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REVIEW ARTICLE

History of the largest global biobanks, ethical challenges, registration, and biological samples ownership

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Abstract

Aims Over the past few years, human DNA sampling and data collection have been improved with the aim of genetic research, clinical care, and future therapies. Since healthcare depends on modern research, it justifies access to biological samples. Therefore, the existence of organized sets of biological samples is essential. These collections are known as biobanks, gene banks, or gene libraries. There are many cases of abuse in relation to the structure of these organizations in the financial, political, individual, and social fields, and also ethical concerns, which are worth of investigation.

Method To this end, in December 2019 a literature review was performed from the PubMed and Scopus online databases. The principal biobanking issues discussed were: (i) overview of the largest global biobanks, and (ii) top ethical biobank issues.

Results and conclusion Only a limited number of studies were reviewed in this research, but the relevant ethical issues were clarified. We worked hard to stay neutral and to express the different authors' views on ethical issues. Differences among the writers and institutions' views were observed, but the main ethical principles of respect are utility, justice, minimizing harm, and motivation to participate in this researches. However, the rapid growth of biobanks creates new issues that are hard to follow and discuss. Therefore, there are issues that have not yet been resolved and should be discussed in the future.

Keywords Biobanking · Informed consent · Data sharing · Research ethics

Introduction

Discovering the causes of complicated diseases depends on understanding the interaction between the biological and environmental factors which increase disease risk. Investigating this relationship is challenging due to many factors, including difficulties in assessing the disease phenotype and reliable assessment of the effects on the environment. On the other hand, there are many subtypes of some diseases which are based on the disturbance of genome expression. In order to determine the impact of those factors for potential therapeutic purposes, comprehensive work on biological samples and clinical evidence is needed. To this end, government and private institutions have developed biobanks or the storage of biological data for researchers worldwide. Due to the different form and number of samples collected, the amount of clinical data, and the disparity in their recognition and use, biological banks are complex (Greely 2007). According to the OECD (Organization for Economic Cooperation and Development), the biobanks include an organized collection of disease-related information with the aim to studying these diseases (Khoei et al. 2016). Watson and Barnes emphasize the importance of biobank classifications, and classify them based on disease, population, genetics, DNA, and RNA (de Souza and Greenspan 2014).

There is also a distinction between databases containing only genetic, clinical information, and databases containing biological samples with/without genetic or clinical information. Stored samples in a biobank can be extracted from clinical & judicial fields, and from research projects that contain clinical samples, surgeries, diagnostic tests, birth products (placenta and umbilical cord), body parts of the deceased,

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donated gametes or embryos, and population biological materials. Also, the sampled data can be individual, familial, or belong to a particular group. These organizations may be storing samples for various purposes (Eduardo 2015).

Two basic goals for these organizations are defined, which are (a) storing the biological materials of individuals for future medical purposes, and (b) storing samples and genetic information for different individuals to identify the involved genes of diseases. Depending on the purpose of the study and the kind of institution conducting the research, different types of public bio-banks have been established, including disease-oriented biobanks, population-based biobanks, and virtual repositories (Davis and Rall 2017). Generally, the uses of such biological and genetic samples are:

1. Developing methods of diagnosing and treating genetic disorder causes sch as multifactorial diseases
2. Epidemiologic studies
3. Preparation of genetic maps and their applied research
4. Pharmacokinetics and pharmacology (Khoei et al. 2016)

The advance in science has led to the widespread use of storage, generating collaboration among biobanks in various countries. For example, there are common genetic research projects focusing on prevalent diseases in developing countries, which require the shipment of stored samples in biobanks from developing countries to developed countries. But because of the legal, ethical, and political gaps between countries, these partnerships have significant constraints. There are concerns about privacy, protecting confidentiality, ways to avoid discrimination, or the use of biological samples in international trade. Therefore, many international ethical guidelines have been presented (Rothstein 2005; Eduardo 2015).

In this review, we initially present a brief report on the history of biobanks. Then the various aspects of ethical challenges, including social and legal aspects, confidentiality, data security, control of access to data, access to biological samples, benefit-sharing, commercialization, intellectual property rights, and genetic discrimination are discussed.

