we provide an overview of the regulation of genetic data since DTC PGT became available for purchase, and we highlight major events that illustrate gaps in regulatory oversight. DTC PGT can benefit consumers by providing certain DNA-based health information, as well as ancestry and genealogy information. But these at-home tests also present potential risks to consumers that necessitate appropriate safeguards. These concerns are heightened in view of the aforementioned large mergers, which have the potential to change company privacy policies[7]. We conclude by offering some policy solutions to help mitigate consumer risks, such as establishing standard data-management practices across DTC PGT companies.

Genetic data regulation

In the 13 years since 23andMe became the first company to market a broad personal genome service directly to consumers, relevant US regulation of DTC PGT companies has thus far focused on whether test kits should be considered medical devices regulated by the US Food and Drug Administration (FDA)[8,9] (Fig. 1). Over time, the FDA reasoned that certain DTC PGT companies offer medical information, and the agency eventually exercised enforcement on their diagnostic tests and mandated they undergo premarket review.

In contrast, the regulation of data aggregated by these companies has received less attention. In the USA, health data, including genetic data, are regulated largely through the Health Insurance Portability and Accountability Act of 1996 (HIPAA), which governs health data collected by a set of covered entities, including providers,

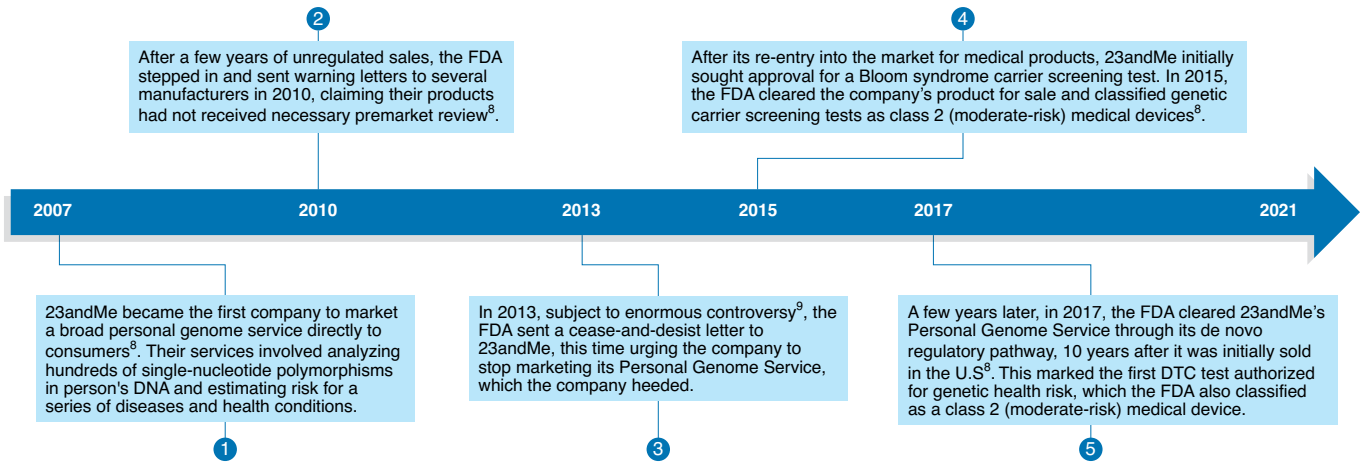

Fig. 1 | A brief history of diagnostic test regulation for DTC PGT. DTC PGT has gone through cycles of regulatory changes in the 13 years since 23andMe became the first company to market a broad personal genome service directly to consumers. Today, the FDA regulates four categories of DTC genetic tests: carrier screening, genetic health risk, pharmacogenetics, and cancer-predisposition tests.

