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Returning a Research Participant's Genomic Results to Relatives: Analysis and Recommendations

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Abstract

Genomic research results and incidental findings with health implications for a research participant are of potential interest not only to the participant, but also to the participant's family. Yet investigators lack guidance on return of results to relatives, including after the participant's death. In this paper, a national working group offers consensus analysis and recommendations, including an ethical framework to guide investigators in managing this challenging issue, before and after the participant's death.

Keywords

return of results; incidental findings; genomics; family; return after death

Introduction

The debate about how to manage individual research results and incidental findings in genetic and genomic research has focused primarily on what information, if any, to offer back to research participants.[1] However, increasing controversy surrounds the question of whether researchers have any responsibility to offer a participant's results (defined here to include both individual research results and incidental findings) to the participant's relatives, including after the participant's death.[2] This question arises in multiple contexts, including when researchers discover a result with potentially important health implications for genetic relatives, when a participant's relatives ask a researcher whether any research results about the participant have implications for their own health or reproductive planning, when a participant's relative asks whether any of the participant's results have implications for a child's health, and when the participant is deceased and the participant's relatives seek information about the participant's genetic results in order to address their own health or reproductive concerns.

The question of whether relatives (a term used here to include genetic relatives as well as family members, such as spouses or partners, without a genetic relationship to the participant – see Definitions box) should be offered any of the participant's research results (whether at the relative's request or in an offer initiated by investigators) is challenging. Ethical and legal approaches to informed consent, research protections, and privacy safeguards in the United States mainly focus on the rights and interests of individual participants. However, first-degree biological relatives have 50% of their genetic material in common (with more distant relatives sharing genetic material to a lesser degree), and other

close relatives may be co-parenting the participant's child or sharing other family caregiving. A research participant's genomic results may thus have relevance for others. For genes with known pathogenic variants whose pattern of inheritance is understood, researchers may face the question of whether to encourage the participant to share results with relatives or whether the investigators themselves should seek to share the results, including after the research participant's death. Sharing through either route may allow relatives to seek genetic counseling and consider genetic testing, for themselves or children.

We consider return of the participant's genomic results to relatives in the research context. This is an emerging issue facing researchers. In contrast, clinicians have long faced questions of whether to alert relatives to a heritable condition or pathogenic variant in the patient because of the possibility that the relative (such as the patient's sibling or adult offspring) may share the same variant. In the clinical context, the dominant recommendation is for clinicians to urge their patients to communicate their genomic results to relatives themselves and offer assistance to their patients if requested, but the primary responsibility of the clinician is to maintain the privacy of patient health information and to avoid breaching patient confidentiality by reaching out directly to relatives to communicate patient health information unless the patient authorizes this.[3] Only in limited circumstances have some authorities recognized a clinician option to share the patient's genetic information directly with relatives: when efforts to seek patient consent to disclosure have failed, serious harm to identified individuals is highly likely without disclosure, disclosure is likely to avert the harm, and the scope of the disclosure is limited to the genetic information needed for diagnosis or treatment.[4] After the patient's death, the federal Health Insurance Portability and Accountability Act (HIPAA) (in institutions covered by that statute) and state law address access to patient health information and generally give rights of access and control to the patient's Personal Representative (PR), who may be the patient's executor. We discuss disclosure to the participant's representative below.

Recognizing the ethics and patterns of access for relatives in the clinical context aids analysis of access for relatives in the research context. Clinicians have a robust duty to care for their patients. In contrast, researchers are committed to generating generalizable knowledge, while conducting their research in a way that respects participants' rights. Because clinicians' first responsibility is to provide care, the argument for their concern to extend beyond the patient to relatives is stronger than in the research context, where the first responsibility is to create knowledge and any duty of care is limited.[5] Yet even in the clinical context, clinicians are not free to reach out to relatives to share a patient's health information; clinicians are generally bound to protect patient privacy, including after the patient's death. Clinicians can only share patient health information in limited circumstances. The clinical context suggests the outer limits of what researchers may do to share a participant's genomic results with relatives. In addition, research designs vary widely; in some contexts, investigators have little or no direct contact with the individual sources of data or specimens, much less their relatives.[6]

Debate has already begun on whether to offer a research participant's genomic results to relatives and possible processes for doing this.[7] Indeed, data are emerging indicating that many people feel they would benefit from or are entitled to be offered genomic results of a

family member.[8] In addition, studies to date have shown that approximately half or more of those surveyed would want their results shared with at least one relative after death.[9] This consensus paper responds to these emerging issues and provides investigators, Institutional Review Boards (IRBs) and other oversight bodies, funders, and all involved in the design of genomic research with an ethical framework and concrete recommendations for when, how, and with whom participants' research results may be shared. We consider the issues raised by sharing results from adult and pediatric participants (including adolescents), both before and after the participant's death.

I. Method

Funded by a grant from the National Cancer Institute (NCI) and National Human Genome Research Institute (NHGRI) at the National Institutes of Health (NIH), we undertook ethical and legal analysis of whether and how researchers might offer a participant's results to relatives, including after the participant's death. We conducted this analysis as part of a larger project that included data collection in an NCI-supported pancreatic cancer biobank and an associated family research registry at the Mayo Clinic.

The project's ethical, legal, and social implications (ELSI) Working Group of national experts was based at the University of Minnesota. The Working Group's expertise spanned clinical genetics and genetic counseling, research genetics and translational genomics, pediatric genetics and genomics, cancer genetics, biobanks, human research protections, law, anthropology, psychology, and bioethics. The Working Group experts met repeatedly over the course of 3 years, benefited from invited presentations by Working Group members and outside experts, and iteratively developed this paper. The group also benefited from meeting with a panel of 4 unrelated individuals enrolled in the Mayo Clinic research registry—a patient with pancreatic cancer and three relatives of pancreatic cancer patients. The Working Group's efforts were also aided by presentations of the project's empirical work, including analyses of interviews and survey data.[10] Research memoranda and assembly of a comprehensive online bibliography further supported the Working Group's progress. In November 2014, the project convened a public conference including presentation of the Working Group's recommendations for reaction and critique.[11] The group reconvened the next day to negotiate further changes. The paper was subsequently finalized by email.

II. Relatives' Access to a Participant's Results at the Present Time

Both ethics and law in the United States protect the privacy and confidentiality of health information about patients and research participants. Mapping the pathways by which this information may currently reach relatives, as well as the reasons that this information may not be shared, helps illuminate the core question: whether relatives should be granted *broader* access. Most germane here are the pathways for access in research. When research access is unclear, we note the relevance of rules surrounding access to clinical health information, where HIPAA plays a large role in governing access to protected health information in a great many health care institutions (what HIPAA terms "covered entities").

A. Current pathways by which a participant's results may reach relatives—A research participant's genomic information can already reach some relatives through several

pathways. These include: (1) direct disclosure by the participant to a relative, (2) investigator disclosure authorized by the participant, (3) investigator disclosure to a relative who serves in a representative capacity (for example, as Legally Authorized Representative (LAR) of the participant for research purposes, surrogate decision-maker for treatment purposes, or Personal Representative (PR) under HIPAA after death), (4) investigator disclosure to a relative because he or she is a parent or guardian of a minor research participant, (5) investigator disclosure to the relative's health care provider for treatment purposes, who then discloses to the relative, and (6) investigator disclosure after participant death to relatives who were involved in the participant's care or in payment for that care.

Most simply, if an adult research participant receives a research result, the participant is free to share this information with relatives. Participants may receive these results through return of results or incidental findings by investigators. They may also receive them by asserting their rights of access to their medical records under HIPAA (and/or state law), if research results are recorded in the medical record or the institution allows access to research records on the same terms as access to medical records. Institutions differ in whether they interpret the medical record (or “designated record set” under HIPAA) to include the research record. For example, some institutions have interpreted the “designated record set” to include the research record,[12] while others have not and have therefore denied participants a copy of the research record.[13] Until the privacy rules resolve this, participant access to the research record will vary by institution. Access will also vary by research practice. If an investigator records any of a participant's results in the participant's medical record, they become accessible to the participant, who may share that information further. In addition, 2014 changes to Clinical Laboratory Improvement Amendments (CLIA) and HIPAA rules may increase access of participants by permitting them direct access to reports in many circumstances.[14]

Relatives may gain access to a participant's genomic results when they serve in a representative capacity, for example as an LAR for research participation, surrogate decision maker for treatment, parent or guardian, or PR after participant death. All of these are types of representatives. Under HIPAA, “a person authorized (under State or other applicable law...) to act on behalf of the individual in making health related decisions is the individual's ‘personal representative’” and can access and disclose the individual's health information.[15] Note that a representative's authority may be limited under state law or by the terms of their appointment; their access to the participant's information would be limited accordingly.

Relatives may also be able to access participant data through their own physicians. HIPAA generally permits disclosure of protected health information to health care providers for purposes of treatment,[16] including treatment of relatives.[17] Thus, HIPAA permits but does not require “a doctor to disclose protected health information about a patient to another health care provider for the purpose of treating another patient (e.g., to assist the other health care provider with treating a family member...). For example, an individual's doctor can provide information to the doctor of a family member about the individual's adverse reactions to anesthetics prior to the family member undergoing surgery.”[18] Although an individual patient may request the restriction of such disclosures, a covered entity or health care provider need not agree to the restriction.[19] Comments to recent final rules specifically

state that “a health care provider may share genetic information about an individual with providers treating family members of the individual who are seeking to identify their own genetic health risks, provided the individual has not requested and the health care provider has not agreed to a restriction on such a disclosure.”[20] Because the rules allow providers to refrain from agreeing to a disclosure restriction requested by the individual, they remain controversial. Indeed, one commentator argues that this HIPAA provision allowing relatives access over the individual's objection “is at variance with established principles of medical ethics and should be ignored by health care providers until a better reasoned interpretation is developed by HHS.”[21]

Once a research participant is deceased, there are additional avenues of family access to a participant's results. The participant may have given Common Rule consent and HIPAA authorization while alive to share research-generated results with relatives, including after death. Even if the participant was not asked for such consent, a person authorized to act for the decedent or that person's estate (for example, the decedent's executor, who may be a relative) would customarily have broad access to and control over health information as the decedent's PR.[22] The PR may decide to share results with relatives. As noted above, HIPAA allows the participant's protected health information to be shared with relatives for their own treatment without authorization from the decedent or their PR,[23] though this provision may be questioned for inadequately protecting individual privacy. Some states similarly allow disclosure of a decedent's genetic information to “assist in medical diagnosis of blood relatives.”[24] Finally, HIPAA allows disclosure after an individual's death to relatives and others who were involved in the decedent's care or payment for that care unless disclosure “is inconsistent with any prior expressed preference of the individual that is known to the covered entity.”[25]

B. Current content of the results that may reach relatives by any of the above pathways—Even though there are already pathways for some access by relatives to a participant's results, it is important to consider the nature of the results likely to be available for potential return to relatives. The results available for potential return are likely to be those identified as relevant to the participant. Most recommendations to date have defined and prioritized returnable results in terms of their importance to the participant's health, reproduction, and personal utility.[26] The recommendations for return in the research context have generally not addressed return to relatives. The existing recommendations for return to participants typically urge return of actionable results indicating a serious health condition, while allowing researchers to exercise discretion in returning additional results that may offer net benefit to participants in terms of clinical care, reproductive decisions, or personal utility.[27] This means that the scope of results that may reach a relative is likely to be limited to those results of potential significance to the participant. This may exclude some results of potential significance to a relative.

