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RESEARCH ARTICLE

The Application of Bioethical Principles in the Use of Pharmacogenomics in Person-Centered Medicine

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ABSTRACT

This study reviews ethical issues encountered in the literature about the use of pharmacogenomics in personalized medicine. Data gathered from Medline, Scopus, and Scielo were grouped as issues belonging to the application of the four bioethical principles. Autonomy: informed consent with vulnerable populations, consent for biobanks, changes in the physician-patient relationship, safeguarding confidentiality; non-malifecence: risks of stigmatization and discrimination, risks in clinical trials; beneficence: risk/benefit assessment in favor of benefit; and justice: pharmacogenetic tests and public health interests, equity concerns. Issues discussed were: reasons in favor and against returning research results from genomic and pharmacogenetic testing, enhancing the participation of vulnerable populations, and the reconsideration of respect for autonomy from a viewpoint too individualistic to a communal perspective since personal reality is constructed in relation to many significant others.

Keywords: Pharmacogenomics, pharmacogenetics, personalized medicine, ethics, bioethical principles

Introduction

The field of Pharmacogenomics studies how genes affect the response of human individuals to drugs[1]. Pharmacogenetics deal with clinical efficacy and/or the safety and tolerability profile of drugs in individuals[2]. While pharmacogenetics focuses on single drug interactions, pharmacogenomics considers a wider approach, incorporating epigenetics and the effects of multiple genes on drug response[3]. Currently, the terms pharmacogenetics and pharmacogenomics are used interchangeably. While genomics deal with the study of the genome and the expressed or non-expressed genes, pharmacogenomics deals with the detection of genetic modifications involved in the response to drugs. This technology allows the development of new diagnostic procedures, prevention methods, and therapeutic products selectively prescribed to patients with the assurance of safetiness and effectiveness. Pharmacogenomics may be clinically applied in three ways: the use of drugs to treat genetically inherited diseases, genetic determination of safety and efficacy of drugs in certain individuals, and designing a drug regimen based on the metabolic enzyme activity of the patient[4]. Personalized or precision medicine refers to treating persons with the right drug for the right patient with the right dosage based on genetic data, including prevention of disease, prediction of efficacy, time to respond, and side-effect profile[5]. Pharmacogenomics may help to develop a person-centered medicine by selecting and providing the right dosage of medicines base on the genetics of patients. Individuals with risk of toxicity or lack of therapeutic response to specific drugs may be identified. The genome of individuals predicts the response to drugs and having the information allows the diminishing of adverse events[6]. The genetic variation of drug response in patients may correlate gene expression or single-nucleotide polymorphisms with drug metabolizing enzymes involved in pharmacokinetics and pharmacodynamics, such as absorption, interaction with drug receptors, biotransformation, distribution in the body, and excretion.

The four principles of bioethics (autonomy, beneficence, non-maleficence, and justice) constitute a good framework for reflecting the ethical issues that arise in pharmacogenetic testing. Bioethical reflection provides a common ground for dialogue among different disciplines and stakeholders involved in this technology.

Materials and Methods

A review of the literature has been performed by searching Medline, Scopus, and Scielo in English, and Spanish using the following keywords: pharmacogenetics, pharmacogenomics, personalized medicine, bioethics and ethics. The search resulted in 8600 articles, of which 90 were chosen since they concentrated the information needed. Ethical issues were grouped as issues belonging to the application of the four bioethical principles: autonomy, non-malifecence, beneficence, and justice.

Application of bioethical principles

The responsibility and challenges of using pharmacogenomics in medicine demand ethical reflection. While there are great expectations for the use of pharmacogenomics in personalized medicine, there are many ethical and social concerns with the practice as well[7]. Among the concerns are limited knowledge of patients, which makes difficult the process of informed consent; participation of vulnerable populations; difficulties with guarantying confidentiality; communication of incidental findings; changes in doctor-patient-relationship with the emphasis on data; possibility of discrimination due to misuse of data by insurance companies and employers; the potential for racial stigmatization due to genetic information; lack of equity due to unavailability of access to personalized medicine for underprivileged people and ethnic minorities. The bioethical principles (respect of autonomy, non-maleficence, beneficence, and justice) provide a framework from which to reflect the ethical and social issues for the use of pharmacogenomics in person-centered medicine for taking the most appropriate decisions[8]. The ethical issues have been classified according to the principles.

