International Policies on Sharing Genomic Research Results with Relatives: Approaches to Balancing Privacy with Access

Rebecca Branum and Susan M. Wolf

Introduction

Debate over return of results and incidental findings to participants in genetic and genomic research has exploded over the last decade. At this point, there is wide agreement that investigators have a responsibility to anticipate discovery of findings that may warrant return, to incorporate in protocols a plan for evaluating such findings, and to offer at least some of these results to participants consenting to such return.[1] However, the issue of how to handle questions from a participant's genetic relatives about their own risk, or whether investigators should alert relatives to a genetic risk they may share, has garnered much less attention. Only recently has the genomic research community begun to debate these questions and offer recommendations.[2]

The question of whether and how to share a research participant's results with relatives is an important — indeed, inevitable — issue in genomic research. Because genetically related family members may share variants identified in the participant, they may seek information about the participant's genomic results. Similarly, when research identifies pathogenic and clinically actionable variants that relatives may share, investigators may well wonder whether to offer information to relatives. Because genomic research frequently involves archiving data and specimens for ongoing analysis, including in research on cancer, the question of sharing results with relatives after the participant's death is also likely to arise.

At present, there is little law and policy directly on point in the United States. As debate on this issue emerges and the need for policy becomes clear, looking to the law and policy of other countries may be helpful, shedding light on policy options and revealing international trends. Further, genomic research is increasingly international, with cross-border cooperation and data sharing. Although countries have different legal systems, precedent, and cultural values, international harmonization of genomics policies, when possible, may facilitate collaboration and advance genomic research.

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International comparison of policies on return of research results to participants themselves has already proven helpful.[3] In two articles, Zawati and co-authors have described the normative frameworks at play in the international return of results debate.[4] Supplementing this work is Knoppers and Dam's[5] helpful analysis of relevant terminology and an examination by Lévesque and colleagues[6] of the views of organizational stakeholders and the ethical underpinning of the return of results debate in the international arena.

This paper endeavors to expand our knowledge base by comparing policies on sharing with relatives, both before and after death, with a focus on national law and policy across a broader range of countries than has been previously examined. Genomics researchers and professionals across the world face the challenge of balancing the privacy and wishes of individuals against the potential utility of genetic information to relatives. The following analysis focuses on laws and policies on relatives' access to the genetic information of participants in genomic research. Using the United States as a comparison, this paper analyzes law and policy in 10 countries and recommends ways that American policy can better reconcile the priorities of privacy protection, respect for autonomy, and consideration of the interests of research participants and relatives.

There have also been efforts to articulate policy that may be applied across borders.[7] In addition, Tassé has published analysis comparing Canada, France, and the United States on their approach to return of results after death.[8]

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Under American law and regulation, genetic or genomic research results can reach relatives in several ways.[9] The simplest way for relatives to access such research results is through the participant, if the participant is willing and able to provide the information. Relatives may also receive these research results from researchers directly when a participant has previously consented to this type of sharing. Beyond these two situations, several interconnected laws and regulations address access to genetic or genomic research results. While this paper focuses on federal law and regulation and we do not analyze state law, states do have privacy laws and laws on genetic testing which may be relevant to sharing genomic research results with relatives.[10] In addition, a few states (such as South Carolina) have passed legislation on sharing an individual's genetic information within families after the person's death, without specifically addressing research results.[11] On the federal level, sharing of genetic research results is addressed by the Privacy Act[12] and regulations issued by the federal Office of Civil Rights under the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule.[13]

The Privacy Act regulates the dissemination of personal information held by federal executive agencies, including the Department of Health and Human Services (DHHS). Under the Privacy Act, agencies may not disclose information, including genetic information, without an individual's consent unless the disclosure is made "pursuant to a showing of compelling circumstances affecting the health or safety of an individual...."[14] To the extent that a federal executive agency holds genetic or genomic data from research, the Privacy Act would permit DHHS to release research results pursuant to the showing of "compelling circumstances" that warrant disclosure.[15] The Privacy Act would apply to the return of research results if the results were shown to present "compel-

ling circumstances affecting the health or safety of an individual."[16] Although some have urged that a "duty to warn" may exist for a subset of research results that are pathogenic and clinically actionable,[17] Department of Justice guidance indicates that "compelling circumstances" has been interpreted to refer to emergencies.[18] It is not clear that circumstances in which a relative might request access to genomic research results would constitute an emergency warranting disclosure without consent under the Privacy Act.

