Applied & Translational Genomics 3 (2014) 23–29

Contents lists available at ScienceDirect

Applied & Translational Genomics

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

Rare disease research: Breaking the privacy barrier

Deborah Mascalzoni [a,*], Angelo Paradiso [b,c,1], Matts Hansson [a]

[a] Centre for Research Ethics & Bioethics (CRB), Uppsala University, Box 564, SE-751 22 Uppsala, Sweden
[b] Direttore Scientifico Istituto Oncologico-Bari, Italy
[c] Direttore Laboratorio Oncologia Sperimentale Clinica Istituto Oncologico-Bari, Italy

ARTICLE INFO

Article history:
Received 8 January 2014
Received in revised form 20 February 2014
Accepted 2 April 2014

Keywords:
Privacy
Research barriers
Informed consent
Private sphere

ABSTRACT

Due to the few patients affected, rare disease research has to count on international registries to exist in order to produce significant research outputs. Data sharing of registries is therefore a unique resource to allow rare disease research to flourish and any lost data will jeopardize the quality of an already extremely difficult research. The rules usually applied to research such as the right to withdraw or the need for specific consent for every use of data can be detrimental in order to get effective results. Privacy rights regulated through traditional informed consent mechanisms have been regarded as a major barrier in order to effectively share data worldwide. Some authors argue that this barrier hampers results that could be beneficial to the patients so that another right will be overstated: the right to quality healthcare. We argue in this paper that privacy has been often interpreted just one-sided as the right to secrecy but it can entail another meaning: the right to manage one's own private sphere. Managing it pertains, not only to the right to deny access, but also to the right to grant access. At the same time research on patient participation and transparency shows that new forms of IT-based informed consent can provide a good balance between the right of individuals to be in control of their data and the opportunity for science to pursue international research.

1. Introduction

The role of genomics in medicine is rapidly and pervasively increasing. Genomics promises many ambitious developments, including personalized and precision medicine, and tailored drugs. Genomics knowledge is full of promise for the development of targeted therapies in rare diseases. In terms of policy, the integration of genomics in health is pervasive, so much so that the Centers for Disease Control and Prevention (CDC) states that genomics plays a role in nine of the ten leading causes of death in the United States and that it foresees the "integration of genomics into pediatric primary care and into public health practices such as screening programs designed on the basis of the genetic likelihood to develop certain diseases (Center for Disease Control and Prevention, 2013)" Genomic research also forms the basis for precision medicine, and is thus important for our understanding of rare diseases. Recent advances in genotyping and sequencing have led to a steep drop in the costs of genome scanning. The introduction of next-generation sequencing and whole genome sequencing has also led to more accurate, precise, and defined procedural outcomes. This accuracy may be used to develop a clinical understanding of what used to be known as general "research results." Biobank infrastructures are commonplace in many hospitals, and large research biobanks have also been created. All these rapid developments in genomics were made possible by huge international efforts to find effective ways to collaborate and share data, samples and technologies. Genomic results are, in fact, based on collections of data that made genome-wide association studies possible. Large data collections are necessary in order to ensure statistical significance, and to create international consortia for data sharing. The European Commission has acknowledged this necessity by supporting research consortia through substantial grants.

Rare 'orphan' disease, or diseases that are either life-threatening or chronically debilitating, affect a very small percentage of the population. Rare diseases are challenging subjects of research, in that there are very few cases upon which researchers may draw conclusions (sometimes fewer than 100 cases in the world). In the United States, a disease is considered rare if it is believed to affect fewer than 200,000 Americans. Conventional levels of statistical precision are unlikely to be met if a trial is required to evaluate treatment of a rare disease. In order to obtain a sample size of statistical significance, researchers often use data from patients in foreign countries. The very existence of rare disease research requires international collaboration and the movement of samples and data across national borders. Although genomic research is full of promise, the need for large data sets will ensure that certain types of genomic research will be difficult to perform. In point of fact, research in rare disease is extremely difficult due to the limited availability of cases.

* Corresponding author. Tel.: +46 18 471 62 32.
E-mail addresses: deborah.mascalzoni@crb.uu.se (D. Mascalzoni), a.paradiso@oncologico.bari.it (A. Paradiso), Matts.hannson@crb.uu.se (M. Hansson).
[1] Tel.: +39 080 555561 0; fax: +39 080 555560.

http://dx.doi.org/10.1016/j.atg.2014.04.003

Rare disease research depends on international registries, since no one registry will house the requisite amount of affected persons to sustain a trial. The sharing of data registries is a unique resource that allows rare disease research to exist. That being said, medical research on biobanks and registries is only as good as the data it uses; lost data will jeopardize the quality of an already difficult research endeavor. To jeopardize genomic research in this way would engender serious consequences for patients with rare diseases, who would not be able to benefit from research results. Consequently, the application of certain research rules (such as the possibility of withdrawal or the need for specific consent) to rare disease research can be highly detrimental. This fact has also been recognized by the European Commission, which requires all member states to have a national research plan for rare diseases in place (Council of Europe, 2009).