The history of biobanking

In 1948, the National Institutes of Health—National Heart, Lung, and Blood Institute (NIH-NHLBI) founded the oldest biobank in the Framingham Heart Study (FHS). In the late 1990s, the Human Genome Project (HGP) began to understand the cause of multi-gene diseases, and the entire human genome data was completely published in 2003. The number of biobanks increased significantly between 1980 and 1999, due to increased demand for suitable samples for research (Kang et al. 2013).

In 1995, the Korean Ministry of Science and Technology developed research centers to gather various biological resources. However, their scale and diversity were limited as they were focused on an individual research project. On the other hand, the Ministry of the Environment established biobanks, but their samples were limited only to environmental disease research, rather than human biobanks (Kang et al. 2013). For this reason, the Ministry of Health and Welfare initiated the Korean Biobank Project (KBP) in 2008 and supported the establishment of biobanks at university-affiliated hospitals. The largest, the National Biobank of Korea (NBK), was established in the central Osong area of South Korea (Kang et al. 2013, b; Park et al. 2013).

In 2005, the UK Biobank was developed by collecting DNA samples and personal information, with the aim of searching for the relationship between diseases, lifestyle, and genes, as well as identifying the risk factors that represent the individual's response to the treatment. Between 2006 and 2010 this center collected samples, and the findings were presented to participants in 2012 after research (Watts 2012; Kang et al. 2013).

Recently, the establishment of biobanks has been increased; 43 biobanks have started operating in different fields based on population or specific disease groups since 2000.

Examples oof the largest biobanks and their objectives are:

1999

- Chernobyl Tissue Bank. Investigation of the prevalence of thyroid cancer in accident-prone areas). Supported by the Governments of Belarus, the Russian Federation, and Ukraine, in conjunction with the European Commission (EC), the WHO, the United States National Cancer Institute (NCI) and the Sasakawa Memorial Health Foundation (SMHF) in Japan (Thomas and Tuttle 2007).

2000

- Estonian Biobank (Estonia). Development of a health, genealogical and genome database to explore connections between genes, environmental factors, and common diseases (Dove 2015).

2002

- UK Biobank (UK). Research on how the health of 500,000 people from all over the UK, between the ages of 40 and 69, is influenced by their lifestyle, the climate, and their genes (Sudlow et al. 2015).
- Marshfield Clinic Personalized Medicine Research Project (US). Evaluation of the genes causing disease, the genes determining drug reactions, and how the environment and genes function together to cause disease (McCarty et al. 2008).

2003

- Biobank Japan (Japan). Evaluation of specific disease pharmacogenetics.
- Generation Scotland (UK). Providing more successful gene therapies based on awareness on the medical, social, and economic benefits of Scotland and its people (Nagai et al. 2017).
- EuroBiobank: a unique biobank network that stores and distributes quality DNA, cell, and tissue samples for rare disease research (Mora et al. 2015).

2007

- Kaiser Permanente Research Program on Genes, Environment and Health (RPGEH) (US). To find out genes and environmental factors which relate to particular diseases (Schaefer 2011).
- CARTAGENE (Canada). Studies genomic factors relating to health and disease in the 45–69-year-old population.
- LifeGene (Sweden). Resource for research in all medical fields to encourage new and groundbreaking research on heredity, environment, and lifestyle (Almquist et al. 2011).

2008

- LifeLines (Netherlands). Longitudinal population-based three-generation research to investigate risk factors for multifactorial diseases and their modifications (Scholtens et al. (2015).

2010

- Taiwan Biobank (Taiwan). Uses genetic and other medical information in a large-scale longitudinal study to investigate genetic factors behind common chronic diseases such as cancer and high blood pressure in Taiwan (Dove 2015).

2013

- Genomics England(UK). Aims to evaluate the sequence of 100,000 NHS[1] genomes from genetic disease patients and their families, and cancer patients) (Baker 2018).

