TU Delft student report

The validity of informed consent with regard to human genetic sequencing.

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Abstract

Modern societies manage an ever increasing amount of data. By mining these data-sets, it is possible to gain understanding of problems. Through a process of informed consent companies have been able to sequence the genome of large populations. Providing insight to the consumer about their family lineage and possible future risks that they could face. As a consequence of providing such services to consumers, companies are in the position where they can monetize a database of information hat they possess. The primary issue that will be addressed is how private genetic data should be handled correctly. As without clear ethical guidance corporations will (un)willingly abuse trust. The result of aiming to maximize asset value can be unethical conduct such as selling the data to third party insurance companies. The apparent need to process larger quantities of data in order to acquire new information to fill our knowledge gaps is a trade off between privacy and anonymity of the individuals within society. Creating an ethical conundrum for companies trying to profit. This research makes a contribution to prove that certain actions when sequencing or using genetic information infringe on privacy and are not morally permissible. Providing greater clarity when trying to decide whether a use case of personal data is ethically permissible. By reviewing modern literature that describes the ethical implications of informed consent and human genome sequencing the research will identify key areas requiring further work to develop the ethics of technology in a way that enables innovation whilst keeping society safe.

Keywords: Informed consent, Technology management, Whole genome sequencing

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1. Introduction

Possibly the strongest argument for human genetic sequencing is the ability to detect those who will be born with rare disorders. As indicated by Posey in *Genome sequencing and implications for rare disorders*

> Genomic studies of neuropathy support a model whereby an aggregation of rare variants in disease-associated genes can influence clinical severity and can contribute to common complex traits [1].

Before age 25, roughly 0,053% of people can be predicted to suffer from diseases with an important genetic component [2]. As shown below in figure 1, in recent times the cost of genetic sequencing has dramatically decreased at a rate much faster than Moore's law. This means that a growing and greater proportion of the population has access to genome sequencing.

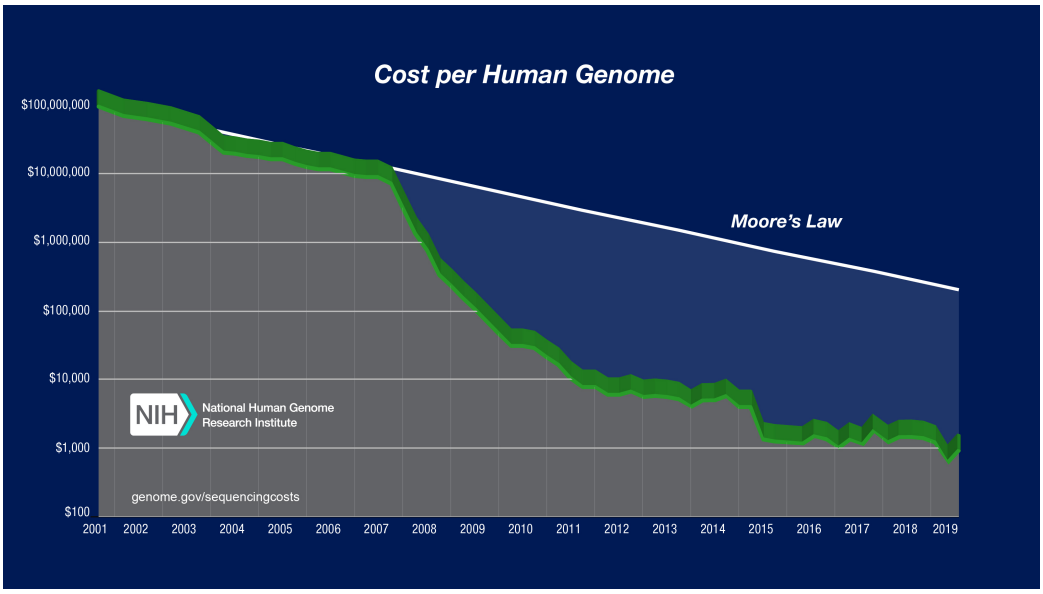

Figure 1 Decreasing cost of sequencing courtesy of the National Human Genome Research Institute [3].

An advantage of early disease detection is to provide treatment earlier. By editing genetic information it may be possible to provide preventative help to some of the most vulnerable in society. We propose to resolve the ethical

challenge that our society has had surrounding the ownership of biological material such as genes and what happens once they have been separated from the human in whom they grew by arguing that humans are not commodities and that selling organs is known to be morally impermissible and thus by extension gene or organ transfer should only be done in an emergency. In the context of human genome sequencing traditional notions of informed consent may not provide a suitable safeguard. For a person to make the best possible decisions it is critical that they are given clear understandable information about the risks associated with what they are about to undertake. In this way they are aware of future danger and can also try mitigate harm. There are further practicalities pertaining to who is required to give consent since a decision from one person may adversely effect a family. The concept of informed consent therefore needs to be extended to include to the extent of what is possible everyone who is connected. Mitigating a situation whereby privacy has been infringed upon. Since private information of a large proportion of the population could easily be collected without their knowledge or consent. [4].