The one domain in which return based on potential significance to relatives themselves has received focused attention is in potential return of a child's genomic research results to parents. In the clinical context, return of a child's genomic results needed for treatment in childhood is well-accepted, but return of results relating to adult-onset disorders has proven more controversial. Historically, recommendations have urged deferring return of results

revealing risk of adult-onset disorders until the child reaches adulthood and can autonomously decide whether to undergo testing and receive results.[28] However, a 2013 policy statement from the American College of Medical Genetics and Genomics (ACMG) suggested that in clinical sequencing, the scope of findings offered to parents should include those of health importance not only during childhood, but also in adulthood, as return of variants associated with adult-onset conditions may benefit the parents (who may otherwise be unaware of their own potential vulnerability) and thus may benefit the child by preserving parental health.[29]

Although the ACMG 2013 statement excludes research and has prompted debate[30] as well as revision on another point in 2014,[31] some commentators focusing instead on research have similarly noted that parents may perceive value in obtaining their child's research results, in part due to potential utility for their own health-related decision-making or in reproductive decisions.[32] Yet neither ACMG in the clinical context, nor commentary focusing on the research context, has urged returning results of no relevance to the child (at the time of testing or in adulthood) and exclusive relevance to parents. Thus, the results considered for possible return remain those of relevance to the participant.

C. Reasons why a participant's genomic results currently may not reach relatives—Data suggest that participants recognize the importance of genomic information to relatives and may identify sharing genomic information with relatives as an important benefit of participating in genomic research.[33] Similarly, in studies of participant communication of their own results related to cancer variants, most participants report either sharing research results with relatives or anticipating that they will share.[34]

However, results may not reach relatives for several reasons. Communicating genomic results can be challenging for individuals who wish to share the information, as it requires an understanding of potentially complex genomic information, the capacity to convey that information, and a willingness to deal with family dynamics.[35] Further, when a relative receives such information and is responsible for sharing it with other relatives, that person functions as a gatekeeper, holding the power to choose who within the family will get the information.[36] When relationships are strained, when parents desire to protect their children from upsetting information,[37] or when the gatekeeper is not a genetic relative,[38] genomic information may not be disseminated within a family. In addition, different individuals and families may understand genetic information and its significance in varying ways, leading to different patterns of sharing genetic information.[39]

Legal fears may also influence whether genetic information is shared. Despite the Genetic Information Nondiscrimination Act (GINA), concerns about genetic discrimination remain, as GINA does not provide protection against discrimination in life, disability, or long-term care insurance.[40] Data suggest that discrimination in employment and insurance coverage is a concern in returning research results.[41]

III. Ethical, Legal & Policy Considerations

The question of whether and how researchers should share a participant's results with relatives raises questions of ethics, law, policy, and pragmatics. We offer ethics

recommendations, while remaining cognizant of the other considerations, in order to offer recommendations that can be put into research practice. U.S. law on return to relatives is not fully clear. At the federal level, HIPAA governs the privacy of an individual's protected health information (PHI) held by a “covered entity,” though HIPAA functions as a floor and more protective state laws will also apply. Additional federal privacy protections (such as those governing data held by the federal government) may apply as well. As noted above, HIPAA will apply to research results in some cases (when considered part of the “designated record set”). However, even when HIPAA privacy rules do not govern, they are one model of privacy protection. Ethics guidelines nonetheless remain distinct from legal rules. We offer an ethical framework that researchers and their institutions should consider in light of applicable law and in the context of individual cases. Where law seems to block sensible and ethical research practice, such law should be carefully scrutinized.

Our Working Group used the following ethical, legal, and policy considerations to guide our formulation of recommendations on sharing a participant's results with relatives:

Protection of individual privacy—Protection of research participant privacy is a core ethical commitment in human subjects research. In genomic research in particular, protecting individuals against the unconsented release of identifying information has been a major and long-standing concern. Although many individual rights end at death, federal privacy rules continue to protect individual health information for 50 years after death.[42] Under HIPAA, individuals generally have the right to forbid sharing their protected health information with others. These legal rules have sound analogues in research ethics, with its commitment to protecting the privacy of identifiable individual information.

Respect for individual autonomy—Respect for individual autonomy is a core commitment in research; this underlies respect for participant choices and informed consent. Respect for autonomy includes respecting the individual's choice of what information to share with relatives. It is consistent with that respect to counsel the individual on what information the person should consider sharing with relatives and to offer help in communicating that information.

Appreciation for the shared nature of genomic information—Supporting the rights of individuals is compatible with supporting families. Counseling individuals on the implications of their results for relatives, urging individuals to consider communicating potentially relevant results to relatives, and offering to help in that process (such as providing written reports or letters that individuals can share with relatives), support both the individual and their relatives. These recommendations aim to respect the rights of individual participants while simultaneously recognizing that a participant's genomic results may have relevance to relatives.

Respect for the pre-death wishes of deceased participants—Recognizing that genomic information can affect relatives does not mean that the wishes of participants should be disregarded, either before or after death. Whether deceased persons retain rights or are capable of being harmed is an ethically and legally controversial question. Courts routinely respect the expressed wishes of the deceased, most commonly in probating a will

and distributing assets. Courts have also held that decedents have interests in the use of their gametes after death.[43] The expressions of a person's autonomy during life are not always enforceable after death,[44] such as when the individual's wishes violate public policy. Several ethical arguments, however, support a baseline of respect for expressed pre-mortem wishes to maintain the privacy of the individual's health information. Human dignity, respect for the autonomy of the pre-mortem decedent,[45] recognition of a social contract,[46] and acknowledgment that privacy interests continue for a significant period after death support generally respecting the expressed pre-mortem privacy preferences of decedents, including explicit wishes regarding the privacy of genomic information, in all but exceptional circumstances.

Researcher responsibilities to research participants—Researchers have duties to their research participants, including respect for participant choices expressed through informed consent, protecting participant privacy and the confidentiality of participant data, and avoiding harm to the participant. Researchers do not owe the same duties to relatives who are not enrolled in the research. Indeed, the researcher will often have no relationship with relatives and may not even have contact information. Even when the relative is a participant in the same or related research, researchers should respect the privacy of each participant. Thus, a living participant's results should generally be offered only to that participant or their representative, unless the participant has consented to sharing the results with relatives. Once the participant is deceased, the participant's representative must generally make decisions about such sharing.

Relationship of research to clinical care—In the clinical context, professionals conveying genomic information to patients that has implications for relatives will generally first counsel the patient to consider communicating this information him- or herself. The clinician may offer to assist by writing a report or letter suitable for sharing or offering to meet directly with relatives. Clinicians are bound to respect the privacy and autonomy of their patients, and thus will generally avoid reaching out directly to relatives unless the patient specifically grants authorization. Indeed, the American Society of Human Genetics (ASHG) has long recognized that clinicians should protect the confidentiality of an individual's genetic information, and would have the latitude to warn relatives directly only in exceptional circumstances in which the patient refused to warn relatives, and “harm is serious, imminent, and likely...and prevention or treatment is available.”[47] Importantly, ASHG framed this latitude to warn in exceptional circumstances as a “discretionary right,” not a duty.[48] Duties to reach out to relatives in the research context should not exceed those in clinical care. As noted above, the clinician's duty of care is more robust than that of an investigator, who may not even be a clinician.[49] Researchers have no greater authorization to reach out to relatives than clinicians.

Recognizing the importance of study design—In the research context, study design may determine whether the return of results to participants and relatives is feasible. Recognizing that studies vary widely in size and design, return of results from some types of research could be cost-prohibitive.[50] In addition, studies irretrievably stripping identifiers may be unable to return results to participants and their relatives.[51] Our recommendations

are intended to be flexible enough to apply to various research designs and do not place obligations on projects unable to return results to relatives.

Scope of participant results for potential sharing with relatives—Previous recommendations on return of genomic results address at length what findings researchers should consider offering to participants. Typically, those are results of high potential health significance and actionability ("should return") or results of health, reproductive, or personal utility that offer net benefit to the participant ("may return").[52] The scope of participant results that a researcher considers for possible return to relatives should generally be limited to those that would qualify for return to the participant him- or herself. To ask the researcher to re-investigate the participant's results looking for added results for potential return to relatives is to significantly enlarge the research burden of return of results, and to do so not for the research participant (to whom the researcher owes direct duties), but for relatives who may not be involved in the research at all. Moreover, the results are those of the participant. Even when those results suggest that the relative has a significant likelihood of sharing a pathogenic and actionable variant, the relative will need to consider undergoing confirmatory genetic testing. For a number of reasons (including the variant's inheritance pattern, as well as possible misattributed paternity or undisclosed lack of genetic relationship), the relative may not have inherited the variant.

Distinction between "should offer" and "may offer"—Ethics and practice standards distinguish actions that "should" be taken from those that "may" be taken. Consensus recommendations to date on return of results to research participants have generally confined "should return" or "should offer" to the category of results that have high health importance and clinical actionability for the participant.[53] However, when considering sharing participants' results with relatives, the health importance for the relative will often not be clear without genetic testing of the relative him- or herself, and the immediate actionability is likely to be undertaking confirmatory testing. For these reasons, as well as the fact that researchers owe fewer duties to relatives than participants, sharing the participant's results with relatives should remain in the category of "may offer" or "may return."

The "duty" or "privilege" to warn and its limits—The "duty to warn" has been much discussed in both law and ethics. In law, a clinician's duty to warn third parties was famously recognized in *Tarasoff*, a California case involving a psychotherapist's failure to warn a third party of the imminent danger posed to her by the patient.[54] Although traditionally understood as a duty owed by clinicians to third-party non-patients who are highly likely to suffer grave harm that can be averted through clinician disclosure, genomic research and the understanding of genetic variation as familial has prompted discussion of a potential duty to warn individuals and their families of pathogenic genetic findings.[55] State case law is inconsistent on a legal duty to warn relatives of hereditary conditions in clinical genetics,[56] but has generally avoided imposing on clinicians a duty to warn relatives directly, instead finding that clinicians discharge their duty by counseling patients to disclose to relatives. However, some authorities have recognized a clinician privilege (rather than duty) to warn relatives without the consent of the patient or representative, but have limited this privilege

to exceptional circumstances in which encouraging the patient to warn the relative has failed and serious harm to the relative is highly likely but can be avoided through disclosure.[57] Courts have not yet resolved the issue of a researcher's duty to warn in genomic research.[58] Given the usual lack of relationship between investigators and third parties who are not themselves research participants, the research (as opposed to clinical) setting, the need for a third-party relative to obtain their own genetic testing upon learning a participant's genomic results to ascertain whether they share the result in question, and the consequent uncertainty about whether disclosure of a participant's results to relatives is highly likely to avert harm, a legal duty falling on researchers to warn relatives of genomic research results seems improbable.

An ethical duty to warn a participant in genomic research has been recognized where “an investigator discovers genetic information that clearly indicates a high probability of a serious condition for which an effective intervention is readily available.”[59] Although the ethics literature on return of research results has suggested that a duty to warn the research participant may exist in certain circumstances,[60] the existence of such a duty or privilege to warn relatives of research participants is less clear.[61] As noted above in the legal context, most researchers will have limited or no relationship with a participant's relatives and thus will lack the duties to relatives that researchers have to participants. Moreover, even in the case of many results that are pathogenic and actionable for the participant, the researcher may not have adequate grounds to conclude that disclosing the participant's results is likely to trigger testing that will then reveal pathogenic and actionable results in the relative and thus will avert harm. Given the fact that researchers will generally have committed to protecting participant privacy and the confidentiality of participant genomic results, those responsibilities will take precedence in most circumstances. Our group debated whether researchers should reach out to relatives to share participant results in exceptional cases -- when the specific participant result is of established pathogenicity and actionability, the genetic relationship between the participant and relative makes the statistical likelihood high that the relative carries the variant, and disclosure to the relative is highly likely to avert imminent harm. These cases will be rare. While a majority of our group concluded that researchers should have the latitude to initiate return to relatives in these cases after ethics consultation, even over the objection of the participant or representative, our group was divided. A minority took the view that researchers should not have this latitude, as participants and their representatives should control access to health information even in such cases.

