4.

Digital informed consent: possibilities and challenges in biobanks for health research

Brígida Riso
CIES-Iscte, Portugal
Faculdade de Medicina da Universidade de Lisboa, Portugal

Cíntia Águas
Investigadora Independente

ABSTRACT

Biobanks are key infrastructures in biomedical research, storing and providing biological samples, personal and clinical data. Informed consent is a central piece of the process, as a means to respect each participants' dignity, integrity and to acknowledge their capacity to express autonomous decisions. Providing adequate information, while ensuring the voluntariness of their decision are essential to an effective consent. Requesting informed consent usually takes place in the context of healthcare, where paper forms are still widely preferred, when not mandatory and when person to person relationships are crucial.
As biobanks are moving fast to implement automated protocols from biological samples processing to data collection, it is relevant to discuss the challenges posed by the digitalization of informed consent. To this end, such transition will be critically discussed using dynamic consent as a starting point to highlight the opportunities of digital tools, but also the relevance of healthcare context.

Keywords: Digital informed consent; Dynamic consent; Biobanks; Health research, Healthcare

INTRODUCTION

Biobanks for health research are repositories aiming at the collection, storing and distribution of biological samples, personal and clinical data to study human health diseases. Although health data collection is a common practice in healthcare, the storing and usage of vast amounts of data in recent decades has emphasized the problems and fragilities of sensitive data sharing in biobanks for health research (Hoeyer, 2012).

On diverse occasions, large-scale repositories, such as populational biobanks in Iceland or the UK, have led to an intense debate on informed consent, data access and privacy protection. With the growth and scalability of biobanking activities, a variety of situations become problematic from the ethical, legal, and social standpoint. The dilemmatic nature of these issues has fed the news outlets and the academic debate, proving their relevance to the continuous implementation of ethical and research integrity practices.

Informed consent has always been at the core of the ethical, legal, and social issues debate surrounding biobanks. Informed consent is key to assure that individuals are aware of what is at stake when their biological samples and associated data are provided for health research and, above all, that their consent to the use of sensitive information about their present and future health has been validly obtained. This procedure is a legal requirement not only in Portugal (Law no. 12/2005, of 26th January, which provisions require that the collection, conservation and usage of biological samples for genetic testing should be subject to an informed consent separate for health care and biomedical research), but also as a general rule in other countries. Informed consent is dictated as a Human Rights issue by the most relevant international guidelines regarding voluntary participation in research, from 1947, with Nuremberg Code, being reaffirmed with the most recent UNESCO Universal Declaration on Bioethics and Human Rights, in 2005. Also, specific guidelines regarding the biobanking activity have been issued by scientific or professional associations, such as the 2006 and 2016 Recommendations of the Council of Europe Committee of Ministers to Member States on Research on Biological Materials of Human Origin, the ISBER Best Practices for Repositories, or the 2016 World Medical Association's Declaration of Ethical Considerations regarding Health Databases (Taipei Declaration).

Informed consent has always been at the core of the ethical, legal, and social issues debate surrounding biobanks

Besides bioethics as a moral endeavor, in which free, informed consent is rooted in the respect for personal dignity and integrity, a different approach,

that of respect for personal privacy, has given informed consent for the treatment of personal data new momentum after the General Data Protection Regulation (GDPR) came into force, becoming even more relevant in the context of a "*databased society*". With this double entendre, informed consent works as both a recognition of the person as a central player in research and as a safeguard of the person's fundamental rights, such as the right to privacy and data control and ownership. Furthermore, consent as a procedure contributes to protect biobanks from liability (Skolbekken *et al.*, 2005).

As scientific research evolves, biobanks strive to catch up to the fast pace of innovation. Modernization includes automatizing different laboratory--related tasks, as well as implementing digital archives and storage modules to keep data safely preserved. This will ease the navigation between large datasets, enabling or destroying the links between sets of information or specific data at will. When digital solutions have already populated almost every dimension of social life, including health, their arrival to the field of biobanking is inevitable. Having this in mind, particular forms of informed consent have been designed as digital by default, such as dynamic consent, both as a model of personal decision-making, as well as a platform to enable it (Kaye et al., 2014).

In the context of healthcare, where samples and data are to be requested, informed consent can be even more significant regarding vulnerable individuals, who can feel deprived of autonomy and powerlessness in their relationship with healthcare providers and researchers

In the context of healthcare, where samples and data are to be requested, informed consent can be even more significant regarding vulnerable individuals, who can feel deprived of autonomy and powerlessness in their relationship with healthcare providers and researchers.

