European Review for Medical and Pharmacological Sciences 2015; 19: 4182-4186

Ethical governance in biobanks linked to electronic health records

L. CAENAZZO[1], P. TOZZO[1], A. BOROVECKI[2]

Department of Molecular Medicine, Clinical Bioethics Laboratory, University of Padova, Padova, Italy
Department of Social Medicine and Organisation of Health Care, University of Zagreb, Zagreb, Croatia

Abstract. – In the last years an alternative to traditional research projects conducted with patients has emerged: it is represented by the pairing of different type of disease biobanks specimens with Electronic Health Records (EHRs).

Even if informed consent remains one of the most contested issues of biobank policy, other ethical challenges still require careful attention, given that additional issues are related to the use of EHRs.

In this new way of doing research harmonization of governance is essential in practice, with the aim to make the most use of resources at our disposal, and sharing of samples and data among researchers under common policies regulating the distribution and the use.

A biobank-specific Ethics Committee could be seen as a new and type of Ethics Committee, that we suggest to be applied to each biobank, with possible different functions.

In particular, considering the possible use of electronic health record data linked to biological specimens in biobanking research, this specific Ethics Committee could draft best practice and ethical guidelines for the utilisation of the EHRs as a tool for genetic research, addressing concerns on accessibility, return of results and privacy and help to educate patients and healthcare providers.

Key Words:
Ethics Committee, Biobanks, Clinical research governance, HERs.

Introduction

Biobanking, the organised collection of biological samples and associated data, ranges from small collections of samples in academic or hospital settings to large-scale national repositories.

Different approaches to regulations of biobanks have appeared both at the national and international levels, sometimes through specific legally binding instruments or by general regulatory texts. Over the years, new questions, difficulties and solutions have appeared. The result is that there is lack of clarity and uniformity in biobank regulation and consideration of this confusing literature and procedures may be difficult to understand.

Nonetheless, it is reductive, on first view, to try to capture in a single term a reality so varied: small and vast collections, managed by private entities and public bodies, containing tumors, tissue, blood, plasma and other forms of DNA. In fact, the term biobank is not yet entirely universal.

Some prefer to talk about "biolibraries", others, such as the French legislature, of "biological sample collections", others still prefer to talk about "biological resource centers" (BRCs) or "specimen banks". Other designations include "genetic databases" or "human genetic research databases" (used by the OECD), "virtual biobanks" (the Human Genome Organisation and the Institute for Genomic Research), "biorepositories" (OECD, International Society for Biological and Environmental Repositories), "tissue banks", "gene banks", and "registries". These examples show just how varied the terminology is and how unbridled the semantic imagination of those involved[1].

However in general terms, a biobank has the following characteristics and elements: an infrastructure (that is, a place and equipment) managed by a public or private body, the accumulation in an organized fashion and over a period of time of biological samples (cells, tissue, urine, genes, or DNA or RNA fragments) and data (clinical information about patients and their families, or even populations, genealogical or biological data, lifestyle information, etc.), for the purpose of medical research.

Corresponding Author: Luciana Caenazzo, MD; e-mail: luciana.caenazzo@unipd.it

A biobank is composed of biological specimens and of the information related to the specimens and their sources. Individual or patient information is part of the biobank and has the same relevance as the tissue sample and for this reason collection of information should be accurate and complete.

In the last years an alternative to traditional research projects conducted with patients has emerged: it is represented by the pairing of different type of disease biobanks specimens with electronic medical/health records (EMRs/EHRs), for example the Electronic Medical Records and Genomics (eMERGE) network[2], the Vanderbilt Electronic Systems for Pharmacogeomic Assessment (VESPA) Project[3] and the Estonian Biobank, that was the first country to implement a nationwide electronic health records system for all citizens[4,5]. In these models of research, a healthcare facility collects biological samples of patients (as indicated above) for research and stores them in a biobank, maintaining a linkage between the sample and the patient's EHR data, that constitute the primary source of phenotypic information.

Incorporating health information from participant in Biobanking research aids in correlating phenotypic information with genetic data and environmental data.

The advantages of collecting EHRs related to genomic information stored in biobanks are costeffctiveness and the potential to reuse genetic and phenotypic information collected during a patient's lifespan, beyond the original study. This is particularly true for dense genetic data such as thosegenerated through genome-wide association studies or large-scale sequencing data[6].

Biobanking Governance

Although biobanking is not new, what distinguishes the present from the past is that the general scientific context has changed, and the scale of biobanking activities, both in terms of the quantity of samples and data, as well as the range of disease areas and institutions now involved in biobanking have increased considerably, especially with the emergence of EHRs-linked biobanks. The other significant change is that these collections are being configured so that they can be used as a resource for the whole scientific community.