2. Informed Consent

2.1. Individual

For an individual to give informed consent it is required that said individual fully understands the topic to be able to make a decision. Furthermore they should be able to convey their consent. We will assume that the individuals are able to communicate their wishes and show that it would still not be possible for them to consent to human genetic sequencing, by using the health sector as an example application of this technology.

It is impossible for all patient on which this technology is used to be knowledgeable on the technical process. The health sector treats the general public, it is a fact that the general public is comprised of individuals of different interests, professions and capabilities. From this it is concluded that there must be individuals who do not have an interest in, or have their profession lie in the field of human genetic sequencing. Furthermore we can conclude that there must be individuals that due to their capabilities are not able to grasp this topic. Thus there exist individuals in the general public that do not understand the topic of human genome sequencing.

Patients are also not able to fully grasp the risks that come with human genetic sequencing. Like other medical data, it needs to be stored in order for it to be used for medical purposes, this to help with appropriate and effective treatment for the individual's conditions and health [5]. Company 23andMe has stated its "longer-range goal is to collect a massive biobank of genetic information that can be used and sold for medical research and could also lead to patentable discoveries" [6]. The storing of data also brings some risks with it. When this data is mismanaged or stolen and released, it becomes accessible to individuals of the public. From here, these individuals can decide to use this data whether lawfully or not. We describe the consequences in greater detail in section Privacy & Discrimination, but one needs to understand that the chance of data getting stolen carries problems with it. This chance of data being stolen is never 0, but the consequences can be huge. Creating a situation where it is difficult to grasp the impact it has on ones life. One off these problems could be identity theft[7], but again it is difficult to grasp in the implications that this can have, making is difficult to provide informed consent. Furthermore, more ways to use released medical data will be discovered as time goes on. But once a dataset is released it is permanently out there, which means these new techniques can be used on it. It is impossible for a patient to consent to future harm of which we are currently not able to determine its impact.

One might say that a doctor can provide the information required for the patient to make their informed decision, but this line of reasoning is flawed. The statement supposes that the doctor is knowledgeable on the topic to the extent where they can explain the topic to a patient in a way that leaves the patients understanding it (fully). This statement also assumes that there is a doctor with the time available to goes through this process for every patient. But these two suppositions are not true. As previously shown there exists patients that are sometimes not willing or capable of grasping the topic. In such a situation it would not be possible for them to be fully informed, which in turn leaves them unable to make a fully informed decision. The increase in time required to explain procedures would come at a cost somewhere. Most likely it will come from the amount of time spent on other patients, which has been shown to decrease patient satisfaction and increases the likely hood of a doctor prescribing medication [8].

To conclude, not all patients are able to grasp the concept of human genetic

sequencing to the extent needed to make a fully informed decision about it, leaving them unable to give informed consent.

2.2. Prenatal and Children

The most common use of genetic sequencing in medicine is the screening of newborns for potential diseases. Enabling better management of genetic disorders. False Positives are the scariest ethical challenge surrounding treatment resulting from genetic testing. A False Positive is someone who is incorrectly diagnosed with a disease [9]. Abortion is a notable ethical challenge associated with prenatal genetic sequencing. Therefore, we propose that genetic sequencing should only be conducted after the embryo is too old to be aborted by its parents.

2.3. Transitive Consent

The issue of obtaining consent for DNA sequencing is further complicated by the fact that someone's DNA doesn't only contain information about that individual, but also about their relatives and community. A person shares half of their DNA with each of their parents and siblings, a quarter with their grandparents. This raises the question of whether an individual's consent is enough, given that the impact of this single decision is shared among many people. In this section we will illustrate this effect of consent being carried over to other people – what we will label as "transitive consent" – with a few examples and discuss its consequences.

Many jurisdictions allow for the collection of DNA samples by law enforcement, whether done with consent or not. DNA databases for forensic purposes are commonplace, and may store data indefinitely. In S and Marper v United Kingdom, the European Court of Human Rights decided that the retention of DNA of individuals who are arrested but never convicted of a crime constitutes a violation of their right to privacy under the European Convention on Human Rights [10]. However, family members of convicted criminals whose DNA is stored undergo the same violation; they may be identified by police solely by their DNA, despite never having been arrested or even suspected of a crime. In some cases individuals hand over DNA samples voluntarily to assist in investigations. In these cases their consent would be taken as enough justification to retain their DNA. Though if the consequences of this are extended to their family members, and these are deemed by the ECHR to be a violation of privacy, the argument can be made that

it is still unlawful.

2.4. Privacy & Discrimination

When the sensitive data stored after genome sequencing is mismanaged or stolen it has serious implications for the individual. There are some implications this has for privacy, first one being that when information is released it makes the individual vulnerable to targeting doxing[11]. By having genetic information available to others, it might motivate them to act hostile because of the information they find, which can lead to bullying, ridicule and abuse. This would result in the person feeling unsafe. Another implication would be the violation of the individual's trust. They have put their trust in an institution, thereby sharing information with them. When data is leaked it will influence the level of trust the person has in the system, which might result in them not seeking treatment in the future.

