Applied & Translational Genomics 3 (2014) 111–115

Contents lists available at ScienceDirect

Applied & Translational Genomics

journal homepage: www.elsevier.com/locate/atg

Review

Genomic knowledge sharing: A review of the ethical and legal issues

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ARTICLE INFO

Keywords:
Genomic information
"Big data"
Confidentiality
Discrimination
Informed consent
Duty to warn

ABSTRACT

The importance of genomic information for care of individual patients and for the development of knowledge about treatment efficacy is becoming increasingly apparent. This information is probabilistic and involves the use of large data sets to increase the likelihood of detecting low frequency events. Duties and rights of patients with respect to this information have been much discussed, including informed consent to the use of individual information, privacy and confidentiality, rights to know or not to know, and individual ownership of information about themselves. But this is only one side of the information equation. On the other side of the equation are duties of information holders: malpractice and duties to warn, responsibilities of data stewardship, intellectual property and ownership, reciprocity, and justice. This article argues that if we take duties of patients to share information seriously, we must also consider duties on the part of information holders about how they protect and use information.

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The importance of genomic information for patient care is increasingly apparent (Institute of Medicine, 2012). Genomic information may be helpful in assessing the likelihood and possible extent of therapeutic response, the possibility of treatment side effects, the risks of drug–drug interactions in a particular patient, and the need to monitor for disease prevention, among other factors. Much of the use of genomic information is probabilistic at best—that is, information about a person's genome, when combined with other information, is predictive but not determinative of therapeutic outcomes. And genomic information has one feature that at least some other forms of individually identifiable health information do not: information about one individual may also convey at least probabilistic information about their genetic relatives. These features of genomic information raise many legal and ethical issues.

Genomic information is initially information about a particular individual's genetic or epigenetic makeup. Thus understood, it raises problems of informed consent to the use of individual information, privacy and confidentiality, rights to know or not to know, and ownership, among other issues. Many of these issues have been much discussed and are familiar.

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http://dx.doi.org/10.1016/j.atg.2014.09.003

Less discussed, by contrast, are the legal and ethical issues raised by the probabilistic nature of much genomic information. Information about an individual's genomic makeup, by itself, rarely yields definitive diagnostic or prognostic information. Cases of the known significance of a single gene—such as the CAG repeats in the HTT gene on chromosome 4 present in Huntington's disease—are rare. Even in such cases, moreover, some of what is known is probabilistic: the number of CAG repeats, for example, is associated with age of disease onset. As genomic medicine is developing today, large data sets establishing correlations between particular genomic features are needed for understanding the possible significance of any individual's genomic characteristics. This probabilistic nature of genetic information raises significant ethical and legal questions on the other side of the information equation: not the patient side, but the information-holder side. These ethical and legal issues, including malpractice and duties to warn, responsibilities of data stewardship, intellectual property and ownership, reciprocity, and justice are much less recognized but no less critical.

1. Genomic information about individuals

As pointed out above, much has been written about the ethical and legal issues raised by genomic information about individuals. This review presents a brief summary of these issues. Although the topics are relatively familiar, understanding them is important both for patient care and for appreciation of the ethical and legal problems on the other side of the information equation. The import of genetic information for individuals gives rise to reciprocal obligations, or so this article contends.

1.1. Genetic information and identifiability

As a preliminary matter, several points about the individual identifiability of genetic information are important to set out. The presence of a particular genetic sequence does not, in the absence of accompanying information, identify an individual. Under the HIPAA privacy rule for the protection of individually identifiable health information, genetic information does not contain any of the first seventeen factors listed for safe harbor de-identification: patient's name, address, telephone number, various dates, Social Security number and other numbers identifying accounts, device serial numbers, photographic images, biometric identifiers, and other similar identifying information (Anon, 2014a). Only the final listed factor for safe harbor de-identification applies directly to genomic information—"any other unique identifying number, characteristic, or code"—in cases in which genetic information is a unique identifying characteristic. By itself, a single nucleotide polymorphism is not unique to a particular individual; however, in combination with other publicly available information about the individual genomic information may permit identification (Gymrek et al., 2013). Such risks of re-identification depend on what other information is publicly available; for example, Gymrek et al. (Gymrek et al., 2013) used information in recreational genetic databases and online search engines such as PeopleFinder to achieve re-identification. Importantly, these strategies can also be used to identify individuals through information from very remote, unknown relatives.

