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Ethical, Legal and Social Issues in Applied Genomics

MSc Genomic Medicine

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Ethical Dilemmas with Direct-To-Consumer Genetic Testing Kits.

Contents

Introduction:

The revolutionary advances in genetic and genomic technologies expanded its markets, reaching the shelves of online and physical stores for anyone to buy. Recently, Direct-To-Consumer genetic testing (DTC-GT) kits were invented and made available for consumers to purchase without the intervention of medical professionals or services (1). They have shown an increase in popularity over the years, and companies such as "23andME, Ancestry, and MyHeritage™ " have capitalised on this interest. They are similar in their accessibility but differ in their focus. For example, 23andMe prioritises diseases and disease risk reporting, while Ancestry and MyHeritage focus on genealogy and ancestry. They offer advantages such as ease of use, general affordability, and the ability to provide an educational opportunity for the public to recognise the importance of genetic tests. The boom in popularity, coupled with the increased interest in private data from companies in the pharmaceuticals and governmental sectors, demanded an increased effort to address concerns surrounding such technologies. General issues associated with DTC-GT include the quality of data produced and their direct impact on health, the psychological and social effect of misinformation and misinterpretation of results, and ethical, public health, and legal concerns. Elaborating on the ethical questions involves expanding on the areas related to consent, privacy, confidentiality, and data processing while accounting for certain perspectives such as social, psychological, political, and legal.

Discussion:

A- Consent:

A simple search in the Oxford English Dictionary (OED) of "Consent "as a noun in the dictionary yields a definition of "permission for something to happen or agreement to do something", with informed consent adding the element of full knowledge of the possible consequences associated. In healthcare, and especially genetic testing, informed consent involves the legal and ethical process of ensuring adequate knowledge of the genetic test, and it includes steps such as an explanation of the test process itself, its reason, and the interpretation of the results. It is followed by a discussion on the advantages and limitations involved until reaching the physical aspect of a signature (2). The aims revolve around protection from harm or coercion, enabling an autonomous decision, and it assumes that the consenter has adequate decision-making capacity. For this reason, the problem facing such technologies in terms of consent can be looked upon from different perspectives. For example, taking the necessity of informed consent to represent a full comprehension of the information. First, the genomic data itself is complex and can be challenging to explain to non-scientific communities. Niemiec, Kalokairinou (3) argue that DTC-GT consumers may not be going through the full process of communicating the relevance and meaning of such tests, given the absence of healthcare providers (HCP) such as genetic counsellors. This raises the question of how we can guarantee that the consumer has indeed fulfilled the criteria of informed consent when a full understanding might be lacking. A second important point related to consent is the ease of unlawful testing when a specimen is obtained without that individual's permission, such as in the case of parents testing their children. This feeds back to an original point of consent, which involves an adequate decision-making capacity that might be absent in children. An example of this incidence is when a mother performed a DTC on her 12-year-old daughter that showed single nucleotide polymorphisms (SNPs) in the *COL3A1* gene associated with "Ehlers–Danlos syndrome type III" (4). The patient was subjected to many tests that revoked the DTC results. Nonetheless, the mother kept seeking professional help (seven cardiologists, two

gynecologists, an ophthalmologist, a gastroenterologist, and six emergency room physicians) subjecting the child to unnecessary emotional and psychological trauma. Moreover, genetic data does not only contain your information; by extension, it might reveal aspects of the health or ancestry of your family. In this scenario, no consent might be given which presents the question of how to formulate true informed consent when the participants involved are not aware of the process in the first instance.