IV. Recommendations on Return of Results from Adults and Children, Living and Deceased

We recommend the continued respect for participants’ privacy and autonomy in genomic research, coupled with specific attention to the question of the circumstances under which relatives may learn of a participant's results including after the participant's death, the types of results that may be shared with relatives, and the underlying reasoning. We summarize our core recommendations in the Summary of Recommendations.

Recommendation 1: Researchers should communicate to prospective participants their policy on sharing participants' genomic results with relatives, should elicit participants' preferences on such sharing including after death, and should invite participants to designate a representative for decisions on sharing results—Researchers should convey to prospective participants their policy on communicating the participant's genomic results to relatives, including after the participant's death. This allows individuals to consider this policy in deciding whether to participate in the research. Formulating such policy helps investigators anticipate the possibility of requests by relatives for familial genomic information, and considering the possibility that investigators may wish to offer information to relatives under some circumstances. The National Cancer Institute's *Best Practices for Biospecimen Resources* urges that when an individual's consent for participating in research is sought, the consent process should address whether individual results will be shared with relatives.[62] Ethics guidance and oversight may be valuable in developing policy and handling individual cases, given the lack of specific federal guidance on sharing genomic research information with relatives. That ethics guidance may come from the IRB, another committee or consultant providing ethics advice within the institution, a committee dedicated to return of results questions, or a combination of these sources.[63]

Investigators anticipating the possibility of sharing results with relatives (either passively or actively) should elicit information-sharing preferences from participants during the informed consent process, including preferences in the event of loss of decisional capacity or death. Investigators should also ask participants to identify their preferred representative to make decisions on access to information when the participant cannot, including after death. (Note that some participants may prefer that multiple family members or others jointly make decisions on access to the participant's genomic results.) Eliciting participant preferences on return and on who should serve as representative can provide guidance. In sharing policy with prospective participants on return of results to relatives, researchers should indicate whether there are circumstances under which results may be shared without approval by the participant or representative.

Recommendation 2: Researchers have no obligation to return results to relatives and no "duty to hunt" for such results—Researchers may address the process of return of results to relatives but are not obligated to engage in such return, to design their studies to facilitate such return, or to search for results germane to relatives. While researchers have a relationship with and obligations toward their research participants, this does not mean that they have the same relationship and obligations with respect to participants' relatives. Indeed, they may have no relationship with relatives at all. There are research designs that enroll and perform genomic testing on a participant plus relatives with some specified genetic relationship (such as family-based research and trio testing of a child and both parents). In those cases, all of these individuals are research participants and each participant's results can be analyzed for health importance and actionability as to that individual.

In deciding whether and to what extent to address return of genomic results to participants' relatives, researchers may consider the feasibility of return to relatives as well as contextual

factors such as the vulnerability of the relatives, the depth of the relationship (if any) between researchers and relatives, and whether relatives have independent access to the genetic information.[64]

Using the participant's sample and data to hunt for additional results that do not meet the criteria for return to the participant but may be of relevance to relatives is problematic. Although offering a participant's results to a relative is based on potential benefit to the relative, there is no “duty to hunt” for results that might be of benefit to relatives. There is wide agreement (though not universal) that investigators have no “duty to hunt” for research results of individual benefit to participants themselves.[65] There is even less foundation for a “duty to hunt” for the sake of relatives who are uninvolved in the research and to whom the researcher owes no duty of care. Using the participant's sample and data in this way serves no research purpose, as it will generally be beyond the scope of research and instead serve the clinical care of relatives. Further, to suggest that researchers should be required to manage not only those results of potential importance to participants, but also additional results of potential importance to relatives, would greatly increase the burden on the research effort.

Recommendation 3: Researchers should generally follow a passive disclosure policy—We recommend that researchers generally consider potential disclosure of participant results only upon request by relatives (or their health care providers), rather than actively seeking out relatives to share a participant's result. Given the importance of using research efforts and funding for research advances, a policy broadly encouraging proactive sharing with relatives would be an ill-advised drain on research time, effort, and funds. Instead, we encourage a passive disclosure policy, where information is shared with relatives upon request. Passive disclosure in studies already returning results to participants would allow interested relatives to request useful information, while minimizing additional burden on researchers.[66] Results returned to relatives will be those of the participant and thus will require confirmatory testing in order to be of use in the clinical care of relatives. The need for confirmatory testing, in addition to the probabilistic nature of inheritance (so that relatives may not even carry the variant in question), and the researcher's lack of a clinician's duty of care argue against an ethical duty to actively return results to relatives. Even devoting research resources to return of clinically significant results to participants has triggered concern about limiting this so as to preserve resources available for the research itself;[67] using research resources for return of results to relatives has still less warrant.

Requests for participant results may follow a research team's disclosure of aggregate study findings, published on a study website, in a newsletter, or in another format. Researchers should be prepared for the possibility that relatives will respond to these group communications by requesting a participant's results.

Recommendation 4: In exceptional cases, researchers may initiate return to relatives—Given the current state of genomic science, the probabilistic nature of inheritance, and the need for relatives to consider confirmatory testing of research results to clarify the actionability of that information in their own care, the majority of research results will not justify active return by researchers. Some exceptional cases, however, may warrant

considering a more active approach. Researchers may ethically consider reaching out to relatives to return genomic information relating to highly pathogenic and actionable variants, when the relative has a high probability of sharing that variant and return to the relative is highly likely to avert imminent harm. The researcher should first seek consent from the participant (if living and able to consent) or participant's representative for contacting the relative and offering the result. Cases in which consent is denied despite careful explanation of the exceptional circumstances will probably be extremely rare and warrant ethics consultation, from the IRB or another entity. While a majority of our group concludes that researchers may consider return to relatives in these rare cases to avert imminent harm to relatives, a minority of our group instead concludes that researchers should defer to the choices of the participant or the participant's representative, even in these cases.

Researchers should seek ethics consultation in any case prior to initiating contact with relatives, who may be unaware of the participant's involvement in genomic research and may not expect or even desire to receive the genomic information. Results should be returned only to relatives who agree to receive them.

Recommendation 5: Researchers should generally respect the choices of research participants, as well as their privacy, before and after death— Researchers should generally avoid sharing a participant's results with relatives against the expressed wishes of a participant. Cases in which the participant has forbidden sharing with relatives will probably be rare. However, in such cases, sharing genomic information against the wishes of a participant raises serious concerns about breach of confidentiality and invasion of privacy. Note that HIPAA rules generally allow individuals to veto sharing of their protected health information, even when the rules describe a pathway for sharing. As noted above, HIPAA rules do allow for sharing an individual's results over their objection for the medical treatment of a relative, but this exception has been challenged for being too broad, given ethics guidelines from ASHG and other sources that confine more strictly the latitude to disclose.[68] In addition, the participant's result will be only indicative of the relative's result and sharing a participant's result with a relative will require follow-up genetic testing of the relative to confirm that the relative indeed has the variant in question. Over time, genomic testing and sequencing will become more broadly available and relatives will more easily be able to obtain their own testing and sequencing if a participant denies access to results.

Recommendation 6: Participants and their representatives should generally control access to the participant's genomic information—In the case of participants who are unable to provide effective consent to sharing (e.g., incompetent adults incapable of providing consent, deceased participants who were never asked about preferences in regard to sharing, and child participants), we recommend that the participant's representative use a two-tier standard to address sharing of their results. Respecting participant privacy and autonomy suggests following the participant's expressed preferences made known while alive and competent. However, if the participant never stated those preferences or was never able to give consent, then their representative will need to reconcile the privacy and personal interests of the participant with the interests of relatives in

obtaining the results. We suggest that a representative lacking the benefit of wishes previously stated by the participant while competent should balance the participant's interests with the relative's need for the information.[69] This aims to reconcile the privacy and other interests of the incompetent participant with the potential benefit to relatives from obtaining the participant's results. Balancing competing interests is not an exact endeavor; however, representatives asked to balance interests should consider the potential utility of the results to relatives and the potential harm to the participant from sharing the results.

In the case of a deceased participant, the representative considering sharing a participant's results with relatives should generally adhere to the participant's previously expressed wishes concerning such sharing. When the participant was not competent to express wishes on sharing with relatives or simply never did so, the representative should decide by balancing the deceased participant's privacy interests against the interests of the relatives.

Note that unless researchers have planned ahead (as recommended above) and asked the participant to designate a preferred representative, they may not know who that representative is. In such cases, a flexible approach may be justified. The researchers may be ethically justified in reaching out, with ethics guidance, to the next-of-kin or a trusted relative of the participant to serve in that capacity. Legal consultation may be helpful in clarifying state law on who may serve in this capacity for a deceased individual.

Recommendation 7: Although parents and guardians of minor participants generally control access to genomic information, preferences of child research participants should be strongly considered—In the case of living research participants who are minors, the question of whether some of the child's results should be offered to relatives should be decided by the parent/guardian, carefully considering the preferences of the child or adolescent who has been informed of the issues and is able to participate in decision making. Although traditionally returning genetic results of child participants has been limited to those that are actionable during childhood,[70] recent recommendations recognize that a child's research results may have significant, actionable implications for the child's parents.[71] The law also provides parent/guardians with significant power over the health information of their children.[72] Although law and societal norms generally defer to parental authority in decision-making regarding a child's health and welfare,[73] parents and guardians should strongly consider the interests and expressed wishes of the child in deciding whether to share the child's genomic information with relatives. In the case of deceased minor participants, the child's representative (frequently the parent/guardian) will have access to the child's records. As in the case of deceased adults, we recommend that the representative balance the privacy and personal interests of the child against relatives' interest in access to the child's genomic information.

Recommendation 8: Results offered to participants and relatives should meet six criteria—Multiple recommendations in the literature suggest the criteria to be used for distinguishing what results to offer back to research participants themselves.[74] Generally, those recommendations distinguish results that (1) should be offered, (2) may be offered in the investigator's discretion, and (3) should not be offered. Research results that **should be** offered to participants are usually restricted to those results that are analytically valid, reveal

an established and substantial risk of a serious health condition, and are clinically actionable, when return comports with law (such as CLIA) and the participant has consented to receiving the result.[75] Research results that **may be** offered to participants are usually results that are analytically valid; reveal an established and substantial risk of likely health importance, reproductive importance, or personal utility; may or may not be clinically actionable but may be valued by participants with return offering net benefit from their perspective; when return comports with law and the participant has consented to receive the result. Note that Berg and colleagues[76] offer a similar scheme (framed as "binning"), but for return of clinical, not research, results.

Because our focus here is development of criteria for return of a research participant's results to relatives, it is important to recognize that the information to be returned is not information about the potential recipient's genes or genome, but rather the participant's. The participant's results may suggest the probability that the relative shares certain variants, including variants that are pathogenic and actionable. However, the relative will need to consider undergoing genetic testing to conclusively determine the presence of that variant in their own genome. When the relative does not share the variant, this may be for reasons including the pattern of inheritance for that variant or misattributed paternity or other misattributed genetic relatedness. Thus, a participant's genomic results will not conclusively reveal that the relative has a genetic variant creating an established and substantial risk of a serious health condition. However, the relative may value the risk information conveyed by the result. The immediate actionability for the relative will likely be to consider having his or her own genetic testing.

This means that the criteria usually stated for cases in which researchers "should return" a participant's results – that the results show the presence of a genetic variant in that person that confers established and substantial risk of a serious health condition that the participant can take clinical action to avoid or treat – do not easily and directly apply to return of a participant's results to someone other than the participant. This supports the conclusion that offering a participant's results to relatives should remain discretionary on the part of investigators. Such return should thus be regarded as an instance of "may return" (rather than "should return"). The criteria we recommend for distinguishing those participant results that **may be** returned to relatives are:

- **(a)** the participant's results are analytically valid;
- **(b)** revealing an established and substantial risk of a likely health condition in the **participant**, with significant potential health implications for the genetically related **relative**;
- **(c)** the result offers potential net benefit to the relative, who may seek genetic testing and have an opportunity to benefit from such testing due to the actionability of the variant;
- **(d)** offering the result to the relative comports with law (including CLIA, HIPAA and state privacy law, and the Common Rule); and
- **(e)** the relative agrees to receiving the result.

