D-5 Identifiability/Confidentiality

Ethical Issues Regarding the Potential for Identifiability of Information in a Public Genotype-Phenotype Database

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The objectives of this presentation are to:
- Describe how technological advances are challenging our current ideas about the identifiability of genetic information;
- Discuss how patients’ informational needs in the context of personalized medicine will further exacerbate these challenges; and
- Discuss the acceptability of providing mutation-specific genotype-phenotype information on a public website.

The proliferation of genetic testing provides patients with unprecedented opportunities to learn more about the genetic component of their risk for disease and simultaneously presents the medical community with the challenge of how to communicate information in such a way that is both understood by patients and is personally meaningful. In the near future, our current paradigm of communicating genetic information to patients primarily through genetic counseling will become inadequate to address patients’ informational needs due to workforce limitations and overwhelming demand. Expected advances in the ability to quickly and inexpensively perform whole-genome sequencing will further overwhelm our current capacity to inform patients about their genetic risk in the traditional manner. It is imperative that the scientific community develop alternative methods to communicate complicated genetic information to patients in order to enable broader use of genetic and genomic testing in medical care.

Driven by the need to obtain more information about the 1800 mutations in the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene, the U.S. Cystic Fibrosis Foundation funded the Clinical and Functional Translation of CFTR (CFTR2) project in 2008. CFTR2 represents an international effort to link every reported CFTR mutation with expert-reviewed clinical parameters and when necessary, studies of the functional effects of the mutation. A website to communicate this information to the CF research and patient communities is being developed by the CFTR2 team.

One of the main ethical challenges in the development of the CFTR2 website is the potential for identifiability of individuals in the CFTR2 database. The historical paradigm in which patient information in public health databases is presented in a de-identified manner is not entirely consistent with the goals of this type of genotype-phenotype database and may not be possible in the context of rare mutations. For example, within the current CFTR2 database, 502 different CFTR mutations are seen in five or fewer patients, and 249 of these are seen in only one individual worldwide. Consequently, information about these individuals on a publicly available database could potentially be identifiable. The proliferation of online patient communities dedicated to specific diseases demonstrates that the informational needs of these patients are not being met currently. These online patient communities are being used by patients, and in the case of CF, patient family members, to seek others who share the same mutation or combination of mutations, to learn additional mutation-specific information. These online exchanges are not being mediated by the medical community to ensure the accuracy of information. It is vital that resources be made available to provide patients and their families with accurate mutation-specific information. The goal is to do this in an ethically responsible manner.
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The Use and Understanding of Certificates of Confidentiality

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Researchers and institutions are ethically and legally obligated to safeguard research participants’ privacy and the confidentiality of their data. Indeed, the success of the research enterprise depends on the public’s confidence that private information will be vigorously protected. Certificates of Confidentiality, authorized by federal law, are an important tool for meeting this expectation. By shielding researchers and institutions from forced disclosure of identifying data in any legal proceeding, Certificates are intended to facilitate participation by reassuring prospective participants about the security of their information and thus allow research to proceed on sensitive topics critical to the public’s health. In fact, Certificates are commonly believed to offer near absolute privacy protection. Their use has recently been promoted in the context of burgeoning efforts to build large-scale research platforms (such as biobanks) and requirements for an unprecedented degree of data sharing.

There is, however, a remarkable paucity of evidence upon which to base conclusions about the strength of the protection Certificates afford. A case that reached the North Carolina Court of Appeals suggests that the full legal effect of a Certificate is unclear. Limited empirical data are available concerning when, why, and how Certificates are used, including stakeholders’ understanding of the protection they provide and how that affects their assessment of research risk. The perceptions of institutional stakeholders, including IRB chairs and institutional legal counsel, are particularly important given the central role they play in developing and implementing policies and practices for recommending or requiring that a Certificate be obtained.

To better understand these issues, we are conducting a multi-faceted study with funding from an NIH R01. In this session, we will present our findings from a survey we are conducting of IRB chairs (n=580) at US research institutions to examine their (i) knowledge and opinions of Certificates and the protections they provide; (ii) institutional policies concerning the use of Certificates; (iii) the role Certificates play in assessments of risk; and (iv) their institution’s experiences with attempts to compel disclosure of identifiable research data.

