



Research on genetic Databases: Duties of Rescue and equal Respect to all

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Research on genetic databases: duties of rescue and equal respect to all

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Abstract

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The ideal exercise of Castellanos et al. asks IRB members to accept or deny a researchers' request for disclosing genes associated with breast-ovarian cancer, a potential clinically significant finding (CSF), to a subgroup of 1500 research participants of a research database of 300,000 subjects (1). Here, we will defend that researchers are under a rational duty to rescue. However, we also argue that only a decision that respects equally the rights and interests of all participants could be a fair and reasonable decision, compatible with ethics and the rule of law. Consequently, IRB members should not only accept the researchers' request to disclose potential CFS to database participants with breast-ovarian cancer genes but also to advocate for an update in the disclosure policy for all participants of the genetic research database.

The main identified problem for accepting this request is that, when enrolled, participants accepted that data would be deidentified and that they would not receive their personal results. The main non-identified problem is that, because of the (growing) nature of our genetic medical knowledge (2), there are (and will be) other CSFs besides BRCA status. Hence, other subgroups of participants in the database may benefit from disclosure besides the BRCA subgroup. Accepting to do it for one subgroup states a precedent. And not doing this for other subgroups in a similar situation would be unfair.

One could easily think of other CSFs (3). For instance, "Marfan Syndrome is an inherited [autosomal] disorder of the connective tissue which provides material and support for the skeleton, muscles, and blood vessels. Marfan patients are at risk of sudden death due to weakening of the wall of the large blood vessel leading from the heart (aorta)" (clinicaltrials.gov, NCT03567460). Although there is no cure for Marfan Syndrome, having the relevant diagnostic information may not only allow individuals to take preventive measures or enroll in clinical trials, but also inform their relatives and test their children for the disorder. The incidence of Marfan is 1 in 5,000 worldwide (4), so a rough extrapolation gives us 60 participants with Marfan in your database.

If our argument is sound, disclosing information to the BRCA subgroup and not doing it for the Marfan subgroup would be unfair. Hence, what is needed from the IRB members and the officials in charge of the research database is updating the policy disclosure of the database rather than a discrete decision for a subgroup. Furthermore,



other research databases have put in place mechanisms to manage information disclosure of CSFs to research participants (5), so in principle it is possible to do it without hindering further secondary research.

At this point, someone may think that denying all requests for incidental findings is the most cost-effective solution that will take into account the interest of all 300,000 participants as equal, since no subgroup will be potentially better off from individual incidental findings than other. However, if the government officials and researchers knowingly do not help research participants and their families to avoid tragic consequences, they might be in breach of the rational duty to rescue research participants (and their relatives) for suffering a terrible disease (6). We agree with Clayton's suggestion that researchers' angst and distress are not a reasonable cause of any ethical or legal obligations (1). However, with the correct ethical theory, we should realize that these feelings may be regarded as the emotional effect of researchers' realizing they are not complying with the rational duty to rescue or help others in what they can, although doing so is not the standard research policy of the database.

So, if our claim that researchers have a rational duty to rescue and this rescue is not impossible is sound, we should pay a closer look at the main identified problem of inform consent. Having consented to no disclosure 20 years ago is a reason with less weight that it might seem, especially if the decision at the time was to participate without disclosure or not participate at all. Extrapolating preferences from the Icelandic survey of Stefánsson (1), the majority (97%) of research participants may care for individual results today. But at the time of signing informed consent, contributing to science might have weighted more than not participating at all. So, the information in the static inform consent form does not reveal the true interests of the participants or how they might have evolved (7). Moreover, a contract between asymmetric parties (such as any contract for a massive service), has not the same moral weight as a contract where two parties with similar bargaining power set their conditions (such as selling a house in a normal situation). Inform consent in research often resembles the former rather than the latter. These considerations show a chink in the armor of any extreme defender of the ethical and legal force of inform consent in research, such as



Clayton (1). However, they do not allow us to disregard the “right not to know” of the minority (9,000 of total participants or 45 participants in the BRCA subgroup), as Stefánsson implies (1). Informing this minority about CSFs would be a disrespect of their autonomy and a moral harm (3).

One practical solution, would be to inform all the participants that there will be a change in the database original policy of disclosure and allow people to opt out if they do not agree. This or any other mechanism that tries to show equal respect between the interest of all participants would be perfectible and may need to be adapted to the context and practical constraints, such as, the list of CSFs that the database will inform or how this list would be updated. However, it would also make the IRBs decision ethical and legally better than any other mechanism not doing so.

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Supplementary Material

New England Journal of Medicine (NEJM) Comment

Title:

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Comment:

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