

Law: Pharmacogenetics Testing: What are the ethical, legal, and social issues?

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Disclosure

Trinh Pham has no actual or potential conflict of interest associated with this presentation

Objectives

- Explain the appropriate informed consent process for genetic testing
- Discuss concerns for genetic discrimination, privacy, and confidentiality with pharmacogenomic testing
- Explain the legal issues relating to ownership and use of large scale genomic data collection, and public versus corporate ownership of genomic research results
- Discuss the justice and equity issues associated with pharmacogenomics testing

Pharmacogenetics vs Pharmacogenomics

Pharmacogenetics

The study of the relationship between an individual's genetic constitution and the person's response to medication

Pharmacogenomics

Studies and compiles all the available information regarding an individual's genetic make-up in order to predict patterns of reaction to medication

Sillon G, et al. Med Law. 2008; 27: 843-857

Pharmacogenomic Testing

- Clarifies appropriate treatments for specific disease subtypes
- Identify genetic variants that predict drug efficacy or toxicity
- Links drug response to individual genetic variations
- Identify genes that code for proteins involved in drug absorption, distribution, metabolism, and excretion

Informed Consent

Disease Genetics

- Effective treatment may not be available
- Possibility of stigmatization or discrimination
- Limits of confidentiality due to effect on relatives
- Concerns about incidental findings

Pharmacogenomics

- Immediate clinical utility
- Does not pose significant risks
- Psychological stakes low

Balance in maintaining personal privacy and public interest in the prevention of harm

Aspects of Informed Consent

- Main clinical drug trial
- Research involving a specific genetic test related to a drug effect
- Unspecified genetic tests to be used in future research
- Clinical setting for treatment decisions
 - Consent obtained by the health care provider
 - Consent obtained by the laboratory

Informed Consent

Broad Consent

In addition to disease or genomic specific research:

- Participants can be asked to agree to storage of their samples and/or data and to the use of their samples/data in future unspecified research

Specific Consent

- Narrowly defined research uses of participant samples and data
- Participants can change their consent preferences over time

<https://www.genome.gov/27559024/informed-consent-special-considerations-for-genome-research/>

Broad Consent

- *Your samples, genomic data and health information will be stored and shared with other researchers*
- *The samples and information will be available for any research question such as:*
 - *Understand what causes certain diseases (for example heart disease, cancer, or psychiatric disorders)*
 - *Development of new scientific methods*

<https://www.genome.gov/27559024/informed-consent-special-considerations-for-genome-research/>

Tiered Consent

If you wish to participate, please check your answers to the following questions. Yes or No

- *May we collect your tissue samples, health information, and genomic information to study [state specific research project]?*
- *May we share your tissue samples, health information, and genomic information with other researchers to study [state specific disease or disorder]?*
- *May we share your tissue samples, genomic data, and health information with other researchers for future research projects related to other topics?*

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Permission to re-contact

Researchers might want to ask you to participate in additional studies. In some cases, you might be a particularly good candidate for a particular study because of your health history or genomic information.

- *May we contact you in the future to get your permission to use your samples, health information, and genomic information for additional studies?*
- *May we contact you in the future to ask your permission for additional samples or follow-up information about your health or medical care?*

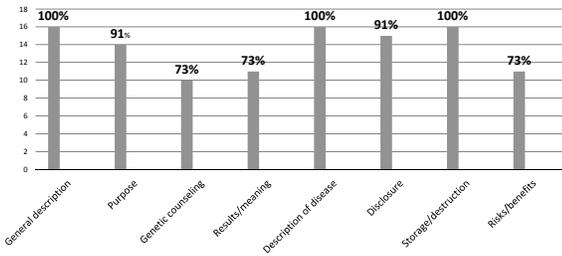
<https://www.genome.gov/27559024/informed-consent-special-considerations-for-genome-research/>

Informed consent for clinical genetics testing

1. Description of the test
2. Purpose of the test
3. Consideration of genetic counseling
4. Potential results and/or meaning of a positive result
5. Description of the disease/condition being tested
6. Individuals to whom results will be disclosed
7. Storage and/or destruction of sample following testing
8. Medical risks and benefits

Haga S, Mills R. Pharmacogenomics. 2016; 17(14): 1595-1605

Analysis of 8 elements of informed consent from responding labs (n=16)



