The Status of Genetic Information and Genetic Testing.

Consequences for Public Health Genomics and the Public Health Genomics European Network (PHGEN).

1. Introduction

In public health, demands are increasingly being made for due consideration to be given to genetic information. Genes and genetic information are often given exceptional and iconic status, due both to the progress made in the field of molecular biology and to the negative overtones arising from the historical association between eugenics and the use of genomic information in public health.\(^1\) The symbolic meaning and status given to genes have resulted in the view that genetic information is fundamentally different from other kinds of health information and should \textit{per se} be protected in a special way.\(^2\) We are not convinced of this position.

Our argument will draw on what we believe to be significant conceptual distinctions and will include a discussion of the status of genetic information and genetic testing, its regulation, and its consequences for public health. This clarification will help to avoid misunderstandings and serves to set out our position on the status of genetic information for future discussions of public health genomics within the Public Health Genomics European Network (PHGEN).

2. “Genetic diseases”, “inherited disorders” and “common-complex diseases”

2.1 “Genetic Diseases”

One often talks of “genetic diseases”, meaning diseases in which gene mutations are to a significant extent causally involved. However, genes are involved in all disease, as they are also...
involved in the physical and mental status we call health. In other words, all diseases and all physiological traits have a genetic component. Genetic variations play a role in almost every disorder by modulating the risk of becoming affected, including the risk of infection because of the role of genetic factors in determining host susceptibility to pathogens. Not every person will develop the disease after coming into contact with a relevant virus or bacterium.

The extremely complex interaction of the genetic endowment of persons (including gene-gene interactions) and environmental and lifestyle factors cannot be underestimated. It is a necessary context for understanding public health genomics. Tom Murray speaks of the artificial nature of a “two bucket theory” of disease wherein one bucket contains “genetic”, the other “non-genetic” exposures. While superficially it might be thought that Huntington’s disease would belong in the “genetic” bucket and “to get run over by a truck” in the “non-genetic” bucket, even they are not entirely without influence from environmental and genetic factors respectively. “To get run over by a truck” presupposes a living human being and humans have genes that contribute to their behaviour and hence the chance that they may or may not be walking on the street at a particular time. Highly penetrant Mendelian disorders such as Huntington’s Disease do not solely depend on having the relevant gene, but on other modulatory genetic and environmental factors. Otherwise the disease would manifest itself in the same way in all persons with an identical gene mutation.

Most diseases do not “neatly fit into either bucket”, in fact, as to the causative role of genes there is a continuum from Mendelian disorders to “getting run over by a truck”. For example genetic factors are known to have a causative role in diabetes, schizophrenia and breast cancer. Gene mutations are significantly involved in only a small proportion of cases of these diseases; in most instances the genetic exposure will confer only susceptibility, with no certainty that the disease will manifest at all. The contributions of the various exposures cannot be distinguished within individuals. Statistical quantification in populations provides an attempt to quantify the impact of the different factors evolving in time in a stochastic way. In this sense it is misleading to ask whether a disease is genetic or environmental and it may be misleading to talk of “genetic diseases”. In conclusion, the term “genetic disease” has no meaning, because it includes any disease: the prefix “genetic” does not indicate a subset of the group referred to as “disease”.

2.2 Inherited Disorders

Rather, one should speak of diseases caused by a single (or small set of) highly penetrant genes inherited in a Mendelian fashion as “inherited disorders”. An inherited disorder may be

---


4 Huntington’s disease (prevalence in Germany up to 1/10,000) is a fatal neurological monogenetic disease. Bearing the mutant huntingtin gene is indeed predictive of an almost 100% certainty of developing Huntington’s Disease, which is most common in the late 40ies or 50ies of a person’s life. However, the point in time of the onset and also the exact course of the disease cannot be predicted. Also it may be that it only breaks out in the 70ies. As such, Huntington’s Disease is a paradigm disease for genetic counselling in the medical setting. Cf. Kunstmann E, Epplen JT (2006) Genetic counselling for the public? Community Genetics 9: 62-66.