This article discusses the opportunities and challenges of implementing digital informed consent in the context of biomedical research, specifically in biobanks. After briefly presenting selected informed consent models, a SWOT analysis clarifies the role of dynamic and digital consent. Beyond its digital form, we propose that informed consent should be discussed as part of a particular social context, where the respect for ethical values, citizens' rights and societal concerns are at stake in daily and institutional relationships.

INFORMED CONSENT: WHAT IT IS AND WHY IT MATTERS

Following a historical path filled with abusive experiments conducted on human beings, respect for autonomy has become a central tenet of bioethics, materializing in two correlated dimensions. The first, considered as negative, refers to not subjecting any participant to unduly influence or coercion, which may condition an otherwise autonomous, valid decision. The second is positive, falling onto the States the duty to promote the conditions needed to guarantee that the decision can be freely made.

Furthermore, informed consent is more than a written formality, or even a mere agreement to a given premise. It implies the voluntary approval of a due course of action, made with prior understanding of substantial or relevant information. It should go without saying that autonomous action also encompasses the possibility of refusal or withdrawal of consent, without fear of reprisal. Consent, either given by the participant or by legal representative, legitimizes the research performed on the person or on their biological and non-biological data. Consent may have yet a meaning of validation, as it is obtained through procedures that satisfy the requirements defining a specific institutional research practice.

Alongside the personal capacity or ability to consent, and to do so free from undue influence, respect for personal autonomy requires that the information supporting a decision to donate samples or data to biobanks is accurate and transmitted in an appropriate way, thus avoiding any form of bias or deception. Individuals should be able to make choices that are coherent with their expectations, wishes and values.

Alongside the personal capacity or ability to consent, and to do so free from undue influence, respect for personal autonomy requires that the information supporting a decision to donate samples or data to biobanks is accurate and transmitted in an appropriate way, thus avoiding any form of bias or deception

The Portuguese legal system has, for the most part, accepted the premises laid out by the most relevant Human Rights and Bioethics declarations. Additionally, in 2014, Clinical Research Law (Law no.21/2014, of 16th of April) had clearly defined informed consent as "the express decision to participate in a clinical trial, taken freely by a person endowed with the capacity to do so or, in the absence of such a person, by his/her legal representative, after having been duly informed of the nature the scope, consequences and risks of the trial, as well as the right to withdraw from it at any time, without any consequences, in accordance with the guidelines issued by the relevant Ethics Committee, which shall include the definition of the appropriate means of providing consent, which shall be in writing where applicable" (Article 2 (l)).

INFORMED CONSENT IN BIOBANKING: SPECIFICITIES AND CHALLENGES

Informed consent in biobanking is widely discussed, occupying the top position when compared to other health research domains (Lossman & Nickel, 2022). Consent works, from a legal standpoint, as a safeguard to all individual and institutional actors involved. Yet it may become a point of contention, as biobanks enable samples and data storage and management for long periods of time, for which frequently the research purposes are not yet envisioned.

There is no single model, or one-size-fits-all format of informed consent – different forms entail different values and possibilities. In biobanks, two main models of consent are commonly considered, depending on their research goal (terminology may differ). Specific consent is contingent to a singular purpose - a particular research project or a specific set of studies - for which the samples and data are to be used. Where it is proposed that samples previously collected and stored with consent for research are to be used for a new research purpose, a separate consent for the different research should be obtained, meaning a new contact with the sample donor, with all the difficulties that go with it, especially in case of large cohorts - the time elapsed, the loss of contacts, the morosity, costs and sheer volume of administrative work, posing obvious constraints to future research.

Serving purposes of prospective research, a broader consent has been considered a balanced alternative to study-specific consent

Still, regarding a model of specific consent, the content of the previous information tends to be as detailed as more intrusive the intervention, or the more sensitive the data collected. It assumes the written form concerning, especially, its risks and outcomes, either expected or contingent, also as a protection from liability regarding the researcher and the research institution, as mentioned before.

Specific consent is usually a one-time, previous to research or in its initial stage. In the case of long-term storage this rigid, time-contingent and case--specific model risks creating insurmountable difficulties, impeding research when recontact is not feasible or even possible (Manson, 2019).

Serving purposes of prospective research, a broader consent has been considered a balanced alternative to study-specific consent (Petrini, 2010). Sought only once as its specific counterpart, it may differ from, yet another variety located at the far-end of the autonomy-control continuum, that of blanket or unrestricted consent (Rothstein, Knoppers & Harrel, 2019) clearly set apart broad and blanket consents. This means consent is given to future research with no limitations (Grady *et al.*, 2015), being subjected to several additional

safeguards, which complement it from an ethical perspective. Broad consent may vary from consent to conduct research in a specific field of biomedicine or addressing a specific pathology, to almost any future research use, for instance in population biobanks (Gefenas *et al.*, 2011). Broad consent, absent the specific research it is intended for, puts its weight behind information policies and ethical review regarding the biobank: it requires an account of the biobank in question, its governance and ethical review framework, its objectives, the areas of research for which it was established, and the procedures in place to return incidental findings, when applicable (Mikkelsen *et al.*, 2019).