Haga S, Mills R. Pharmacogenomics. 2016; 17(14): 1595-1605

Sample text from components of the informed consent	
General description	"The DNA test(s) detect small differences (variants) in DNA which can affect the way drugs work and are metabolized in your body and/or detect potential side effects"
Purpose of test	"Pharmacogenomics testing determines how genetic makeup affects my response to medication"
Counseling	"Genetic counseling is recommended prior to, as well as following genetic testing"
Results/meaning	"DNA results may indicate whether or not you have this condition or are at risk for developing this condition. Indicated whether or not you are a carrier for this condition, predict that another family member has or is at risk for developing this condition, predict that another family member is a carrier of this condition"
Description of disease tested	"Genotyping of CYP2C9, CYP2C19, and VKORC1 for metabolism status to determine proper initial dosage of warfarin to avoid bleeding events or overdose"
Disclosure	"Because of the complexity of genetic testing & the important implications of the test results, results will be reported only through a physician, genetic counselor or other identified health care provider"
Storage/destruction	"The sample will be destroyed at the end of the testing process or not more than 60 days after the sample was taken..."
Medical risks/benefits	"Side effects of having blood drawn are uncommon, but include..... Other risks that may be experienced...include: related emotional issues, impact on life-changing decisions, potential genetic discrimination and loss of confidentiality"

Haga S, Mills R. Pharmacogenomics. 2016; 17(14): 1595-1605

Assessment Question #1

In the clinical, non-research setting, choose true or false for each statement

1. A signed informed consent is required for pharmacogenomics testing
2. Pharmacogenomic tests may be considered to be the same as routine clinical laboratory tests and does not require informed consent
3. A verbal informed consent is sufficient for pharmacogenomics testing
4. There is clear guidance on the informed consent process for pharmacogenomic testing

Issues to Address for Informed Consent for Genomic Data

- Information may be relevant for family members and reproductive decision-making
- Individuals may be susceptible to a broad range of conditions
- Risks of carrying a diagnosis may be uncertain or unclear
- The data may be reinterpreted and change in relevance over time
- Privacy concerns in part because of the risk of re-identification

Disclosure Obligations

- Many genetic variants have clinical relevance for more than one condition
- Pharmacogenetic tests may generate incidental or ancillary information unrelated to the original purpose of testing

Are physicians obligated to disclose ancillary or incidental information?

Types of Incidental Information

- Medically preventable conditions
- Medically relevant results with unclear treatment implications
- Results without personal health implications, but which may be useful for reproductive planning
- Results of uncertain significance

<https://www.genome.gov/27559024/informed-consent-special-considerations-for-genome-research/>

Dissemination of Incidental Information

- Whether individual results will be returned, and if so, what types of findings may be returned
- Whether summary-level study results will be given to participants
- When and how results will be returned to participants
- Whether results may be returned by secondary investigators if samples or data are deposited in a biobank or data repository

<https://www.genome.gov/27559024/informed-consent-special-considerations-for-genome-research/>

Factors to consider in the informed consent

- **Scope and intent of participant's informed consent (IC) for research**
 - Future use of tissue/blood samples collected today?
 - How will the sample be stored?
 - Who will have access to the samples?
- **Collection and banking of DNA samples**
 - Pharmaceutical company sponsored clinical drug trials vs academic institution
 - Who owns the genetic information?
 - Who has access to the individual's genetic information?
- Who is responsible for oversight in the process of ensuring confidentiality and destruction of genetic material?

Sample/Data Banking and Collection

- Biorepositories or Biobanks
 - Repositories that store and distribute biospecimens and associated data
- Databases or data repositories
 - Repositories that store and distribute only data are referred to as databases or data repositories.

NIH expects investigators to obtain explicit consent for participants' genomic and phenotypic data to be used for future research purposes and to be shared broadly through databases repositories

<https://www.genome.gov/27559024/informed-consent-special-considerations-for-genome-research/>

Sample/Data Banking and Collection

- Secondary investigators can access de-identified individual-level participant data through NIH-designated data repositories
 - Defined by the submitting institutions based upon the participants' informed consent
 - Only if participants explicitly consent to allow unrestricted access to and use of their data for any purpose

<https://www.genome.gov/27559024/informed-consent-special-considerations-for-genome-research/>

What happens to data/sample after:

- **Change in participation status**
 - Discussion should include whether the investigators and/or secondary investigators might continue to use the participants' stored samples or genomic data after participants have withdrawn from the study
- **Closing of repository**
 - Participants should understand whether samples and/or genomic data will be destroyed or transferred if the repository closes

Moore v Regents of University of California

- Mr. Moore's biological specimens were collected by the defendant's physician for research project
- Unknown to the patient, the results of the research led to a patent application by the defendant
- The plaintiff sued the defendant claiming deprivation of property interest, lack of adequate informed consent, breach of fiduciary duty

The court ruled Mr. Moore did not retain right of ownership of his biological specimen that was used to develop a new product.