2017

- The EuroBiobank. Composed of 25 representatives from nine European nations, including Germany, Hungary, Italy, Malta, Slovenia, Spain, the UK and Turkey, as well as Israel and Canada) (Mora et al. 2015).
- FinnGen (Finland). A European Biobank focused on the origins of diseases and their treatment (Dove 2015).
- Hospital-integrated biobank, Pilsen (Czech Republic). Initially this biobank focused on previous samples collected from patients; the main diagnoses of interest were breast cancer, prostate cancer, colorectal cancer, and lung cancer. In 2014 the repository of biological material at the University Hospital in Pilsen changed its status to "biobank" and became a member of the Czech national BBMRI-ERIC node, the biggest biobank infrastructure in Europe (Kinkorová et al. 2019).

Seventy percent of them are in Europe; 60 % of the sponsors of these biobanks are governmental or national institutes, and 16 to 17% of biobanks are funded by non-governmental public services corporations, universities, and hospitals (Kang et al. 2013).

Guidelines for the management and quality assurance of biobanks

The International Society for Biological and Environmental Repositories (ISBER) and the Organization for Economic Cooperation and Development (OECD) provide general guidelines for research on human subjects. They highlight the importance of the independence of individuals in the decision. The Belmont Report in 1979 defined three specific ethical principles, which were: respect for individuals (autonomy and informed consent), beneficence (risk assessment and benefits), and justice (equitable application of research and subject selection). in any research, this should always be respected (Kang et al. 2013).

There are many guidelines for biobank management, including those of ISBER and the OECD mentioned above. ISBER has "Best Practices for repositories: collection, storage, retrieval, and distribution of human biological materials for research" which is used for biobanks. In 2009, the OECD Council adopted recommendations to provide guidelines for the establishment and management of Human Biobanks and Genetic Research Databases (HBGRDs). Each institution should have its own supervisory board, the Institutional Review Board (IRB), to ensure the implementation of ethical principles. The IRB is an administrative institute established to protect the rights and welfareof people involved in human research (OECD 2009; Astrin et al. 2012; Kang et al. 2013, b; Souza and Greenspan 2014).

Informed consent and requirements

The obtaining of informed consent can be written, verbal, broad consent (see definition below), by email, and by telephone or fax. In many institutions, verbal consent may be used for specific therapeutic procedures but is not permissive for

[1] National Health Service

research. For example, for an emergency clinical issue, informed consent by phone or legally authorized representative may be acceptable, but is rarely approved for research. For certain cases, printed documentation for the consent may be emailed or faxed, allowing the person time to study it (Can et al. 2008). In 2016, the Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), and Health and Human Services (HHS) published guidance for Investigators, institutional review boards (IRBs), and sponsors. This guidance provides guidelines on the use of electronic systems application and their procedures for obtaining electronically informed consent (eIC) in the use of medical products and clinical investigations (FDA 2016).

There are various perspective declarations of informed consent for the use of material research and data stored in biobanks. They contain broad consent (open consent for any type of research with the stipulation that future studies are conducted only when an independent donor protection body such as the IRB declares the proposed research to be ethical), restricted or specific consent (consent for specific research), tiered consent or multi-layered consent that needs many choices to clarify the subject of the research (giving the right to choose from the list of subsequent investigations that may occur during the first research), and blanket consent (OAuth, open authentication, without any limitations to research) (Master et al. 2012; Eduardo 2015; Kinkorová et al. 2019). The International Society for Biological and Environmental Repositories (ISBER) and the Biobanking and Biomolecular Resources Research Infrastructure – European Research Infrastructure Consortium (BBMRI-ERIC) assist in the preparation of informed consent documentation (Kinkorová et al. 2019).

Biobanks tend to receive broad consent with the lowest risk and at the same time, they have to protect the privacy of individuals and confidentiality of information. Since many patients are reluctant to be re-contacted again, getting this type of consent for any type of research is justified. However, they want a guarantee that the biobank will not use their samples and information unethically. Many people believe that broad consent is not truly informed, but rather a general license that benefits the research interests of the Biobanks. In fact, informed consent must be exclusive and related to relevant research (Eduardo 2015).

The following topics should be listed in the contents of the consent form. In addition, the individuals must sign with awareness of the rules in the form (Nijhawan et al. 2013; Manti and Licari 2018).

For new collections of data and samples

1. Verification by the ethical committee that there is a fair balance exists between risks and benefits.
2. Providing special protection for vulnerable individuals and groups in accordance with the general principles in their best interest.
3. Determining how individuals can access the stored or shared samples, and the duration of their storage with respect to the types of research.