At the conclusion of this session, attendees will be able to:

1. Describe the role of Certificates in protecting research participants
2. Discuss available data concerning IRB perceptions, policies, and experiences with Certificates
3. Identify critical considerations for the development of policies to address the strengths and limitations of the protections Certificates provide

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3 Beskow LM, Dame L, Costello EJ. Certificates of Confidentiality and compelled disclosure of data. Science 2008; 322(5904): 1054-5 [PMC2694567].
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Non-welfare interests in the uses of de-identified materials

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Most discussion of the ethical challenges raised by the growth of research biobanks relies on the assumption that the only ethically relevant interests are those that concern risks to subjects’ welfare or well-being. Once materials have been collected, and any further risks have been reduced to near-zero by de-identification, it follows that no further protection of the interests of research subjects is required.

The history of US research subject protections encourages this assumption. Starting with the Belmont Report, the ethical protection of human subjects has centered almost exclusively on protection against risk. This emphasis is reflected in the rules determining when research is exempt from US Federal regulation, or is eligible for expedited review. It is also reflected in the rules governing the use of less-stringent informed consent processes, when the research involves no more than “minimal risk.” These features of US research protections have led a number of commentators to argue that research on de-identified archived materials is exempt from Federal regulation, a conclusion that the US Office of Human Research Protections accepts. Other ethical codes, like the Declaration of Helsinki, make similar assumptions.

Regardless of the history or scope of existing regulations, as an ethical matter it is highly debatable whether personal risk is the only kind of interest requiring ethical respect and protection. As Allen Buchanan has pointed out, people may have a variety of interests in the purposes or the implications of research making use of materials that they have contributed.

In this presentation, I will explore three questions with regard to non-welfare interests. First, what’s the evidence that people have these interests in research uses of biological materials, or that they affect their willingness to contribute to biobanks? The evidence will turn out to be spotty and inconclusive, on both counts. Second, what’s the moral weight of such interests? If we have a duty to accommodate them, is it for pragmatic, or for principled reasons? And third, if we should accommodate them, how should we do so? I will use the example of complicity in research some contributors might find morally objectionable to explore the second and third questions in some depth.

Objectives:

1. Appreciate the nature and ethical relevance of “non-welfare” interests.
2. Understand the importance of the distinction between pragmatic and principles reasons for accommodating these interests.
3. Understand how a close ethical analysis of the nature of such interests can guide biobank policies.
Public opinion and deliberation about ethical issues in genetic testing: Comparing qualitative, quantitative and elite views

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As the public debates ethical and policy issues in genetic testing and research, how will those opinions change? This question is addressed through a large-scale study of public opinion and deliberation by the American public. The sample was assigned randomly to one of three groups: group one deliberates in synchronous electronic focus groups on-line on three separate occasions (N= 1824) and answers surveys at baseline, before and after discussion, and at the end of project; group two responds to all the surveys but does not deliberate (N=398); group three answers surveys at baseline and end-of-project only (N=1532).

Five broad issues were assessed in the surveys and were discussed in the deliberative groups under the direction of moderators. These issues were selected by an elite panel of advisors and included: the duty to warn; biobanking; genetic discrimination; direct to consumer genetic testing (DTCGT); and personalized medicine.

The nationally representative core sample included 3210 people at baseline with an oversample of African Americans (N=544) for a total sample (N=3754) at baseline. The sample was 55% female, 46 years of age on average, 7% Hispanic, 20% African-American, and 27% with a HS education or less. Those assigned to the group discussions were allocated randomly to one of 60 groups which met on three occasions for about an hour to discuss topics through created scenarios. All textual exchanges were captured and stored for later evaluation.

Three broad types of responses are compared: survey responses to policy opinions in three topical areas (biobanking; direct to consumer testing; duty to warn); qualitative responses revealed in participants’ comments in discussion; and elite opinion on the same topics as revealed in published reports from research groups, courts, and commissions. Survey responses are compared from baseline to post-discussion to assess change in policy opinions after exposure to a range of online opinion relative to changes in persons that do not discuss. Qualitative description of themes supplements quantitative responses. Elite opinions are employed as interpretive guides allowing evaluation of the direction of opinion change.

Results cannot be summarized here but three broad trends have emerged: control over one’s own genetic data, mistrust of commercial entities, and the preference for more rather than fewer options even when risks are present. In the DTCA scenario, people believe that the availability of online genetic tests is a good idea (M=3.65, SD=1.30) but that it is also risky (M=3.94, SD=0.86). These findings are consistent with concerns raised by various expert groups.

Learning objectives: (1) What opinions and reasons do the public at large hold regarding public policies and ethical concerns for duty to warn, biobanking and direct to consumer genetic testing? (2) Do these opinions change when people are exposed to diverse opinions from those not expert in comparison to those not exposed? (3) When change is observed, is the direction of change toward greater “collective intelligence” – that is toward that of experts’ opinions – or not?