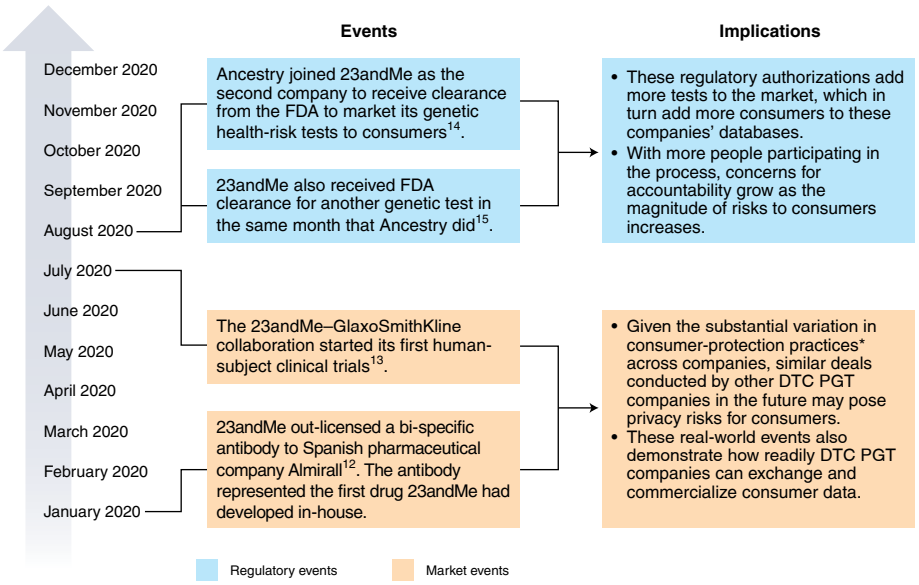

Fig. 2 | The market landscape for DTC PGT companies in 2020. The select market and regulatory events over the past year shown here illustrate implications for current and future potential consumer risks to data control, agency and discrimination.

health plans and healthcare clearinghouses. HIPAA places restrictions on the collection, storage and exchange of health information. The HIPAA Privacy Rule sets forth a basic set of standards that the entities covered must follow to receive authorization to use or disclose patients' protected health information. Because the entities covered are generally required to obtain consent from a patient before sharing protected health information for purposes other than improving the quality of patient care, covered entities such as hospitals are not permitted to sell this information without authorization from the patient[10].

Subsequent federal legislation on health-data protections, such as the Health Information Technology for Economic and Clinical Health Act of 2009 (HITECH) and the 21st Century Cures Act of 2016, typically expanded the regulatory oversight authorized by HIPAA. HITECH encouraged meaningful use of electronic health records (EHRs), granting reward payments to healthcare providers if they met certain EHR-management criteria, such as whether their EHR system could maintain an active medication list or identify patients with certain diseases, and levying stronger penalties for violations. HITECH also expanded HIPAA's privacy and security protections so they applied to business associates in addition to covered entities. The 21st Century Cures Act addressed health data by seeking to facilitate seamless EHR usage and prohibit information blocking.

Because most if not all DTC PGT companies are neither HIPAA-covered entities nor business associates of HIPAA entities, they largely fall beyond the purview of the legislation. This is in contrast to the experiences of other health-data aggregators, such as those that deal with EHRs. Because EHR companies deal with data obtained from covered entities as their business partners, they become classified as business associates under HIPAA and are subject to the range of federal health-data legislation, including requirements to de-identify patients' health information before selling data. However, DTC PGT companies are not currently subject to the same requirements.

Although few federal laws on health data exist outside of HIPAA, the Genetic Information Nondiscrimination Act of 2008 (GINA) currently provides limited protection in the context of genomics. GINA specifically prevents discrimination, by employers and health-insurance providers, that is based on genetic information. Unlike HIPAA, GINA does not narrowly define covered entities and does apply to data collected by DTC PGT.

Although DTC PGT companies have seen little governance on their data-collection practices in the USA, recent advancements have been noted in Europe. Genetic data, like other forms of data, are covered by the General Data Protection Regulation (GDPR), adopted in 2016 and implemented in 2018 (ref. [11]). Unlike HIPAA, which targets specific healthcare stakeholders in order to regulate data protection, the GDPR applies to all industry sectors by addressing data generally rather than by targeting specific companies. The GDPR establishes a floor for data protection, privacy and transfer that reaches far beyond US federal regulation. For example, it allows people to request that their identifiable health information be deleted.