The fact remains that the individual did not want their genetic information released to the public, yet is experiencing the consequences. Consequences the company storing the data is responsible for as "One is responsible for, as it were ... in a straightforwards way." [12]. Which falls in line with the agency the company has over its actions. There are also implications regarding discrimination that come to mind. Companies could use the sequence information to discriminate, an example being an insurance company that charges more to a person with a higher risk of getting certain illnesses, or refuses to accept them as a client. Just like the discrimination in which contraceptives are not covered under insurance [13]. The data could also be used in decision processes. When a potential employer or dating partner looks you up online and finds your genetic information, it can not be guaranteed that this information will not be used in the decision making process. While there are laws in place that try reduce the amount of discrimination happening [14], it does not prevent it from happening. Where there now is a way to combat this injustice, it still holds that it would not have occurred if the genetic sequence was not available. Furthermore by having the data accessible it will impose a mental strain of not knowing when you are being discriminated against, and when you are being treated fairly.

3. Conclusion

The main contribution of this scientific ethics research is the closing of the current knowledge gap by describing the relationship between morality and the management of technology. Identifying the fundamental moral challenges associated with the handling of human genetic information. Obtaining consent for DNA sequencing is complicated by the fact that a persons's DNA does not only contain information about that individual, but also about their relatives and community. Therefore when an individual hands over their genetic information for sequencing they are also handing over the genetic information of others. Technological management risks are associated with the storage of genetic information which is required for the training of an AI model. The consequences of data mismanagement or theft is that important private information becomes accessible for malign intentions. For example, companies such as those in the insurance industry may use the genetic information to unfairly discriminate by charging an exorbitant amount of money to a person with a higher risk of certain illnesses, or refuse to accept them as a client. By failing to address the ethical challenges presented by this research in an appropriate manner our society condones and further exacerbate unethical actions.

4. Future Research

There are significant challenges identified surrounding informed and transitive consent along with individual privacy being infringed upon. These concerns warrant attention and need to be incorporated to ensure that society is kept safe. Individual ownership of genetic information is a potential system that may adhere to these constraints whilst still fostering critical innovation required. This model is built on the foundation whereby each individual is the sole owner of their own genetic information. An individual may hand over their information to be checked by a professional with a pretrained AI model for health care reasons. After a maximum period of six month all information stored must be deleted. Individual ownership deals with the challenge of developing an AI that requires training data. Genetic information can only be handed over in some anonymised form for a limited period of time. After training the AI this data must be deleted. Allowing scientists to make breakthroughs in medicine without putting individuals at risk by limiting the number of people who at any one time could have their personal information hacked and placed into the wrong hands.

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References

[1] J. E. Posey, Genome sequencing and implications for rare disorders, Orphanet journal of rare diseases 14 (1) (2019) 153.

[2] P. A. Baird, T. W. Anderson, H. B. Newcombe, R. B. Lowry, Genetic disorders in children and young adults: a population study., American journal of human genetics 42 (5) (1988) 677.

[3] NIH, The Cost of Sequencing a Human Genome (2020).
URL https://www.genome.gov/about-genomics/fact-sheets/Sequencing-Human-Genome-cost

[4] H. T. Greely, Legal, ethical, and social issues in human genome research, Annual Review of Anthropology 27 (1) (1998) 473–502, pMID: 15977340. arXiv:https://doi.org/10.1146/annurev.anthro.27.1.473, doi:10.1146/annurev.anthro.27.1.473.
URL https://doi.org/10.1146/annurev.anthro.27.1.473

[5] D. Safety, Understanding the importance of medical history (2011).
URL http://www.ddssafety.net/sites/default/files/attachments/10-06-11/FAMedicalHistory_0.pdf

[6] G. J. Annas, S. Elias, 23andme and the fda, New England Journal of Medicine 370 (11) (2014) 985–988.

[7] S. Romanosky, R. Telang, A. Acquisti, Do data breach disclosure laws reduce identity theft?, Journal of Policy Analysis and Management 30 (2) (2011) 256–286.

[8] D. C. Dugdale, R. Epstein, S. Z. Pantilat, Time and the patient–physician relationship, Journal of general internal medicine 14 (Suppl 1) (1999) S34.

[9] J. R. Botkin, E. Rothwell, Whole genome sequencing and newborn screening, Current genetic medicine reports 4 (1) (2016) 1–6.

[10] P. Walker, European court rules dna database breaches human rights, The Guardian (2008).
URL https://www.theguardian.com/uk/2008/dec/04/law-genetics

[11] D. M. Douglas, Doxing: a conceptual analysis, Ethics and information technology 18 (3) (2016) 199–210.

[12] A. Sen, Well-being, agency and freedom: The dewey lectures 1984, The journal of philosophy 82 (4) (1985) 169–221.

[13] S. A. Law, Sex discrimination and insurance for contraception, Wash. L. Rev. 73 (1998) 363.

[14] U. G. Assembly, Universal declaration of human rights (1948).