For existing data and samples

1. The use of stored anonymous samples where it not possible to reveal the names should not be for other purposes than what was initially intended.
2. Using anonymous samples, ensure absolute confidentiality, allowing more use of the samples. Although preserving the sample IDs requires more informed consent from individuals, it leads to effective research and re-contact with individuals, especially when a suitable therapeutic option becomes available.
3. To ensure efficacy, the sample anonymization methods should be in accordance with an international standard.
4. In the case of existing samples, researchers must re-contact with people to obtain consent for new research. If not practicable, the approval of an ethical institutional review board (IRB) should be given to make use of the samples with the lowest risk to donors.
5. If people limit the use of their samples to the period of their life, this restriction should be applied after their death. If this restriction is not specified, the research could proceed, as a request for re-consent is not necessary (Nijhawan et al. 2013; Eduardo 2015).
6. Remember to discard old samples and data. The use of such samples for new research purposes needs the ethics committee's approval.

For population studies

1. If the topic of the research is a population, the individual's informed consent must be obtained. The group leader's consent is required; however, this does not mean that the leader's consent should be replaced with the individual's informed consent.
2. The cultural distinctions with respect to the rights of minority groups must be considered in the form of consent.
3. If sampling is done by a group from another country, the country's related rules should be followed to protect individual rights (European Society of Human Genetics 2003; Budimir et al. 2011).

Information scope

Researchers should have enough knowledge about the implications and consequences of predictable benefits and risks to make an informed decision. They should evaluate the possible

risks and make people aware of them. On the other hand, organizations and individuals must have a common system and language to communicate This is even more important for international Biobanks (Eduardo 2015; Fransson et al. 2015).

Source

The source of biological samples collected for the research should be clear.

Intended purpose

The purpose of using samples should be clearly stated.

Secondary use of the sample:

The reuse conditions of samples should be specified. If there is no existing new consent, the feature of first consent for secondary use should be evaluated before using them, because it is difficult to control the secondary use of them when biological samples are stored in biobanks (Eduardo 2015).

Data sharing

Policies should be considered for access to the biological samples and data by third parties such as insurers, employers or law enforcement agencies. The necessity of observing these principles by Biobanks to share resources with third parties leads to the loss of the Biobank's public confidence among people, especially if causing a social stigmatization or discrimination. The consequences of the loss of privacy can significantly affect people's tendency to participate in Biobank research. Therefore, Biobanks must always ensure the highest level of support for participants (Critchley et al. 2015; Eduardo 2015).

Release of information

Participants should have a right to be informed about the results of research on their health or relatives. Sometimes the treatment may be impossible and being aware of the results will not benefit them. Some researchers are opposed to giving the results to the participants because they believe that the purpose is not providing clinical care, but the development of science and knowledge. On the other hand, they believe that research laboratories do not operate according to clinical laboratory standards. There is an agreement in this regard that individuals should only be told about the outcomes which will improve their health or conditions (Budimir et al. 2011; Eduardo 2015).

Understandable communication

Providing participants with the information should be simple, brief, and clear. Observing this principle for vulnerable populations with a low level of education is a major barrier to informed consent due to the complexity of the consent issues (Eduardo 2015).

Access to data

In 2015, Marco Capocasa et al. performed an online analysis to determine access to the information and samples in 238 biobanks. This research attempts to analyze the extent of access and reuse of data and biological samples stored in biobanks using an analytical approach. Just 46 biobanks replied in that research, and most of the participating institutions were from the United States. This research showed that the amount of access to samples and their data was 95.7% and 85.4% respectively, given the scientific community's general consensus regarding access to the data and knowledge of them. The amount of access, though, was not free and unconditional. This does not mean that for unrestricted access to biobank services all these barriers need to be overcome. Many of these obstacles actually guarantee some of the donor rights, including anonymity and lack of violence. Those barriers should, therefore, be seen as "necessary." Not all organizations should have access to the biological resources in the same way, but they must follow a common operating principle (Capocasa et al. 2016).

