The ethics of dead participants: policy recommendations for biobank research

ABSTRACT

Respecting people's consent choices for use of their material and data is a cornerstone of biobank ethics. Participation in biobanks is characteristically based on broad consent that presupposes an on-going possibility of informing and interacting with participants over time. The death of a participant means the end of any interaction, but usually not the end of participation. Research on causes of death makes biobank material from deceased participants extremely valuable. But as new research questions and methods develop over time, the question arises whether stored biobank material from deceased persons still can be used on the basis of their broad consent. In this paper, we discuss policies for post mortem use of biobank material, including consent options, proxy consent, and criteria for limitation of types of use and duration of storage. We conclude that the interests of participants in biobank research are best served by asking at enrolment if and how the biobank material may be used after death. We state that the use of biobank material from deceased participants should be delimited both by their consent and by the prevailing broad consent choices of living participants. Biobanks also need to inform participants at enrolment about the duration of storage of biobank material, or at minimum have procedures for deciding how long material will be stored for and for which purpose. For older collections, in the absence of such information or consent options, relevant authorities should decide.

BROAD CONSENT AND DEAD BIOBANK PARTICIPANTS

In medical research, the informed consent of participants is a fundamental requirement. Medical research participants should not be deceived or coerced into taking part, but should be offered comprehensive information about the risks, benefits and purposes involved. In this way, the participant can give a voluntary consent to take part in the specific project that he or she has been informed about.

In *longitudinal* (long-term) research biobanks, data collected from participants through questionnaires, interviews, measurements, clinical examinations and analyses of biological material, are stored for later use and combined with new analyses of biological material,

including genetics and epigenetics. This *biobank material* may also consist of connecting properties of such stored data to events earlier or later in life, gathered from medical and other records, and including cause of death.

Biobank participants are typically asked to give a *broad* consent[1]to take part in these broadly defined projects, agreeing to broadly defined goals, research methods and governing procedures for their biobank material. Their consent is also *long term*, valid for decades of use in medical research. Biobank participants thus give their consent to projects that stretch out wide both thematically and temporally. The specific nature of longitudinal biobank projects is unknown at the time of consenting, as new interests, knowledge and methodology continually give rise to unforeseen future research projects.

To ensure that the participants are properly informed, broad consent requirements include giving biobank participants regular updates on the use of biobank material, having easy access to opt-out mechanisms, and demanding renewed consent or renewed ethics committee assessment in case of substantial changes in the use of the material. Currently, the opportunity of offering personal web pages for biobank participants gives increased possibilities for updates and continuous specific consent options.

As research biobanks set up over the last decades continue their existence, an increasing amount of stored material will be derived from deceased participants. Especially for research on causes of death, access to biobank material of deceased participants is of great value. But how can the ethical framework of broad consent be fulfilled after the death of a biobank participant? Obviously, it is no longer possible for the biobank institution to update the dead participant, nor possible for the dead participant to renew or withdraw his or her consent.

What is the significance of this predicament? Does the death of a participant mean that the ethical basis for further use of the material ceases to exist, because the broad consent requirements become impossible to fulfil? Or does it rather mean that the basis for any restrictions on the use of the material is annulled, because dead participants simply cannot be harmed and informed consent loses its meaning?

In this paper, we will briefly consider the symmetry between risks of harm for living and dead biobank participants, before we offer a broad overview over diverging points of view emerging from current international documents and biobank consent practices, highlighting the need for clearer guidelines. We proceed to discuss how biobank institutions can acknowledge and accommodate the interests of biobank participants in respectful handling of their contribution after death. Based on this discussion we give recommendations

for good biobank practice concerning the possibility of continued use of material from dead participants for research purposes.

POST MORTEM HARM OF BIOBANK PARTICIPANTS

Even though there is some mention in existing regulation of how to deal with biobank material of dead participants in a proper way, it might still seem strange and strained to talk about *harming* dead participants, since they obviously are insusceptible to any pain or adverse health effects. Interestingly, however, the same objection has been levelled at strict protection of *living* biobank participants: Biobank research is largely non-invasive, as inclusion is restricted to the use of tissue already procured from medical treatment or minimally invasive procedures such as giving a blood sample. Thus the participants are susceptible to no or only negligible risk of bodily harm. No consent has therefore traditionally been regarded as necessary for using stored tissue from hospital biobanks.

