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INFORMED CONSENT IN GENETIC RESEARCH

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Abstract

Recognizing the ethical, legal, and social implications (ELSI) of genetic testing becomes crucial for physicians in the face of complex medical issues, as they are increasingly expected to counsel their patients regarding the medical, psychological, and social responses arising from genetic information.

Genetic medicine, with its extreme complexity and the potential repercussions on an individual's life, raises important questions in the ethical, deontological, and legal realms of medicine, playing a primary role in personalized medicine.

The aim of this paper is to underscore the significance of informed consent and to provide insights into the ethical procedures associated with genetic testing.

Keywords: informed consent, genetic, genomic testing, ELSI.

Introduction

Every individual working in the field of biosciences must adhere to the principles of bioethics, which entails consistently taking responsibility for ethical decision-making. We believe that the most significant shift in ethical considerations within biomedicine arises from the sequencing of the human genome and the emergence of new biotechnologies enabling diagnostic approaches, as well as novel possibilities for treating and preventing diseases.

Genetic information may carry profound implications for patients/subjects, their relatives, and the community they inhabit, thus impacting society as a whole.

Respecting patient confidentiality by refraining from disclosing genetic test results to third parties may lead to a conflict between the well-being of the subjects and the potential benefits for their family members if they are aware of the test results. Striking the right balance between privacy and confidentiality in genetic information, with a focus on the interests of family members, poses a current ethical and social challenge.

The power of genetic testing renders it particularly susceptible to potential misuse. Concerns about privacy arise because numerous individuals, institutions, and organizations may be interested in knowing the genetic status of an individual, leading to the potential for stigmatization, discrimination, and other adverse effects not only on the research results but also on the patient and their immediate and extended family.

Specifically, the potential for social stigmatization and discrimination may manifest in insurance, employment (even regarding genetic information disclosed by consumers), or among authorized genetic counselors and nurses present during testing [1, 2, 3].

These instances highlight challenges with other societal agencies and institutions such as blood banks, adoption agencies, the military, the police, and schools [1].

It has been suggested that educational and legal institutions may take an interest in the genetic status for identifying learning difficulties [4, 1] and decision-making in custody and paternity disputes [4]. Medical benefits, purportedly, have been denied to retirees suffering from diseases with a known genetic basis [4], a matter that can be particularly relevant in incorporating genetic sampling into demographic studies on population aging.

Naturally, these benefits must include the undeniable value and utility in forensic issues.

Objectively, determining the degree of risk of genetic discrimination in health insurance and other institutions is challenging. Examples of genetic discrimination, as found in the previously mentioned studies, have led to the formation of legislation in many states and at the federal level through The Health Insurance Portability and Accountability Act (HIPAA) [4, 5]. The informational potential of genetic testing raises ethical, legal, and social issues (ELSI), emphasizing the importance of securing the confidentiality of test results and establishing legislation that allows selective and maximally secure access to this information [6].

The most important elements related to genetic testing are informed consent, protection of privacy, genetic counseling, and issues related to minors.

Informed Consent

Informed consent is a fundamental principle of ethics in human subject research (OHRP & DHHS Citation 2018; National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (NCPHS) Citation 1979, [7-9].

In a medical intervention or procedure, informed consent is a legitimate assumption for any healthcare provision and is thus a crucial element in establishing a successful therapeutic relationship between the physician and the patient.

The implementation of this principle implies dedication from the physician to provide the patient with the necessary kind of information regarding their health condition and to what extent to furnish information about the diagnostic and therapeutic activities required for improving health conditions. The increased use of genetic testing, particularly genetic sequencing, has introduced many new challenges for physicians and researchers when obtaining informed consent.

The decision-making process for the patient becomes problematic when genetic tests are the subject of information. The difficulties in the decision-making process arise from the complexity of genetic mechanisms and their interactions, including environmental factors. Such complexity leads to uncertainty about the causes of genetic diseases and an inadequate understanding of the patient's information. Therefore, genetic tests must be accompanied by all the necessary information to illustrate the potential implications of the results, including possible false-negative or false-positive results, concepts of predisposition to risk factors for diseases, and the available options for the patient [9].

This communication process is a prerequisite for enabling a free and informed choice from the available options.

Regardless of who defines the relevant content of informed consent and whether clinical or research studies/projects are in question, there is a certain general consensus that patients are often overwhelmed with extensive health information, and they frequently perceive it as irrelevant to their questions. Consequently, they lose enthusiasm for focused and reliable answers.

This is applicable to patients with lower health literacy who may be overloaded with information [10], and, based on our experience, to patients with high health literacy who may focus on information that is not central and crucial to their decision-making. Many of these challenges are related to the patient's need to understand enough essential information.

The physician should prioritize the patient and provide sufficient information to a "reasonable patient" who needs to make the right choice regarding whether they will proceed with the suggested intervention or not [11 Ge]. Informed consent necessitates decision-making capacity, but this capacity may be uncertain in families with suspected genetic conditions, intellectual disabilities, autism, or neurodegeneration. In such cases, informed consent might be sought from a legally authorized representative [12 In].

