



Return of raw data in genomic testing and research: ownership, partnership, and risk–benefit

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The Alabama Genomic Health Initiative (AGHI) is a state-sponsored and institutional review board (IRB)-approved research initiative that carries out large-scale genotyping and returns results for medically actionable genetic variants to adult volunteers in Alabama, as well as genome sequencing to select individuals with a phenotype suggestive of a genetic condition. Recently, an initiative participant requested access to their entire genotyping results (“raw data”), analogous to what occurs for several direct-to-consumer genetic testing companies. Protected health information (PHI), and related patient rights to access this information under the Health Insurance Portability and Accountability Act of 1996 (HIPAA), certainly include information *about* genetics tests, genetic counseling, or genetic education. However, the full set of *unanalyzed* data extracted from a person’s biospecimen should not be regarded as protected health information as defined by HIPAA. A “genetic test” is defined by HIPAA as “*an analysis* of human DNA, RNA, chromosomes, proteins, or metabolites, if the analysis detects genotypes, mutations, or chromosomal changes” (45 CFR 160.103) emphasis. Because AGHI generates data under a research protocol, “raw” data, which have not undergone clinical analysis, are not regarded as falling under HIPAA. This understanding was offered and confirmed by the University of Alabama–Birmingham (UAB) IRB, and is consistent with specific recommendations A and B under recommendation 12 of the National Academies of Sciences, Engineering, and Medicine for return of research results:¹¹

A. Because the designated record set (DRS) is intended to include information used to make decisions about individuals, those decisions should be based on test results that are of sufficient quality to be valuable for decision making. Accordingly, the Office for Civil Rights (OCR) of the Department of Health and Human Services (HHS) should define the DRS to include only individual research results generated in a CLIA-certified laboratory

or under the externally accountable quality management system for research laboratories;

B. OCR should require all Health Insurance Portability and Accountability Act (HIPAA)-covered entities that conduct research on human biospecimens to develop a plan that is reviewed and approved by the IRB for the release of individual research results in the designated record set to participants in a responsive manner when requested under HIPAA;

In discussing the request among the members of the ethics working group of AGHI, several competing concerns were recognized, including our responsibilities as researchers, potential risks to the participant, and the importance of transparency, engagement, and partnership in human genomic research. A consideration of these concerns led us to a consensus recommendation for return of raw genomic data in AGHI, and may help guide discussions and approaches more broadly as the landscape of population-based genomic testing continues to expand.

Our first task was to ascertain the moral rights and obligations pertinent to the issue at hand. Rights claims would likely be grounded in participant claims of ownership of the raw data generated by their biological material, while obligations might be drawn from reasonable participant expectations stemming from the health professional–participant relationship.

While ownership claims for voluntarily donated biological material do not have legal standing,¹ a plausible moral case can be made based on rights of research participants to control of their body and its parts.² Such a moral claim is commonly recognized by oversight committees and federal regulations through the right of a participant to withdraw consent at any time³ and disallow further use of their biological material in research. However, access to raw data as a potential component of a moral ownership claim would be

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related to the ability to make discoveries from biological material; a claim that, like ownership of donated biological material itself, does not have legal standing.⁴ While this does not preclude a successful moral claim, the burden falls on the claimant to establish this moral extension of ownership. At present, it is unclear if or how moral claims of “ownership” might extend beyond control of biological material to include positive access to data derived from the biological material, including genotyping and/or genome sequencing data.

Nor can we see a plausible argument for an inherent or implied obligation on the part of a health-care initiative/institution to return nonclinical data as part of health research. While a case has been made for a fiduciary obligation to return genetic “incidental findings” that are unrelated to primary testing purposes in the context of clinical testing,⁵ raw data that is insufficient and/or unsuitable for clinical use does not fall within this realm. In addition, the features used to justify this fiduciary duty—accurate results for highly penetrant conditions and for which intervention may prevent serious morbidity—are, by definition, inapplicable to the raw data in question. Indeed, it is the unsuitability of raw data for clinical decision making that creates concern.