Broad consent for future research on banked samples may be acceptable, especially when the following components are present: "1) initial broad consent, 2) a process of oversight and approval of future research activities, and 3) wherever feasible an ongoing process of providing information to or communicating with donors. These features promote the ethical acceptability and scientific value of future research with biospecimens and demonstrate respect for donors' contributions" (Grady *et al.,* 2015: 37).

The use of digital tools in healthcare allows for a continuous communication and engagement over time, enabling participants to review and update their decisions, to receive the information and feedback most suited, to give new inputs

Still, times have evolved, as have the participants' and society's perceptions of data ownership, control and right to information, which broad consent may fail to address. Respect for autonomy increasingly entails respect for privacy, essentially with a view to ensuring the research participant effective control over his or her personal information (Manson, 2019).

On the other hand, digital platforms, social media, algorithm-led research, are becoming staples of everyday life. Dynamic consent dates back to these societal shifts and the growing demands for the adoption of digital health strategies, data sharing and collaborative research at a global level. The use of digital tools in healthcare allows for a continuous communication and engagement over time, enabling participants to review and update their decisions, to receive the information and feedback most suited, to give new inputs (Teare *et al.,* 2020) and even to take part in the design of future research.

To help us develop a fuller awareness of the dynamic consent as a possible model for biobanking, the most relevant features of the model were compiled into a SWOT (Strengths, Weaknesses, Opportunities and Threats) analysis grid (figure 1). Examining these positive and negative elements, both internal and external, may help understand the usefulness of dynamic consent models from an effectiveness standpoint.

INTERNAL	
Strenghts	**Weaknesses**
Timely, two-sided virtual communication and feedback Tailor-made, interactive levels of information and consent Traceable, organized information Continuous scaling with less costs	Loss of direct, face-to-face contact Lack of training or information on how to use the platform Risk of incompatibility with other biobanks' procedures Dependent on software updates
Opportunities	**Threats**
Continued engagement for future research Possibility to review consent Better control of the participants over their samples and data Promoting literacy and trust	No participant activity: continued agreement or lack of interest? Consent "fatigue"/burden Too many subsequent changes to consent may jeopardize research Informational exclusion of some populational groups
External	

Figure 1. SWOT Analysis of Dynamic Consent.

APPLYING DIGITAL INFORMED CONSENT TO BIOBANKS

Biological samples and data collection is usually a process initiated in the context of healthcare provision. In this setting, many factors intervene and are responsible for influencing the possibilities for participants' decision-making or the training of health professionals (Arregui Egido & Villalobos-Quesada, 2022). For example, the vulnerability brought about by a disease condition, the power relationships between health professionals/researchers and eventual participants, or the level of trust in health care systems. Also, individual variables, such as the ability to interpret information, or health literacy, may influence whether a choice is truly informed. As the request to participate in research by giving samples and data happens in a limited time (*e.g.* medical appointment), a digital dynamic consent has the potential to prolong this relationship in the future and over time, thus enabling the provision of detailed information for different research studies while

A digital dynamic consent has the potential to prolong this relationship in the future and over time, thus enabling the provision of detailed information for different research studies while making use of the interactive potential of digital technologies

making use of the interactive potential of digital technologies (Heslop *et al.,* 2020). Digital consent could also contribute to health literacy by providing tailor-made, interactive information, and feedback. This continuous process of validating consent in different points of the data life cycle could also contribute to promote a closer relationship between participants and researchers, maximizing their opportunities for significant, collaborative decision-making.

However, the application of informed consent as a digital tool also entails weaknesses and possible threats. When considering populations with lower levels of health literacy, in a vulnerable condition or experiencing impairments due to acute or chronic illnesses, the application of digital consent could contribute to a sense of disengagement or dehumanization, caused by the loss of contact with healthcare providers or researchers, now substituted by a digital interface. Also, the constant need to request consent from time to time can cause a consent fatigue that may incur in further disengagement and ultimately consent withdrawal.