In these last years the importance of biobanks is testified by the great increase, in the scientific literature, of papers that consider new applications, new research in both public and private contexts, and new ethical challenges in biobanking[7,8].

Even if informed consent remains one of the most contested issues of biobank policy[9], other ethical challenges still require careful attention, given that additional issues are related to the use of EHRs: these include the protection of vulnerable subjects, the safeguarding of privacy, the communication of research results to donors, the conflicts over patenting, the access, the need for open science, the rights of donors to retain a property claim or control over their samples and data. In particular it is necessary to pay attention to the management of healthcare information collected from patients in different research projects[10,11] that can overwhelm the original purpose of the research and the related informed consent. Furthermore, the ethical policy has to take in consideration the fact that some patient's EHR data are collected for healthcare purposes, without specific informed consent.

Biobanking enables a new way of doing research: research projects are now frequently global, involving international teams, cross-border networks of expertise, members of international scientific societies belonging to different institutions around the world, which pool and share samples and data; this is crucial in order to make investigations more robust, more targeted, and more economical. The use of EHRs related to biobanks may enable this new way of doing research, and it could benefit from the creation of teams for phenotyping and genetic data analysis, facilitating communication and spread of expertise among research teams.

In this new way of doing research harmonization of governance is essential in practice, with the aim to make the most use of resources at our disposal, and the sharing of samples and data among researchers under common policies regulating the distribution and the use. Furthermore governance harmonization among different biobanks in different countries could ensure an equal protection of autonomy, dignity and fundamental rights of patients and research participants, helping researchers in their activity and ensuring a flexible framework that should not be an obstacle for the technical progress of the biobank, and offering to all communities the opportunity to benefit from the results obtained. Governance harmonization could guarantee access controls and security measures in order to avoid breach of partecipants' privacy and the risk of stigmatization of specific groups.

For these reasons biobank harmonization has become a key issue in the field of biobanking, both in terms of regulation and governance, with respect to peculiar challenges of EHRs-related biobank.

In response to biobanks challenges, different regulation and governance mechanisms have been proposed and adopted across Europe, and a great effort has been made to achieve governance harmonization and standardization of regulation in the European context, as shown in different European projects[12,13]. In general, regulation applies to the formal structures of law and legally constituted regulatory bodies. In the specific field of biobanking, it may be difficult to achieve absolute standardization of regulating legal instruments, given the great variability of national regulatory frameworks, which are often fragmented. Furthermore, research practices in different medical areas could be different. All these factors may cause conflicts between a necessary level of diversity in ethical positions and an indispensable common base of principles and procedures to manage these issues in order to harmonize the procedures. A European legal instrument covering clearly the requirements for biobanking is difficult to attain and diversity among Countries in the regulation of biobanks still remain[14-16]. For example there are different national requirement of samples and data across borders which creates difficulties when samples and data must be shared within international biobanks consortia, researchers face with different levels of accessibility among countries, with the risk of multiple applications for the same research project to different regulatory institutions[17].

Rather than regulation, governance should be considered as an overarching concept that includes regulation and also less constructed mechanisms that indicate behavioral norms. For harmonization in governance, there is an urgent need of an evaluation of existing governance systems to see how they should be modified, adapted or improved to accommodate, among biobanks, the different research practices. The purpose of this harmonization is obtaining comparable results and sharing useful biological samples and data, maximizing the use, productivity, and value of biobanks.

New ethical issues coming into the biobanking debate concern the responsibilities and role of custodians of the biobank in relation to research participants and other stakeholders, the kinds of ownership rights that exist over the samples, the development of a fair and equitable system of access for researchers wishing to use the biobanks and the benefits of shared results[7].

In this context, the development of ethical guidelines and a systematic involvement of Ethics Committees – which should be networked – could be useful instruments to address and discuss new kind of ethical issues, rarely encountered and so far applied only in the Ethics Committees of big national biobanks, such as the UK Biobank EGC (Ethics and Governance Council)[18].

Biobanks and Ethics Committees

Governance has emerged as a prime principle in the role of different types of Ethics Committees when it comes to biobanking practices.

Ethics Committees have been permanent fixture of healthcare provision during the last three decades.

The function and the purpose of the research Ethics Committee is to ensure that the research is designed in conformity to relevant ethical standards. However, it also has the task of assessing the adequacy of the design of the study reviewed[19].

The healthcare Ethics Committee (HEC) or clinical Ethics Committee or hospital Ethics Committee deals with making treatment decisions. HECs are usually not required by the law, and they are composed of individuals from different backgrounds with different professional perspectives and experiences who come together and discuss problematic issues involving conflicting values in clinical settings. In general, healthcare Ethics Committees have three functions: education, case review and recommendation or formation of policies and guidelines[20,21].