HIPAA privacy regulations safeguard the privacy of protected health information (PHI), including genetic or genomic information contained in the designated record set.[19] This record set includes all medical and billing records; any record "used, in whole or in part, by or for the covered entity to make decisions about individuals"; and any "item, collection, or grouping of information that includes protected health information and is maintained, collected, used, or disseminated by or for a covered entity."[20] This may include the research record or research results recorded in the medical record, but would only apply to information housed by covered entities.[21] HIPAA regulations define covered entities as "health plans, health care clearinghouses, and health care providers who electronically transmit any health information in connection with transactions for which [D]HHS has adopted standards."[22]

Three HIPAA regulations provide avenues for relatives to gain access to genetic or genomic information without the participation or consent of the individual. First, HIPAA regulations permit health care providers to disclose protected health information to other health care providers for the purpose of diagnosis and treatment of another patient, including relatives.[23] Individuals may request that their information not be shared, but covered entities and health care providers are under no obligation to agree to such restrictions.[24] Covered entities may also disclose a decedent's PHI to relatives involved in the care (or payment for care) of the decedent prior to his or her death, unless sharing would be inconsistent with the individual's expressed wishes.[25] Relatives may additionally gain access to a decedent's PHI through the decedent's personal representative as defined by state law — typically a surviving spouse or relative — who, under HIPAA, is granted the same access rights that the individual enjoyed during his or her life.[26] The personal representative granted access to health records may also have direct access to lab reports due to recent regulatory changes, including after death.[27]

The provision allowing a relative's physician to request access to the individual's genetic results for the purpose of diagnosing or treating the relative has been criticized by Mark Rothstein as inadequately protective of the individual's privacy.[28] Rothstein argues that third-party access (including relatives' access) to an individual's genetic information has long been limited in the United States and that the current interpretation of the Privacy Rule damages privacy and the physician-patient relationship.[29] American professional associations have articulated policy that is more restrictive than the Privacy Rule provision that Rothstein criticizes. The American Society of Human Genetics (ASHG) has addressed sharing genetic information with relatives on two occasions. In a 1996 statement, ASHG stated that "[r]esearch results or samples should not be given to any of the subject's family members by the investigator without explicit, written permission of the subject, except under extraordinary circumstances."[30] ASHG's 1998 statement addressing both clinical and research activities elaborated, stating that "[d]isclosure should be permissible where attempts to encourage disclosure on the part of the patient have failed; where the harm is highly likely to occur and is serious and foreseeable; where the at-risk relative(s) is identifiable; and where either the disease is preventable/treatable or medically accepted standards indicate that early monitoring will reduce the genetic risk"[31] and that "[t]he harm that may result from failure to disclose should outweigh the harm that may result from disclosure."[32] These guidelines thus provide more stringent protections against the disclosure of genetic information without the source individual's consent than do current federal and state statutes and regulation.

The Privacy Act and HIPAA do not protect all genetic and genomic research results. The Privacy Act applies only to data maintained by federal executive branch departments and HIPAA compliance is only required by "covered entities" and only with regard to PHI contained in the "designated record set." Institutions interpret current HIPAA regulations differently and not all institutions consider research data to be part of the designated record set, to which a participant or personal representative would have access.[33] In addition, genetic research results may not be generated or held by a "covered entity" under HIPAA, and thus may not be subject to HIPAA's regulations. Further, research institutions composed of both heath care and research components may be designated as "hybrid entities," limiting the application of many HIPAA requirements to only those portions of the institution that are part of a "health care component."[34]

In the U.S., genetic and genomic research results not subject to the Privacy Act or HIPAA are nonetheless likely to be protected through the Common Rule. The Common Rule, which applies to human subjects

research that is conducted or funded by any of the federal agencies and departments that have signed on to the Common Rule[35] or conducted by an entity rendering a Federalwide Assurance (FWA) that all of its research will be covered by the Rule,[36] requires that consent documents contain "[a] statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained."[37] This suggests that the prospective research participant must be told what results will or will not be available to relatives (so the participant may decide whether to participate in the research on that basis) or must agree to any disclosure of their findings to relatives, at least while the participant is alive. However, unlike the protections of HIPAA that extend for 50 years beyond the death of an individual, the Common Rule only applies to "human subjects" who, by definition, must be "living."[38] Because Common Rule protection ends at death, relatives may have access to genetic or genomic research results not protected by the Privacy Act or HIPAA following the death of a participant.