5 Not all Mendelian disorders are highly penetrant.

defined as a disease caused by inherited factors producing the disease in most persons with that genetic factor(s), irrespective of their other genes and their environment. Such genetic factors may be denoted “genetic defects”. “Mutations” may be genetic defects, but most mutations are not. The term “mutation” indicates today a sudden and inherited change in DNA structure. In older population genetics it denoted rare genetic variations – meaning they had been recently produced, because otherwise they would either have been removed from the population by genetic drift, or drifted to a prevalence to be maintained by Hardy-Weinberg equilibrium. The threshold is about 2% heterozygote prevalence: All variants exceeding 2% prevalences were denoted polymorphisms. The recent term “rare polymorphism” is a conceptual misunderstanding, as is the recent interpretation that a mutation necessarily is causing a disease. This nomenclature is the working tool for geneticists. To avoid confusion, the public debate should use other terms intuitively understood by the public. “Inherited disorder” is such term.

Inherited disorders include e.g. Huntington’s disease, cystic fibrosis and polycystic kidney disease. Due to the very high penetrance, predictive power and familial dimension of these disorders, their presymptomatic – including prenatal – diagnosis is to be conducted in genetic services with the provision of appropriate genetic counselling. It may be noted in passing that special counselling services are also provided e.g. in the context of presymptomatic HIV testing, so the provision of the service is not contingent upon a disorder being inherited but on the meaning of the test results for affected persons. We also suggest that we should avoid the use of the term “complex diseases” as all diseases are complex and result from multiple factors, both genetic and environmental. In order to distinguish rare “inherited disorders” from common diseases, we use instead the term “common-complex diseases” to refer to the disorders, such as cancer or heart disease, that are the focus of public health practice.

It is among the aims of public health genomics to ascertain the genetic component or susceptibility for these “common-complex diseases” and to use this knowledge in a responsible way for prevention, diagnosis, prognosis and treatment.

We will differentiate and use the following terms in the following way:

**Inherited disorders** are Mendelian disorders with high penetrance. Their prevalence tends to be low.

**Common-complex diseases** have wide prevalence. Genetic variations are or are expected to be identified that contribute to developing the disease.

3. Genetic testing, genetic information and personal health information

3.1 Health information characteristics in focus

Those who espouse genetic exceptionalism argue that there are characteristics of genetic information which might lead to the necessity of treating information derived from DNA or RNA differently from other medical or health related information. We present these character-
istics in focus and the concerns that arise from them, and suggest that these concerns are not exclusive to the information generated by analysing DNA or RNA. Much of what we say here is derived from Tom Murray’s seminal article on the subject. In the light of these discussions we will discuss the terms “genetic information” and “genetic test” themselves.

3.1.1 Concern for kin

The concern for kin means that genes can be passed on to children and as such can affect the wider family and future generations. However, a family can be most seriously affected by non-genetic information as well, such as common infectious or chemical exposures, such as tuberculosis or lead poisoning, and, as mentioned earlier, HIV/AIDS. The familial nature of genetic information concerns privacy, confidentiality and the fundamental right (not) to know issues. However, these issues are not exclusive to genetic information.

3.1.2 Concern for stigmatisation and discrimination

The fear is expressed that knowledge derived from analysing DNA allows for the stigmatisation and discrimination of individual persons or at-risk groups. Nevertheless, even though genetic information might give grounds for stigmatisation and discrimination, this is not a property of genetic information alone. There is a long history of stigmatisation and discrimination of persons affected by diseases such as leprosy, epilepsy, mental disorders, malformations, AIDS or indeed of those who are HIV positive.