Questions Related to Participants and Researchers in Genetic Scientific Research

The primary role and, of course, the benefit of research participants are to serve as sources of data. The duty of researchers is to protect their life, health, integrity, dignity, the right to self-determination, privacy, and confidentiality of the personal information of the subjects of the research.

The questions encompass general principles related to risk assessment, scientific requirements, research protocols and registration, the function of ethical committees, the use of

placebos, provisions post-trial, and the publication of research [12]. Since the primary goal is directed toward scientific research rather than the patient, additional relevant information in clinical trials or research studies in the form of informed consent must be provided.

Informed Consent - Before and After the Introduction of Genomic Sequencing

Before the introduction of next-generation sequencing (NGS), genetic testing followed an iterative process in which clinicians conducted a differential diagnosis.

They started by testing one or two genes that were likely to provide a diagnosis. If the initial test yielded a negative result, they would proceed to test other genes. NGS has revolutionized this approach, enabling the rapid and cost-effective acquisition of a significant amount of genetic information. This has led to the widespread adoption of panel-based genetic testing and increased utilization of exome and genome sequencing for both clinical and research samples.

The traditional approach to genetic counseling for informed consent had an educational focus, providing information about the testing process, potential benefits, risks, limitations of the test, and potential treatments for which the testing would be conducted [13].

The most significant risks associated with clinical genetic testing are psychological and social (anxiety, stress from presymptomatic knowledge that someone might develop a genetic condition for which there may not be any treatment or prevention, as well as stigma and discrimination due to such a genetic test). Among family members, differences in opinions may cause stress and mutual conflict.

The advent of the era of personal genomics brings opportunities for personalized medicine. Recent genomic research has revealed a large amount of personal data about the genome with the help of NGS and data analysis techniques [14, 15]. However, at the same time, this has raised concerns about the ethical, legal, and social implications (ELSI) that require additional considerations [16].

As sequenced and analyzed data become more advanced and complex, research participants face greater difficulties in understanding the content of the study and their rights, benefits, and risks. Therefore, in the literature, authors increasingly address key topics such as informed consent, data sharing, and the return of results [17-19].

Availability of Genomic Data and Informed Consent Challenges

The availability of genomic data has triggered numerous challenges related to informed consent [20], prompting the question of whether previously accepted standards for informed consent for tests with such expansive implications can be met [21, 22].

Many specific challenges for informed consent in the context of genomic sequencing revolve around defining the need for appropriate information and understanding [23]. In human genomic research, the concept of informed consent differs from the original concept in many aspects.

Physicians often cannot determine how much information is needed for the patient to make an informed decision [13, 24].

Striking a balance between too many or too few details when obtaining informed consent for genomic testing underscores the importance of approaching consent as a dialogue between the doctor and the patient.

This is because the physician must gather information about the patient's values, goals, preferences, and concerns to determine what information the patient may need to make an informed decision. The patient should also have the opportunity to ask questions about the shared information and obtain additional information that may be necessary for giving informed consent.

Genomic research fundamentally uses human samples with less invasive methodologies and focuses on genomic information that affects not only the participant but also family members and relatives [25]. Additionally, personal genome research includes information about the personal genome and functionally undiscovered genome sequences, thus posing more unexpected risks for participants. However, despite biobanking human samples and sharing personal genomic data being currently conducted to facilitate future research, they

potentially involve many more questions regarding privacy and the unrestricted use of samples and data. As a result, the role of informed consent becomes more diverse in personal genome research.

The recent increase in research activities has raised concerns about ethical and legal issues. Many large institutions have already started using whole genome and exome sequencing in clinical settings [26, 27, 28]. Consequently, the ELSI discussion related to clinical practice has become more intense in academic circles [29].

The forensic scientific community has adopted the same principles of informed consent for medical research on humans, most commonly in procedures for human identification.

DNA analysis with informed consent is used in solving cases in forensic medicine, such as custody disputes over a child through maternity or paternity testing, discovering perpetrators and crime victims, mass disaster accidents, or the release of innocent persons sentenced to prison.

There are known cases of prison release by proving their innocence in inmates who have spent decades in prison. Informed consent may pose a challenge in cases of sudden cardiac death, especially in young people, requiring a multidisciplinary approach that includes genetic counseling and the possibility of additional testing consent from family members.

Conclusion

Anthropological, social, customary, and legal standards vary across each country, making it very challenging, if not impossible, to establish internationally standardized principles, procedures, and working principles. In the literature, the term "flexibility" is frequently encountered, primarily addressing the establishment of universally applicable principles that align with the essence of informed consent in each individual country.

It is essential for fundamental principles to be present in every country, considering anthroposocial changes and principles of action in cases of obtaining informed consent. In our view, the significant mistake lies in the notion that we should replicate the practices of wealthier and more developed countries.

The application of basic principles, with due consideration and adaptation to the specificities of each country, is necessary. Automatically adopting informed consent from richer, more developed countries, positioned higher on the global influence scale, undermines the intellectual capacities that exist independently of a country's standard.

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