Current U.S. law on sharing a participant's genetic or genomic research results with relatives is thus complex. Analysis must consider whether the Privacy Act, Common Rule, or HIPAA applies (as well as any state law provisions) and whether the results are in the designated record set. The rules also differ before and after the death of the participant. Depending on which regulatory provisions apply, privacy protections for the participant's genetic or genomic information may yield in the face of a relative's need. An unresolved tension also remains between the balance struck by ASHG allowing family access to clinical genetic information without proband consent only under narrow circumstances and HIPAA's more generous access provisions. How U.S. policy will specifically address relatives' access to a participant's genomic research results before and after death remains to be fully resolved, though emerging recommendations[39] should help guide this policy evolution. This paper's comparison to law and policy in other countries may help as well.

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Methodology

In order to compare approaches in other countries, this paper catalogs and examines the law and policy on sharing of genetic information in 10 countries roughly similar to the United States: Australia, Austria, Canada, France, Israel, Japan, New Zealand, Singapore, Sweden, and the United Kingdom. We identified countries with law and policy governing return of genetic research results to relatives using the International Compilation of Human Research Standards (ICHRS) (2013)[40] assembled by the U.S. Office for Human Research Protections (OHRP). The ICHRS "enumerates over 1,000 laws, regulations, and guidelines that govern human subjects research in 104 countries." This compilation is assembled by OHRP for use by "researchers, IRBs/Research Ethics Committees, sponsors, and others who are involved in human subjects research around the world."[41] The ICHRS is updated annually and in-country authorities are permitted to submit corrections and verify

entries published by OHRP.[42] To ensure the accuracy of our analysis, we collected only those laws and policies listed in the 2013 edition of the ICHRS with an indication that they had been verified by in-country authorities.

From the full list of countries with verified entries on the ICHRS, we narrowed our analysis to countries classified as having "very high human development" as determined by the United Nations Human Development Index (HDI), in order to compare the United States with countries that are roughly similar.[43] HDI measures three dimensions of human development (health, education, and living standards) along with four indicators (life expectancy at birth, mean years of schooling, expected years of schooling, and gross national income per capita). Author R.B. retrieved the laws and policies listed in the ICHRS for the 49 "very high human development" countries with verified entries. She then identified those 29 countries with laws and policies available in English in the original or in translation. Analysis was finally narrowed to the 10 countries with laws and policies relevant to the return of genetic research results to relatives. Laws that addressed access to genetic research results by "third parties" were included, as "third parties" could include relatives.

The collection and analysis of these documents took place in 2013. To ensure timeliness in advance of publication, the documents collected in 2013 were compared to the laws and policies listed in the 2014 ICHRS.[44] Where comparison showed that the 2013 documents had been updated or replaced, the superseding documents were collected and then analyzed, replacing the 2013 documents in our collection. No research on the laws or policies of countries was conducted outside of ICHRS. Due to this limitation, laws and policies on relatives' access to genetic research results may exist in addition to those that were analyzed, whether due to absence of additional material in ICHRS or the unavailability of a law or policy in English.

Given the language and breadth limitations, this analysis is not intended to be comprehensive. Case law, regulation, and policies not included in the ICHRS or not available in English may contain relevant information, but are not captured by our methodology and thus are beyond the scope of this analysis.[45] Rather, this article provides a comparative analysis of approaches to relatives accessing genetic research results in order to illustrate options and glean lessons that the United States might consider in clarifying and improving its own approach to this complex issue.

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Results

The above methodology identified 10 countries with law and policies on sharing genetic research results with relatives (or third parties): Australia, Austria, Canada, France, Israel, Japan, New Zealand, Singapore, Sweden, and the United Kingdom. **Table 1** lists attributes of the law and policy in those countries. In 8 of these countries, the law and policy identified apply only to research results. The Israeli Genetic Information Law is ambiguous as to whether it applies to clinical or research information and the Swedish Genetic Integrity Act applies to all genetic information.