3.1.3 Concerns for easy accessibility of information and identification

Some maintain that DNA is a unique material that will individually identify a person and that it is ubiquitous as cells from saliva or hair are everywhere. This claim can be refuted with the following arguments. Cells from saliva, hair or skin are indeed easily accessible. However, what is ubiquitous is rather the sample containing the DNA, not the information itself. Other health information, however, can easily be obtained. Consider for example infrared thermal cameras at airports used to screen the body temperature of passengers – although high temperature does not say much about a causing disease. Furthermore, the genome does not offer a

---


unique chance to identify individuals. The iris is even more unique than the set of a person’s genes that may be shared among identical twins.

3.1.4 **Long-term storage and use for other purposes than originally consented for**

There is concern that tissue containing human DNA can be stored for many years and indeed DNA may be stored almost indefinitely. This leads to the possibility that the genome can be analysed for reasons other than what was originally consented for. Or, a genetic variation was tested for and later turns out to be also of predictive value for other disorders. To use samples in the medical context for other purposes than consented for is nevertheless also in principle true for conventional biochemical diagnoses, even though the sample’s stability is not so strong as the stability of DNA. It is reported for example from the Dutch Bloodbank that 14 years after samples had been taken they were searched for antibodies for other purposes than originally intended.⁹

3.1.5 **Concern for prophecy**

The predictive power of genetic analysis leads to the potential to make probabilistic estimates about a person’s future health. But genetic prediction is not unique in this: The biochemical diagnosis of a positive status of HIV, Hepatitis B or high blood cholesterol can also foretell the risks and probabilities of a person’s future health as do some easily observable factors (e.g. working as a ballet dancer and the risks of damaging one’s feet or being a heavy smoker). Knowledge about carrying certain viruses, about having a high blood pressure or about a person’s lifestyle may indeed have greater predictive power than information about a particular genetic variation in an individual.

3.1.6 **The origination of health information**

Genetic information might in some cases stem from the analysis of a person’s genome but at the same time could also come from analyses at the phenotype level. An example is inherited disorder autosomal dominant polycystic kidney disease (ADPKD), an autosomal inherited disorder. A person with the genetic predisposition for ADPKD is susceptible to developing multiple cysts in the kidneys. These cysts grow during lifetime and almost always lead to kidney failure later in life. The predisposition to developing ADPKD and subsequent renal failure can be detected in two ways in asymptomatic persons: at the genotypic level by molecular diagnostics, or at the phenotypic level by ultrasound or computer tomography. A diagnosis for ADPKD on the phenotype level is possible if the person’s family history is known and makes him a person being at risk.

Knowledge that an individual has ADPKD has the same meaning for that person irrespective of whether he or she obtained this piece of information by genotypic or phenotypic measures. No matter how the information was generated, the medical and social implications of the diagnosis are the same.

Information obtained by analysis of DNA or RNA has some characteristics conventional health information has as well – e.g. familial implications, potential for stigmatisation and discrimination, identification, use for other purposes, predictive power.

With regard to some inherited disorders, the diagnosis of these disorders can also be made by analysis on the phenotypic level. Hence, some clarification is to be given about what could be meant by “genetic information” and “genetic testing”.

3.2 Conceptualisation and definition of “genetic information”

In genetic discourse one often hears the term “genetic information” as a locus of hope and concern. The discussions in this paper have so far shown that we have to define precisely the nature of “genetic information” and its relationship to “health information”. We discuss this below and also the need to distinguish between its meaning as “information about an inherited disorder” and “information derived from the analysis of DNA and RNA”\(^\text{10}\).

For example, when we see a woman we have, in some senses, accessed “genetic information”. With a high certainty we know that she is likely to have two X-chromosomes. Also, we get genetic information when using ultrasound for ADPKD with a person at risk for ADPKD. Other sources from conventional medical practice deliver genetic information, amongst them radiology, family history and the biochemical analyses of tissue, blood and plasma. The diagnosis of a syndrome may be made purely on the gestalt observed by an experienced clinician. Examples include bilateral retinoblastoma and polyposis in the colon. This may also lead to knowledge about the underlying genetic variation. Genetic information can also be derived from the analysis of DNA.