The consent of children

There are many ethical concerns about the potential use of children, including the duration of research, providing the consent, and the procedure to obtain it (Eduardo 2015). Informed consent can be obtained from parents; however, as soon as possible it should be obtained from children. In some instances, research is conducted without the consent of the parents or children, but the research should guarantee that is safe for children. Researchers must always respect the child's fear or disagreement for participation in the research. Taken together, any research on children should be reviewed with the ethics board (Budimir et al. 2011).

Waiver of consent

The human ethics committee can relinquish the need for consent if it carries minimal human risk. In such cases, there is sufficient privacy protection and an adequate plan to protect the confidentiality of the data.

Death or inability of the participants

You need a strategy to make decisions about the biological samples and data in a period of participants' disability or death (Eduardo 2015). Ethical guidelines should have a procedure for the study's post-mortem use of personal data, so informed consent procedures in this situation are transparent during initial consent, and relatives should receive individual research findings (Müller et al. 2020).

Who can announce consent

Ideally, obtaining the informed consent from the participant in the research is in ideal conditions with an analysis of the positive and negative aspects, and without any sense of time or other pressure. But this is not always possible. In many cases, the designated delegate performs the consent process for the patient or vulnerable individuals, and for minors. In medical cases, individual competence is determined by the degree of injury, illness, pain, etc., evaluated by the researcher's discretion. In fact, balanced satisfaction means consent from the person who is not involved in the research (authorized representative). To improve the process of obtaining informed consent from individuals, the use of comprehensive brochures or complex content expressions should be avoided (Can et al. 2008).

Respect for cultures

In the process of obtaining consent, the biobanks should respect the cultural and religious sensitivity of the participants, and of the research community (Eduardo 2015).

Inappropriate informed consent

Although all type of consent taken from the people is 'informed', some writers examine the reasons for the suitability of informed consent as the 'gold standard' to ensure ethics in research. As stated in the Nuremberg act, in informed consent, individuals must be aware of the nature, duration, purpose of the experiment, the method and the equipment. It is necessary to consider all the expected risks, as well as health effects. Those specifications were fulfilled in the Helsinki Declaration. The new edition of 2008 notes that it is important to analyze the financial capital, advantages, and the right to withdraw from the study. However, it is difficult to meet this stage of the informed consent rules, for the following reasons:

1. Genetic research does not consider people with blood relationships associated benefits and risks to third parties, because an informed consent is only associated with the individual. Unlike other medical information, obtaining the sample of a person in genetic research does not only provide information about the sample donor but also includes others. For example, genetic tests on a family member indicate the genetic status of other family members.
2. Biobanking research is prospective and cannot be called informed consent because at the time of declaration of agreement the individual has no information concerning the future. There is little information about the type of investigation which will be carried out on data and samples at the time of declaration of consent. The Helsinki Declaration and other informed consent models assume that at the beginning of a specific research project, the goals, benefits, and risks must be completely recognized. This is simply not possible, and even in the best case only the general fields of research are known.
3. Biobanks are not research projects but a "research source" or "library of science". Therefore, informed consent is not a suitable option for future projects. The Helsinki Declaration believes that the consent for any research is impossible because in such situations, referrals to donors for obtaining consent for any new study relies on previous data. For this reason, biobanks have opposed informed consent and tended to use other consent models such as broad consent with ethical principles and the lowest individual risk.
4. It is not clear that the right to withdraw from research and consent is fully implemented and respected by the biobanks (Widdows and Cordell 2011).

Given these reasons, the most ethical issues in the field of biobanks are obtaining informed consent and the risk of withdrawing the report. As stated, consent is considered notified by following the first concept, i.e. autonomous, and the decision of the individual participant is focused on performing research or preparing future research (knowing full genetic information about the disease and its treatment) and does not mean signing an unconditional consent document. It is understandable that humans should be properly informed. On the other hand, it is easier to understand what form of consent the person provides.We express below the kinds of consent and the conditions associated with them, and finally, in most biobanks, we introduce the best kind of consent for research projects. For example, the open consent that allows a sample to be used for future testing, or a specific consent that covers all testing purposes and allows withdrawal from consent. Dynamic consent is suggested to make informed consent, allowing withdrawal from research at any time.

