Biobanks are repositories for human material, such as tissue samples and DNA, that can be used for research purposes. Biobanks can be extremely large-scale, with the UK Biobank having collected samples from over 500,000 individuals[1]. The combination of genetic data with the health, lifestyle, and demographic information of each participant makes biobanks a formidable resource[2] for medical research.

It has generally been considered an ethical requirement that informed consent be obtained from any study participants. This holds true for biobanks. Uniquely for biobanks, due to their massive scale, this ethical requirement would entail substantial resources and time dedicated to consenting each of tens of thousands of participants. Further, repeatedly consenting willing participants could over time lead to poor retention rates.

To avoid this, researchers have introduced the concept of *broad consent*, where participants provide blanket consent to studies conducted with a specific aim or by a specific group. This allows participants to consent to multiple studies at once, including studies for which details like aims, methods, and design have not yet been determined (hereafter referred to as *future studies*. For clarity, I will refer to the individual who broadly consents to future studies as the *participant*).

Most definitions for informed consent require that information be disclosed and understood by a competent participant such that they may make an autonomous decision[3]. The important implication here is that the broad consent model cannot offer a high level of disclosure – since future studies have not yet been conceived, their details cannot be communicated. This has led ethicists to question whether broad consent can be considered informed, and therefore ethical[4].

The question I seek to address in this essay is, can broad consent be informed? In this essay, I explain the most frequently used argument in favour of broad consent, as explained by Gert Helgesson in his article, *In Defense of Broad Consent*. Then, I consider several important objections, ultimately proposing that the practice of broad consent be adapted to address these concerns.

A discussion of Helgesson's *In Defense of Broad Consent*.

The main objection to broad consent is that it cannot be fully informed. This objection rests on the idea that failure to convey necessarily unavailable details would result in a failure to adequately inform the participant. Therefore, to fully address this objection, we must understand the knowledge requirements for informed consent.

Traditionally, participants are deemed adequately informed when they have been given full knowledge of the nature and risks of the study. Some investigators address this by increasing the quantity of information shared with participants, in accordance with the dogma that more information is always better. However, some have questioned whether this is truly in line with the spirit of informed consent[5,6]. To illustrate this: it has been shown, when asking consumers to make quality evaluations of hospitals, that communicating important information (like number of registered nurses per 100 patients) and omitting less important or relevant information (like the number of beds) increases the percent of consumers selecting the correct 'highest quality hospital' option[7]. Thus increasing the quantity of information communicated eventually reduces comprehension in consumers. This is critical to informed consent: information must both be disclosed *and* understood by a competent participant; if the quantity of information disclosed is such that comprehension is compromised, then researchers would have failed to inform in a similar way to if they had not conveyed sufficient details altogether.

It is therefore clear that the knowledge requirements for informed consent cannot be every study detail, as this may eventually reduce understanding in the participant. What should be the knowledge requirements for informed consent? Helgesson argues that informed consent is possible when the participant has all the information she would require to make an autonomous decision. This definition, being almost tautological, seems a strong alternative to our traditional requirement of full knowledge disclosure. With this new definition, the knowledge requirements for informed consent would be satisfied so long as further disclosure would have no impact on the participant's decision-making process.

Helgesson also acknowledges variation in an individual's information preferences. He then argues that, in accordance with this individual variation, the knowledge requirements for an autonomous decision may differ from individual to individual.

With this in mind, we should return to the primary objection to broad consent (as given by the influential Árnason 2004 paper)[4]:

> *If we are to preserve a meaningful notion of informed consent for participation in research, it should only be used about specified research where the participants are informed about the aims and methods of a particular research proposal. There is no such thing as "general informed consent." The more general the consent is, the less informed it becomes. It is misleading to use the notion of informed consent for participation in research that is unforeseen and has not been specified in a research protocol.*

Árnason believes that the lack of information disclosure inherent to the process of broad consent precludes all individuals from giving informed consent. His argument, however,

rests on the assumption that disclosing less information makes the participant less informed. His argument is in line with our traditional understanding of the knowledge requirements for informed consent.