1. Respect of autonomy or respect for persons

The respect of autonomy implies that research subjects and patients will be free to make their own choices and act voluntarily according to their values, beliefs, and preferences. When using pharmacogenetic tests, clinicians and researchers should provide to patients and research subjects the rationale behind using them, making clear that it is a voluntary procedure subject to informed consent.

Genetic testing is unique since it has a predictive value showing the risks for future diseases in individuals and in their offspring and remains stable during life[9]. Genetic information is considered of sensible nature since there are risks

of discrimination or stigmatization. Stigmatization refers to labeling a person linked to genetic information as having a disease or condition. Discrimination refers to treating persons differently based on genetic information. Care must be taken that individuals understand that in pharmacogenomic research they are giving permission to pharmaceutical companies to link personal and family information to genetic research, which may risk the respect for privacy[10]. The DNA samples that patients provide contain information about the whole genome. Therefore, researchers receive more information that is required from patients. When doing informed consent, researchers must inform about what and how information from genetic testing will be used.

Informed consent with vulnerable populations

In many countries, indigenous populations require tribal oversight and community approval before carrying out individual informed consent and some problems may be encountered since many have been skeptical about participating in genetic research and rejected blood sampling[11,12]. Indigenous participation may be enhanced by several approaches that may help: collaboration with community leaders, cultural competency, a process of deliberation with the community for the way of receiving results, improving research transparency, and supporting the community with capacity building[13,14]. Community advisory boards may also help to support pharmacogenetic tests in vulnerable populations[15].

There are ethical considerations regarding children as a vulnerable population. Individualized genome-based therapy has the potential to improve drug efficacy with adequate dosing, reducing rates of toxicity and overall health outcomes for children, but there is less information than for adults[16]. Assent rather than consent is required for those between 12 and 18 years in most country legislations, but in general, it is difficult for children to understand the benefits and risks of genetic information and that this may include health problems that will occur in their future life[17,18]. Generally, a dialogical process with family, psychological and social support, and genetic counseling at and post-diagnosis are recommended, which may take considerable time[19]. Pharmacogenomics uses complex terminology which should be adapted to the age of participants. For children less than 12, it is considered that they do not have competence for taking decisions so the permission must be given by parents or guardians. Some authors recommend that children younger than 12 may participate in the decision process according to their capabilities[20]. For minors between 12 and 18 years, it is considered that they have a developing capacity to participate in decision-making for health care and research. This means to obtain the minor agreement to participate providing they understand the necessary information given, but when there is a danger for the health of the child and there is no other way to improve it, guardian permission may be sufficient. However, it has been reported that direct-to-consumer companies provide pharmacogenomic testing requiring only legal guardians to sign consent for their children without assent[21]. Returning of research results must also be explicated in the consent process specifying to whom the data will be available and it is recommended that only clinically relevant and informative results must be communicated to the family, advising also when data is inconclusive[22].

Consent issues for biobanks

Very often samples are stored in biobanks. The following issues have been found with the informed consent for biological materials stored in biobanks used for genetic research including pharmacogenomic: questions about how much information should be given, that communication must be understandable, benefit sharing with participating community and research subjects, ownership issues, intended purposes, secondary use, data sharing with research and health care institutions, consent of vulnerable populations including children, consent when there is death or incapacity of donors, respect of culture, returning research results including incidental findings, how data and biological materials will be store, transfer of biological materials including overseas, right to withdraw with disposal of biological materials when requested, safeguarding confidentiality and privacy, waiver of consent[23]. Another problem is the quality of informed consent process since deficiencies have been found in the information provided to donors of biological samples for informed consent[24]and in understanding the terminology used[25]. Greater patient knowledge of genetics has been associated with a more positive attitude towards pharmacogenomic testing[26,27].

In biobanks, the type of consent may be:

A) Broad: open to any kind of research and use
B) Restricted: A unique specified use, any secondary use requires new informed consent
C) Tiered: By choosing among a possible list of secondary uses

D) Optional: Choosing between broad or restricted

For the biobank and researchers, the broad model looks more efficient for informed consent, since this allows greater control of the use of data and also because many donors do not wish to be contacted again or become difficult to localize them[28]. But considering the risks, some authors think that broad consent is not true consent but a generic authorization of use sacrificing the right of the donor to decide in favor of research interests[29]. For psychiatry patients, it is considered that for the storage of samples waiving of consent is not possible and opt-out consent procedure either because of incompetence and being that the risks are not minimal[30].