Consent to participate in biobank research may be provided in any written or verbal form. Informed consent requires the sharing of information and training between the researcher and the participant. Often knowledge provided to individuals may be confusing or irritating, which is why considering their

interests requires time to participate in the study. In this case, the researcher must provide information and address concerns more than once, or provide a period of time between the submission of information and the signature request in the consent form. Individuals may consult with family members, close friends, or trusted advisors during this waiting time to participate in the study.

Verbal consent

In certain cases, policy disregards the need for written consent and enables researchers to receive verbal consent. In this scenario, the researcher should take the following steps:

Step 1: the researcher should orally clarify all the research details (purpose, methods, dangers, benefits, choices for participation, etc.) and allow people plenty of time to ask questions.
Step 2: following this verbal clarification, the researcher should provide a data sheet containing a description of the research process which gives them ample time to review research involvement. This period can last from a couple of minutes to several hours depending on the person's ability to assess the processes, threats, benefits, and potentials.
Step 3: After providing enough time to read the datasheet, the researcher should answer each of the person's questions.

Written consent

Written consent is not just signing the form. The study material should be clarified orally, and the information should be shared between the researcher and the participant; signing the consent form is part of the procedure. Informed consent includes providing the person with an opportunity to review the material, have their questions answered, and eventually ensuring that people have understood the subject matter. According to console law, the agreements should be based on the authority of a person, and the individuals must be 18 years old.

Individuals of legal age can provide informed consent. A legal representative should receive the consent of minors or individuals with medical disturbance. The agreement should be written and extra assistance should be provided to vulnerable persons in the best possible way, based on general standards and laws.

Reconsent

Providing a signature does not mean granting full consent. The basis of informed consent is that any new problems that arise during the study (such as a change in the design and the research risk/benefit, relevant research outcomes, etc.) can affect the subject of the agreement. Can the participants' decision be determined by whether the research is continuing or not?

In these situations, the researcher sends a letter revising the consent form and sending a cover letter with a request for reconsent that explains briefly what has changed since the original declaration of consent. The modified consent form is intended to update the consent words with emphasis on the revision. The person must sign up for a revised consent form (Can et al. 2008).

Store, transfer and make available data

Applying the security mechanisms to ensure the confidentiality and long-term protection of genetic information is an absolute condition. These mechanisms must be performed before sampling, Including programming standardization, sample tracking, computer, and data encryption (European Society of Human Genetics 2003). The storage format and length, the mode of transmission of samples (if necessary, the international transfer of data), access to them and, monitoring by different participants, can be done in different ways:

Identifiable Specimens are labeled with a specific individual identification number, samples or data.

Traceable or coded Each sample is registered with a code that is not unique and not labeled on it.

Encrypted Sample encryption offers a higher degree of security and is a multi-character code shared with third-party data. Intervention by a third party is necessary to trace the individual samples and information identities.

Anonymized The relation between the sample/data and the individual's identity is irrevocably interrupted after collecting. In fact, all personal information with any other data that could identify the patient and be revealed to the recipient must be removed.

Anonymous There is no relation between the sample/data and a given person right from the start of the study. The samples are stored anonymously from the beginning (Eduardo 2015).

ISO (the International Organization for Standardization) and IEC (the International Electrotechnical Commission) provides instructions to anonymize data with privacy purposes, which we will discuss in two categories: non-perturbative methods (reduce the detail in the data by suppression of certain values) and perturbative methods (creating uncertainty around in the true values). According to this classification, non-perturbative methods include the type of coding (global

recoding, top, and bottom coding) and local suppression, and perturbative methods include micro-aggregation, noise addition, and rank swapping, and shuffling (BS ISO/IEC 20889:2018; https://sdcpractice.readthedocs.io/en/latest/anon_methods.html, https://www.iso.org/obp/ui/#iso:std:iso-iec:20889:ed-1:v1:en).

These anonymization methods are based on three international standard procedures:

The first anonymization technique means that the database incorporates protocols for tracker detection, and when a tracker is identified, it avoids answering questions about sensitive information.

The second anonymization technique is that it is not possible to search on the original database, but only on a derived database that contains a copy of the original data from which no data can be inferred for any person. This database is created by removing data that may challenge individual privacy. Solutions include replacing absolute data with relative data (e.g., age rather than date of birth), eliminating personal identifiers such as social security numbers, and generalizing data such as registration of age groups with specific codes instead of the absolute age of individuals.