To return to Helgesson's argument, and to our revised understanding: if there are individuals for whom additional disclosure would not influence their decision-making process, then the information requirements for informed consent have been met. Broad, informed consent is therefore theoretically possible for those individuals who would not require details like specific aims and methods. In this way, Helgesson gives us an account of how broad consent may also be informed.

A response to Helgesson's objections: the limits of imagination.

We have established that the knowledge requirements for informed consent depend on the individual. These knowledge requirements are met when giving further information would not influence an individual's decision-making process. This makes it possible for a subset of the population to give broad, informed consent.

It therefore becomes important to ensure that broad consent is only obtained from this specific subset of the population; failure to do so would mean that the consent obtained is not informed and thus not ethical. How can researchers ensure this? Helgesson suggests that the lack of information inherent to the broad consent process should be explained to potential participants. These potential participants must then imagine what information they would require to make an informed decision about participating.

An important objection follows from this line of thought. It is possible that the participant may fail to imagine that she would require more information than is provided during the broad consent process, as there are limits to her imagination. Subsequently, without being confronted by this information during the consent process, she might give uninformed consent. For the purposes of this essay, I will refer to this issue as the *limits of imagination risk* (LIR).

Helgesson addresses this objection in two ways. First, he argues that for many (if not all) consent processes, researchers often convey only some salient study details to protect participants from information overload. Therefore, in all consent processes, researchers expose participants to LIR. Since this objection applies equally to broad and traditional consent cases – and given that we consider traditional consent practices ethical – Helgesson argues that we already accept LIR.

However, it seems that the process of broad consent makes the participant particularly vulnerable to failures of this nature. To illustrate this, take the example of a research group investigating novel treatments for leukaemia. The participant feels strongly that she would accept significant physical harm (e.g. bone marrow sampling) to further research in this area. She may then give enthusiastic broad consent to the use of her stem cells. However, the participant is vegan and feels strongly opposed to the use of animal models in research. When giving broad consent to this research group, she may fail to imagine that their research aims, centred around a human bone marrow cancer, could involve the use of live mice. If the leukaemia group were to implant human donor stem cells into living mice,

furthering their research aims by allowing invasive observation of the disease, this would clearly demonstrate a failure of imagination on her part. If, however, she was involved in a conventional consent process, she would naturally be made aware of the use of mice and refuse to give consent for participation. It therefore seems clear that the LIR is much greater in broad than traditional consent.

Helgesson alternatively addresses the "limits of imagination" objection by stating that this risk is one that participants must estimate for themselves[8]:

> *The response here has to be similar to the one given to the first argument: this will have to be a calculated risk for those giving broad consent. This risk is not as such unacceptable from an autonomy perspective if it is pointed out beforehand. Nor would it be unacceptable from a participant safety perspective to allow broad consent, because researchers and ethical review boards (ERBs) are obliged to make sure that participation in research does not involve unacceptable risks.*

In arguing that LIR must be a calculated risk, Helgesson puts the onus of calculating LIR on the individual. The assumption Helgesson makes in this argument is that the average participant can calculate such risk. Does this reflect reality?

The layperson is incapable of making optimal decisions in many specialised areas of life. There is often too much evidence for and against any decision for any single individual to adequately synthesise[9]. We acknowledge this in everyday life, for example by allowing climate scientists to inform us about climate change, or by allowing lawyers to advise us on legal issues.

In the same way, I argue that it is entirely unreasonable to expect a layperson to be able to estimate the LIR associated with biobank-based studies. Under traditional consent, we may ask medically trained experts to appreciate study details and anticipate what may be important to explain to the layperson; this minimises LIR. But in the case of broad consent, where there are no study details to appraise, the participant can only be informed that these details are undetermined. It is unethical to expect the participant to estimate LIR on this basis. We ought not to rely on these estimations to justify broad consent.