Biobank participants' interest in privacy and integrity protection is however increasingly recognized. Currently, the information and biological material from the participants are widely held to belong to their private sphere. The integrity and privacy risks concern information going astray, or being used for projects and purposes that the participant does not endorse. The participant is also granted a right (not) to know risk information concerning oneself and one's family members.

Although debated[2], we maintain that there are good arguments to speak of the possibility of harming dead people, or of people having surviving interests after their death[3]. The possible risks of harm for dead biobank participants are to a large degree the same as for living participants: Unwanted information from analyses of material and data from the participant with possible implications for relatives, confidential information being made public, unwanted use of material and data in new kinds of research, unwanted use by commercial and other actors because of new ways of sharing and storing, unwanted use of material and data for other purposes than health research, unwanted linkage of data to other registries, unwanted changes in how and by whom assessments are done of proper use and access to data, etc.

Being exposed to risks of harm in terms of privacy and integrity infringements, biobank participants do not want their submitted questionnaires to be misused by biobank researchers (for instance to be given to a biographer), irrespective of any chance that they will ever become aware of this. This kind of interest seems in TM Wilkinson's term *symmetrical*

between living and dead participants: Death does not make a decisive difference to the interest in integrity in question.[4]

Likewise, death does not seem to make any changes in a participant's decision not to take part in certain types of projects. The same goes for interests in who gets access to the material. If a living participant does not endorse the use of his or her material by drug companies for instance, it seems reasonable to adhere to this preference when the participant dies.

PARTICIPATION AFTER DEATH IN INTERNATIONAL POLICIES AND GUIDELINES

The rights and duties connected with the use of material of deceased participants are not widely addressed, and policies or regulations on the use of biological material of deceased participants are few and divergent. A recent review paper found that in the 30 German consent templates and 10 prominent international guidelines identified, none explicitly mentioned how to dispose of biobank material after death.[5] Another review paper reports that just 4 out of 22 international ethical and legal guidelines (very briefly) addressed the effects of death on participation in biobank research. Only 2 out of 54 biobank consent forms and information documents directly addressed the fate (no withdrawal after death) of research material and data collected before the death of a participant. The very diverging points of view on the matter are reflected in the statement that "most international guidelines do not foresee the impact of death, American law only applies to living individuals, and Canadian guidelines barely distinguish between the rights of living and deceased participants".[6]

Some mention of the impact of death on disposal of biobank material can nevertheless be found in international documents. WHO state in a report that the "death of an individual who has provided a genetic sample or genetic information does not represent the end of the ethical responsibilities that are owed in respect of the material or information. Death only affects the primacy of the interests of the sample source, and does not extinguish them."[7] What remains unclear here is what it means that ethical responsibilities do not fall away with death. To whom do we have continuing responsibilities, and how should these responsibilities be dealt with in practice?

Most biobank documents gloss over the question of post mortem use of material by mentioning or presuming *indefinite* storage for research purposes. In a few documents, however, three particular aspects of post mortem use are considered. Firstly, regarding the legitimate *duration of storage* of material from participants in longitudinal studies, OECD

advises that "how long the human biological material, the data and information may be stored will vary according to the nature and potential uses of the specimens or data."[8] A second aspect concerns whether the deceased has any *surviving interests* in the use of his or her biobank material. In its commentary on taking post mortem material, the UNESCO International Bioethics Committee suggests that decedents retain privacy interests: "DNA testing of the dead is potentially an infringement of privacy rights which the deceased enjoyed during his or her lifetime. There are, however, legitimate purposes which might be served by testing the dead (...) [U]nless it is known that the deceased held an objection to the procedure, there might be a presumption of altruistic intent and testing might be permissible."[9] The European Society of Human Genetics holds that decedents retain some authority, such that "concerning post mortem uses of material, a policy of unrestricted access cannot be justified on the grounds that the risk or harm for the subject are no more an issue. If individuals restrict use of their sample when they are still alive, those restrictions apply after their death."[10]

A final aspect concerns the question of *how, and by whom, decisions should be made* regarding post mortem use of material. Should options regarding post mortem use be included in consent forms? Should relatives and ethical committees decide on post mortem use? The UK 100,000 Genomes Project allows a role for relatives. Although the use of material in most instances will be continued after a participant's death, they state: "If relatives of the decedent have a different view after the participant has died then this will be handled sensitively by the patient's medical team and Genomics England. The relatives' wishes will usually be taken in consideration."[11] The Italian CHRIS Study lets participants decide on the post mortem use of their material, by offering this choice in their consent form: "In the event of my death or sudden loss of legal capacity, I decide that: my material and data are destroyed / my material and data are anonymised / my material - taking into account the limitations of the declaration of consent - is completely made available for research purposes".[12] In this way, the authority over the post mortem use of the material is firmly placed in the hands of the participant.