Changes in the physician-patient relationship

A shared decision-making in health care relies on a good physician-patient relationship and on the comprehension of the patient, which requires a good level of literacy on the topic[31]. Physicians need to have patience and time to go over the meaning of genetic predictions about health taking into consideration that patients may have problems in understanding probabilities and they must avoid reducing patients to their genetic characteristics in the exchange of information[32]. This fact adds pressure to physicians who have very little time in most situations and prefer taking decisions based on data that is difficult to understand by patients who may feel under pressure to optimize their health and to contribute with data [33]. The problem may be aggravated for minorities due to language problems and difficulty to understand drug-genes interactions[34]. Family members may wish to know whether they have inherited the trait, so that the privacy of the patient may enter into conflict with the right-to-know of family members[35]. Pharmacogenetic tests may reveal additional sensitive information about the patient who may wish not to be shared to others. When performing pharmacogenetic tests ancillary or secondary information may be produced about disease prognosis, predisposition to other diseases, or possible inheritance to family members. Physicians favor preserving the confidentiality and privacy of patients due to potential conflicts regarding secondary genetic information but there is also the duty to report them to patients when they are serious and predictable[36], [37].

Safeguarding confidentiality

Confidentiality for personal data is needed for the protection of genetic information so that third parties will not have access according to the will of the donor. Generally, confidentiality is guaranteed by coding the information and separating personal data from genetic information, and assigning a person in charge to safeguard data. Making biological materials anonymous is not favored since most studies need associated data. Also, full anonymity prevents researchers from giving back research results to participants, which is considered an obligation as it is to preserve confidentiality[38],[39]. The Declaration of Helsinki, CIOMS guidelines, and the UNESCO Declaration about Human Genetic Data specify the need to safeguard confidentiality. Genomic information may be stored in computerized databases which must be safeguarded since employers and insurance companies may wish to have access to this information for their interests. However, complete protection of privacy may be difficult in direct-to-consumer genetic testing that is proposed in the internet[40].

2. Non-maleficence: avoiding harm to other human beings

Risk of stigmatization and discrimination

A possible harm in the use of genetic information is the stigmatization or discrimination of individuals and groups. Being diagnosed with mutations associated to disease or behavior problems, such as violence or addiction, generates to be marked as having a pathology or condition which affects individuals and also families or ethnic groups. Discrimination may occur in having difficulties finding a job or in an increase in health insurance fees, or higher fees for medications with a small chance of efficacy[41]. Genotyping vulnerable populations may cause suspicion and rejection and it has been proposed that generalizations must be avoided at the time of publishing results[42]. An example was the stigmatization of the Maori ethnic group of New Zealand, which was stigmatized as violent due to a misleading publication about the frequency in the group of the gene monoamine oxidase which degrades neurotransmitters with amine and has been associated with major depression and risk behaviors, such as aggression, addiction and gaming[43]. In Mexico, the National Institute for Genomic Medicine was created to study the genome of Mexicans having the goal to promote preventive medicine, but the Project originated a social controversy and rejection due to the lack of understanding and prejudices about the real purpose[44].

Personalized medicine may further find genetic differences with biological and economic impact. There is a difference between genetic tests to reveal disease mutations and pharmacogenomic tests that only look at genes related to the metabolism or mechanism of action of drugs. Some argue that pharmacogenomic characterization is less likely to raise sensitive issues that require confidentiality and the possibility of stigmatization than genetic testing about disease risk assessment, but others consider that it may be true for genotyping highly penetrant Mendelian disorders but not for common complex disorders in which pharmacogenetic testing may become an important financial risk assessment[45]. Additionally, polymorphisms relevant to drug response may overlap with disease susceptibility, thus having the risk to stigmatize for that disease, but these overlaps are rare[46]. On the other hand, patients less likely to respond to treatment revealed by pharmacogenetic tests would have a greater risk of increase in insurance fees[47]. However, Nuffield Council Report considers being unlikely that pharmacogenomic information will be used by itself for increasing premiums since most pharmacogenetic tests are of low predictive value[48]; on the other hand, with the development of the field insurance, companies may come forcing to take pharmacogenetic tests to choose the right drug for individuals and patients may feel under pressure to optimize their health and to contribute with data[49],[50].