Another type of Ethics Committee is represented National Bioethics Committees, which are governmental bodies usually formed by the governments according to specific legal requirements. Their main function is to issue recommendations and opinions on specific ethical issues, to participate in the drafting of legal provisions and to encourage and participate in public debate on current bioethical issues. Their recommendations are usually not binding, but rather of a consultatory nature[22].

The great variability of types of biobanks raises different issues for different types of Ethics Committees.

National Bioethics Committees could be essential in drafting general biobanking regulation

and National biobanks guidelines and their opinion could be of paramount importance, in absence of legal standards, as referring statement of soft law, meaning a normative instrument "weaker" than the binding force of the traditional law.

The functions of a healthcare Ethics Committee may be of importance in writing ethical guidelines establishing rules and procedures and in discussing particularly complex cases involved in biobanking management, for example particular donors' requests on withdrawal of consent or samples, on the management of left over tissues from diagnostic or therapeutic procedures or tissues procured form deceased individuals, and communicating these guidelines both to healthcare professionals and patients.

Finally, when it comes to biobanking, it may be important, especially for biobanks with a large number of data samples, to establish their own Ethics Committee. A good biobank Ethics Committee should embody all of the functions of a healthcare Ethics Committee, research Ehics Committee and national bioethics committee as a sort of a mixed type Ethics Committee.

A biobank-specific Ethics Committee could be seen as a new and type of Ethics Committee, different from the three type of currently existing Ethics Committee that are: research Ethics Committee, healthcare Ethics Committee and national bioethics committee. McHale has called it "specialist ethics or ethics and governance committee", for the first time referring to the UK biobank project, as an independent guardian of the frameworks and legal instruments that safeguard the project of UK Biobank. We suggest this type of Ethics Committee to be applied to each biobank, with possible different functions. It may monitor and the inform the public about the research done and functioning of the biobank; it could be useful in fostering interests of research participants, giving approval for data exchange and transfer, revising guidelines and working frameworks, if needed, regarding recruitment access or handling complaints. Another function of this new Ethics Committee could be monitoring and managing the collaboration between public and private biobanks, with the purpose to guarantee equitable access to genome-related EHRs. Finally, one of its functions stands on its own and this is the function of governance in a specific scope of that specific biobank[23]. The composition of this Ethics Committee can not be separated by the presence of essential figures such as the biobank's director, the ethics consultant, the patients' and researchers' representative, the epidemiologist.

With the widespread use of electronic health records linked to biological specimens in health care, the biobank Ethics Committee could draft best practice and ethical guidelines for the utilisation of the EHRs as a tool for genetic research, addressing concerns on accessibility, return of results and privacy and help in educate patients and healthcare providers. Furthermore, bioethics committee could be useful in providing ethically oriented strategies for combining consent to research with the management of access to EHR.

It is clear that depending on the type of biobank being developed the Ethics Committee may have different functions and tasks. In certain cases it may be more of a research Ethics Committee, or may be more similar to a health care Ethics Committee. Depending on the national level of biobank organization, it may have tasks similar to a national bioethics committee but still retain its primary function.

Conclusions

A biobank-specific Ethics Committee could be applied to each biobank with possible different functions and tasks in relation to the type of biobank. In particular, considering the possible use of electronic health record data linked to biological specimens in biobanking research, this specific Ethics Committee could draft best practice and ethical guidelines for the utilization of the EHRs as a tool for genetic research, addressing concerns on accessibility, return of results and privacy and help in educate patients and healthcare providers.

Specific focus groups within these committee should be aware of the specific incoming organizational, ethical, legal and social challenges of EHRs-related biobanks research, which may be different from those routinely analyzed within their daily activities.

A future effort towards implementation of relevant ethical guidelines could help governance harmonization in response to new challenges in these biobanks structure, as well as systematic coordination and involvement of biobanks-specific Ethics Committees could ensure a consistent and coherent ethical framework for biobanks to operate successfully, empowering their enforcement and mitigating differences in samples and data collection and management.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