The manifold sources of genetic information already tell us that the specific circumstances of the source can hardly be a decisive criterion to provide a special regulatory regime for “genetic information”. Rather, it should be the predictive power, the implications for the affected persons and the potential for discrimination/stigmatisation that might argue for treating certain types of “genetic information” in a special way. In this sense we suggest that there may be some grounds for treating genetic information, meaning “information about an inherited disorder”, differently and with great care. However, these characteristics may also be found in other situations, such as presymptomatic HIV testing.

We would argue that DNA information relating to low penetrance genes known to be involved in cholesterol metabolism or breast cancer do not fall into such a category, and that most “information derived from the analysis of DNA or RNA”, being no better predictors of heart disease or cancer than routine medical data such as blood pressure, cholesterol, age of menarche or menopause, or dietary fat intake, should be treated not differently to other types of personal health data, clinical, biochemical or radiological. Knowledge of such information

---
may allow a more accurate assessment of an individual’s risk of developing the disease but will not result in the predictive power seen in its application to inherited genetic disorders.

Genetic information is information about a person’s genetic makeup. However, this information might be derived from many sources, not only analysis of DNA or RNA. The source does not say much about the moral or social relevance of the property of the information gained. In other words, the handling of the information should be decided by the implications of the information, not by the source of the information.

Genetic information about inherited disorders, though, is of a different morally relevant quality, primarily because of its high degree of predictability and its relevance for other family members.

3.3 Genetic testing – a conceptual differentiation

When we discuss the exact way (if any) in which genetic information should be regulated in society, what aspects might we consider as being relevant to this question? What should we have in focus when reflecting on these matters? One fundamental consideration is how we use the terms “genetic information” and “genetic test”? In this paper we define a genetic test as a test from which “genetic information” is derived. We have, in turn, spoken of the need to clarify the distinction between “genetic information” as “information about an inherited disorder” and “information derived from DNA or RNA”. A radiological or biochemical test is in this sense a “genetic test” if it is a test designed to provide “information about an inherited disorder” but not otherwise.¹¹

The purpose of regulation in this sphere is to prevent improper use of genetic information. However, regulators need to keep the two separate meanings of “genetic information” in mind to avoid inconsistent and illogical policies. If the intention is to regulate “tests for inherited disorders” it would be inconsistent to regulate their diagnosis only through the use of DNA technology but not from any other means. It would be similarly inconsistent if they sought to regulate tests derived from DNA technology irrespective of purpose or context, since by so doing they would, in the context of common-complex diseases, place a greater regulatory burden on genotypic tests than on phenotypic tests that might have a greater predictive power.

Our stance is that we see no reason to regulate DNA based tests purely for the reason that they are DNA based, and that attempts to do so are based on the conflation of the two different meanings of genetic information that we have discussed above. We use DNA testing to verify diagnoses or for the categorisation of tumour pathology or for susceptibility to infectious diseases. It would clearly be inappropriate to confer special status on these tests simply because they involve analysing DNA.

While not necessarily advocating it, we do accept that there may be grounds for protecting persons subjected to highly predictive information in the context of inherited disorders. However, if this is to be implemented the regulations should apply to all diagnostic modalities and not just to DNA based diagnosis. But even in this situation arguments can be adduced to suggest that such regulation should only be implemented after careful consideration since to give “information about inherited disorders” special status may lead both to discrimination of those with inherited disorders and those who do not. The notion that people with inherited disorders should be subject to a more comprehensive protection compared to people who have no inherited disorders may well lead “to unjustified unequal treatment of persons affected.”

These remarks in no way argue against the view that the protection of personal health information is essential – quite to the contrary. Our stance is that all personal health information should be adequately protected and that, if it is so protected, there will be no need for extra protection for information just because it is based on the use of DNA. We accept that special consideration may, however, need to be given to predictive testing in inherited disorders which are best managed within specialist services and which should include the provision of genetic counselling by appropriately trained health professionals.

Genetic Testing = refers to any test/diagnosis that delivers genetic information; including conventional testing.