Risks in clinical trials

Pharmacogenetics may increase effectiveness and diminish side effects of drugs based on genetic information which may be used in clinical trials for diminishing adverse events. Although clinical trials using drugs for medication may reduce costs by performing the tests in smaller targeted populations known to have less probability of adverse events, in post-marketing surveillance there may be a problem affecting the non-maleficence principle, since the unknown adverse reactions will appear in this phase only[51].

In clinical trials, one of the complaints in developing countries is that populations from these countries may be exploited as subjects since there are many obstacles in being benefited after research is finished due to financial constraints[52].

3. Beneficence: to ensure that our actions achieve more benefits than harmful effects

Risk/benefit assessment in favor of benefit

There may be many benefits in personalized medicine: risk prediction, improvement of effective prevention, improvement of quality of health care on accessibility, effectiveness, and affordability of drugs [53]. Some authors believe that in risk/benefit assessment, the benefits of pharmacogenomics for patient well-being and the cost of health care outweigh the risks[54]. Some authors consider that the use of pharmacogenomics in clinical trials will improve the fair selection of subjects since there will be less probability of damage by choosing those with low adverse reactions or side effects and those with greater chances to benefit[55]. But whether there will be a greater cost-efficacy is debatable, drugs are responsible for only a small portion of health care costs and genomics is only one of several factors influencing adverse drug reactions[56]. In clinical trials, it is not clear whether the cost will diminish. The cost of performing pharmacogenetics tests and analysis of data is high and a large number of patients may still be required at least in phases 3 and 4, since adverse reactions may be infrequent[57]. Some authors believe that pharmacogenetic companies will spend less in obtaining FDA approval of drugs, but these savings may not be passed to patients[58]. On the other hand, if there is a technology that predicts that a drug is harmful to an individual, then it is unethical not to carry out the test[59].

4. Justice: to treat others fairly without exploitation or deceit. Achieving equity

Pharmacogenetic tests and public health interests

In general, pharmacogenetic testing has a high cot triggering restrictions on its use in middle and low-income countries, affordable only for a small proportion of the population. This generates inequalities in benefits. Generally, there is no political will to include pharmacogenomics as a public service. Cost-effectiveness must be evaluated before considering financing genetic tests by public system. The following factors must be evaluated for approving the cost[60]:

- A strong association between polymorphisms and the clinical relevant effects
- Prevalence of genetic variants sufficiently present as justifying performing genetic tests
- Determination of a genotype with relevant impact on the quality of life, mortality, or diminishing therapeutic cost

- Use of genetic tests (versus standard procedures) which signifies a considerable reduction in adverse events
- Sensibility, specificity, and associated costs previously identified
- Consideration of additional costs such as genetic counseling

Additionally, other factors apart from cost must be considered for implementing clinical pharmacogenetics: the perception of patients, consistency in clinical recommendations, well-trained pharmacogeneticists, and commitment of healthcare personnel[61,62,63].

Equity concerns

In research, the stratification of groups of patients based on genetic information may cause less participation of populations with a low response (orphans) since the development of tests for them will not have profit[64]. Orphan populations already exist when extremely rare diseases are left aside from research to develop treatments and the use of pharmacogenomics may create new orphan populations[65]. Increasing the expenses of drug development in minorities is not favor by governments, pharmaceutical industry and insurance companies[66,67]. The pharmaceutical companies may be reluctant to market drugs for poor ethnic groups. Some authors promote the inclusion of minority populations in genomic research for being able to receive more benefits[68].