The last criterion—agreement from the relative to receive the result—is a standard part of communicating genomic results that respects the relative's right to decline such information. In some cases, the relative will be seeking a specific genomic result from the participant; investigators should confirm that the relative understands the implications of receiving the result and still wishes to receive it. In other cases, the relative may not have a clear sense of the content of the participant's results and may have greater need for education and counseling.

Recommendation 9: Researchers should offer to support communication of results by participants or their representatives—Although researchers' obligations to participants differ from those of clinicians, researchers should offer support for accurate communication of research results, when participants or their representatives seek to communicate those results to relatives. Researchers may consider options including (a) providing written results and educating the participant or representative on how to share those with relatives, (b) providing the contact information of one or more genetics professionals to assist with understanding and sharing the information, and/or (3) communicating the result to a genetics professional or clinician of the participant's or representative's choosing, to aid communication to the relative. In addition, researchers may use a website, newsletter, or other means of aggregate return to offer all participants information on project findings. We discuss the recommended process for return in section VII below.

Recommendation 10: Further research is needed on return of a participant's genomic results to relatives—Because the practice of sharing a participant's research results with relatives is not yet widespread, investigators should collect data to evaluate this practice. Data would be helpful on the types of results that prompt consideration of such sharing; the attitudes of research participants and relatives toward sharing; the investigator time, effort, and cost involved; which pathways for sharing are used, with what consequences, including the impact on family dynamics; and the experiences of relatives who receive information as well as what further action they take, including their own genetic testing or sequencing. These data will help inform further development of policy on sharing a participant's results with relatives.

V. Processes for Sharing Results with Relatives

The following process recommendations for offering results to relatives differ depending on whether the participant is alive or deceased, has (or previously had) decisional capacity, and whether the participant is a minor. Note that in all cases, relatives themselves will need to agree to receipt of the participant's results before those results are communicated to them.

Scenario A: Living adult research participant (Figure 1)—In the simplest case, a living adult participant receiving results may be counseled about the implications of those results for relatives. If the participant consents, or previously consented, to sharing with relatives, then discussion can proceed on whether the participant wishes to share the results with relatives or prefers that the investigator or a genetics professional reach out to relatives.

Once a living adult participant has been counseled on reasons for sharing their genomic results with relatives, the participant's preferences on sharing should generally be honored, out of respect for the participant's autonomy and privacy. However, cases will arise in which the participant either is not competent to decide, or cannot be consulted (perhaps because the participant is lost to follow-up). In such cases, the participant's representative (who may be an LAR, surrogate decision-maker, another authorized representative, or a trusted family member) should decide. Lacking expressed guidance from the participant, the representative should balance the participant's privacy and personal interests against the interests of relatives, as described above.

As discussed above, exceptional cases may arise, involving highly pathogenic and actionable variants whose disclosure to relatives is highly likely to avert imminent harm. In those cases, if the participant refuses to authorize sharing the results or the representative refuses, researchers should seek ethics consultation on sharing findings with relatives.

We note that HIPAA rules provide an additional route of access applicable to HIPAA-covered entities: a physician treating a relative may request an individual's information to identify the relative's genetic health risks.[77] Faced with such a request, the individual may refuse to authorize disclosure, but the provider holding the information need not agree.[78] However, as noted above, this exception to privacy protection has been sharply criticized.[79] Given the fact that research depends on participant trust and that protecting participant privacy is a core obligation of researchers, we urge researchers to proceed with caution and seek ethics (and legal) consultation if faced with such a physician request on behalf of a relative but the participant asks the researcher to refrain from sharing results.

Scenario B: Deceased adult research participant (Figure 2)—After the death of the adult participant, the participant's representative will generally control access to their health information. If relatives actively seek results, they should be urged to consult the representative for authorization to have access. As noted above, we recommend a general policy of passive disclosure at the request of relatives (if their access is then approved), rather than the researcher actively initiating return of a participant's results to relatives. However, we again note that exceptional cases may arise in which the case for return to relatives is strong because those cases involve potential return of highly pathogenic and actionable variants whose disclosure is highly likely to avert imminent harm to the relatives. In those cases, researchers should seek ethics consultation on the possibility of more active return. Consultation with and notice to the participant's representative will still be warranted.

If the deceased adult participant consented to sharing results with relatives, then that provides strong grounds for the representative to authorize it. Similarly, if the participant forbade such sharing (especially if he or she was explicit about forbidding posthumous sharing), that provides strong grounds for the representative to refuse access. However, if the participant was silent on sharing or not competent to decide, the participant's representative should balance the deceased participant's privacy and personal interests against the interests of relatives.

Representatives may vary in the strength they assign to a participant's interests after death. HIPAA sends mixed signals, recognizing that privacy interests continue after death but also allowing access under some conditions when a relative's physician seeks information, as noted above.[80] However, as a practical matter, researchers may find it important to offer prospective participants a choice on posthumous disclosure in order to recruit participants for long-term genomic studies or to recruit cancer patients and others with conditions that limit their life expectancy.

Again, we note that exceptional cases may arise, involving highly pathogenic and actionable variants whose disclosure to relatives is highly likely to avert imminent harm. In those cases, if the participant's representative refuses to authorize sharing the results, researchers should seek ethics consultation on sharing findings with relatives.

Scenario C: Living child research participant (Figure 3)—In the case of a living child participant, sharing their research results with relatives will generally require the permission of the parent/guardian. When the child is able to participate in decision-making, the child's well-informed preferences should also be accorded significant weight. As is customary, the child's preferences should be given increasing weight in adolescence and as the participant approaches full decisional capacity.

If the parent or guardian and the child participant agree to sharing results with relatives, sharing may proceed. Similarly, if they both refuse permission to sharing with relatives, that choice should generally be respected. Where they have been silent, they should be consulted; if they agree to sharing or refusal, that choice should be honored.

The case in which the parent/guardian and child disagree is challenging and may require ethics consultation. Holm and colleagues have taken an initial position that their project will not return results when parents and adolescents disagree, though they will examine each case, expect their approach to evolve, and would nonetheless return results that "predict[] imminent risks of severe harm that can be prevented only by disclosure."[81] Those authors were considering return of results to participants, so the issue was potential harm or benefit to the adolescent. We focus here instead on return of a participant's results to relatives; the issue is the potential intrusion on the child's privacy and other interests *versus* potential benefit to relatives. This is a different question that requires complex consideration of individual rights as well as the needs of others. We recommend generally allowing the parent/guardian of a minor to decide this question, but also urging the parent/guardian to strongly consider any well-informed preferences expressed by the child. However, cases in which the child (especially if an older adolescent) wishes to block sharing genomic results with relatives will need ethics consultation. In general, we urge efforts to respect the adolescent's privacy and preference not to share results.

In the case of living child research participants, we again note that exceptional cases may arise involving highly pathogenic and actionable variants whose disclosure to relatives is highly likely to avert imminent harm. In those cases, if the parent/guardian refuses to authorize sharing the results, which the child may object to as well, researchers should seek ethics consultation on sharing findings with relatives.

Scenario D: Deceased child research participant (Figure 4)—In the case of a deceased child participant, a relative's request for access to the child's research results should generally be referred to the child's representative, who is likely to be the parent/guardian. If the representative finds that the parent/guardian agreed to sharing (or now agrees upon being asked) and the child (if able to participate) did not object, the representative should respect those preferences and may authorize sharing. Similarly, if the representative finds that the parent/guardian refused to agree to sharing (or now refuses upon being asked) and the child (if able to participate) did not object, sharing should not proceed. The more challenging cases are likely to be those in which the representative can find no past guidance and cannot consult the parent/guardian (perhaps because they are unavailable or they too are deceased), and cases in which the parent/guardian and child (if able to participate) have disagreed. The representative should balance child's privacy and other interests against the interests of relatives to whom results would be returned. In cases in which the parent/guardian and child disagreed, the representative should consider both perspectives, and may need ethics consultation.

Here again, in the case of deceased child research participants, we note that exceptional cases may arise, involving highly pathogenic and actionable variants whose disclosure to relatives is highly likely to avert imminent harm. In those cases, researchers should seek ethics consultation on sharing findings with relatives.

VI. Conclusion

As the debate surrounding the return of genomic results to research participants has developed, the issue of return to family has emerged, including after the death of the research participant. Guidance is needed. Indeed, some investigators are already encountering requests from relatives for access to this information. Because researchers generally have duties to research participants but not their relatives, the fact that the relative may not carry the genetic variant of concern, and the potential added cost to the research enterprise of return to relatives, we suggest that researchers may consider responding to a relative's request by sharing a participant's result (with appropriate authorization from the participant or a representative, as outlined here), but that return to family is not ethically required. As discussed above, in exceptional circumstances in which researchers identify a highly pathogenic and actionable result that the relative is likely to carry and disclosure is highly likely to avert imminent harm, a majority of our group concluded that researchers may consider initiating return to relatives, with ethics consultation. As the costs of sequencing and other types of genetic testing diminish, relatives will have other options to pursue their own testing and receive information important to their own health care. Until the time that such sequencing and testing are readily available, however, investigators will face the challenge of addressing the importance of genomic information to participants as well as relatives.

The goal of this paper is to offer consensus recommendations on how to handle return of results to relatives, including after the death of the research participant. We offer recommendations that strive to respect the wishes of the participant, while recognizing that those wishes may not be known and that relatives may seek a participant's genomic

information, including after the participant's death. Genomics researchers should plan how they will address the question of return of results to relatives, incorporating that plan in their protocols. We encourage researchers to ask participants for their preferences regarding sharing results with relatives, both before and after death. Respecting participants' wishes while taking seriously the needs of relatives calls for the creation of policy and pathways addressing return of genomic results to relatives.

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References

1. Wolf SM, et al. Managing Incidental Findings and Research Results in Genomic Research Involving Biobanks and Archived Data Sets. Genetics in Medicine. 2012; 14(4):361–384. [PubMed: 22436882] Fabsitz RR, et al. Ethical and Practical Guidelines for Reporting Genetic Research Results to Study Participants. Circulation: Cardiovascular Genetics. 2010; 3(6):574–580. [PubMed: 21156933] Wolf SM, et al. Managing Incidental Findings in Human Subjects Research: Analysis and Recommendations. Journal of Law, Medicine & Ethics. 2008; 36(2):219–248.

2. Battistuzzi L, et al. Communication of Clinically Useful NGS Results to At-Risk Relatives of Deceased Research Participants: Toward Active Disclosure? Journal of Clinical Oncology. 2013; 31(32):4164–4165. [PubMed: 24101050] ; Lolkema MP, et al. Ethical, Legal, and Counseling Challenges Surrounding the Return of Genetic Results in Oncology. Journal of Clinical Oncology. 2013; 31(15):1842–1848. [PubMed: 23589552] , at 1846; Bombard Y, Offit K, Robson ME. Risks to Relatives in Genomic Research: A Duty to Warn?" American Journal of Bioethics. 2012; 12(10): 12–14.; Bredenoord AL, van Delden JJM. Disclosing Individual Genetic Research Results to Deceased Participants' Relatives by Means of a Qualified Disclosure Policy. American Journal of Bioethics. 2012; 12(10):12–14.; Chan B, et al. Genomic Inheritances: Disclosing Individual Research Results From Whole-Exome Sequencing to Deceased Participants' Relatives. American Journal of Bioethics. 2012; 12(10):1–8. [PubMed: 22974017] ; Fullerton SM, et al. Beneficence, Clinical Urgency, and the Return of Individual Research Results to Relatives. American Journal of Bioethics. 2012; 12(10):9–10. [PubMed: 22974018] ; Office of Biorepositories and Biospecimen Research, National Cancer Institute, NCI Best Practices for Biospecimen Resources (2011), available at <http://biospecimens.cancer.gov/bestpractices/2011-NCIBestPractices.pdf> (last visited June 12, 2014), at 38 [hereinafter NCI Best Practices 2011] ("The informed consent document should state whether individual or aggregate research results will be released to...the participant's family and, if so, the mechanism....").