As we recognize the challenges posed by a digital informed consent, we need to move towards to a digital approach that considers ethical values and research integrity at the core of its design

Thus, it is relevant to note, as Wiertz and Boldt (2022) suggested, that more than the means by which consent is implemented, the context in which it is procured should be taken into account when considering any applicable models. In this scenario, the responsible to request informed consent will play a major role in contextualizing informed consent or by providing additional explanations. This is still true for digital informed consent. Considering the environment implies not only paying attention to human factors, but also to social and cultural context, what includes the public trust in healthcare, or in science. As mentioned by the authors, this could make a difference in the effectiveness of informed consent, highlighting the need to go beyond the digital informed consent forms to promote a more trustworthy and sensitive environment to informed decision-making.

FINAL REMARKS

The most up to date informed consent forms and processes are already designed to run in digital environments. While this change seems to be the next step in promoting better informed choices, increasing the participation levels or health literacy, digital consent forms still have flaws and disadvantages.

As we recognize the challenges posed by a digital informed consent, we need to move towards to a digital approach that considers ethical values and research

integrity at the core of its design. When considering digital informed consent for biobanks, one has to take into account that this tool is usually presented to eventual participants in healthcare services. Thus, in this context, we must invest in the promotion of trustworthy, inclusive environments that could maximize the strengths and opportunities brought by using digital tools. This will be key to provide a digital informed consent solution that not only serves the purpose of health data storage for research purposes, but it also prepared to deal with the unforeseen premises of future research.

REFERENCES

Arregui Egido, L., & Villalobos-Quesada, M. (2022). Improving the Practice of Obtaining Informed Consent for Biobanking in Clinical Settings. *Biopreservation and Biobanking*. http://doi.org/10.1089/bio.2021.0158

Gefenas, E., Dranseika, V., Cekanauskaite, A., & Serepkaite, J. (2011). Research on human biological materials: what consent is needed, and when. In *Biobanks and tissue research* (pp. 95-110). Springer, Dordrecht. https://doi.org/10.1007/978-94-007-1673-5_7

Grady, C., Eckstein, L., Berkman, B., Brock, D., Cook-Deegan, R., Fullerton, S. M., ... & Wendler, D. (2015). Broad consent for research with biological samples: workshop conclusions. *The American Journal of Bioethics*, *15*(9), 34-42. https://doi.org/10.1080/15265161.2015.1062162

Hoeyer, K. L. (2012). Size matters: The ethical, legal, and social issues surrounding large-scale genetic biobank initiatives. *Norsk Epidemiologi*, *21*(2), 211–220. https://doi.org/10.5324/nje.v21i2.1496

Kaye, J., Whitley, E. a, Lund, D., Morrison, M., Teare, H., & Melham, K. (2014). Dynamic consent: a patient interface for twenty-first century research networks. *European journal of human genetics : EJHG*, *November 2013*, 1–6. https://doi.org/10.1038/ejhg.2014.71

Loosman, I., & Nickel, P. J. (2022). Towards a Design Toolkit of Informed Consent Models Across Fields: A Systematic Review. *Science and engineering ethics*, *28*(5), 1-19. https://doi.org/10.1007/s11948-022-00398-x

Manson, N. C. (2019). The ethics of biobanking: Assessing the right to control problem for broad consent. *Bioethics*, *33*(5), 540-549. https://doi.org/10.1111/bioe.12550.

Mikkelsen, R. B., Gjerris, M., Waldemar, G., & Sandøe, P. (2019). Broad consent for biobanks is best–provided it is also deep. *BMC medical ethics*, *20*(1), 1-12. https://doi.org/10.1186/s12910-019-0414-6

Petrini, C. (2010). "Broad" consent, exceptions to consent and the question of using biological samples for research purposes different from the initial collection purpose. *Social science & medicine*, *70*(2), 217-220. https://doi.org/10.1016/j.socscimed.2009.10.004

Rothstein, M. A., Knoppers, B. M., & Harrell, H. L. (2016). Comparative approaches to biobanks and privacy. *Journal of Law, Medicine & Ethics*, *44*(1), 161-172. https://doi.org/10.1177/1073110516644207

Skolbekken, J. A., Ursin, L. Ø., Solberg, B., Christensen, E., & Ytterhus, B. (2005). Not worth the paper it's written on? Informed consent and biobank research in a Norwegian context. Critical Public Health, 15(4), 335–347. https://doi.org/10.1080/09581590500523319

Teare, H. J., Prictor, M., & Kaye, J. (2021). Reflections on dynamic consent in biomedical research: the story so far. *European journal of human genetics*, *29*(4), 649-656. https://doi.org/10.1038/s41431-020-00771-z

Wiertz, S., & Boldt, J. (2022). Evaluating models of consent in changing health research environments. *Medicine, Health Care and Philosophy*, 1-12. https://doi.org/10.1007/s11019-022-10074-3