On the other hand, to match the autonomous part of consent, there is debate about how truly autonomous consumers are when they opt-in to such tests. The idea of no external forces/coercion influencing their decision is questionable. For example, marketing strategies for such companies might involve the use of emotionally charged notions such as “Know your genome” or “take control of your healthcare” which leads to the consumer acting by exploiting their vulnerabilities and selling a powerful narrative of self-discovery, health empowerment, and the promise of personalised insights. Although these claims can be true, there is a significant downplay of the risks and limitations associated with their test, via a manipulative marketing strategy. For example, while assessing the ethical concerns of DTC tests, Panacer (5) mentions that 23andMe in their “consent for research” section, highlighted buzzwords such as “to make discoveries” and “ may benefit others in the future” while emitting this highlight when discussing the pharmaceutical companies' access to their data. Moreover, their decision might be affected by economic and accessibility considerations when certain promotional periods, such as holiday promos, or discounts give the illusion of accessibility and time-sensitivity. In addition, someone who is already on a budget might perceive this discount as a unique opportunity, further devouring one’s autonomy in making choices.

In summary, DTC genetic testing might offer a chance to increase awareness about genetics and personalised medicine, and there have been successful stories around that. However, there are still many ethical dilemmas that have not been addressed yet. The complexity of genetic data, the absence of an intermediary professional body and the for-profit aspect of these companies encourage us to dive deeper into trying to answer such questions.

B- <u>Confidentiality and Data Privacy:</u>

Another ethical question that presents itself when dealing with DTC tests is confidentiality and data privacy, which are distinct but related concepts. Professor Emily Jackson in her books about medical ethics (6), emphasises the importance of confidentiality based on deontological (duty-based) and teleological (consequentialist) reasoning. The deontological reasoning describes the patient's right to privacy and complete control over their sensitive information, which aligns with the scope of the issues facing DTC tests. Genetic data was shown to positively influence and accelerate scientific research. Withholding such information might negatively affect current and future patients from receiving the necessary treatment. Nevertheless, balancing this with individual confidentiality and privacy raises ethical questions about how data is managed. To that end, policies and measures were invented to address confidentiality and data privacy concerns, such as the "Health Insurance Portability and Accountability Act (HIPAA)" of 1996 which prohibits the use and disclosure of protected health information (PHI) in the United States, data protection laws in the United Kingdom, anonymising the data and the requirement of a physician in health-related genetic testing.

Despite these policies, they are not international and there are multiple fronts in which confidentiality and privacy concerns were questioned, with many cases showing instances of breaches. For example, ever since their inception, the companies selling the tests were subjected to public mistrust due to the willingness to easily share data such as their raw genetic data, statistics, and ancestry, with third-party players. Two of the most controversial partnerships were when 23andME partnered with GlaxiSmithKline© in 2018 to discover drug targets, and Ancestry and Caligo, a GOOGLE company, investigating the longevity of certain families (7). This shows that even with laws and policies in place, these powerful companies can still find loopholes through which they can make huge profits on the accounts of consumers.

Another concern here is the possibility of data breaches facilitated by the computerised and cloud archives. For example, in the first quarter of 2023 6.41 million data records were leaked in worldwide data breaches (8), costing millions of dollars, with each data record estimated to cost 165 US dollars. In addition to being costly, it carries the risk of a heavy psychological

effect on the people whose data were leaked. An example of that is when hackers accessed the data of 7 million 23andME users (9) , targeting data points exclusively about Ashkenazi Jews. The company claimed that the reason for this hack was due to people reusing passwords (Hajdenberg, 2024), showing an aptitude for evading responsibility which was later settled in court. This suggests a reluctance to take full responsibility and accountability for the trusted data, which clashes with the very notion of confidentiality. Given the fact that full legal and moral obligations bind the agreement with the expectation that companies are fully accountable for safeguarding consumer information. In addition, psychological consequences incurred from such breaches can be unsettling with varying degrees of anxiety, stress, or even a fear of discrimination, especially within minority ethnic groups that were historically subjected to appalling torments.

Many other issues need attention when privacy is mentioned. The fact that anonymising data can be reversed is especially concerning. In a Forbes article by Pitts (10), they described a new lab technique that can identify genetic markers tied to specific physical traits, such as eye or hair colour. They mention an MIT student who was able to decode supposedly anonymous genetic samples and discern the identity of five people in less than a day. Linda Avey, a cofounder of 23andMe, has explicitly admitted that "it's a fallacy to think that genomic data can be fully anonymized"(10). The potential for harm is astronomical if genetic data are linked to specific individuals such as in the case of using it to not employ someone based on their risk of developing certain diseases or to discredit politicians and world leaders. Genetic testing companies have not been candid about these dangers affecting privacy, facilitated via an elusive “Term of Service” in a language that can be difficult to interpret and described as “college-level language”, and refusing to disclose how long they store the data or how it can be used. Consumers are sharing their intimate data without suitable fortifications.