As discussed below, 3 of the 10 countries that address sharing genetic information with relatives (Japan,[46] New Zealand,[47] and the United Kingdom[48]) address the complexities of sharing genetic information after the death of a participant. Of the 10 countries analyzed, France and Sweden[49] take the most protective stance in regard to an individual's genetic information. One country (Australia)[50] requires that all consent documents warn participants that life-threatening information may be shared with relatives, even if the participant objects. Among the remaining seven countries, genetic information is generally kept confidential and consent is required for sharing. The

Table 1
Attributes of International Policies on Sharing Genetic Research Results with Relatives

	Applies only to research-generated results	Participants should be provided with information on whether or how results will be shared with relatives	Addresses posthumous sharing of results	May be shared over objection or without consent of participant
Australia[115]	Yes	Yes	No	Yes
Austria[116]	Yes	Not addressed	No	Ambiguous
Canada[117]	Yes	Yes	No	Yes
France[118]	Yes	Not addressed	No	No
Israel[119]	Ambiguous	Not addressed	No	Yes
Japan[120]	Yes	Not addressed	Yes	Yes
New Zealand[121]	Yes	Yes	Yes	Ambiguous
Singapore[122]	Yes	Not addressed	No	Yes
Sweden[123]	No	Not addressed	No	No
United Kingdom[124]	Yes	Yes	Yes	Yes
United States[125]	No	Not addressed	Yes	Yes

requirement for consent, however, is modified by various exceptions that permit the disclosure of results to relatives, as discussed below.

A. Three Countries Address Posthumous Sharing of Research Results

Of the 10 countries whose law and policy address sharing of research results with relatives, only three specifically address whether results may be shared after death: New Zealand, Japan, and the United Kingdom. New Zealand also addresses access to stored specimens. In its "Ethical Considerations Relating to Research in Human Genetics," New Zealand requires that "[r]esearchers must specify the procedure to be followed if the participant, or a relative of the living participant, or a relative of the deceased participant, requests access to stored genetic material or information generated by the research. Consent to participation should cover post death requirements."[51] The Japanese "Fundamental Principles of Research on the Human Genome" require that "[w]here a surviving family member (blood relative) requests disclosure of the donor's genetic information, the director of the research institution shall, after presenting to the ethics review committee the reasons for or the necessity of the disclosure request by the surviving family member (blood relative) determine a response based on the opinions of the ethics review committee."[52] Policy in the United Kingdom only addresses access by relatives to results obtained from post-mortem research.[53] In that circumstance, "[a]rrangements must be described for the respectful disposal of material once the research is completed, and for the reporting of the findings of the research to relatives, if they wish it."[54]

Thus, none of these provisions clarifies the substantive conditions under which researchers should grant relatives access to a participant's genetic information after the death of the participant. Instead, these three provisions are procedural. New Zealand requires researchers to anticipate possible requests, to specify a procedure to be followed in the event of such a request, and to address these issues with participants in the research consent process.[55] Japan states that if such a request is received, the director of the research institution should consult with the ethics committee, and then decide how to respond.[56] Finally, the United Kingdom requires that participants and relatives be informed of the "arrangements" for reporting post-mortem research results to relatives wishing to receive the information, but does not address what findings may or should be returned.[57]

B. Only France and Sweden Strictly Limit Access to an Individual's Genetic Information

Of the 10 countries with laws or policies governing the sharing of genetic results with relatives, only two — France and Sweden — strictly limit the access of relatives to a participant's genetic information and

always require consent or authorization for access. A French guidance document from 1991 states, "[n]o result concerning the characteristics of the genome of an individual is to be provided to parents, third parties or any public or private organisation without the explicit consent of the individual."[58] The Swedish Genetic Integrity Act states that "[u]nless by virtue of provisions laid down by law, no party may inquire into or use genetic information about the other party in connection with an agreement. No person may effect access to genetic information about another person without authority."[59] Thus, France appears to require consent from an individual for others, including family members, to access genetic results. Sweden appears to require authorization for such access; presumably that authorization could be in the form of consent by the individual or approval by a court or similar authority.