Gene Testing = is a subgroup of genetic testing. Gene testing is the analysis of DNA or RNA.

The focus of regulations should be personal health information and how it is or can be used. Personal health information can be derived from genetic testing that has a special predictive value – basically found in inherited disorders, no matter what the source of the information is (e.g. DNA analysis by Huntington’s Disease, ultrasound by ADPKD). Health information has to be object of appropriate data protection.

Gene testing per se is no sufficient reason for special regulations and special professional standards.

Relevant criteria for (non-)regulation and (non-)setting of professional standards for all health information are:
1. Predictive power and its implication for the person affected
2. Implications for family / others
3. Potential for stigmatisation / discrimination

---

4. Conclusion and consequences for Public Health Genomics and PHGEN

The characteristics of genetic information, as “information from the analysis of DNA” are not sufficiently different to justify different treatment and regulation from that of other types of personal health information.

Genetic information per se deserves no “status apart” just because some (but only some) of it derives from molecular diagnostic techniques. To confer special protection on genetic information per se would be overtly discriminatory against both those with inherited disorders and those without. We accept the argument that there should be particular safeguards (such as the use of formal genetic counselling) when considering the use of diagnostic and predictive tests in inherited disorders, or to ensure that people with these diseases or predispositions to these diseases will, for any reason, not become the subject of unfair discrimination. However, we reject the view that the same arguments can be used in the context of DNA tests generally or of common complex disorders.

The implication of this stance for PHGEN is that it should be sensitive to the multiple meanings of the term “genetic information” and take care in defining how the term is used. In its recommendations PHGEN has to make sure that the ethical principles of primum nil nocere, bonum facere, justice and respect for human dignity and self-determination are considered. As such, there have to be safeguards to prevent people from being stigmatised, discriminated and to keep up privacy, the right to know and the right not to know and confidentiality in reasonable ways. Also, services should be delivered in such a way that persons will understand the meaning of their health information – a goal that is a challenge to achieve when genetic testing is directly marketed to the consumer without any clinical context. However, this does not exclusively apply to information derived from analysing DNA or RNA and has to be guaranteed for all personal health information, including “conventional” phenotypic health information that is also relevant to common-complex diseases – such as blood pressure, infections and injuries.

The provision of safeguards for the use of genetic tests, even for those with inherited disorders, does not necessarily require exclusive laws and regulations. PHGEN must show that existing laws and regulations for the protection of personal health information are insufficient to deal with genetic information before it considers the use of special genetic norms. Even then it would need to be sure that the remedy does not lie in a modification of general data protection legislation rather than by the implementation of special regimes for DNA based information.

The assumption that DNA-tests per se are to be treated in a unique way implies an acceptance of genetic reductionism or genetic determinism. Genetic reductionism is the oversimplistic supposition that phenotypic traits of human beings are a linear consequence of genetic factors. Genetic determinism is the notion that our genes exclusively make us the persons we are. PHGEN has the task to counteract genetic determinism and reductionism. Another task of PHGEN is to offset actions where genetic information is mystified and demonised. To achieve a more balanced public debate will further a rational approach of using genomics to improve public health.

---


irrational, PHGEN has to take into account and be responsive to the fears that prevail in the population. Public and professional education has to be among the tasks in the field of public health genomics.

The work of PHGEN should be sensitive to the use and salient characteristics of personal health information – such as predictive power, relevance to other persons, potential for discrimination and stigmatisation. Personal health information has to be protected by regulations and professional standards. Special attention always has to be attached to inherited disorders.

However, before suggesting special “genetic laws/regulations” it has to be examined if existing standards, regulations, laws, and safeguards would not be sufficient and already include genetic information.

PHGEN has to focus on recommendations on educative measures to normalise the perception of genetics.

**Literature**


Acknowledgments:
Working on this paper was supported by the “Public Health Genomics European Network (PHGEN)” funded by the European Commission (Project Number 2005313). The opinion expressed is the opinion of the authors not necessarily of other network members.