C- Data Quality, Interpretation and Impact:

DTC genetic tests question the data produced, its interpretation, and its impact. There are examples where the DTC-GT showed promise, by having a positive impact such as in the case

of screening for pathogenic variants in BRCA genes, where certain women reported " being grateful" for the results (11). However, despite this occasional success, issues remained. To begin, the mentioned tests when used for health-related purposes do not encompass the whole genome and can easily miss certain relevant information. Kilbride and Bradbury (12) mention that there are two main tests available, 'Narrow Tests' where they screen for a subset of the relevant variants, and 'Broad Tests' which include a certain number of genes. Therefore, the clinical utility is heavily affected. For example, 23andMe before the latest FDA 510k clearance used genotyping to report only 3 variants in BRCA1/2 genes. This means that everyone who took the test before this clearance and received an "all clear" result will need to reassess their situation which can be psychologically demanding. In addition, even after the addition of 41 variants (44 variants to be screened now), it is still lacking in terms of clinical utility since there are thousands of variants associated with increased breast and ovarian cancer risks. Additionally, even with the broad tests of multiple genes inclusion, worries persist because they include genes with an unfounded risk estimate. For example, BARD1 is a gene screened for in the panel, and despite showing a moderate increased risk of breast cancer in patients with pathogenic variants, more research is needed for more definitive risk estimates(13). Furthermore, the risk of false positives and false negatives can be potentially misleading and might lead to either unnecessary stress in case of false positives, or false reassurance in case of false negatives. Tandy-Connor, Guiltinan (14) conducted a review of the raw genetic data of consumers using DTC genetic tests and found that 40% of variants in different genes were false positives and some variants allocated the "increased risk" notion in in DTC raw data were reported as benign in other clinical sources. This emphasises the profound limitations of DTC tests and the importance of re-interpretation of data by a verified clinical entity. Therefore, additional questions emerge when discussing the accuracy and interpretation of the results as who should be held responsible for or liable for its validity. Additionally, given the fast advancement of scientific research and the emergence of new information, what happens when a previously low-risk result is found to be high-risk? Are the companies liable or obliged to contact the consumer?

Moreover, despite that many companies state that their results are for educational and informative use and not to diagnose, treat or prevent a condition (terms-of-service), there is doubt about whether the consumers even read these statements given the small print they are

written in and the use of a ticking box to agree. This feeds back to the informed consent part where consumers might not be equipped to fulfil the ethical question of consent. From a societal/economic perspective also, Niemiec, Kalokairinou (15) indicate a strong point when assessing the clinical validity of DTC tests when they ask the question of the implications on the public health system. Should the consumer receiving potentially health-altering news contact their HCP in their public health system? Especially given the absence of an intermediary professional. How this will affect the public health system? Moscarello, Murray (4) mentioned that incorrect third-party interpretation of genetic data augmented the demand for clinic appointments. If patients were to be able to receive consultancy regarding their results in the first place, it could lead to unnecessary follow-ups that will consume already limited public health resources and displace access to medical care in urging cases.