The third technique is to apply statistical noise (for example, adding a small random number) to the responses, which blurs the results so that it is difficult to determine with certainty individual data. This approach makes an attacker's findings useless, but the findings of such blurred queries would still be useful to a researcher (Benschop et al. 2020; Eder et al. 2012).

Ownership of biological samples, data and profit-sharing

There is a query as to who could become the sample's owners through biobanks, or whether the participants are still the sample's real owners? One author looked into this topic and concluded that the participants are the true owners. But other writers disagree with this view, arguing that if the sample is anonymous, it is no longer connected with the original owner and belongs to the bank (Budimir et al. 2011; Chalmers 2011). But in some situations, donor ownership is retained, and permission to use the material must be ontained. Yet other writers believe that the individual's sample does not belong to the individual. Some writers have proposed that donors, researchers, and organizations could share ownership of samples (Simon and Robienski 2009; Budimir et al. 2011; Chalmers 2011).

Most biobanks agree to set legal representatives for both parties. Some people also believe that samples should not have ownership determined because they believe a commodification of personal data would prevent extensive research. This issue has not been completely discussed and resolved yet. Also, in international research, the ownership of the biological samples should be clarified. In these studies, developed countries often take advantage of the instability of international cooperation. There is a conflict over who has the right to use, to distribute biological samples, and to produce products. Therefore, the level of commercialization and the rights of participants to take advantage of income from the study should be thoroughly defined (Budimir et al. 2011).

Children and illiterate adults as participants in the study

Participation by children in biobanks poses ethical problems which are not identical to participation by adults. Children (or, more accurately, minors) have little capacity to consider the ethical and other biobank issues. Most biobanks refuse to carry out research involving children because of specific ethical concerns, the protection of the general public ,and the media. It poses many needless risks for biobanks. For this reason, children's research lags behind adult research. And from an ethical point of view, work involving children should be performed at minimum risk (DAVIDSON and O'BRIEN 2009; Hens et al. 2009; Levenson 2010; Budimir et al. 2011).

Another problem involves knowledge sharing. Some writers claim the sharing of children's data is forbidden before they reach adulthood (Gurwitz et al. 2009; Budimir et al. 2011). Many writers strongly oppose this, however, because they believe such a plan may significantly delay the study (Brothers and Clayton 2009; Hansson and Maschke 2009; Budimir et al. 2011).

Furthermore, parents appear to be aware of the findings of the study concerning their children. Most scholars agree that would not be ethically acceptable in this situation. Parents are entitled to decide about the involvement of children in biobank research. Parents can provide informed consent on behalf of their children instead; however, they should be conscious of the findings before puberty. Another concern involves the outcomes of certain child genetic results and a potential cure for them. This has not been discussed by many scholars, but an article by Hens et al. suggests that this knowledge should be returned to the parents (Hens et al. 2011). While this topic is not listed as a separate subject in the articles, the same ethics are used for participants who are not eligible. Including those suffering mental disorders. They will, for example, always be guarded and exposed to the minimum danger. For them, a supervisor has to sign an informed consent (Molnar and Bencsik 2006; Chalmers 2011).

Confidentiality and privacy

Concerns regarding data protection and information security are growing. Policies to protect individuals' genetic

information and privacy include labeling and encoding samples and data, restricting access by the environmental banks, and so on to different extents(Eduardo 2015; National Cancer Institute 2016). The USA signed into law in 1996 the Health Insurance Portability and Accountability Act (HIPAA), setting new and regulatory standards to define patients' protected health information (PHI). Inappropriate information disclosure will affect patient insurance, job opportunities, and privacy (Souza and Greenspan 2014; National Cancer Institute 2016).

Inspectors who handle and access data and persons are committed to the legal and ethical security of private information. Data programming is the most appropriate way of ensuring privacy. There is a consensus that simple, double, or even triple sample and data encoding provides a satisfactory level of privacy, because one to three codes are required to create a link between the sample and data (Greely 2007; Hansson 2009; Budimir et al. 2011).