3. National Cancer Institute, Cancer Genetics Risk and Counseling Physician Data Query: The Option of Genetic Testing. 2014available at <http://www.cancer.gov/cancertopics/pdq/genetics/risk-assessment-and-counseling/HealthProfessional/page5> (last visited June 12, 2014); Forrest LE, et al. Communicating Genetic Information in Families: A Review of Guidelines and Position Papers. European Journal of Human Genetics. 2007; 15(6):612–618. [PubMed: 17392704] ; American Society of Clinical Oncology. American Society of Clinical Oncology Policy Statement Update: Genetic Testing for Cancer Susceptibility. Journal of Clinical Oncology. 2003; 21(12):2397–2406. [PubMed: 12692171] , at 2403; Clayton EW. What Should the Law Say About Disclosure of Genetic Information to Relatives? Journal of Health Care Law & Policy. 1998; 1(2):373–390. [PubMed: 16281334]

4. See Offit K, et al. The 'Duty to Warn' a Patient's Family Members About Hereditary Disease Risks. JAMA. 2004; 292(12):1469–1473. [PubMed: 15383518] ; American Society of Human Genetics Social Issues Subcommittee on Familial Disclosure. Professional Disclosure of Familial Genetic Information. American Journal of Human Genetics. 1998; 62(2):474–483. [PubMed: 9537923] ; Clayton, supra note 3, at 383; Andrews LB, et al.Committee on Assessing Genetic Risks, Institute of Medicine (IOM), Assessing Genetic Risks: Implications for Health and Social Policy. 1993National Academies PressWashington, DC, at 278.

5. Burke W, Evans BJ, Jarvik GP. Return of Results: Ethical and Legal Distinctions Between Research and Clinical Care. American Journal of Medical Genetics Part C: Seminars in Medical Genetics. 2014; 166(1):105–111.; Richardson HS. Moral Entanglements: The Ancillary-Care Obligations of Medical Researchers. Oxford University Press2012New York: at 44; Garrett JR. Ethical Considerations for Biobanking: Should Individual Research Results be Shared with Relatives? Future Medicine. 2012; 9(2):159–162.

6. Bledsoe MJ, et al. Practical Implementation Issues and Challenges for Biobanks in the Return of Individual Research Results. Genetics in Medicine. 2012; 14(4):478–483. [PubMed: 22323073] Beskow LM, Burke W. Offering Individual Genetic Research Results: Context Matters," Science Translational Medicine. 2010; 2(38):38cm20.

7. Graves KD, et al. Communication of Genetic Test Results to Family and Health-Care Providers Following Disclosure of Research Results. Genetics in Medicine. 2014; 16(4):294–301. [PubMed: 24091800] ; Lolkema et al., supra note 2, at 1844, 1846; Milner LC, et al. Relationships Matter: Ethical Considerations for Returning Results to Family Members of Deceased Subjects. American Journal of Bioethics. 2013; 13(10):66–67. [PubMed: 24024819] ; Rothstein MA. Should Researchers Disclose Results to Descendants? American Journal of Bioethics. 2013; 13(10):64–65. [PubMed: 24024818] ; Taylor HA, Wilfond BS. The Ethics of Contacting Family Members of a Subject in a Genetic Research Study to Return Results for an Autosomal Dominant Syndrome. American Journal of Bioethics. 2013; 13(10):61. [PubMed: 24024816] ; Bombard et al., supra note 2; Bredenoord and van Delden, supra note 2; Chan et al., supra note 2; Fullerton et al., supra note 2; Rothstein MA. Disclosing Decedents' Research Results to Relatives Violates the HIPAA Privacy

Rule. American Journal of Bioethics. 2012; 12(10):16–17. [PubMed: 22974022] ; Tassé AM. The Return of Results of Deceased Research Participants. Journal of Law, Medicine & Ethics. 2011; 39(4):621–630.

8. Radecki Breitkopf C, et al. Preferences Regarding Return of Genomic Research Results to Relatives of Research Participants, Including After Participant Death: Empirical Results from a Cancer Biobank. Journal of Law, Medicine & Ethics. 2015 __, no. __. : __-__; Fernandez CV, et al. Attitudes of Parents Toward the Return of Targeted and Incidental Genomic Research Findings in Children. Genetics in Medicine. 2014; 16(8):633–640. [PubMed: 24434691] , at 635, 637; Bollinger JM, et al. Public Preferences Regarding the Return of Individual Genetic Research Results: Findings from a Qualitative Focus Group Study. Genetics in Medicine. 2012; 14(4):451–457. [PubMed: 22402755] , at 455; Meulenkamp TM, et al. Communication of Biobanks' Research Results: What Do (Potential) Participants Want? American Journal of Medical Genetics. 2010; 152 Part A(10): 2482–2492. [PubMed: 20799322] , at 2489-90; Murphy J, et al. Public Expectations for Return of Results from Large-Cohort Genetic Research. American Journal of Bioethics. 2008; 8(11):36–43. [PubMed: 19061108] , at 40.
9. Allen NL, et al. Biobank Participants' Preferences for Disclosure of Genetic Research Results: Perspectives From the OurGenes, OurHealth, OurCommunity Project. Mayo Clinic Proceedings. 2014; 89(6):738–746. [PubMed: 24943692] , at 743, with Radecki Breitkopf et al., supra note 8, at [PAGE] and Table 3, and Amendola LM, et al. Patients' Choices for Return of Exome Sequencing Results to Relatives in the Event of their Death. Journal of Law, Medicine & Ethics. 2015
10. See, e.g., Radecki Breitkopf et al., supra note 8.
11. See Consortium on Law and Values in Health, Environment & the Life Sciences, Conference, "Should We Offer Genomic Results to a Research Participant's Family, Including After Death?" (November 6, 2014), available at <http://consortium.umn.edu/conference/should-we-offer-genomic-results-research-participant-s-family-including-after-death> (last visited May 9, 2015).
12. See, e.g., Mercy College, HIPAA & Research: What Do I Need to Know? available at <https://legacyweb.mercy.edu/my-mercy/faculty-resources/institutional-review-board/application-guidelines/hipaa-research-what-do-i-need-to-know/> (last visited February 4, 2015).
13. See, e.g., Johns Hopkins Medicine, Office of Human Subjects Research--Institutional Review Boards, HIPAA Questions and Answers Relating to Research, available at <http://www.hopkinsmedicine.org/institutional_review_board/hipaa_research/faq_research.html> (last visited February 4, 2015).
14. See 42 C.F.R. § 493.1291 (2014); 45 C.F.R. § 164.524 (2014); U.S. Department of Health and Human Services, CLIA Program and HIPAA Privacy Rule; Patients' Access to Test Reports; Final Rule, 79 Federal Register 7290-7316 (2014); Evans BJ, et al. Regulatory Changes Raise Troubling Questions for Genomic Testing. Genetics in Medicine. 2014; 16(11):799–803. [PubMed: 25255365] , at 801 ("[W]hen HHS published the Privacy Rule many years ago, it interpreted the term 'CLIA-exempt' as also including non-CLIA research laboratories for purposes of the § 164.524 individual access right. Forgetting this history, the recent amendments eliminated a § 164.524 exception that kept 'CLIA exempt' laboratories from having to comply with § 164.524. This inadvertently put HIPAA-covered, non-CLIA laboratories squarely in the crosshairs of individuals' new § 164.524 access right." (footnote omitted)).
15. U.S. Department of Health and Human Services, Health Information Privacy, Personal Representatives, at <http://www.hhs.gov/ocr/privacy/hipaa/understanding/coveredentities/personalreps.html> (last visited April 18, 2015), construing 45 C.F.R. § 164.502 (g) [hereinafter DHHS, Personal Representatives].
16. 45 C.F.R. § 164.502(a)(1)(ii) (2014).
17. 45 C.F.R. § 164.502 (2014); D. McGraw, "Privacy and Health Information Technology," Journal of Law, Medicine & Ethics 37, Supp. 2 (2009): 123-149, at 136; Office of Civil Rights, U.S. Department of Health and Human Services, FAQ: Under the HIPAA Privacy Rule, May a Health Care Provider Disclose Protected Health Information About an Individual to Another Provider, When Such Information Is Requested for the Treatment of a Family Member of the Individual? available at <http://www.hhs.gov/ocr/privacy/hipaa/faq/disclosures_to_friends_and_family/512.html> (last visited July 17, 2014); U.S. Department of Health and Human Services, Frequently Asked Questions About Family Medical History Information, available at <http://www.hhs.gov/ocr/privacy/familyhealthhistoryfaqs.pdf> (last visited May 10, 2015) [hereinafter

HIPAA FAQ] (“The HIPAA Privacy Rule permits…. a doctor to disclose protected health information about a patient to another health care provider for the purpose of treating another patient (e.g., to assist the other health care provider with treating a family member of the doctor's patient).”); U.S. Department of Health and Human Services, Preamble to Final HIPAA Privacy Rule (2000), at 48, available at <http://aspe.hhs.gov/admnsimp/final/PvcPre03.htm> (last visited July 17, 2014) (“We agree that family members may need access to the protected health information of a deceased individual, and this regulation permits such disclosure in two ways. First, a family member may qualify as a ‘personal representative’ of the individual (see § 164.502(g)). Personal representatives include anyone who has authority to act on behalf of a deceased individual or such individual's estate, not just legally-appointed executors. We also allow disclosure of protected health information to health care providers for purposes of treatment, including treatment of persons other than the individual. Thus, where protected health information about a deceased person is relevant to the treatment of a family member, the family member's physician may obtain that information.”)