RESPECTING DECEASED BIOBANK PARTICIPANTS' INTERESTS

The few guiding statements in documents regarding post mortem use of biobank material thus revolve around these three issues: protection of participants against post mortem harm, duration of storage, and authority of deciding over the material. Of these three, the protection of participants against post mortem harm is central, because the reasons for deciding on a time limit of storage or for a governing model depend on the premise that post mortem harm can be done.

Protection of participants against post mortem harm

A challenge in deciding on the use of material from participants emerges when the content or the context of biobank research on their material changes after their death. Substantial changes might make the given consent *insufficient* because it does not comprise of improvements in how research is done, or *irrelevant* because of unforeseen kinds of research, changes in how research is governed, or even changes in moral norms in society. If the content of the consent is old-fashioned and insufficient it might still be interpretable to fit the current situation. But if the content of the consent is irrelevant it might become an open question which interests the deceased participant has.

For such new types of research that deceased participants have not explicitly consented to, a proposal might be to handle the material in the same way as material from non-consenting contributors to research, like patient biopsies that are stored after diagnostics. In many jurisdictions, such material can be used with certain restrictions, for instance anonymization, or only for research that cannot be performed otherwise and that can be highly beneficial for society. Maybe the same restrictions should apply to material from deceased participants in biobanks? We do not think so.

Although it is true that no explicit consent was given for the new type of research, deceased participants once made a conscious decision to contribute to research and it may thus be correct to presume an altruistic intent, as pointed out by UNESCO.[13] It would therefore be wrong not to respect this altruistic intent and refrain from using material from the deceased, or anonymize the material by default.

Regarding new kinds of research on or use of biobank material, introduced after the death of a participant, such use will simply not be covered by their consent. But current participants' choices may give indications for prevailing preferences. When living participants generally accept the new type of research by giving renewed or fortified consent and when the new type of research is included in broad consents given by contemporary biobank participants, we may assume that the new type of research or use has become generally accepted. We can further assume that deceased participants would have been positive to this new type of research and would consent to it, unless there are specific indications that the participant did not want to contribute to the kind of research in question.

Our argument here is not that the current participants are given the task to understand the past moral sensitivity and will of deceased participants, but that it is reasonable to assume that the deceased participants would have had the current sensitivity if still alive. This means that material can be used for current generally accepted types of research or use, but not for new kinds of research or use that are controversial (for instance if it requires a specific consent by living participants, in addition to their broad consent to take part). In the same vein, if specific consent choices were made by the deceased, these should be respected.

With time, controversial research questions and methods may become common and uncontroversial, and be transferred from specific consent choices to broad consent. Also, research and use that we now regard now as permissible might become unacceptable in the future. Such changes in research ethical norms might give good reasons to protect dead participants from their previous choices.

Duration of storage

As mentioned, with time there can be great changes in the nature of biobank research: Changes in research topics and aims, how research is financed and approved of, how, why and to whom biobank material is shared, as well as political and moral changes in society at large. The time dimension is ethically relevant both in terms of how the use of biobank material may change with time, and in terms of how the moral significance of the decedent changes with time. Are the concerns and wishes of the deceased eternally valid - or do they fade with time? WMA state that for biobanks, "[g]overnance arrangements must include (...) arrangements for the length of time for which the data or material will be stored."[14] Likewise, the General Data Protection Regulation, legally binding for all EU member states from May 25, 2018, also requires time restrictions on the storage of personal data, where "time limits should be established by the controller for erasure or for a periodic review."[15]

Could biobank material become common property some years after the death of a participant, for instance a generation (30 years), based on a conception of dwindling post mortem interests of the deceased and relatives with time? It seems reasonable to offer participants a say in this. In the same line of reasoning, it could be argued that there should be a moratorium period of no use of biobank material for some time after a participant's death, to make sure that the material is not used against the participant's intended use at least the first time after death. To make this a general rule, however, seems to go against the altruistic intent of the consenting participants.

Another possibility would be to destroy the material after the death of the participant, or after a certain amount of time, because future changes in research, societal norms or governing mechanisms cannot be foreseen. This would prevent or limit unwanted post mortem contribution to research or other unwanted use. On the other hand, such a policy would destroy valuable research material and again potentially go against the altruistic intent of the consenting participants. If it is possible to ask the participant, we think it is reasonable to offer the choice of destruction of material after the death of the participant, or after a certain amount of time after the participants' death.