Consumer risks. In the past year, several high-profile regulatory and market events[12–15] have illustrated the widespread use and commercialization of genetic data aggregated by DTC PGT companies (Fig. 2), such as the out-licensing of a bi-specific antibody to a pharmaceutical company by 23andMe[12]. These events raise questions about regulatory gaps related to who should maintain control of these data, how these data should be stored and shared, and discrimination risks. Furthermore, there are concerns about changes in privacy policies that can occur if a company is sold or acquired.

Data control and agency. To their credit, major DTC PGT manufacturers have made some effort to enable consumer control over their data. However, given the lack of regulatory oversight on this issue, policies can vary widely across manufacturers, and respect for consumer agency remains largely subject to the voluntary goodwill of DTC PGT companies[16–18] (Table 1).

Risks of discrimination. When test manufacturers share or sell consumer data for other purposes and to other institutions, they expose people to the risk of re-identification and harmful predatory and discriminative practices by third-party actors. As one example, life-insurance companies could disproportionately charge consumers on the basis of their genetic health risk for certain diseases. Due to protections conferred by GINA, genetic-based health-insurance or employment discrimination is currently not legal in the USA. However, many other programs and policies, such as life insurance, disability insurance and mortgage lending, are not protected by GINA[19,20]. Simply de-identifying data is insufficient on its own to mitigate discrimination risks to consumers, as data aggregators can pool multiple data sources and re-identify people through probabilistic matching[21].

Disparities in benefit sharing. Consumers enter the data market by taking a diagnostic

Table 1 | Consumer risks

Highly variable informed consent policies	Re-identification risks	Limited optionality within data-sharing
One research study[a] surveying a sample of the privacy policies and/or terms of service of DTC PGT companies found that companies widely varied in their disclosures of how consumer genetic information would be shared with third parties[16].	Researchers have demonstrated that minimal additional information is needed to re-identify a person from de-identified data[18]. Certain DTC PGT companies seek to gain consumer consent for sharing de-identified data; however, these practices are also not standardized across the industry[b].	23andMe's privacy statement allows two levels of data sharing after consumers opt in to third-party sharing: the first is for general research, and the second is for the explicit sharing of individual-level data[17].
The finding above is in contrast to the case for EHR companies, for which HIPAA requires that they use identifiable information only as the Privacy Rule permits or, alternatively, de-identify information.	The inherent risk above that is present in sharing genetic data necessitates that DTC PGT companies go beyond the standard of data-protection practices for EHR companies, as simple de-identification alone may not be sufficient.	Within the confines noted above, consumers do not have the ability to selectively grant use of their data to specific third parties or restrict use across geographies.

People have agency over their data when they consent to how data about them are used, but there remain highly variable informed-consent policies, concerns about re-identification risks for people from de-identified genetic data, and limited optionality within data sharing. [a]Approximately 40% of companies provided consumers with no information on third- party sharing at all; those that mentioned third-party sharing still differed on how to manage personally identifiable genetic data, with few companies declaring the explicit purposes behind data-sharing to third parties. [b]From the same aforementioned survey, 78% of DTC PGT companies included provisions in their privacy policies to share de-identified or aggregate genetic data to third parties without additional consumer consent[16].

test and consenting to allow the test manufacturer to use their data. For their participation, consumers' return is the test results that they paid for as a service from the company. Manufacturers profit twice: the first time by selling the test, and the second time by selling consumers' data. Consumers effectively, and voluntarily, often pay for their data to ultimately be sold.

Data commercialization is rising in many sectors, not just DTC PGT, with some experts sounding alarms and calling for reform. Some experts argue that people should have property rights to data, and others call for people to be paid for their time to generate data, as a type of labor fee[22,23]. Select companies are recognizing an opportunity to return more benefits to consumers than just test results. Some are, for example, offering equity stakes in their companies in exchange for people's data. Although the payouts may be marginal, this approach could allow people, in addition to companies, to share in any profit gained through their data. LunaDNA, a community-owned platform for health research containing EHR data, offers people who share health data on their platform ownership shares in the company, with proceeds passed back to the community as dividends[24]. Paying people for their data is of course not without its own ethical challenges, including worry that privacy will become a luxury product, which would lead to non-representative datasets for research and open up additional regulatory loopholes.