18. HIPAA FAQ, supra note 17.
19. Id.; 45 C.F.R. §164.522 (2014).
20. U.S. Department of Health and Human Services. Modifications to the HIPAA Privacy, Security, Enforcement, and Breach Notification Rules Under the Health Information Technology and Economic and Clinical Health Act and the Genetic Information Nondiscrimination Act; Other Modifications to the HIPAA Rules; Final Rule. 78 Federal Register. 2013:5566–5702. at 5668.
21. Rothstein MA. HIPAA Privacy Rule 2.0. Journal of Law, Medicine & Ethics. 2013; 41(2):525–528. at 528.
22. 45 C.F.R. § 164.502 (g) (2014). See also DHHS, Personal Representatives, supra note 15. Note that once the research participant is deceased, the PR for the decedent will generally have broad authority over health information even if there was no specific grant of authority over health decisions. See id.
23. See supra note 17.
24. South Carolina Statutes § 38-93-40 (2014). For a compendium of state genetic privacy statutes, see National Human Genome Research Institute (NHGRI), Genome Statute and Legislation Database, available at <https://www.genome.gov/PolicyEthics/LegDatabase/pubsearch.cfm> (last visited Sept. 1, 2014).
25. See 45 C.F.R. § 164.510 (b)(5) (2014).
26. Wolf et al. (2012), supra note 1, at 378; Fabsitz et al., supra note 1, at 578; Wolf et al. (2008), supra note 1, at 219.
27. Wolf et al. (2012), supra note 1, at 378; Fabsitz et al., supra note 1, at 575-76.
28. American Academy of Pediatrics and American College of Medical Genetics. Policy Statement: Ethical and Policy Issues in Genetic Testing and Screening of Children. Pediatrics. 2013; 131(3): 620–622. [PubMed: 23428972] , at 621 [hereinafter AAP & ACMG 2013]; Ross LF, et al. Technical Report: Ethical and Policy Issues in Genetic Testing and Screening of Children. Genetics in Medicine. 2013; 15(3):234–245. [PubMed: 23429433] , at 237-38; American Society of Human Genetics Board of Directors and American College of Medical Genetics Board of Directors. Points to Consider: Ethical, Legal, and Psychosocial Implications of Genetic Testing in Children and Adolescents. American Journal of Human Genetics. 1995; 57(5):1233–1241. [PubMed: 7485175] [hereinafter ASHG & ACMG 1995].
29. Green RC, et al. ACMG Recommendations for Reporting of Incidental Findings in Clinical Exome and Genome Sequencing. Genetics in Medicine. 2013; 15(7):565–574. [PubMed: 23788249]
30. Clayton EW, et al. Addressing the Ethical Challenges in Genetic Testing and Sequencing of Children. American Journal of Bioethics. 2014; 14(3):3–9. [PubMed: 24592828] Burke W, et al. Recommendations for Returning Genomic Incidental Findings? We Need to Talk! Genetics in Medicine. 2013; 15(11):854–859. [PubMed: 23907645] McGuire AM, et al. Ethics and Genomic Incidental Findings. Science. 2013; 340(6136):1047–1048. [PubMed: 23686340] Wolf SM, Annas GJ, Elias S. Patient Autonomy and Incidental Findings in Clinical Genomics. Science. 2013; 340(6136):1049–1050. [PubMed: 23686341]
31. ACMG Board of Directors. ACMG Policy Statement: Updated Recommendations Regarding Analysis and Reporting of Secondary Findings in Clinical Genome-scale Sequencing. Genetics in

Medicine. 2015; 17(1):68–69. [PubMed: 25356965] (noting approval by the ACMG Board of Directors in September 2014).

32. Madadi P. Ethical Perspectives on Translational Pharmacogenetic Research Involving Children. Pediatric Drugs 17. 2015; 1:91–95.; Holm IA, et al. Guidelines for Return of Research Results from Pediatric Genomic Studies: Deliberations of the Boston Children's Hospital Gene Partnership Informed Cohort Oversight Board. Genetics in Medicine. 2014; 16(7):547–552. [PubMed: 24406460] , at 550-51; Kleiderman E, et al. Returning Incidental Findings from Genetic Research to Children: Views of Parents of Children Affected by Rare Diseases. Journal of Medical Ethics. 2014; 40(10):691–696. [PubMed: 24356209] ; AAP & ACMG 2013, supra note 28, at 621; Haga SB, Zhao JQ. Stakeholder Views on Returning Research Results. Advances in Genetics. 2013; 84:41–81. [PubMed: 24262096] , at 52.
33. Bui ET, et al. Do Participants in Genome Sequencing Studies of Psychiatric Disorders Wish to Be Informed of Their Results? A Survey Study. PLoS One. 2014; 9(7):e101111. [PubMed: 24983240] ; Bennette CS, et al. Return of Incidental Findings in Genomic Medicine: Measuring What Patients Value–Development of an Instrument to Measure Preferences for Information from Next-Generation Testing (IMPRINT). Genetics in Medicine. 2013; 15(11):873–881. [PubMed: 23722871] , at 878; Facio FM, et al. Motivators for Participation in a Whole-Genome Sequencing Study: Implications for Translational Genomics Research. European Journal of Human Genetics. 2011; 19(12):1213–1217. [PubMed: 21731059] , at 1215; O'Daniel J, Haga SB. Public Perspectives on Returning Genetics and Genomics Research Results. Public Health Genomics. 2011; 14(6):346–355. [PubMed: 21555865] , at 353; Meulenkamp et al., supra note 8, at 2490; Murphy et al., supra note 8, at 40. See also sources cited supra note 9.
34. Bui et al., supra note 33 (in a psychiatric genome sequencing study, more than half of respondents anticipated sharing results with relatives and most felt personally responsible for informing family members); Graves et al., supra note 7, at 298 (in a study of individuals in a colon cancer registry, most of whom were positive for a variant associated with colon cancer reported sharing results with family); Esplen MJ, et al. Colorectal Cancer Survivors Undergoing Genetic Testing for Hereditary Nonpolyposis Colorectal Cancer: Motivational Factors and Psychosocial Functioning. Clinical Genetics. 2007; 72(5):394–401. [PubMed: 17892499] , at 397 (in a study of Canadian survivors of colorectal cancer, most anticipated sharing their genetic results with family members).
35. Peters JA, et al. Unpacking the Blockers: Understanding Perceptions and Social Constraints of Health Communication in Hereditary Breast and Ovarian Cancer (HBOC) Susceptibility Families. Journal of Genetic Counseling. 2011; 20(5):450–464. [PubMed: 21547418] MacDonald DJ, et al. Women's Perceptions of the Personal and Family Impact of Genetic Cancer Risk Assessment: Focus Group Findings. Journal of Genetic Counseling. 2010; 19(2):148–160. [PubMed: 19902342] Hallowell N, et al. Communication About Genetic Testing in Families of Male BRCA1/2 Carriers and Non-carriers: Patterns, Priorities and Problems. Clinical Genetics. 2005; 67(6):492–502. [PubMed: 15857416] Foster C, et al. Juggling Roles and Expectations: Dilemmas Faced by Women Talking to Relatives About Cancer and Genetic Testing. Psychology & Health. 2004; 19(4):439–455.Claes E, et al. Communication with Close and Distant Relatives in the Context of Genetic Testing for Hereditary Breast and Ovarian Cancer in Cancer Patients. American Journal of Medical Genetics. 116 Part A. 2003; (1):11–19. [PubMed: 12476445]
36. Peters et al., supra note 35, at 453.
37. Ormondroyd E, et al. Communicating Genetics Research Results to Families: Problems Arising When the Patient Participant Is Deceased. Psychooncology. 2008; 17(8):804–811. [PubMed: 18688787] ; Hallowell et al., supra note 35.
38. Koehly LM, et al. Characteristics of Health Information Gatherers, Disseminators, and Blockers Within Families at Risk of Hereditary Cancer: Implications for Family Health Communication Interventions. American Journal of Public Health. 2009; 99(12):2203–2209. [PubMed: 19833996]
39. Atkinson P, et al. Kinscapes, Timescapes, and Genescapes: Families Living with Genetic Risk. Sociology of Health & Illness. 2013; 35(8):1227–1241. [PubMed: 23957884]
40. Rothstein MA. GINA, the ADA, and Genetic Discrimination in Employment. Journal of Law, Medicine & Ethics. 2008; 36(4):837–840.
41. Bui et al., supra note 33; Lohn Z, et al. Incidental Findings from Clinical Genome-Wide Sequencing: A Review. Journal of Genetic Counseling. 2014; 23(4):463–473. [PubMed: 23709124] ; Bevan JL, et al. Critical Social Theory Approaches to Disclosure of Genomic

Incidental Findings. Nursing Ethics 19. 2012; 6:819–828.; See generally Green RC, Lautenbach D, McGuire AL. GINA, Genetic Discrimination, and Genomic Medicine. New England Journal of Medicine. 2015; 372(5):397–399. [PubMed: 25629736]

42. U.S. Department of Health and Human Services, Modifications to the HIPAA Privacy, Security, Enforcement, and Breach Notification Rules Under the Health Information Technology for Economic and Clinical Health Act and the Genetic Information Nondiscrimination Act; Other Modifications to the HIPAA Rules, 78 Federal Register 5566-5702 (2013), at 5689.
43. Woodward v. Commissioner of Social Security, 760 N.E.2d 257 (Mass. 2002); Hecht v. Superior Court, 20 Cal. Rptr.2d 275 (Cal. Ct. App. 1993).
44. Saleh v. Reichert, 104 D.L.R. 4th 384, 391 (Can. Ont. Gen. Div. 1993).
45. Smolensky KR. Rights of the Dead. Hofstra Law Review. 2009; 37(3):763–803.Strong C. Ethical and Legal Aspects of Sperm Retrieval after Death or Persistent Vegetative State. Journal of Law, Medicine & Ethics. 1999; 27(4):347–358.
46. Partridge E. Posthumous Interests and Posthumous Respect. Ethics. 1981; 91(2):243–264.
47. American Society of Human Genetics Social Issues Subcommittee on Familial Disclosure, supra note 4, at 482. See also other sources cited supra note 4.
48. American Society of Human Genetics Social Issues Subcommittee on Familial Disclosure, supra note 4, at 474.
49. Wolf et al. (2008), supra note 1, at 228, 232; Richardson HS, Belsky L. An Ethical Framework for Thinking About the Clinical Care that Researchers Owe Their Subjects. Hastings Center Report. 2004; 341:25–33. [PubMed: 15098404] .
50. Bledsoe MJ, et al. Return of Research Results from Genomic Biobanks: Cost Matters. Genetics in Medicine. 2013; 15(2):103–105. [PubMed: 22935716] ; Wolf et al. (2012), supra note 1, at 373; Beskow and Burke, supra note 6.
51. Bledsoe et al., supra note 50, at 103; Wolf et al. (2012), supra note 1, at 366, 375-76.
52. Wolf et al. (2012), supra note 1, at 373; Fabsitz et al., supra note 1, at 575-76, 580.
53. Wolf et al. (2012), supra note 1, at 373; Fabsitz et al., supra note 1, at 575.
54. Tarasoff v. Regents of the University of California, 17 Cal. 3d 425 (Cal. 1976).
55. Shah SK, et al. What Does the Duty to Warn Require? American Journal of Bioethics. 2013; 13(10):62–63. [PubMed: 24024817] ; Bombard et al., supra note 2; Wolf SM, et al. The Law of Incidental Findings in Human Subjects Research: Establishing Researchers' Duties. Journal of Law, Medicine & Ethics. 2008; 36(2):361–383.; Offit et al., supra note 4; Clayton, supra note 3.
56. See Molloy v. Meier, 679 N.W.2d 711 (Minn. 2004); Safer v. Estate of Pack, 677 A.2d 1188 (N.J. App. 1996), cert. denied, 683 A.2d 1163 (N.J. 1996), but see N.J. Stat.10: 5-47 (restricting disclosure of an individual's genetic information); Pate v. Threkel, 661 So. 2d 278 (Fla. 1995).
57. See Clayton, supra note 3, at 383.
58. For a rare case in which plaintiffs alleged a duty to disclose a research result – a positive newborn test for cystic fibrosis -- see Ande v. Rock, 647 N.W.2d 265 (Ct. App. Wisc. 2002).
59. Beskow and Burke, supra note 6. See also Shah et al., supra note 55; Bombard et al., supra note 2, at 13.
60. Beskow and Burke, supra note 6.
61. Fullerton et al., supra note 2; Garrett, supra note 5, at 161.
62. NCI Best Practices 2011, supra note 2, at 38.
63. For discussion of different oversight models for return of results issues, including an Informed Cohort Oversight Board (ICOB) and a Return of Results Oversight Committee, see, e.g., Wolf et al. (2012), supra note 1, at 374, and sources cited therein.
64. Beskow and Burke, supra note 6.
65. Jarvik GP, et al. Return of Genomic Results to Research Participants: The Floor, the Ceiling, and the Choices in Between. American Journal of Human Genetics. 2014; 94(6):818–826. [PubMed: 24814192] , at 823; Presidential Commission for the Study of Bioethical Issues, Anticipate and Communicate: Ethical Management of Incidental and Secondary Findings in the Clinical, Research, and Direct-to-Consumer Contexts (2013), available at <http://bioethics.gov/sites/default/files/FINALAnticipateCommunicate_PCSBI_0.pdf> (last visited June 12, 2014), at 91-93; Clayton

EW, McGuire AL. The Legal Risks of Returning Results of Genomics Research. Genetics in Medicine 14. 2012; 4:473–477., at 476; Wolf et al. (2012), supra note 1.