One of these policy options – common property, moratorium period, time limit or destruction after death – could be implemented by the relevant authority for already existing material from now deceased participants, as further detailed in the next section. For new or still living participants we think participants should be offered consent options regarding post mortem use, as illustrated in Box 1.

Authority to decide on the post mortem use of biobank material

Does offering participants consent options regarding post mortem use further mean that they should decide on such use in detail? This would enable participants to take control of the use of material after death, and avoid unwanted use in a specified way. The nature of the possible future use might, however, be hard to specify for participants, and consent choices may be hard to interpret if slightly insufficient or irrelevant. The decisions of the participant might also go against the wishes of living relatives in cases where they can be regarded to have a legitimate say, for instance regarding projects entailing predictive testing for hereditary diseases. These considerations should lead to caution in offering specific consent options for post mortem use.

When no choices are made by the participants concerning post mortem use, the use of proxy decisions by relatives might also be a possibility. This line of policy is challenging, as we know that it may be difficult to appoint and reach proxies, and that proxies may have difficulty deciding in line with relatives' wishes.[16]

We suggest that when no decision is made or can be made by the participant, relevant authorities should decide. In making such decisions, a governing principle could be that while most of the interests of participants fade with time after death, some might remain, at the same time as the potential for significant changes in use of biobank material increases with time after death.

POLICY RECOMMENDATIONS AND CONCLUDING REMARKS

In this paper, we have demonstrated the need for biobank policies regarding the handling of biobank material from deceased participants. Our conclusions have direct practical indications for the government of biobanks. Biobank institutions should have explicit policies on how material from deceased participants is managed, and inform researchers and participants of the ethical issues of doing research on biobank material from deceased participants.

Table 1 provides an overview of the possible policies discussed in our paper, including the main arguments for and against each element in a comprehensive policy of handling biobank material from dead participants.

TABLE 1. OVERVIEW OF POSSIBLE POLICIES

POLICY	PRO	CONTRA
Protection of participants against post mortem harm		
A. Use of dead participants' material is to be considered in the same way as the use of data and material from non-consenting persons	Dead participants are unable to change consent options/opt-out	Disrespect of dead participants altruistic intent
B. Dead participants' material can only be used for research types that were known at the time participants were still alive/included in the consent information material	Makes it clear for participants, biobanks and relevant authorities what is comprised of by the consent	Does not respect participants' broad consent to take part in future use of material, including types of research that go beyond those known at the time of death
C. Use of dead participants' material follows the prevailing consent choices of living participants	Most likely to be the correct interpretation of the broad consent given by the deceased	Could include participants in types of research they would not have consented to
POLICY	PRO	CONTRA
Duration of storage		
A. Destruction of the material after a participant's death	No danger of unwanted post mortem use of material	– Waste of valuable research material – Goes against altruistic intentions of the participant

B. Time limit of X years to use of material	– Offers participants a definite participation period – A pragmatic solution to deal with unforeseeable changes in the use of biobanks through time – Reduced danger of unwanted post mortem use of material	– Waste of valuable research material – May not fully respect altruistic intentions of participant
C. Moratorium: no-use period of time, after which it will be allowed to use the material	The significance and vulnerability of dead individuals weaken over time, both for the deceased and relatives	– Partly waste of valuable research time – May not fully respect altruistic intentions of participant
POLICY	PRO	CONTRA
Authority deciding over the material		
A. Dead participants' material can only be used in accordance with detailed consent by the deceased participant	Enables participants to specify the use of material after death	Might be hard to specify for participants, and may go against wishes of relatives
B. Dead participants' material can only be used in accordance with consent by proxies	– Continued assessment of aspects of participation, and possibility of withdrawal, is part of broad consent – If relatives are the ones that can be harmed by improper use of material, they should decide on the use	– The deceased might not want to appoint any proxy – Proxies might lack a good understanding of the wishes of the deceased – Identifying, reaching and replacing proxies might present considerable practical problems – Proxies' interests may clash with participant's interests
C. When no adequate decisions are made by the participant, relevant authorities should decide	Enables post mortem use of material in line with ethical assessment by relevant authority	Might go against the interests of the deceased participant, relatives and/or researchers

As biobank participants' broad consent leaves room for interpretation, we argue that their material as a general rule may be used post mortem for new types of research that are included in broad consent forms in use after their death. The material should not be used for types of research that require additional specific consent by new participants, as the purpose of specific consent options is to allow general participation even if you decline to contribute to a specified part of the biobank research.