Establishing safeguards

The majority of the concerns described here exist due to the exemption of DTC PGT companies as HIPAA-protected entities, which effectively allows them to avoid the bulk of US health-data regulation. In contrast, European countries may more easily avoid these concerns through data protection conferred by the aforementioned GDPR. To target the root of the problem, US policymakers could consider strategies to bring DTC PGT companies under the umbrella of HIPAA regulations. Expanding the definition of covered entities to include DTC PGT companies (or even pharmaceutical companies in general) may be one route to accomplishing this objective, as was recently proposed for health data recorded on personal digital devices, such as smartwatches[25]. Complementary to HIPAA changes, GINA should be amended to reflect the market developments since its passage in 2008, and should thereby restrict genetic-based discrimination across a broader range of contexts. In particular, insurance companies offering life and disability coverage, lenders, credit agencies and landlords should be banned from acting on genetic information.

If they were subject to HIPAA, DTC PGT companies, regardless of market share, would be required to standardize their data-consent practices and user agreements. Classification as an entity covered by HIPAA would also limit DTC PGT companies in how they sell and share identifiable data. This solution would strengthen the regulation of DTC PGT companies to be on par with EHR company regulation and would address the most pressing concern of companies sharing identifiable genetic data. However, because HIPAA does not currently apply to de-identified data, additional safeguards may still be needed to protect genetic data.

If DTC PGT companies were to be included under HIPAA, the Department of Health and Human Services (HHS)—charged with implementing HIPAA regulation—may be well suited to tackle this problem. This department could issue a rule that establishes quality standards for the collection of private genomic data. HHS could consider imposing clearer standards of informed consent, with specifications for both identifiable data and de-identified data. Data sharing could be restricted to specific uses, such as population health research, as well as drug research and development. Moreover, all DTC PGT companies could be required to obtain detailed consent from consumers through user-friendly choice architecture for data sharing.

Beyond HIPAA-based enforcement, the FDA could provide supplemental consumer protection by building off its oversight of DTC PGT entities classified as medical devices. Previously, the agency required DTC PGT companies to conduct studies demonstrating comprehension of genetic test results by the users. Through its existing role in clearing tests, the FDA could also require that DTC PGT companies assess whether consumers comprehended what they consented to in terms of data usage and sharing. On the basis of these user studies, test manufacturers could amend their consent documents until an appropriate level of consumer understanding was reached.

Bringing DTC PGT into people's homes has expanded access to healthcare information and has potentially accelerated drug discovery at a scale that might not have been possible without its widespread use. But it has also come with potential risks. In establishing adequate regulatory safeguards, the federal government can better protect consumers and their health information, ensuring that the health and commercial benefits of DTC PGT are realized without compromising consumers' agency or enabling discrimination. ❐

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Author contributions

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Competing interests

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Africa needs to prioritize One Health approaches that focus on the environment, animal health and human health

Urbanization, armed conflict, and deforestation in African countries have increased the risk of zoonotic infections, which requires a One Health approach focused on the environment, animal health and human health.

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The past two decades have witnessed a global increase in the frequency of emerging and re-emerging infectious-disease epidemics. African countries have experienced the devastating impact of successive epidemics that are projected to have caused a loss of over 227 million years of healthy life and an annual productivity loss of over US$800 billion across the continent[1]. Between 2016 and 2018, over 260 infectious-disease epidemics, disasters and other potential public-health emergencies were identified in Africa, with 41 (79%) of the 52 countries in the region recording at least one epidemic during that period[2]. The five top causes of disease epidemics were cholera, measles, viral hemorrhagic diseases, malaria and meningitis.

The 2014–2016 West African outbreak of Ebola virus disease and the ongoing COVID-19 pandemic have further exposed the vulnerability of health systems in Africa[3] and have amplified the threat posed by zoonotic spillover of infectious diseases to the health and economic security of the continent. Increasing trade and migration of people between and among African nations increases the risk that disease outbreaks within Africa rapidly cross international borders to impact global health security[4].

Increasing interspecies interactions

There is compelling evidence linking the disruption of the human–animal–environment interface with