C. Most Policies Envision Some Form of Access by Relatives

In contrast to the French and Swedish policies, Australia, Austria, Canada, Israel, Japan, New Zealand, Singapore, and the United Kingdom (8 countries out of 10) envision circumstances in which genetic information may be shared with relatives without the consent of the source individual or over that person's objection. **Table 2** indicates the approach of these countries to sharing results with relatives. Seven of the 10 countries analyzed create a privacy-protective default in which either the wishes of the participant will be respected or the participant's results will be

Table 2

Circumstances under which Results May Be Shared with Relatives

Note: Table lists only those 8 countries that permit sharing with relatives. Omitted are France and Sweden.
Key requirements for sharing information with relatives are in **bold**.

Australia	"[I]f the research discloses that a family member may be at risk of a life-threatening or serious illness for which treatment is available or pending, this information may, with approval of an HREC, be offered by a clinician to the family member, even if the research participant does not consent to this."[126]
Austria	"Individual results should only be passed on to third parties in exceptional cases."[127]
Canada	"Participants in genetic research shall have an opportunity to express their preferences about the sharing of information with relatives or others. These preferences may be subject to overriding considerations that may warrant disclosure of information to relatives in exceptional circumstances (e.g., if genetic research reveals information about a serious or life-threatening condition that can be prevented or treated through intervention.)"[128]
Israel	"Notwithstanding the objection of the subject, the information may be transmitted to another treating practitioner if the Ethics Committee, after having heard the subject, is convinced of all of the following: 1. communication…is required for the maintenance of the health of the relative or to improve such person's health, and for the prevention of death, illness, or serious disability of such relative, including an unborn relative; 2. communication of the genetic information is the only way of achieving the object referred to in paragraph 1); 3. the benefit to the relative as a result of communication of the genetic information to the treating practitioner is greater than the harm that would be caused to the subject by communication of the genetic information, or the reasons given by the subject for not transmitting the information to the treating practitioner are not reasonable, in the circumstances of the case."[129]
Japan	Bioethics Committee: "Fundamental Principles of Research on the Human Genome":[130] "In principle, blood relatives or families of participants may be informed of the genetic information of the participant only when a participant gives his/her own permission. Personal information pertaining to a participant may not be disclosed to his/her blood relatives or family against his/her will. Notwithstanding the principle described in the preceding paragraph, if the genetic information obtained from the research leads to the conclusion that a portion of the genetic characteristics of the participant is or may be connected to the aetiology [*sic*] of a disease, this conclusion may be disclosed to his/her blood relatives following authorization by the Ethics Committee, and only if preventive measures or treatment have already been established for the disease in question." Ministry of Education: "Ethical Guidelines for Human Genome/Gene Analysis Research":[131] "A research director shall not, in the absence of consent from the donor, in principle, disclose the donor's genetic information to any person other than the donor."