1.2. Informed consent

When individuals provide information about themselves for medical treatment, including for a genetic test, the parameters of informed consent are relatively clear. Individuals can be told what uses of their information are contemplated; standard notices of privacy practices inform patients that their information may be used for treatment, payment, or health care operations. For much information collected in treatment, however, the possibility of future use in research has not been included explicitly in any consent process, thus posing the question of the permissibility of later research use. Because large sets of data may be necessary to identify the significance of low-frequency genomic variants, this problem can be expected to persist. One work-around has been to permit the research use of information that has been de-identified or that has been stripped of sufficient identifiers to qualify as a HIPAA limited data set (Anon, 2014b).

Re-use of information originally collected in research raises related issues. One recent study concludes that although almost 90% of participants in an NIH-funded genetics research were willing to allow the submission of their data in de-identified form to dbGaP, the database of genotypes and phenotypes at NIH (dbGaP, n. d), over two-thirds of them also wanted the researchers to ask their permission (Ludman et al., 2010).

As discussed above, genomic information may not be sufficiently de-identifiable to facilitate the work-around of stripping out identifiers. To allow the use of identifiable information in research, the Advanced Notice of Proposed Rule-Making (ANPRM) for revisions to current human subjects research protections published by HHS in 2011, would allow general consent to any future use of data in research (Anon, 2011). The ANPRM did, however, also suggests that especially sensitive research such as stem cell research or research about reproduction might require more explicit consent. Genetic information, because of its implications for others, may raise questions about the need for explicit consent. At the same time, it may be difficult to anticipate in advance what uses of genomic information might be desirable or what their risks might be. If so, it will need to be argued that sufficiently broad consent still may be informed consent (Sheehan, 2011).

The NIH Genomic Data Sharing Policy, issued August 27, 2014 (National Institutes of Health, 2014), requires all NIH-funded research generating large-scale human (and non-human) genomic data to be submitted to NIH. Data are to be de-identified in accord with the rules governing research with human subjects and the HIPAA Privacy Rule. For studies initiated, specimens collected, or cell lines created after the effective date of the Policy, NIH expects investigators to obtain consent for subsequent data use and broad data sharing. These consents must explain whether data will be shared through unrestricted or controlled-access repositories. For studies, specimens, or cell lines antedating the Policy, NIH requires investigators to consult with their IRB or relevant privacy board to determine what sharing is consistent with consents and to indicate any required limits when data are submitted to NIH. The Policy's encouragement of consent to broad data sharing can be expected to place additional pressure on the responsibilities of data-holders discussed below.

1.3. Privacy and confidentiality

Privacy protects individuals from unwarranted access to the person; confidentiality protects information about the person from unwanted use or disclosure. Both have been thought to raise special issues regarding genomic information. That genetic information about one person can be used to infer information about genetic relatives poses the privacy-like concern that information may be gleaned about individuals without direct access to them or even their knowledge. In part because of what may be exaggerated beliefs about its predictive power, genetic information has also been thought to be especially risky. These concerns led to the federal statute giving special protection from discrimination on the basis of genetic information in employment and health insurance, the Genetic Information Non-Discrimination Act (Prince and Berkman, 2012).

Such genetic exceptionalism may be unwarranted, however (Rothstein, 2008). Other health information—such as diagnoses of infectious diseases—may be at least as and potentially more risky and stigmatizing than genetic information. Although genetic information may seem unique in its possible implications for relatives, other health information such as a household member's exposure to toxins may also reveal information about relatives. That there is reason to question genetic exceptionalism, however, does not abate the potential risks to