The need for extensive data sharing has profound implications for privacy regulation and for personal data management. The proposed use of a unique identifier for research in rare disease (i.e., an identifier code that is applied to subject data and is shared by all researchers working on that same data) has opened up new questions about security, specifically concerning the chances of re-identification born from cross-matching data from different research centers. The Office of Rare Diseases Research at the National Institute of Health (NIH) has launched a pilot project to establish the Global Rare Disease Patient Registry and Data Repository (GRDR) (NIH Office of Rare Diseases Research, 2012). The goal of this registry is to establish a data repository for de-identified patient data, which will be aggregated using Common Data Elements (CDEs) and standardized terminology. This data (which will be available to all investigators) will enable the analysis of many rare diseases, and will facilitate various biomedical studies (including clinical trials) to develop drugs and therapeutics, thereby improving the healthcare and quality of life of many millions of people. De-identification of patient data will also utilize the Global Unique Identifiers (GUID) system, which can link patient data to biospecimen data sets (NIH Office of Rare Diseases, 2012).

The protection of personal data has been a major concern in genomic research. Evolving privacy regulations and existing legal frameworks have already had an important impact on research and its future development. Loss of confidential data may negatively affect participants in research studies. Health data are considered especially sensitive, and as a result, severe restrictions are imposed on researchers and investigators. E-commerce and banking regulations, for example, are often applied to research data, the better to create a safe environment for sensitive data. However, these regulations end up creating strict and unspecific privacy rules that, in the context of rare disease, may detrimentally impact the use of the limited data that is currently available for research. It is therefore critical to understand the role of privacy as a personal right, and to analyze privacy in the context of other rights by assessing its impact on individuals, families and society.

2. Discussion: privacy as a barrier to quality research

Biobanks and medical registries with aggregated clinical data are vital to the development of higher standards of medical diagnosis and personalized treatments. The rapid development of pharmacogenomics underscores the need for these infrastructures as stable libraries for new and future developments. These infrastructures have been heavily criticized as constituting a great risk to individual and family genetic privacy. Privacy has been identified as "The Issue" around which researchers have assessed the ethical and legal dimensions of data and sample collection. Privacy has therefore played a dominant role in the regulation of biobanks and registries, and has been the focus of many restrictions; as such, privacy has often been conceived of as a barrier to research and development (Mascalzoni et al., 2013; Hansson et al., 2013). Many countries have enacted regulations that require specific consent for the use of data in research. LIBE hopes to change a current EU proposal by introducing an exception that would prohibit secondary use of existing data without explicit consent (Mascalzoni et al., 2013). This exception could drastically reduce researchers' reliance on existing resources, which were, in large, collected in the past under the purview of different regulations. It is well known that re-consent (even when possible and practical) results in loss of participation — a huge cost to research efforts.

Privacy has often been regarded as the capacity to identify a person using his or her own data. The power of genetics to identify research subjects has played a significant role in discussions on privacy. In this context, privacy entails the protection of a person's identity (and, therefore, his or her dignity) in relation to his or her health and genetic data.

This paper considers a broader conception of privacy, as it relates to individuals and groups in the private sphere. Mainstream interpretations of privacy (which have been privileged through regulation) regard privacy as a "secret area," in which personal data and data-flow techniques are protected to ensure anonymity.

This paper demonstrates that privacy is, indeed, a large concept, and that even if privacy is heavily associated with secrecy, it entails a broader area of significance that includes the personal sphere and its management. Not only does privacy management imply a negative personal right to non-interference (such as limiting undesired access and making personal information secret) but it also implies a positive right to determine and manage personal information, and to actively have a say in one's own private sphere (Hansson, 2008).

2.1. Privacy regulations

Soft law provisions, professional codes of conduct and legislation constitute the normative patchwork that guides scientific discovery. Striking a balance can be difficult; moreover, scientific development has revealed dilemmas that existing regulations are unable to solve.

The balance between freedom of research and protection of research participants has been difficult to achieve. In the context of genomic research, privacy is a major issue. Although privacy is recognized as a human right (Council of Europe, 2006; Unesco 2003), it is important to acknowledge that privacy is not absolute, and that it needs to be evaluated and balanced against constitutional rights.

The Convention on Human Rights and Biomedicine is a European cornerstone (Council of Europe, 1997a). The aim of this Convention is the protection of dignity and human rights in relation to biomedicine. The Convention sets forth the norms for the conduct of ethical and legally-sound research. Article 10 of the Convention states that: "everyone has the right to respect for private life in relation to information about his or her health," and that "everyone is entitled to know any information collected about his or her health". Article 5 states that a medical intervention may only be carried out if the subject gives his or her free and informed consent, and is also given the right to withdraw his or her consent. Recently, certain authors have criticized these restrictions (Hansson, 2012) as hampering the scope of Article 3 of the Convention, which enshrines a right to "equitable access to health care of appropriate quality."

Privacy provisions, if applied literally, would severely hamper research efforts and prevent patients from enjoying good-quality standards of healthcare. Poor-quality diagnostic tests and treatments can be harmful to patients, and thus can violate the primary medical ethical principle of "do no harm." In practice, balancing medical benefits and privacy risks is inherently as well as situationally complex. Quality is not only a normative requirement in health care, but also a necessary condition for the prevention of harm and for the development of preventative and diagnostic treatments. Quality assurances have an intrinsic value in the implementation of the right to health care (Hansson, 2012). This principle is recognized in Article 12(a) of the 1997 Universal Declaration on the Human Genome and Human Rights, and underscores the need for shared benefits in research: "[b]enefits from advances in biology, genetics and medicine, concerning the