Japan (continued)	"1. Where a proxy consenter (excluding persons in 2. and 3.) requests disclosure of the donor's genetic information, the director of the research institution shall, after presenting to the ethics review committee the reasons for or the necessity of the disclosure request by the proxy consenter, determine a response based on the opinions of the ethics review committee. In making this determination, the director of the research institution shall confirm that either of the following conditions has been met: 1) Where there is a requirement for the protection of the life, body or property of an individual, it is difficult to obtain the consent of donors; 2) Where there is a particular requirement for the improvement of public health, it is difficult to obtain the consent of donors" "2. Where a surviving family member (blood relative) requests disclosure of the donor's genetic information, the director of the research institution shall, after presenting to the ethics review committee the reasons for or the necessity of the disclosure request by the surviving family member (blood relative), determine a response based on the opinions of the ethics review committee." "3. In cases where a donor is a minor and his/her proxy consenter has requested disclosure of the minor's genetic information, the research director may disclose the information to the proxy consenter. Where, however, the minor is aged 16 years or older, the research director shall check the intention of the minor and respect that intention. The research director shall also report to the director of the research institution when, as a result of disclosing the minor's genetic information, there is concern about discrimination against the donor, denial of fostering or negative impacts on treatments. The director of the research institution shall, prior to disclosure, seek opinions of the ethics review committee where necessary regarding the propriety of disclosure and the details and method thereof, and shall seek dialogue with the minor and his/her proxy consenter." "4. Even if a donor has not requested disclosure of his/her own genetic information to blood relatives, when all of the following conditions are met, a research director may convey to the donor's blood relatives information regarding any drug responses or disorders having a genetic predisposition derived from the donor's genetic information: 1) It is discovered that the donor's genetic information is highly likely to have a serious impact on the life of the donor's blood relatives and, at the same time, there is an effective treatment protocol. 2) The director of the research institution, who has received a report set forth in 1) from a research director, seeks opinions of the ethics review committee regarding the propriety of disclosure and the details and method thereof, including consideration of, in particular, the following matters, and, based on those opinions, reaches a conclusion, upon consultation with the research director, that necessary information should be provided to blood relatives: (a) The possibility that blood relatives are afflicted with the same disorder etc. (b) The impact on the life of the blood relatives (c) Whether or not there is an effective treatment protocol, and the blood relatives' state of health (d) Details of the explanation on the disclosure of research results given at the time of the informed consent 3) In view of the conclusion reached in 2), the research director seeks the understanding of the donor again, and endeavors to obtain consent regarding the provision of necessary information to the blood relatives; 4) The intention of the donor's blood relatives to request that information be provided is checked after giving an adequate explanation."
New Zealand	"Research participants should be informed that, if the research generates information of relevance to the health of other family members, their consent will be sought to disclosing the information to those members of their family. Researchers should define the mechanism for obtaining participants' consent to disclose their information to other family members."[132]
Singapore	"There may be circumstances when obligations of confidentiality cannot be absolute. For example, there may be legal duty for the investigator to warn family members of genetically-based risks of severe harm."[133]
United Kingdom	"For the use of tissue taken post mortem, the consent of the person concerned before they died, or of the relatives of the deceased, must always be obtained. Agreeing to such research involves relatives in difficult choices. Arrangements must be described for the respectful disposal of material once the research is completed, and for the reporting of the findings of the research to relatives, if they wish it."[134]
United States	"No agency shall disclose any record . . . [unless there is] a showing of compelling circumstances affecting the health or safety of an individual if upon such disclosure notification is transmitted to the last known address of such individual…."[135] "[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."[136]

kept confidential. However, these defaults are subject to exceptions, discussed below.

AUSTRIA

The least descriptive among these policies is the 2007 Austrian policy document issued by the Bioethics Commission at the Federal Chancellery titled, "Biobanks for Medical Research."[60] The policy states simply that "[i]ndividual results should only be passed on to third parties in exceptional cases"[61] without defining what would constitute "exceptional cases" warranting the sharing of results.

AUSTRALIA

Rather than create a default in which all genetic results are presumed confidential, Australian policy carves out a category of results that a participant may not prevent from being shared. The fact that some results may be shared even over the objection of the participant, however, must be addressed in consent documents prior to enrollment in research. The policy states, "[I]f the research discloses that a family member may be at risk of a life-threatening or serious illness for which treatment is available or pending, this information may, with approval of an HREC, be offered by a clinician to the family member, even if the research participant does not consent to this."[62] Although this policy may provide access to a participant's genetic data if the data show a risk of serious and treatable illness and the ethics committee approves offering the information to the family member, the policy is made available in advance of participation so that individuals who are unwilling to share genetic information may decline to participate in the research.

CANADA

Unlike Australian policy that requires that individuals be made aware that results may be shared without their consent, the Canadian TriCouncil policy states that "[p]articipants in genetic research shall have an opportunity to express their preferences about the sharing of information with relatives or others."[63] These preferences, however, may be overridden in "exceptional circumstances" — language also used in Austrian policy. Rather than provide a comprehensive analysis of what constitutes "exceptional circumstances," however, the Canadian TriCouncil policy provides a single example: "e.g., if genetic research reveals information about a serious or life-threatening condition that can be prevented or treated through intervention."[64] Although the "serious or life-threatening condition" language echoes the circumstances under which information may be shared under Australian policy, the Canadian TriCouncil policy would presumably permit disclosure in other such "exceptional circumstances" not limited to the single example given.