Can we sidestep the limits of imagination risk?

Is there still a way to give broad, informed consent? It may be useful to consider a hypothetical case. Jane is very interested in world events. She has, in the past, walked to a nearby newsstand and read the headlines before committing to purchasing the *New York Times*. Now, she is considering getting a subscription. This would save her the daily walk. However, this also commits her to paying for the newspaper every single day, whether it is a slow news day or not.

Here, Helgesson's justification would be akin to asking Jane to estimate her interest in future headlines, and then to subscribe based on this calculation. Whatever predictions Jane makes is likely to poorly align with which world events truly come to headline the *New York Times*.

And yet, it seems an entirely ordinary exercise of autonomy for any individual – expert or not – to commit to a newspaper subscription. How is this possible? Because people do not subscribe to newspapers on the basis of any prediction they have made about how interesting future headlines may be. They simply choose to trust the reporters to write interesting papers.

This is an important distinction. I have argued that it is not ethical to ask the participant to estimate her own LIR, as she is not an expert and is thus ill-equipped to make such calculations. I appeal, however, to our intuitive sense that a subscription to the *New York Times* is not unethical. We can then apply this to the case of broad consent. The participant cannot give broad, informed consent to her participation in future studies – the LIR is too great. In the same way, it would be unreasonable to expect Jane to predict that she would enjoy reading about the future events that may come to headline the *New York Times*. However, Jane may trust the reporters to write interestingly – and in the same way, the participant should be able to give broad, informed consent to having a *medical ethicist* make decisions regarding her participation on her behalf.

Practically speaking, this medical ethicist would evaluate biobank studies as they are conceived, and then anticipate what elements of the study each participant may find acceptable or unacceptable. If the medical ethicist were to predict that the participant would find a specific method or aim unacceptable, the ethicist would be obligated to withdraw the participant's tissue sample or data from the relevant study. This entire process could take place without the participant's input.

To ensure that the medical ethicist could make these value judgements on the participant's behalf, they could conduct a series of interviews at the point of tissue and data collection for storage in the biobank. Alternatively, a questionnaire could be used, upon which ethical values like veganism and an opposition to the use of animals in research could be communicated.

In this way, the knowledge requirement for giving informed, broad consent would specifically pertain to the ability for the medical ethicist to evaluate on behalf of the participant. The ability for a medical ethicist to make these value judgements can be made known to a participant in entirety – through interviews or questionnaires – and so I argue that there is minimal associated LIR.

It is still the case that specific study details like aims and methods cannot be important to the participant's decision-making process if broad consent is to be informed and ethical, as the medical ethicist cannot replace this lack of knowledge. However, the existence of the medical ethicist reduces the LIR to acceptable levels. Relying on the medical ethicist should make broad, informed consent possible.

Objections to the *New York Times*: is slavery analogous to broad consent?

It may be argued that the similarity between biobank research consent processes and the *New York Times* subscription does not prove that such decision-making is ethical. For example, the freely-made decision to sell oneself into slavery is also analogous to a

subscription to the *New York Times*. In both, one decides not to make further decisions each day[10]. Yet selling oneself into slavery seems almost self-evidently incompatible with autonomy[10], whilst the decision to commit to a *New York Times* subscription seems equally self-evidently permissible. Where does the scenario of broad consent to biobank research fall between these two extremes? What separates a *New York Times* subscription from slavery?

One potential distinction that can be made is that of the harm which we can expect to come from such a decision[10]. A poor day of reporting is minimally harmful, whereas the potential harms that come from slavery are undeniable. Therefore, to judge the ethics of broad consent, some evaluation of the potential harm could be made.

However, even if we were to completely remove all physical and emotional harms associated with slavery, it still seems we would find slavery objectionable. At the same time, many people voluntarily enter professions which put them at the risk of great harm: those who become soldiers, for example, may regularly endanger their physical and emotional wellbeing. The profession is still considered an ethical career path. The same is not thought of slavery. It therefore seems that our ethical issues with slavery do not arise from the associated harm.