<https://www.courtlistener.com/opinion/2608931/moore-v-regents-of-university-of-california/>

Data Storage

Electronic Health Records (EHR)

- Who should have access to the individual's genetic information
- How can the information be protected against unauthorized access
- How much of patient's genetic status should be included in EHR & under what restrictions?

Privacy and Confidentiality

- Information about an individual's genome simultaneously provides information about his or her relative
- Genomics research results may also reveal unexpected information about family relationships
- Use of coding techniques to preserve patient confidentiality

Participants should be informed about the circumstances under which such information would and would not be disclosed to them or to family members

Shields AE. Addiction Science & Clinical Practice. 2001

Considerations for the family

- *Before joining the study, you may want to consider discussing your plans and this study with your family members.*
- *Because certain conditions and traits run in families and are inherited through genes, this study is recruiting biologically-related family members. This study will compare family members who have [disorder] and family members who do not have [disorder].*
- *You may learn something about your genome that relates to the health of your relatives. If so, your relatives might want to know so that they can decide whether to get tested or follow up in other ways. It is also possible that they might not want to know.*
- *It is possible that we will learn that assumed family relationships are incorrect (such as learning that a child is adopted or has a different father). [Possibly] We will not give you these results. [OR] We will tell you these results only if they are relevant to your health*

<https://www.genome.gov/27559024/informed-consent-special-considerations-for-genome-research/>

Pate v Threlkel

- March 1987, Marianne New received treatment for medullary thyroid carcinoma, a genetically transferable disease
- In 1990, Heidi Pate, New's adult daughter, learned that she also had medullary thyroid carcinoma
- Pate and her husband alleged that the physicians knew or should have known of the likelihood that New's children would have inherited the condition genetically
- The physicians were under a duty to warn New that her children should be tested for the disease

<https://h2o.law.harvard.edu/cases/4109>

Pate v Threlkel

- The Florida Supreme Court Ruled:
 - A physician has a duty to warn patients of the genetically transferable nature of the condition for which they are being treated
 - Warning the patient of the familial implications of genetic testing satisfied the duty to informing the patient's children
 - It is not specifically required that the information to be transmitted to the patient's children

<https://h2o.law.harvard.edu/cases/4109>

Assessment Question #2

Potential issues with privacy or confidentiality with pharmacogenomics testing include:

- Possible loss of privacy with identification of incidental findings that may affect relatives also
- Privacy not being maintained or secured even when genetic data is anonymized
- Ability of physicians to inform patients or relatives the incidental findings from pharmacogenomics testing
- All of the above

Genetic Discrimination

Genetic Discrimination

The different treatment of an individual by his or her employer or insurance company due to a known genetic disorder or polymorphism

Genetic Stigmatization

A social process that begins with distinguishing and labelling some feature of a person such as occupation, disease, or skin color

Shields AE. Addiction Science & Clinical Practice. 2001

Genetic Information Nondiscrimination Act of 2008 (GINA)

Title I Genetic Nondiscrimination in Health Insurance

1. Health insurers may not use genetic information to adjust a group plan's premiums, or, in the case of individual plans, to deny coverage, adjust premiums, or impose a preexisting condition exclusion
2. May not request, require, or purchase genetic information for underwriting purposes or prior to enrollment
3. May not request or require individuals or their family members to undergo genetic testing or to provide genetic information

<https://www.eeoc.gov/laws/statutes/gina.cfm>

Genetic Information Nondiscrimination Act of 2008 (GINA)

Title II Prohibiting Employment Discrimination on the Basis of Genetic Information

- Prevents employers from using genetic information in employment decisions such as hiring, firing, promotions, pay, and job assignments.
- Prohibits employers from requiring or requesting genetic information and/or genetic tests as a condition of employment.