ISRAEL

Unlike Canadian policy, the Israeli Genetic Information Law describes discrete circumstances under which information may be shared. In all circumstances, sharing of information under the Israeli Genetic Information Law is limited to transmission between treating practitioners and only after Ethics Committee consultation.[65] The Ethics Committee must then find that three situations exist. First, the communication must be "required for the maintenance of the health of the relative or to improve such person's health, and for the prevention of death, illness, or serious disability of such relative."[66] In addition, the "communication of the genetic information [must be] the only way of achieving these goals." Finally, "the benefit to the relative as a result of communication of the genetic information to the treating practitioner [must be] greater than the harm that would be caused to the subject by communication of the genetic information" or "the reasons given by the subject for not transmitting the information to the treating practitioner are not reasonable, in the circumstances of the case."[67]

The Israeli Genetic Information law has several unique features not seen in the laws and policies of other countries. First, it defines relatives to include the "unborn," implying that the heritability of a condition may warrant disclosure. Also unique to the Israeli approach is the requirement that benefit to the relative receiving the information outweigh the harm to the participant of disclosing his or her genetic information, a provision echoing the 1998 ASHG policy on genetic privacy.[68] Finally, Israel is the only country to explicitly address the dilemma created when a participant is able to prevent useful information from reaching relatives. Permitting an Ethics Committee to evaluate whether a participant's refusal to share is "reasonable" may allow the transfer of useful genetic information to relatives; however, the provision also puts the Ethics Committee in the position of evaluating complex family dynamics.

JAPAN

Japan sets forth the most descriptive and complex requirements for when genetic or genomic information may be shared with relatives. Japan addresses sharing of research results in two documents: the "Fundamental Principles of Research on the Human Genome" and "Ethical Guidelines for Human Genome/Gene Analysis Research." These two documents, however, vary in their approach to disclosure of genetic infor-

mation, the latter taking a more nuanced approach, addressing research results obtained from minors, return of results after death, and return of results to proxy consenters.

The Japanese Council for Science and Technology Bioethics Committee's policy titled, "Fundamental Principles of Research on the Human Genome,"[69] provides the simplest explanation of whether and how genetic information may be shared with relatives. The "Fundamental Principles" document is intended to "serve as 'the Constitution' in human genome research, and relevant guidelines must be formulated based on these Fundamental Principles to provide a more detailed rules that should be adhered to in the course of research."[70] This document states that "in principle, blood relatives…may be informed of the genetic information…only when a participant gives his/her own permission."[71] This principle, however, is not without exception. When "the genetic information obtained from the research leads to the conclusion that a portion of the genetic characteristics of the participant is or may be connected to the [etiology] of disease, this conclusion may be disclosed to his/her blood relatives following authorization by the ethics committee, . . . only if preventive measures or treatment have already been established for the disease in question."[72]

The Ministry of Education's "Ethical Guidelines for Human Genome/Gene Analysis Research" applies to all human genome and gene analysis occurring after 2001 and is based on the "general principles" of the above "Fundamental Principles of Research on the Human Genome."[73] The "Ethical Guidelines" state, "[a] research director shall not, in the absence of consent from the donor, in principle, disclose the donor's genetic information to any person other than the donor."[74] However, this general guidance does not apply in some circumstances. The policy outlines four complex exceptions to the requirement that a participant consent to sharing, depending on whether the results are requested by a proxy consenter, results are requested by a surviving blood relative, results of a minor participant are requested by a proxy consenter, or the research director determines that communication is appropriate.[75]