D- Data Storage and Future Use:

Another pressing ethical concern with DTC genetic testing is data storage and the potential future use of genetic information. There is ambiguity when DTC genetic test companies address the data storage and future use. This introduces questions about the ownership of genetic data and whether consumers truly understand and consent to its long-term storage and use. Laestadius, Rich (16), when assessing DTC-GT company's compliance with transparency guidelines, discusses that there is a clear variation between companies on how long the biological samples and genetic data are held. For example, they found that only half of the companies assessed had a clear policy that the genetic data would be or could be requested to be destroyed. Even in the companies that shared such policies, some mention a clear detail of where the biological samples and data are stored and who has access, while others only mention a location (e.g. Data stored at our facility in X address) (16). In addition to data storage, there is ambiguity on whether data may be accessed, used and sold to third-party companies. Niemiec and Howard (17), while reviewing ethical challenges in genomic research by traditional and DTC genetic companies, stated that all companies researched may allow access to data when required by law such as a court order. For example, “Gene by Gene” which

is a commercial genetic testing company, states in their terms of service (TOS) agreement that the samples may be "*retained for in-house laboratory use*". They mention that by opting in for research, the consumer relinquishes all rights to any commercial products or services that may be developed with such data (terms-of-service). For this and more, it should provoke an international regulatory committee to monitor and regulate such companies to ensure that ethical maneuvers are used when dealing with human genetic data. This is especially important because, in the event of huge breaches that might result in public outrage, it will negatively affect the genetic research community, by jeopardising the public trust in genetic research. With these fine print TOS paragraphs, we run the risk of commercialisation of human genetic data. For example, 23andME not only used the data for its internal research but sold the data of participants with an increased risk of Parkinson's disease to a biotech company for research (18). It is even more problematic when public funds are used to fund research by these companies, such as in the case of 23andME, where they secured 1.4 million dollars from the NIH (National Institute of Health)(19). While the benevolent aspect of using genetic data for the "better of all" is enticing, we must keep in mind that companies after all are interested in profit and will take measures to find exploitable gaps for more profit.

Beyond the ethical and practical question of DTC genetic tests, there are some broader societal, psychological, and public health concerns associated with it. For example, the results are received via email and without professional support for interpretation. Therefore, the possibility of experiencing anxiety, and panic increases astronomically with negative results reports. Bloss, Wineinger (20) mention that more than a third of DTC-GT consumers shared their results with their primary care provider, which feeds back into a previous point where misinterpretation and false results might lead to an increased burden on the healthcare system. Furthermore, social dilemmas seem to be aggravated in certain instances by DTC-GT, especially when dealing with discrimination, and racial and ethnic identity. For example, in a previous example describing the data leak in 23andME where they targeted Ashkenazi Jews, there was a mention of distress when one consumer found that they had Ashkenazi Jewish ancestry which put him and his family on the target list of the hackers causing severe distress (9). In addition, DTC might deepen social inequalities as those who can afford these tests will

gain an advantage by having insight into their genetic predisposition giving them a better chance of survival.

Additionally, racial identification has also been touched by genetic tests and was exploited for personal gain. This was seen in 2014 when an American citizen tried to take advantage of the "disadvantaged business enterprise" (DBE) program, designed to help minority- and women-owned businesses, where he submitted the results of his DNA test showing a 4% sub-Saharan African ancestry and claiming he was at a disadvantage (21). This would affect any legislation made about the inclusion criteria of a minority or disadvantaged group. With the increasing entitlement of people, especially the younger generation, we might be in for a fight to define even racial identity.

Conclusion:

In conclusion, DTC-GT has undeniably revolutionised public access to personal genetic information, allowing consumers to explore their ancestry, health risks, and even disease predispositions from the convenience of their homes. However, complex ethical, legal, and societal challenges are associated with it. There are issues of consent and how truly informed it is, confidentiality and data privacy, data security, and the accuracy of health information. In addition, the absence of intermediary healthcare professionals in the process complicates making informed decisions. Results misinterpretation could lead to unnecessary psychological stress and strain on public health systems. Moreover, the risk of data breaches, falling into the wrong hands, and the lack of transparency in data storage, access, and usage, highlight a growing need for stricter regulation procedures and policies. Despite the promising results of genetic data for personalised medicine and scientific discovery, it carries the risk of exploitation, leading to discrimination, and further deepening of racial and ethnic injustices. Finally, to unlock the full potential of genomic/genetic knowledge without the risks, there must be an international, collaborative effort by governments, policymakers, healthcare professionals, consumers, and the companies themselves to prioritise consumer protection and address the ethical questions.

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