<https://www.eeoc.gov/laws/statutes/gina.cfm>

Patient Protection and Affordable Care Act (PPACA) and GINA

PPACA

- Certain health insurance issuers may only vary premiums based on certain specified factors (i.e., tobacco use, age, geographic area, and self-only or family enrollment)
- Prohibits discrimination by group health plans and health insurance issuers on the basis of health status and specifically includes genetic information as a health status related factor

GINA

- A group health plan and a health insurance issuer may not adjust premium or contribution amounts on the basis of genetic information
- Allows employers, employment agencies, labor organizations, and training programs to acquire genetic information pursuant to the offering of health or genetic services, including services offered as part of a wellness program

https://www.genome.gov/pages/policyethics/geneticdiscrimination/crs_gina_and_aca.pdf

Equal Employment Opportunity Commission (EEOC) V Northern Santa Fe Railway Company (settled 2001)

- The company asked for blood samples after about 125 railroad workers had filed reports of work-related carpal tunnel syndrome (CTS)
- Thirty six workers contacted - telling them they had to have a medical exam.
 - Blood was drawn from 22 of the workers and testing was completed on 15 at the time the EEOC sued
 - Employees not asked to consent to the use of blood sample for genetic testing
- The tests were intended to determine which workers might be genetically inclined to develop CTS, allegedly with the hope of denying them workers' compensation benefits

<https://ergoweb.com/genetic-testing-and-carpal-tunnel-syndrome-settlement-final/>

EEOC V Fabricut (settled 2013)

- First lawsuit for a GINA violation
- Fabricut violated GINA and the Americans With Disabilities Act ("ADA")
 - Unlawfully asking a job applicant for her family medical history in a pre-employment, post-job offer medical examination
 - Allegedly rescinding applicant's job offer based on the belief that she had carpal tunnel syndrome

<https://www.eeoc.gov/eeoc/newsroom/release/5-7-13b.cfm>

Assessment Question #3

Which of the following is NOT an example of genetic discrimination?

- A person being asked to provide blood sample for genetic testing to determine if he or she is a poor metabolizer of drugs prior to insurance coverage
- Higher insurance premiums for an individual who tests positive for a specific genetic variation
- An individual being advised to obtain genetic testing after his/her sister and brother is diagnosed with colorectal cancer
- All of the above are examples of genetic discrimination

Justice and Equity in Pharmacogenomics

- The burdens and benefits of new technologies should be shared in an equitable fashion
- An individual's race, economic status, or "draw" in the genetic lottery should not affect the individual's access to medical treatment
- Questions regarding the possibility of pharmacogenomics rectifying or exacerbating the inequalities that exists in today's U.S. health care system

Justice and Equity in Pharmacogenomics

- **Pharmacogenomics stigmatization**
 - Individuals categorized as "difficult to treat" or as "nonresponders"
 - May affect ability to obtain health care access
 - Possible psychological implications on the individual
- **Economic access to the benefits of pharmacogenomics**
 - Will it increase the socioeconomic division?
 - Will drugs be more expensive with premium pricing?
 - Will there be less access to drugs for lower socioeconomic groups?
 - Will Medicaid or private insurance pay for these therapies?

Challenges of Pharmacogenomic Testing Access: Equity and Justice

- **Ensure equal access**
 - Engage patients, providers and policy makers
 - Community health centers
 - Medicaid coverage
- **Modes of dissemination**
 - Media saturation
 - Concentrate information to minority-serving providers
- Communicate benefits in a culturally competent, accessible, and appropriate manner that mitigate concerns about genetic testing

Shields AE. Addiction Science & Clinical Practice. 2001

Challenges of Pharmacogenomic Testing Access: Equity and Justice

- **Provider comfort level**
 - Interpretation of genetics information
 - Incorporation/integration into clinical practice
- **Patient comfort level**
 - Knowledge, attitudes, experiences
 - Trust or mistrust
 - Patient population
 - Low socioeconomic status
 - Minority communities
 - Education level
 - Religion

Shields AE. Addiction Science & Clinical Practice. 2001

Pharmacogenomics and Race

- Self-identified race is inadequate proxy for human genetic heterogeneity
 - Racial heterogeneities mask genetic diversity
 - Should not equate race with genotype
- Focus on race obscures understanding of environment
- Use of race variables increases potential for discrimination and stigmatization

Shields AE. Addiction Science & Clinical Practice. 2001

Assessment Question #4

Equity and justice in the attainment of pharmacogenomics testing may be attained by:

- A. Ensuring providers are knowledgeable about ordering and interpretation of genetic tests
- B. Investment in infrastructure and clinical capacity for healthcare providers to order pharmacogenomics tests
- C. Media saturation to reach people of all socioeconomic positions
- D. All of the above

Summary

- Genetics testing should distinguish between **pharmacogenetics-guided** therapy and testing for **disease susceptibility**
- Informed consent is a crucial component for individuals deciding to participate in clinical research
- The possibility of discrimination and stigmatization associated with pharmacogenomics testing needs to be considered
- Ensure privacy and confidentiality for employment and payer coverage decisions
- Equal access to the benefits of pharmacogenomics testing needs to be addressed by healthcare policies