Determine people's participation and maintain trust

The right to regain individual consent increases respect for the participants, but creates other problems for the organization in terms of continuing the research. In some cases, it is practically impossible, but this right should not be denied and the individual even has the right to request the removal of his or her related items. But the biggest threat to biobanks is the collective withdrawal of participants from research. If this occurs, the biobanks will be impacted not only by no income but also by substantial systemic losses. In order to solve this problem, biobanks have created various participation patterns, including complete collaboration, the involvement of individuals in advance research, and future creation, up to the model that has no partnerships and only informs them through the biobank. to hereDetermine the participation pattern for individuals to safeguard biobank interests (Widdows and Cordell 2011; National Cancer Institute 2016).

Guarantee and maintain public trust

Gaining public trust is the most critical condition for biobanks to perform successfully. This can be done by having continued education and privacy. The lack of public confidence can cause adverse effects on biobanks, but the main victims will be the people who expect medical progress improvements (Hansson 2011).

All articles which have reviewed the role of the biobanks in the field of public opinion reflect the desire of people to engage in biobank research (Hoeyer et al. 2004; Kettis-Lindblad et al. 2006; Kaufman et al. 2009; Johnsson et al. 2010; Budimir et al. 2011). Some people do not really grasp the biobanks' true goals, but they also seem to be interested (Hoeyer et al. 2005; Budimir et al. 2011). It seems that biobanks currently have an acceptable level of people's support. They will, however, need to continue to cultivate a degree of public confidence. Providing satisfaction and maintaining the privacy of individuals is important for this public trust to continue (Tutton et al. 2004; Hansson 2005; Budimir et al. 2011).

All articles reviewed in the field of public opinion about the functioning of biobanks confirm people's interest in participation in biobank researches.

Commercialization

Policies and regulations about the commercialization of biobank samples and the possibility of using the human body vary greatly between different communities. This possibility is accepted in some societies, while others are based on principles that categorically prohibit the sale of parts of the human body (Evers et al. 2012).

Although the main focus of biobanks is on the research and promotion of medical knowledge, the participation of people does not prevent the use of private companies for data. This raises several ethical issues, including (1) preventing the improper exploitation of results, (2) ensuring participant equity in research, and (3) balancing the costs and benefits (Rothstein 2005; Budimir et al. 2011).

Pharmacology research by pharmaceutical companies is a common example of the commercialization of biobanks (Joly and Knoppers 2006; Budimir et al. 2011; Chalmers 2011). They support research that would potentially contribute to better and future-profitable care. Genealogy patents are also profitable, and many companies tend to support such research to take advantage of them (Andrews 2005; Cambon-Thomsen et al. 2007). But how should the costs and benefits be balanced? How should the intellectual property be shared between companies, researchers, and participants? Others (people, scientists) assume that donors will eventually profit from the results of the research and do not share them, but is this really a moral issue?

Generally, because the creation and maintenance of biobanks is expensive, their developers are seeking private investment to upgrade the long-term sustainability of these research tools. This issue encourages biobanks to cooperate with private institutions. While these types of partnerships are often necessary and can facilitate the transfer of useful technologies and methods, the commercialization of biobanks also raises a number of concerns that need to be discussed in the development of these partnerships and related policies. These include: adverse consequences on public trust; consent challenges, such as the re-consent requirement; potential disputes

over ownership and sharing of biological data and samples; and challenges about the use and control of resources in the event of bankruptcy of biobanks or loss of financial support (Eder et al. 2012).

Conclusion

Only a limited number of studies were reviewed in this research, and the relevant ethical issues were clarified. We worked hard to stay neutral and to express the different authors' views on ethical issues. Differences among the writers and institutions were observed, but the main ethical principles of respect are utility, justice, minimizing harm, and motivation to participate in this research activities. However, the rapid growth of biobanks creates new issues that are hard to follow and discuss. Therefore, there are issues that have not yet been resolved and should be discussed in the future.

Declaration

Conflict of interest This article does not contain any studies with human participants or animals performed by any of the authors. We know of no conflict of interest associated with this publication, and there has been no financial support for this work that could have influenced its outcome. We declare that this manuscript has not been published before and is not under consideration for publication anywhere else.

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