Nonetheless, we believe there *are* strong reasons to provide a path for AGHI participants to access their raw data, justified by the promotion of public trust in science, and the idea that patients and/or participants should be partners in research studies. Public trust in research based on biological materials is especially important given the example of Henrietta Lacks, whose family’s lack of insurance coverage effectively denied them access to treatments based on discoveries that relied on HeLa cells. The idea that there is a partnership between researcher and participant, together with transparency with regard to how biological material may be used in research studies, is also articulated in the All of Us and precision medicine initiatives.⁶

A path for AGHI participants to access their raw data should also come with oversight and potential restrictions, and is based on the well-established precedent that lack of knowledge and understanding required to safely utilize a health-care resource may create risk to the participant. Indeed, the idea of restricting access to certain medications through both prescription and FDA approval is based upon a fundamental recognition of this beneficence-based concern. Worries about risks related to premature reaction to false positives,⁷ false reassurance from negative test results,⁸ and overreaction to contextually meaningless results⁹ are among the most commonly cited concerns about genetic testing, and themselves threaten public trust in the reliability and wisdom of the enterprise itself. These risks are exacerbated by return of raw data, which might be utilized and uploaded to unreliable, unvalidated, and flawed interpretive algorithms and apps.

Balancing the above values and concerns, we have decided to make access to raw data available to AGHI participants, provided they enroll in a genetic counseling protocol for return of these data. Under this protocol, approved as an

addendum to our original IRB, participants undergo education to understand the limitations of the raw data, the reasons why it is deemed unsuitable for health-care decision making, and how those risks may be mitigated. Requiring participation in this separate protocol serves as a “speedbump” to ensure that requests for raw data are deliberate and thoughtful, while allowing a clear path whereby participants can mitigate risks associated with access to raw data. Our approach attempts to balance the value of true partnership with concerns to assure context and limitations of data are understood. The protocol is activated only upon a participant-initiated request for raw data.

Our protocol for access to raw data was developed by the AGHI genetic counseling working group, which includes genetic counselors and medical geneticists. The protocol (1) seeks to ascertain the motivation for seeking raw data so that unwarranted expectations can be addressed, (2) describes how different genotyping platforms may affect interpretation of genetic test results, (3) clarifies the role of prior information and assumptions in using genetic test results to make health-care decisions, and (4) explains the potential risks of false positive results, and the importance and process for obtaining clinically validated confirmatory testing. It is important to note that return of raw data is not, under this protocol, contingent upon “acceptable” motivations: ascertaining these motivations are relevant only to ensure that genetic *counseling* covers potential uses envisioned and explains potential risks adequately.

Our approach strikes an appropriate balance between respect for participant autonomy and beneficence-based duties to protect against the misuse or misinterpretation of raw data. Even the most prominent proponent of social and political autonomy—John Stuart Mill—recognized that intervention is justified to assure contextual knowledge (through, for example, his famous “bridge example” wherein one may forcibly stop an individual from crossing a bridge that they are unlikely to know poses significant danger).¹⁰ In addition, this approach is consistent with recommendations of the National Academies of Sciences, Engineering, and Medicine¹¹ for return of individual research results. Specifically, we have:

1. Determined the conditions under which individual research results will be returned to participants (recommendation 1): at participant request and with genetic counseling.
2. Developed a quality management system (recommendation 2) and ensured adequate infrastructure to generate high-quality results (recommendation 4): these are in place for all AGHI testing.
3. Ensured the high quality of results returned to participants (recommendation 3), and enabled understanding of individual research results by participants (recommendation 10): see (2) above and through the genetic counseling protocol.
4. Incorporated participant needs, preferences, and values in decision making about the return of individual research

results (recommendation 5). This is the primary purpose of this protocol.

In addition, utilization of the ethics working group and IRB advice reflect procedures developed to support and to incorporate review of plans regarding return of individual research results (recommendations 6, 7, and 8), and will, through its conduct under an IRB-approved research protocol, expand empirical evidence relevant to return of results (recommendation 11). Finally, by making available raw data to individual participants, this approach promotes transparency (recommendation 9).

DISCLOSURE

The authors declare no conflicts of interest.

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