I therefore turn to autonomy as the most important distinction. A newspaper subscription and the choice to enter slavery both seem a decision not to make further decisions. However, the consequences these decisions have on one's future autonomy are disparate. Whilst a newspaper subscription has no bearing on one's ability to make future autonomous decisions, slavery – by definition – is limiting.

Having established what separates these two examples, we must return to our discussion of broad consent. Does broad consent limit the participant's ability to make future autonomous decisions? Certainly, broad consent mirrors the *New York Times* subscription in that neither situation limits her expression of autonomy in other areas. Consenting to participate in biobank research, for example, has no effect on that same individual's travel plans later that year. This is also true of a *New York Times* subscription. Entering slavery, however, would certainly affect one's travel plans.

It can be argued that the participant's broad consent limits her future autonomy in that she has now committed – even autonomously – to her ongoing participation. This objection can be addressed in the same way that one addresses ongoing and newly unwanted subscriptions: intrinsic to the process of broad consent should be the understanding that the participant may, at any point, change her mind and be released from future participation. Biobank researchers ought to ensure that this be made simple and accessible for participants.

Conclusion

An ethical solution to the massive consent requirements for biobank studies would enable medical research on an incredible scale. In this essay, I have argued that broad, informed consent can be given so long as it meets several important conditions. First, it can only be given by the participant for whom specific details about study design would not influence

her decision-making process. This would then allow the limited available information inherent to broad consent to sufficiently inform the consenting individual. The participant would have to determine for herself that these unavailable details would not be important. However, because there is a risk that the participant may fail to imagine some information that would sway her decision-making process, it must be made clear to her that she cannot consent to her participation in future studies directly. The second condition is therefore that the participant must consent to having a medical ethicist (and relevant overseeing ethics review boards) make decisions regarding her participation based on their estimations of her values. Thirdly and finally, to protect the participant's autonomy once she has given broad consent, she must be able to withdraw her participation at any point.

BIBLIOGRAPHY

1. England and Wales. UK Biobank. https://www.ukbiobank.ac.uk/.
2. Master, Z., Nelson, E., Murdoch, B. & Caulfield, T. Biobanks, consent and claims of consensus. *Nature Methods* vol. 9 Preprint at https://doi.org/10.1038/nmeth.2142 (2012).
3. Beauchamp, T. L. Informed consent: Its history, meaning, and present challenges. *Cambridge Quarterly of Healthcare Ethics* vol. 20 Preprint at https://doi.org/10.1017/S0963180111000259 (2011).
4. Árnason, V. Coding and consent: Moral challenges of the database project in Iceland. *Bioethics* vol. 18 Preprint at https://doi.org/10.1111/j.1467-8519.2004.00377.x (2004).
5. Bester, J., Cole, C. M. & Kodish, E. The limits of informed consent for an overwhelmed patient: Clinicians' role in protecting patients and preventing overwhelm. *AMA Journal of Ethics* vol. 18 Preprint at https://doi.org/10.1001/journalofethics.2016.18.9.peer2-1609 (2016).
6. Rosenbaum, L. The Paternalism Preference — Choosing Unshared Decision Making. *New England Journal of Medicine* **373**, (2015).
7. Peters, E., Dieckmann, N., Dixon, A., Hibbard, J. H. & Mertz, C. K. Less is more in presenting quality information to consumers. *Medical Care Research and Review* **64**, (2007).
8. Helgesson, G. In defense of broad consent. *Cambridge Quarterly of Healthcare Ethics* **21**, (2012).
9. Hardwig, J. Toward an Ethics of Expertise. in *Professional Ethics and Social Responsibility* (1994).
10. Sheehan, M. Can broad consent be informed consent? *Public Health Ethics* **4**, (2011).