References

1) Bellivier F, Noiville C. Les Biobanques. Paris: Press Universitaries de France, 2009.
2) Gottesman O, Kuivaniemi H, Tromp G, Faucett WA, Li R, Manolio TA, Sanderson SC, Kannry J, Zinberg R, Basford MA, Brilliant M, Carey DJ, Chisholm RL, Chute CG, Connolly JJ, Crosslin D, Denny JC, Gallego CJ, Haines JL, Hakonarson H, Harley J, Jarvik GP, Kohane I, Kullo IJ, Larson EB, McCarty C, Ritchie MD, Roden DM, Smith ME, Böttinger EP, Williams MS; eMERGE Network. The Electronic Medical Records and Genomics (eMERGE) Network: past, present, and future. Genet Med 2013; 15: 761-771.
3) Bowton E, Field JR, Wang S, Schildcrout JS, Van Driest SL, Delaney JT, Cowan J, Weeke P, Mosley JD, Wells QS, Karnes JH, Shaffer C, Peterson JF, Denny JC, Roden DM, Pulley JM. Biobanks and electronic medical records: enabling cost-effective research. Sci Transl Med 2014; 6: 234cm3.
4) Tiik M, Ross P. Patient opportunities in the Estonian Electronic Health Record System. Stud Health Technol Inform 2010; 156: 171-177.
5) Milani L, Leitsalu L, Metspalu A. An epidemiological perspective of personalized medicine: the Estonian experience. J Intern Med 2015; 277: 188-200.
6) Denny JC. Chapter 13: Mining electronic health records in the genomics era. PLoS Comput Biol 2012; 8: e1002823.
7) Harris JR, Burton P, Knoppers BM, Lindpaintner K, Bledsoe M, Brookes AJ, Budin-Ljøsne I, Chisholm R, Cox D, Deschênes M, Fortier I, Hainaut P, Hewitt R, Kaye J, Litton JE, Metspalu A, Ollier B, Palmer LJ, Palotie A, Pasterk M, Perola M, Riegman PH, van Ommen GJ, Yuille M, Zatloukal K. Toward a roadmap in global biobanking for health. Eur J Hum Genet 2012; 20: 1105-1111.
8) Budimir D, Polasek O, Marusi A, Kolci I, Zemunik T, Boraska V, Jeronci A, Boban M, Campbell H, Rudan I. Ethical aspects of human biobanks: a systematic review. Croat Med J 2011; 52: 262-279.
9) Caenazzo L, Tozzo P, Pegoraro R. Biobanking research on oncological residual material: a framework between the rights of the individual and the interest of society. BMC Med Ethics 2013; 14: 17.
10) Refolo P, Sacchini D, Minacori R, Daloiso V, Spagnolo AG. E-recruitment based clinical research: notes for Research Ethics Committees/Institutional Review Boards. Eur Rev Med Pharmacol Sci 2015; 19: 800-804.
11) Overby CL, Tarczy-Hornoch P. Personalized medicine: challenges and opportunities for translational bioinformatics. Per Med 2013; 10: 453-462.
12) Beier K, Schnorrer S, Lenk C, Hoppe N. The Ethical and Legal Regulation of Human Tissue and Biobank Research in Europe. Göttingen: Universitätsverlag Göttingen, 2011.
13) Beier K, Lenk C. A Unified European Approach on Tissue Rsearch and Biobanking? A comparison. In Lenk C, Sándor J, Gordijn B. Biobanks and Tissue Research: The Public, the Patient and the Regulation. Dordrecht Heidelberg London New York: Springer Science & Business Media, 2011.
14) European Commission. Biobanks for Europe – A challenge for governance 2012, available online at: http://www.coe.int/t/dg3/healthbioethic/Activities/10_Biobanks/biobanks_for_Europe.pdf
15) Martín Uranga A, Martín Arribas MC, Jaeger C, Posadas M. Outstanding ethical-legal issues on biobanks. An overview on the regulations of the Member States of the Eurobiobank project. Rev Derecho Genoma Hum 2005; 22: 103-114.
16) Biobanks in Europe: Prospects for Harmonisation and Networking 2010, available online at: http://ftp.jrc.es/EURdoc/JRC57831.pdf
17) Kaye J. From single biobanks to international networks: developing e-governance. Hum Genet 2011; 130: 377-382.
18) UK Biobank Ethics and Governance Council, available online at: www.egcukbiobank.org.uk
19) Macpehrson Cox C. Research ethics committees: a regional approach. Theor Med Bioeth 1999; 20: 161-179.
20) Slomka J. The ethics committee. Providing education for itself and otEHRs. HEC Forum 1994; 2: 31-38.
21) Drane JF. Basic facts about health care ethics committees. In Drane JF. Clinical bioethics. Kansas City: Kansas City Sheed and Ward, 1994.
22) Sabatier S. Comparative study on national ethics committees and similar bodies. In Glasa J. Ethics committees in Central and Eastern Europe. Bratislava: Bratislava Charis IEMB, 2000.
23) McHale JV. Accountability, governance and biobanks: the ethics and governance committee as guardian or as toothless tiger? Health Care Anal 2011; 19: 231-246.