However, responsibility for equity depends on policymakers and governments who should support the disadvantaged[69]. It would be ethical to include vulnerable minority populations in policy decision-making for treatment and resource planning[70]. Insurance and regulations are needed to prevent inequality, and protect vulnerable populations with low access[71]. The problem is that the use of race variables may increase the potential of discrimination especially, for vulnerable populations. Many physicians believe that personalized medicine is only available for some subpopulations and that racial/ethnic background is a consideration to be taken; the most important factors to guide therapy are: family history, drug-drug interaction alerts in medical records, and biomarker measurements[72]. Several clinical guidelines for common health conditions list racial/ethnic background as a factor to be considered in research and clinical management and drug labeling practices promoted by the FDA include the notion that genetic profiles are important for the selection of medications[73]. But, exploring potential differences based on race in pharmacological response may provoke fears of mistreatment in races who have suffered from discriminatory practices, such as African Americans in the US. This population has a low enrollment in pharmacogenomic research studies due to mistrust to research, concerns about genetic testing, and about the amount of blood collected[74]. The risk is that vulnerable minority populations will be left under-studied in pharmacogenetic research or unwarranted from using the drugs that result from research. Developing countries have other barriers, such as low resources for clinical care, few pharmacogenetic clinical trials, scientific and technical barriers to genotype pharmacogene variants, and socio-cultural distrust[75]. Indigenous populations have as a general barrier the mistrust derived from traditional research practices which have not been sensitive to community needs[76]. Linking race or ethnic groups with genetics may provoke stereotyping of diseases as assigned to certain groups with a simplistic conceptualization[77]. However, clinicians often are influenced in their decisions by the existing literature in scientific journals which use racial/ethnic categories in research[78,79]. The use of racial and ethnic categories may be also rooted in politics by attributing the differences in health status to biology rather than to class or socioeconomic factors, shifting away the blame to the government which should work in diminishing social differences[80]. Racial and ethnic categories are confounded with social determinants of health in many contexts, such as socioeconomic status, education, housing, income, environmental exposure or diminishing access to health care[81,82]. Some countries, such as Mexico and India, claim sovereignty over their genomes as biologically distinct, based on racial/ethnic constructs with the rationale of protecting their population from exploitation by the pharmaceutical industry, but this position contributes to the racial/ethnic categorization[83,84]. Indigenous populations fear that pharmacogenetic testing may not improve the health care for these populations unless a research is done addressing cost-effective problems and to avoid discriminatory practices[85]. Some authors believe that generalizations must be avoided due to the considerable variations that exist among members of a race or ethnic groups[86]. The Nuffield Council also recommends not subdividing according to ethnic or racial categories for pharmacogenetic testing, but tests must be validated on the populations in which they are to be used [87]. Some authors consider ancestry as a variable rather than race is a better approach when designing research and that more research is

necessary in pharmacogenomics for underrepresented groups[88,89], but ancestry is still a form of race classification. Real predictors are found by testing the genotype of individuals without the need to consider that belong to a specific group[90]. However, many clinicians still today use racial or ethnic categories due to the lack of resources for pharmacogenetic testing. Some authors believe that personalized medicine will replace the racial and ethnic identity approach in health care when there will be enough resources available at the individual and collective levels, including financial, informatics, legal protection, and sufficient infrastructure[91].

Discussion

Returning of genomic research results have been highly discussed, some in favor others against[92,93]. The problem is aggravated when the results obtained were not covered in the initial research question. Arguments against returning research results are: respecting the autonomy of subjects who do not wish the return, unconfirmed or invalidated results may do more harm than good, unnecessary psychosocial distress, the potential for discrimination, and returning the research results is contrary to the intent of research, which is to provide general results for public's benefit. While those in favor are: the result may be of value for the research subject (empowering), helping to make lifestyle decisions, or be clinically important in predicting immediate or long-term risk[94]. This rationale applies also in pharmacogenetic testing since knowing the adverse effects of drugs may have health implications and may be less problematic than disease susceptibility results. It has been considered that compared with disease susceptibility results, pharmacogenomic results, from studies predicting adverse responses to drugs, are medically actionable, may offer benefit immediately, and are associated with minor psychosocial and life choice consequences[95]. Some surveys suggest that patients, physicians and pharmacists are supportive of sharing pharmacogenomic test results and patients are also in favor of personally maintaining their test results[96]. But often pharmacists consider that they cannot counsel patients adequately about the results of pharmacogenetic tests due to the lack of knowledge[97,98].

An important issue is to enhance understanding and participation in vulnerable populations. This may be enhanced by a process of deliberation with community leaders to adapt to their needs taking into consideration their culture in order to agree in the way of receiving results and in the benefits for the community. Research is needed to gather sufficient information so that vulnerable populations are not let aside from benefits. Increase use of personalized medicine in health care will occur when there will be enough resources available at the individual and collective levels, including cost effective results, social and ancestry data, legal protection, and sufficient infrastructure in every context[99].