Regarding duration of storage, we argue that biobanks should let participants decide at enrolment how long their material may be used after their death, or at least inform participants about the duration of storage (*see* Box 1). The minimum required for all biobanks would be to have procedures in place for how decisions on continued storage are taken.

When no guidelines are in place, and no consent can be obtained from participants anymore, we conclude that relevant authorities such as ethics committees or independent steering committees should decide on the use of the material. Such authorities should balance the interests of the participants and presumed altruistic intent against societal interests, with the prevailing content of contemporary broad consent as the guiding principle. Again, deceased participants should not be included in forms of research that require additional specific consent. Such a policy is appropriate to respect deceased participants' wishes to benefit to research and to society, while avoiding use of the material for controversial types of research that deceased participants may not have consented to.

CONSENT OPTIONS/POLICY
The use of data and biological material from you will be stored indefinitely for use as described in the information sheet of the biobank. Do you allow that your data and biological material is available for future types of research that are unknown now, but which are included in the broad consent given by future biobank participants, as long as these do not go against any specific consent restrictions from you? ☐ Yes, after my death, data and material from me can be used as described above ☐ No, after my death, data and material from me can only be used as described in the current biobank information sheet ☐ No, after my death, data and material from me can only be used as described in the current biobank information sheet for X years after my death

☐ No, in case of death I withdraw my consent, and all data and material from me must be deleted

Box 1. Informed consent template

REFERENCES

[1] Broad consent, in different versions (*see* for instance reference 2), is used in biobank research worldwide, with the exception of some jurisdictions, most notably France. Cf. also recital 33 of GDPR, see reference in endnote 19. More narrow and specific consent types are also in use, especially in diagnostic and thematic research biobanks.

[2] See for instance **Taylor J.** The Myth of Post Mortem Harm. *American Philosophical Quarterly* 2005;**42**(4):311–22.

[3] We do not elaborate on this position here, but refer to an earlier article by one of the authors. The question of harming dead persons is a complicated one, but a thorough discussion of this question is outside the scope of this paper.

[4] **TM Wilkinson**. Last rights: the Ethics of Research on the Dead. *Journal of Applied Philosophy* 2002;**19(1)**:31-41.

[5] **Strech D.** A template for broad consent in biobank research. Results and explanation of an evidence and consensus-based development process. *European Journal of Medical Genetics* 2016;**59**:295-309.

[6] **Tassé AM.** Biobanking and deceased persons. *Human genetics* 2011;130;**3**:418.

[7] **WHO.** *Genetic databases: Assessing the Benefits and the impact on Human and Patient's Rights.* World Health Organization 2003.

[8] **OECD** Guidelines on Human Biobanks and Genetic Research Databases. 2009.

[9] **Rumball, S & McCall Smith, A** *Human Genetic Data: Preliminary Study by the IBC on its Collection, Processing, Storage and Use.* Paris, UNESCO International Bioethics Committee. 2002:18.

[10] **ESGH.** *Data storage and DNA banking for biomedical research: technical, social and ethical issues: Recommendations of the European Society of Human Genetics.* European Journal of Human Genetics 2003;**11**;S2:S8–S10. The ESGH and UNESCO statements pertain to the type of use of material of dead persons in general, but in the second statement there is a distinction between those who have consented while alive and those who never consented. In line with this distinction, it might be argued that the basis for UNESCO's "presumption of altruistic intent" is stronger for consenters.

[11] **Genomics England.** https://www.genomicsengland.co.uk/the-100000-genomes-project/faqs/ethics-and-consent-faqs/ Accessed 22.12.2016

[12] **CHRIS.** http://chris.eurac.edu/de/ethics/Pages/Informierte-Einwilligung.aspx. Accessed 22.12.2016

[13] **See reference 8: Rumball, S & McCall Smith, A**

[14] **WMA.** *Declaration of Taipei on Ethical Considerations regarding Health Databases and Biobanks.* World Medical Association. 2016.

[15] GDPR, point 39, http://eur-lex.europa.eu/legal-content/en/TXT/?uri=CELEX%3A32016R0679 accessed Jan. 10, 2018

[16] In addition, proxies may have a personal interest in how the material is handled, for instance when it comes to genetic dispositions and disclosure of research results to participants that may either harm or benefit them. Of course, if the primary aim of the policy is to promote the interests of living relatives, this is not a major problem. A discussion of to protect the interests of the living is as such, however, outside the scope of this paper.