CASE WESTERN RESERVE UNIVERSITY
SCHOOL OF MEDICINE

Informed Consent and Genetic Research:

Risks, Uncertainty and Genome-Wide Association Studies

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This morning…

Consent Process
- Goals
- Participants
  - Boundaries

GWAS
- What is it?
- How is it different from other research?
- What can it serve as a reminder for good practice?

Genetic Research
- Harms
  - Actual, potential and perceived

The Informed Consent ***Process***

Incorporates research participants' perspectives: values, fears and expectations into the decision to enroll in and continue participation in a research study.

Give information, stress important facts, empower participants to be able to make a choice, and work within a context where there is a huge difference in the knowledge of the parties.

Informed consent and documents usually include:

- Research purpose and procedures
- Potential benefits
- Provisions for confidentiality
- Contacts for additional information
- Additional costs
- Notification of significant new findings
- Voluntary participation and the right to discontinue participation without penalty

- Risks and discomforts
- Alternative procedures or treatment
- Research-related injury
- Unforeseeable risks
- Consequences of discontinuing research participation
- Approximate number of subjects

The relationship: Investigators and Research Subjects

Researchers need subjects to participate

Participants must volunteer

Must understand the choice that is being presented

Both sides need to understand the boundaries

What is GWAS?

Research studies that explore the connections between specific genes (genotype) and their outward expression (phenotype)

Goal is to discover genetic factors that contribute to the development, progression, and treatment of disease

Possible because of technology that allows for quick and accurate analysis of whole genome samples

Requires large numbers to identify statistically significant genetic variations

Points to Consider for IRBs and Institutions
http://grants.nih.gov/grants/gwas/gwas_ptc.pdf
11/29/2007

NIH Policy for sharing GWAS Data:

Who?

NIH Supported or Conducted Genome-Wide Association Studies (effective as of January 25, 2008),

- Data Sharing Plan is part of the grant application and proposal

What?

Policy that creates a database (The **d**ata**b**ase of **G**enotypes and **P**henotypes or "dbGaP"), a repository at the National Center for Biotechnology Information (within the National Library of Medicine)

- Genotype: consists of single nucleotide polymorphisms (SNPs) – between 300,000 to 1 million SNPs per sample
- Phenotype: data on health conditions, behavioral characteristics and measureable or observation traits

NIH Policy for sharing GWAS Data: Institutional and IRB consideration…

Information gathered (SNP pattern) is unique to individuals, vary among ethnic groups, and possible to identify family relationship.

"It is anticipated that technological and analytical capacity available to the public is likely to enhance the feasibility of SNP pattern identification in the future."

Duty to minimize risk to participants, IRBs/Institutions must ensure that 18 identifies outlines in HIPAA are removed, that all data submitted is de-identified and coded, and that "submitting institution" has "no actual knowledge" that remaining information could be used to identify subject (alone or *in combination with other information*)

Points to Consider for IRBs and Institutions 11/29/2007

Database: Process Overview

NIH Funding

IRB reviews protocol

Submitting Institution sends a Certification to the NIH GWAS data repository stating that:

- Data submission is consistent with laws, regulations and policies
- What uses and restrictions are included in consent form
- Participant identities will not be disclosed
- Collection of data was consistent with 45 CFR 46

Database: Process Overview

Request Access to the Data

- Qualified investigators from academic institutions and commercial organization (domestic and foreign)

NIH Data Access Committee (DAC) reviews requests

- Federal staff

Notice of Decision

- Given access instructions and passwords

Data Use Monitoring

- Researchers submit annual data use reports
- DAC monitors data usage and potential issues

GWAS "Points to Consider" regarding Informed Consent

Retrospective Studies:

- Waiver of consent under 45 CFR part 46 does not apply because the NIH GWAS repository does not *involve* human subjects research
- Is the original consent adequate?
  - Broad enough to cover NIH GWAS repository?
  - Specific enough to "inform" subject of this possibility?
    - *Future genetic studies, what data would be shared, condition of data (de-identified), and open regarding storage/entity*

GWAS "Points to Consider" regarding Informed Consent

Prospective Studies:

"From an ethical standpoint, the informed consent process and document should make it clear that participants' DNA will undergo genome-wide analysis and that genotype and phenotype data will be shared for research purposes through the NIH GWAS data repository."

Points to Consider for IRBs and Institutions

11/29/2007

GWAS "Points to Consider" regarding Informed Consent

Scope (permissive and restrictive)

- Genetic research and analysis
- Future use and *broad* sharing of coded phenotype and genotype data for research
- Submission of coded data to a government health research database

Limitations:

- Types of Research?
- Location of Research?
- Types of Medical Condition or Disease Studied?
- Duration of Storage?
- Limitations on Access (only non-commercial researchers)

GWAS "Points to Consider" regarding Informed Consent

Benefits

• Public benefit through the advancement of science

Risks

• Distinguish between genetic (DNA/single gene) and genomic (interaction among genes) research?

  • A tree verses a forest

• Privacy risks (your data will be released to the public, insurers, employers, law enforcement officers

• Security breaches

• Relevant risks to family members

• Relevant risks to identifiable populations or groups?

GWAS "Points to Consider" regarding Informed Consent

Return of Research Results

- Procedures in place to report back to investigator with key/code
- Under what conditions/findings
  - Clinical validation
- Method of contact (institutional website vs. direct contact)
  - Question of scope / boundaries

Privacy and Confidentiality

- Who has the information, what is the level of care/responsibility required

GWAS "Points to Consider" regarding Informed Consent

Withdrawal of Consent

- Who is the contact person?
- What institution?
- What about children who are enrolled who reach the age of maturity?
- Proxy Consent?

- Clear understanding that once data is released from the NIH GWAS Database – it cannot be withdrawn
  - Future or further release of information

GWAS "Points to Consider" regarding Informed Consent

Other Considerations:

- Commercial Use
- Cultural Considerations
  - Consent
  - Stigma
  - Special laws

The challenge

There is a lot of information to considered when designing a protocol, drafting a consent form, and recruiting a research participant into your GWAS study.

The NIH GWAS database is something that must be incorporated into the study

How do we not treat it like an "add on"

Some Suggestions

Separate GWAS study from the discussion of and consent relating to the database

Allow time to discuss

Admit to uncertainty and ignorance

Draft the consent form questions (limitations and scope) with your specific research population in mind

- Values and motivations

More about GWAS…

Best Practices in Genetics Research Meeting

Monday, July 20, 2009
4:30pm—6:00pm
Case Western Reserve University
School of Medicine
Department of Bioethics, TA 200

US Department of Health and Human Services

Genome-Wide Association Studies (GWAS)

Points to Consider for IRBs and Institutions

Thank you

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