66. Chan et al., supra note 2, at 7. Note that individual research studies may decide to experiment with active return to family for the purpose of collecting data on that practice.
67. Burke et al., supra note 5; Bledsoe et al., supra note 50, at 104.
68. Rothstein, supra note 21, at 528.
69. Our group considered whether the representative should use a 3-tier standards similar to the 3-tier standard that surrogates use to make treatment decisions for a living patient who has lost decisional capacity: (1) follow the patient's expressed preferences if known, (2) otherwise decide as the patient would as best that can be determined based on the patient's known values (in an exercise of what is often called “substituted judgment”), or (3) if those values are unknown, decide in the patient's best interests. See, e.g., N. Berlinger, B. Jennings, and S. M. Wolf, The Hastings Center Guidelines for Decisions on Life-Sustaining Treatment and Care Near the End of Life (New York, NY: Oxford University Press, 2d ed. 2013). However, our group concluded that deciding about sharing research results with relatives, including after death, was not the same as deciding a patient's treatment. In deciding about sharing results with relatives, the interests of both the participant and the relatives need to be considered, and in genomic research, the standard needs to apply after participant death. A simpler standard that respects participant preferences if known, but then gives the representative the latitude to balance the participant's privacy and personal interests with the relative's interests thus seemed more appropriate.
70. Anastasova V, et al. Communication of Results and Disclosure of Incidental Findings in Longitudinal Paediatric Research. Pediatric Allergy and Immunology. 2013; 24(4):389–394. [PubMed: 23692330] , at 392-93; AAP & ACMG 2013, supra note 28, at 621; Ross et al., supra note 28, at 237-38; ASHG & ACMG 1995, supra note 28, at 1233.
71. Holm et al., supra note 32, at 551; Kleiderman et al., supra note 32; AAP & ACMG 2013, supra note 28, at 621-22; Haga and Zhao, supra note 32, at 52.
72. 45 C.F.R. § 164.502(g) (2014); Office for Civil Rights, U.S. Department of Health and Human Services, Does the HIPAA Privacy Rule Allow Parents the Right to See Their Children's Medical Records? available at <http://www.hhs.gov/ocr/privacy/hipaa/faq/right_to_access_medical_records/227.html> (last visited July 21, 2014).
73. Strong KA, et al. In the Absence of Evidentiary Harm, Existing Societal Norms Regarding Parental Authority Should Prevail. American Journal of Bioethics. 2014; 14(3):24–26. at 25. [PubMed: 24592835]
74. Wolf et al. (2012), supra note 1; Fabsitz et al., supra note 1; Wolf et al. (2008), supra note 1.
75. Wolf et al. (2012), supra note 1, at 378; Fabsitz et al., supra note 1, at 575-77.
76. Berg JS, Khoury MJ, Evans JP. Deploying Whole Genome Sequencing in Clinical Practice and Public Health: Meeting the Challenge One Bin at a Time. Genetics in Medicine. 2011; 13(6):499–504. at 501-02. [PubMed: 21558861]
77. U.S. Department of Health and Human Services, Modifications to the HIPAA Privacy, Security, Enforcement, and Breach Notification Rules Under the Health Information Technology and Economic and Clinical Health Act and the Genetic Information Nondiscrimination Act; Other Modifications to the HIPAA Rules; Final Rule,78 Federal Register 5566-5702 (2013), at 5668.
78. Id.
79. Rothstein, supra note 21, at 528.
80. As also noted earlier, some states similarly offer posthumous access to an individual's health information to treat a relative. See South Carolina Statutes, supra note 21.
81. Holm et al., supra note 32, at 549.

Summary of Recommendations

1. Researchers in genomic research projects should anticipate the potential for requests by relatives for participant results by communicating to prospective participants how the researchers will handle such requests and the project's policy on return of genomic results to relatives. If there is any potential for return of such results to relatives, the researchers should **ask participants their preferences** for sharing results with relatives, including after the participant's death, and should invite participants to identify their preferred representative to make decisions about relatives' access to their genomic results, including after their death.

2. Researchers are not obligated to return a participant's results to relatives, to design their research to facilitate this, or to search for results relevant to relatives. However, researchers **may participate in return** to relatives (as outlined below).

3. Researchers may urge a participant to disclose research results to relatives, but should generally refrain from otherwise initiating a process of sharing with relatives. A **passive disclosure policy** of responding to a relative's requests for a participant's research results is preferable to an active disclosure policy of researcher-initiated contact in most cases of returning results to relatives.

4. A majority of our group concludes that researchers may be ethically justified in actively reaching out to a participant's relatives to offer genomic information in the exceptional circumstance of discovering highly pathogenic and actionable variants that the relative is likely to carry, and whose disclosure is highly likely to avert imminent harm. Ethics consultation is warranted in such cases. A minority instead concludes that participants and their representatives should control access to the participant's genomic results, even in these rare cases.

5. Researchers should generally protect the choices of research participants, as well as the privacy of participant results. If a relative requests access to a research participant's results, the researcher may clarify what results are sought and why, to address any misunderstanding about the general type of results available and their familial implications. However, the researcher should then direct the request to the adult participant, if living and competent to decide. Otherwise, the request should be directed to the adult participant's representative (who may be the Legally Authorized Representative, Personal Representative, another authorized representative, or a trusted family member).

6. The adult participant or participant's representative should decide whether to share the result(s) with the relative requesting the

information. If the participant lacks decisional capacity or is deceased, the representative should generally follow the participant's wishes, if previously expressed. When the participant did not express or was unable to express such wishes, the representative should balance the participant's privacy and other interests against the interests of the relative in accessing the participant's result(s).

7. When the **research participant is a minor**, the participant's representative (who is likely to be the parent/guardian, but may be a different individual) should decide whether to share the result(s) with the relative. The representative should generally be guided by the decision of the parent/guardian on access by relatives, strongly considering any expressed preferences of the child (if able to participate).

8. **Participant results that may be returned** to a relative are results: (a) that are analytically valid; (b) that reveal an established and substantial risk of a serious health condition in the participant with significant health implications for the relative; (c) whose return offers net benefit to the relative, who may seek genetic testing or sequencing and have an opportunity to benefit due to the actionability of the variant; (d) that may be offered to the relative consistent with relevant law (including CLIA, HIPAA, state privacy law, and the Common Rule, as applicable); and (e) whose receipt has been agreed to by the relative.

9. When a participant's results are to be offered to a relative, the researcher should offer support for **communication of the results** by the participant or the participant's representative. At the participant's request, the researcher may facilitate the referral of the participant or representative to a health care professional who can assist in better understanding the results.

10. **Further research is needed** to analyze the circumstances in which relatives request a participant's results, the type of results sought, how those requests are handled, research participants' attitudes toward sharing, and outcomes. These data can refine recommendations for sharing participant results with relatives.

Definitions used in this paper

Incidental finding—"a finding concerning an individual research participant that has potential health or reproductive importance and is discovered in the course of conducting research but is beyond the aims of the study" (Wolf et al. 2008, at 219)

Individual research result—"a finding concerning an individual contributor that has potential health or reproductive importance and is discovered in the course of research, when the finding is on the focal variables under study in meeting the stated aims of the research project" (Wolf et al. 2012, at 364)

Relatives—used here to include both genetic and social family members

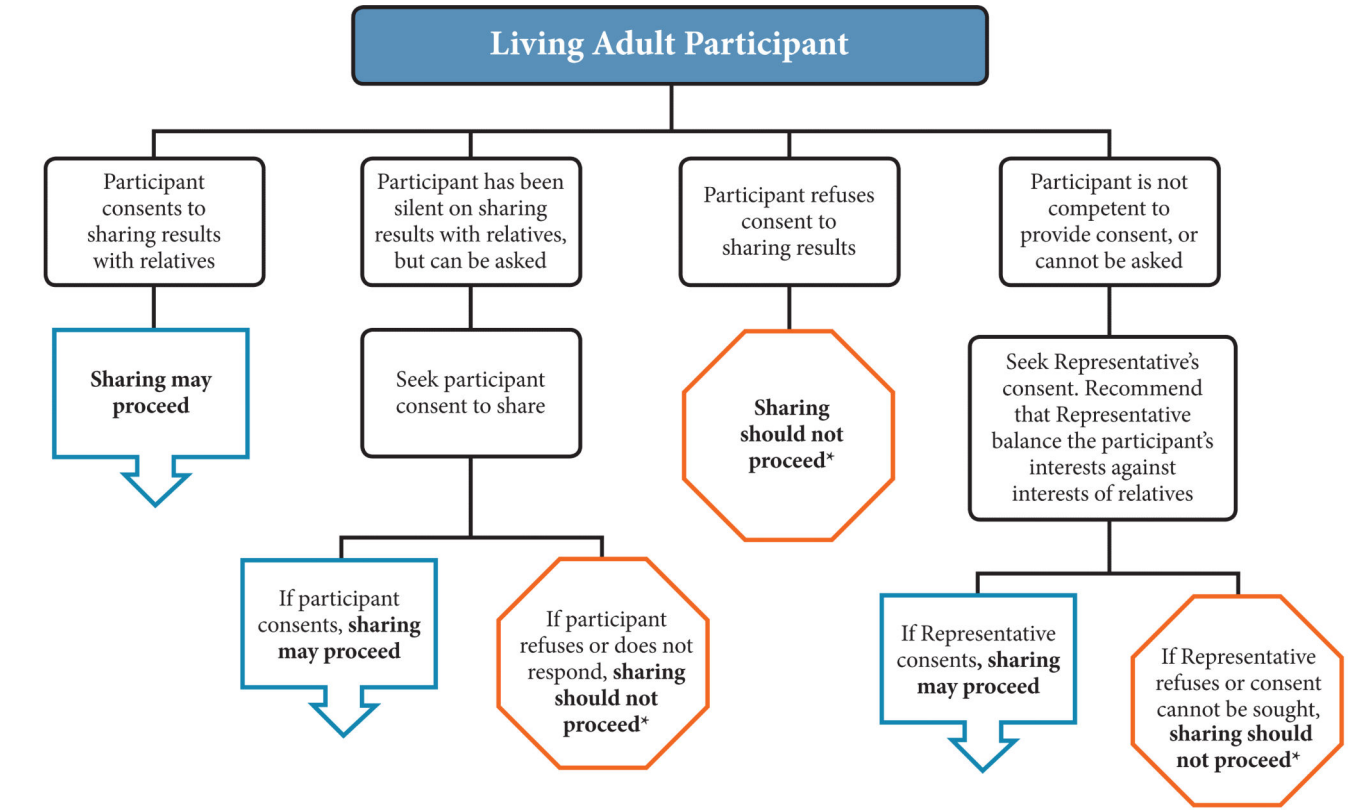
Representative—We use the term "representative" to refer to the person legally authorized to access a participant's genomic results. In different contexts, the representative may vary. A Legally Authorized Representative (LAR), Executor, Next of Kin, Spouse or Partner, or Parent/Guardian may qualify, depending on applicable federal and state law. HIPAA uses the term "personal representative" to refer to the authorized representative, including after the participant's death.

Active Return—return of results to participant or relatives initiated by the researcher without the request of the participant or relatives

Passive Return—used here to define return of results in which a participant or relatives receives results only after requesting results from researchers – not at the initiation of the researcher

Personal Representative (PR)—the term used under HIPAA to refer to the person serving as the participant's representative (see definition above), including after death. Note that HIPAA defers to state law for specification of who this posthumous representative is; state law may define the PR, for example, as the individual whom the participant names in a will as executor)

Legally Authorized Representative (LAR)—"an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research" (DHHS Common Rule § 46.102(c))



* In exceptional circumstances involving highly pathogenic and actionable variants whose disclosure is highly likely to avert imminent harm, researchers should seek ethics consultation on sharing findings with relatives.