A highly debatable question in pharmacogenetic testing refers to the individualistic versus communal approach in the application of autonomy and justice principles. In the reflection on the principle of respect for persons, respect for autonomy should be reconsidered from a viewpoint too individualistic to a communal perspective, taking into account that an individual is not isolated but his/her reality is constructed in relation to many significant others. The moral theory should complement autonomy with relationships as claimed by some feminist authors[100]. The right to protect personal data is not absolute. It must be balanced with other fundamental rights. When research is done, there are other interests apart from respecting privacy, such as using genetic data for the benefit of others. Genetic information contains valuable information not only for the individual but for family members and others who share a similar genetic heritage. Confidentiality measures are necessary for fear of stigmatization or discrimination, but persons may choose, they may be reluctant to certain types of research and favor others. For samples stored in research and health care institutions, it has been proposed a tiered informed consent in which participants may give broad consent only for certain types of research or research uses[101]. For example: for specific diseases, for only public-funded research, for specific research institutions, or specific researchers. The Council for International Organizations of Medical Sciences (CIOMS) in its International Ethical Guidelines for Biomedical Research Involving Human Subjects of 2016 accepts broad consent for unspecified use of biological materials when the Institutions that have stored with a proper governance system and also it may be substituted by an informed opt-out procedure, in which the material is stored and used for research unless the person from whom it originates explicitly objects. The informed opt-out procedure must fulfill the following conditions: 1) patients need to be aware of its existence; 2) sufficient information needs to be provided; 3) patients need to be told that they can withdraw their data; 4) a genuine possibility.

Waiver of consent is also possible under the approval of a scientific ethical review committee, since retrospective studies may use old biological samples stored from which it is not possible to obtain informed consent. CIOMS guidelines establish the following conditions:

- There is minimal risk to human subjects
- The waiver will not adversely affect the rights and welfare of the subjects
- There is sufficient protection of their privacy
- There is an adequate plan to protect the confidentiality of data
- There is no known or likely reason for thinking that participants would not have consented if they had been asked
- Research design responds to an important inquiry
- The research will not be possible if the request of informed consent is enforced

The individualistic approach determines also that individuals look for answers by themselves by approaching offerings on the internet. Some companies are offering Direct-to-consumer pharmacogenomic tests by directly ordering the tests advertised online, either with or without a prescription by a physician. The offerings generally are limited when selecting specific genes or a range of gene variants or alleles, not offering others. This can influence the interpretation of results and the accuracy of predictions that individuals do not know[102,103]. Some factors affect the accuracy of phenotype prediction, such as gene dosage, modifier genes, drug-drug interactions, or environmental effects. For individuals alone is difficult to understand that many times there is a problem about the quality of evidence that links genetic variants to functional effects and that there is no clinical utility of certain genotypes for specific genes[104].

The principle of justice demands a distribution of the benefits of personalized medicine for all racial and socioeconomic backgrounds, but this seems difficult with current health care systems in most countries and differences among countries. This principle demands consideration of the common good over an individualistic approach[105]. Government policymakers must look for the welfare of the larger community and differentiated groups favoring those at disadvantage. In research, pharmacogenetic testing should be performed in collaboration and partnership with vulnerable populations[106]. Additionally, there are several barriers in developing countries on performing pharmacogenetic testing: the cost is high in comparison with other diagnostic procedures, fragile health care systems with debts in implementation, the cost-effectiveness of tests, lack of access for most due to lack of financing by the public system, lack of training and equipment infrastructure, lack of genetic counseling, adjustment to focus on diseases with greater morbidity in each country[107,108,109,110].

The problem of increasing health insurance fees due to genetic differences may be solved with a health insurance system in which costs are shared equally by affiliates. Government Policies may help as well. In the US, for example, the Genetic Information Nondiscrimination Act of 2008 prohibits genetic discrimination in matters involving health insurance and employment. The Act prohibits insurance companies to require the purchase of genetic tests and to use genetic information to adjust premiums, deny coverage or impose restrictions based on preexisting conditions. The Act prohibits companies with 15 or more employees to require or use genetic information, including medical history, for hiring. However, patients may not be protected from genetic discrimination in long-term care insurance.

Conclusions

Clinicians and researchers need taking decisions not only on technical or scientific problems but also related to ethical problems such as rights or responsibilities. The acceptance of pharmacogenetic tests in routine clinical settings depends on the resolution of ethical standards to satisfy the different stakeholders. A balance must be found between social benefits, individual benefits, and scientific development. Government policymakers must look for the welfare of the larger community and differentiated groups favoring those at disadvantage.

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