Figure 1.

Recommended pathway for considering the sharing of a living adult participant's results with relatives.

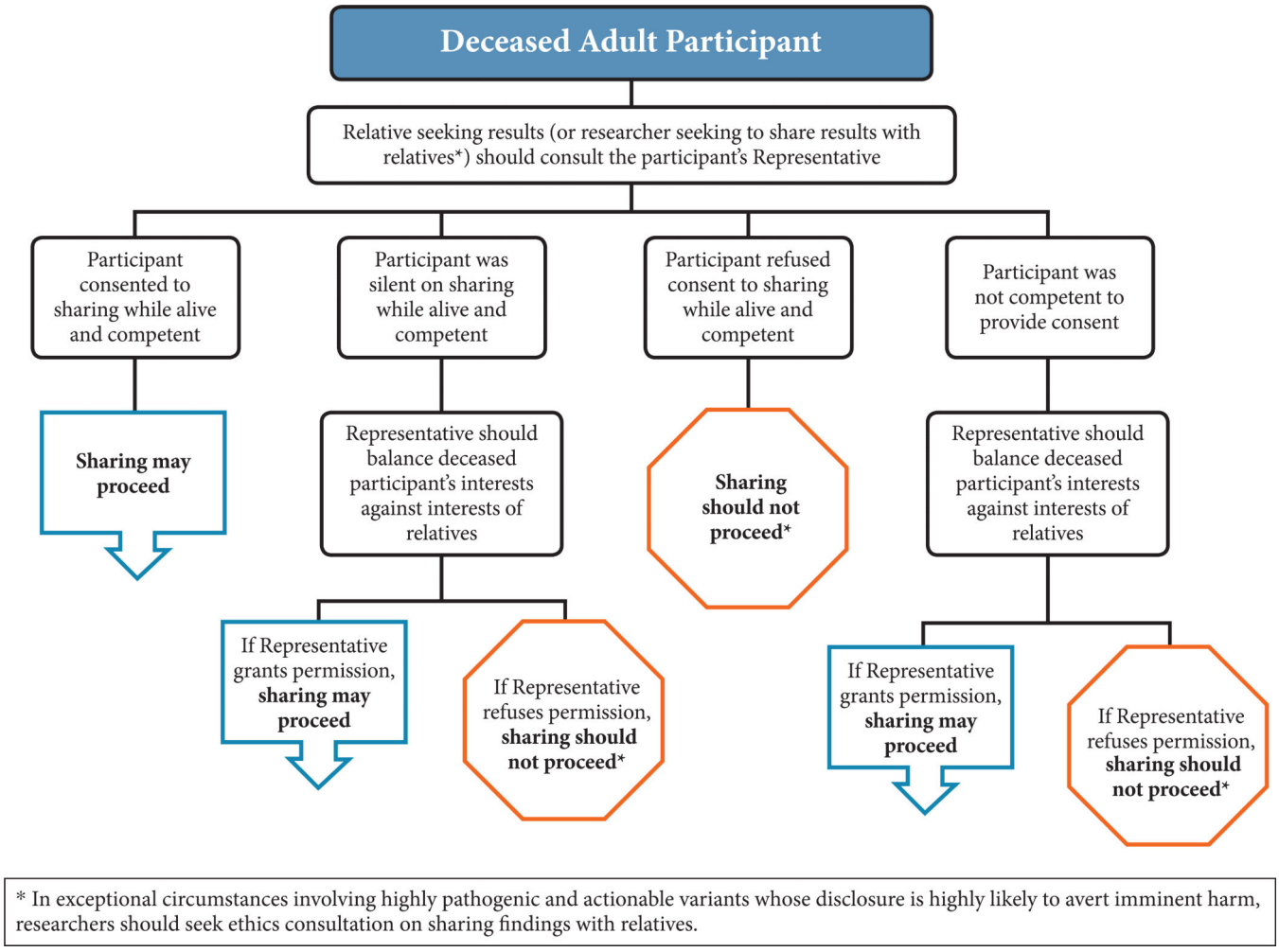
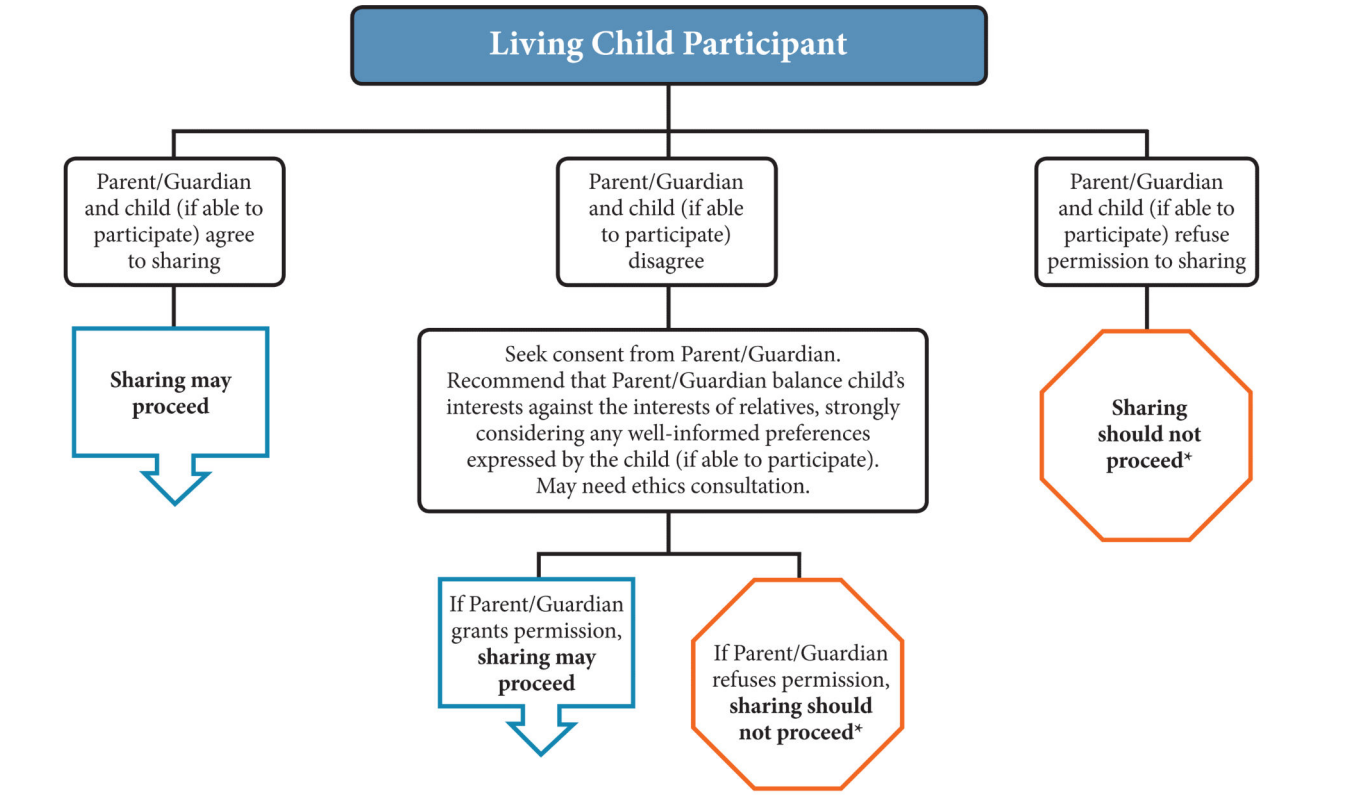


Figure 2.
Recommended pathway for considering the sharing of a deceased adult participant's results with relatives.



* In exceptional circumstances involving highly pathogenic and actionable variants whose disclosure is highly likely to avert imminent harm, researchers should seek ethics consultation on sharing findings with relatives.

Figure 3.
Recommended pathway for considering the sharing of a living child participant's results with relatives.

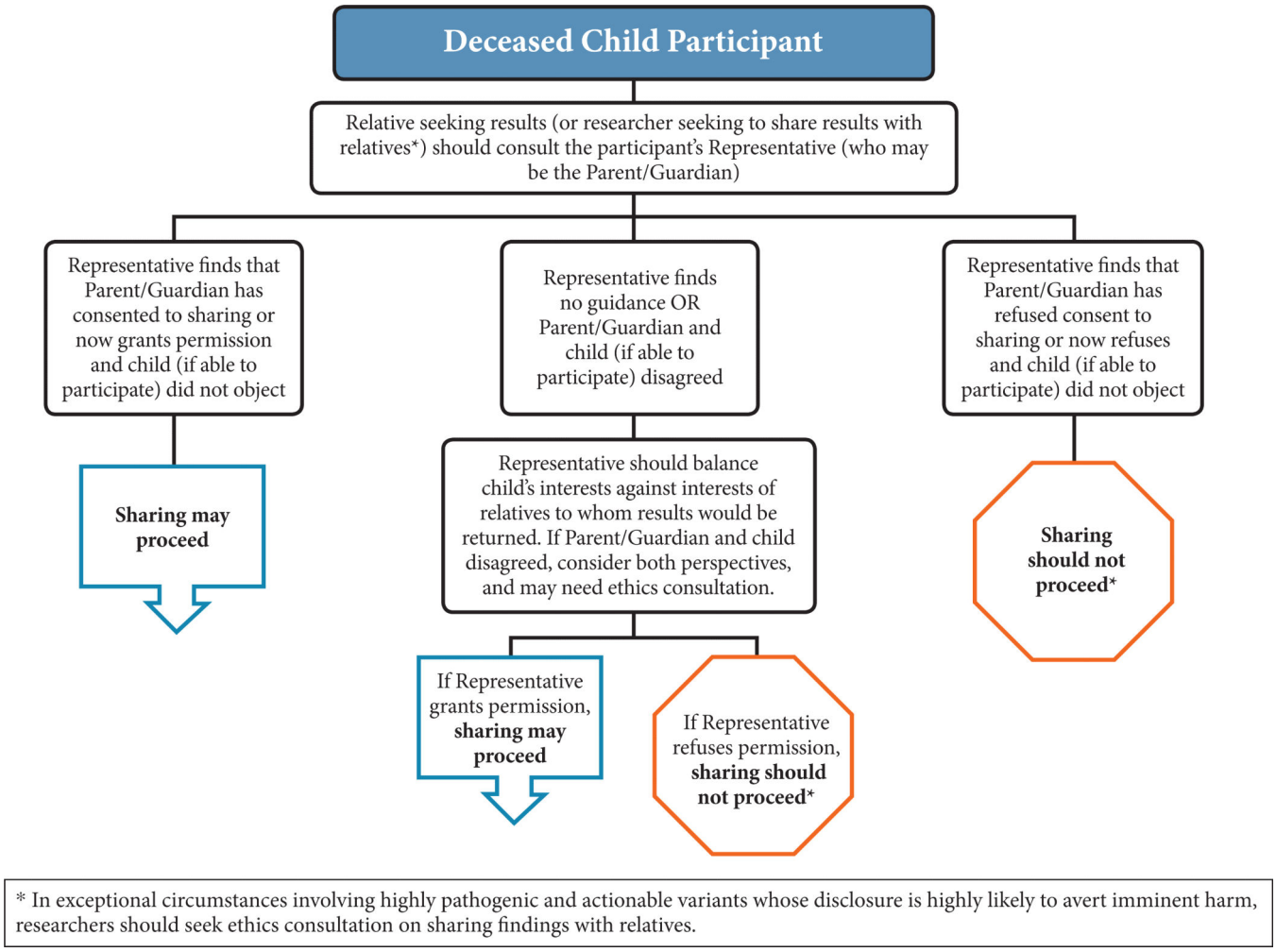


Figure 4.

Recommended pathway for considering the sharing of a deceased child participant's results with relatives.