The first scenario addressed is disclosure to a "proxy consenter," defined as "a person who gives informed consent in place of a donor when the said donor is incapable of giving informed consent."[76] In this case, the genetic information may be disclosed to a proxy consenter only after the director of research consults with the ethics review committee and it is determined that either (1) "there is a requirement for the protection of the life, body or property of an individual, [and] it is difficult to obtain the consent of donors" or (2) "there is a particular requirement for the improvement of public health, [and] it is difficult to obtain the consent of donors."[77] In the second scenario, when a surviving blood relative requests access to genetic information of a participant, "the director of the research institution shall, after presenting to the ethics review committee the reasons for or the necessity of the disclosure request by the surviving family member (blood relative), determine a response based on the opinions of the ethics review committee."[78] Third, a proxy consenter may be granted access to a minor's genetic information when the proxy consenter requests it. However, if the child is age 16 or older, the research director must "check the intention of the minor and respect that intention" regarding disclosure of his or her genetic information.[79] Finally, when a donor has not requested disclosure but "[i]t is discovered that the donor's genetic information is highly likely to have a serious impact on the life of the donor's blood relatives and, at the same time, there is an effective treatment protocol," the director of research must consult with the ethics review committee to determine whether information should be shared by considering four matters: (a) "[t]he possibility that blood relatives are afflicted with the same disorder," (b) "[t]he impact on the life of the blood relatives," (c) "[w]hether or not there is an effective treatment protocol, and the blood relatives' state of health," and (d) "[d]etails of the explanation on the disclosure of research results given at the time of the informed consent."[80] After weighing these four factors, the research director must try to obtain donor consent prior to disclosing the genetic research results to relatives.[81] Japanese policy is thus the only policy among those reviewed that addresses several different ways in which genetic research results might be requested by relatives or identified by researchers as important to share with relatives.

New Zealand

In comparison to the above Japanese policies, the Health Research Council of New Zealand provides a policy of relative simplicity. Like Australia, the New Zealand policy states that participants should be made aware in advance of how their genetic information may be shared. Unlike Australia, however, the New Zealand policy states that "[r]esearch participants should be informed that, if the research generates information of relevance to the health of other family members, their consent will be sought to disclosing the information to those members of their family. Researchers should define the mechanism for obtaining participants' consent to disclose their information to other family members."[82] In contrast to Australian policy stating that under some circumstances partici-

pants will have no choice as to whether their information is shared with relatives,[83] New Zealand policy gives participants a choice by seeking consent prior to disclosing the information to relatives. Although the policy states that there should be established mechanisms for obtaining consent to disclose results to relatives, it does not directly address whether this consent may be overridden in some cases or whether the lack of consent or ability to obtain consent (for example, if the participant has died or cannot be found) precludes sharing with relatives. For this reason, the policy is ambiguous as to whether results can be shared over objection or without the consent of the participant.

Eight out of 10 countries' laws and policies indicate that results are generally considered confidential, but that some circumstances may permit sharing of this information without consent or over objection of the participant. Although the inability to obtain consent (after a participant's death, for example) presents different ethical and policy implications than overriding the refusal of a living participant to share their results, only one country (Japan) has policy that addresses this distinction. The conditions required to override or forego obtaining consent from participants vary among countries.

SINGAPORE

Among the policies examined, Singapore's "Ethical Guidelines on Research Involving Human Subjects" is an outlier, as the only policy to reference the potential legal duty of researchers to disclose genetic information to relatives. This policy states that "[t]here may be circumstances when obligations of confidentiality cannot be absolute. For example, there may be legal duty for the investigator to warn family members of genetically-based risks of severe harm."[84] Although the policy does not specifically address sharing results without consent or over the objection of a participant, it appears to imply that both scenarios are possible when a legal duty to share exists. Although this is the only policy to explicitly mention a potential legal duty, its focus on circumstances posing risk of "severe harm" echoes the approaches of Australia, Canada, Israel, and Japan.

UNITED KINGDOM

The policy from the United Kingdom refers briefly to the sharing of results with relatives and addresses only sharing after the death of the participant. The policy, "Research Governance Framework for Health and Social Care," states that consent to participate in post-mortem research may be provided either by the living participant or by relatives following the participant's death.[85] The policy then states that "[a]rrangements must be described for…the reporting of the findings of the research to relatives, if they wish it."[86] Whether a participant consents or family members enter a deceased individual into research, the policy implies that results of some sort may be returned to relatives. Because relatives can enter an individual into research post-mortem, consent of the individual is not required for participation in the research, nor is it required for return of results to relatives.

D. Conditions for Access by Relatives Vary Among Countries

Eight out of 10 countries' laws and policies indicate that results are generally considered confidential, but that some circumstances may permit sharing of this information without consent or over objection of the participant. Although the inability to obtain consent (after a participant's death, for example) presents different ethical and policy implications than overriding the refusal of a living participant to share their results, only one country (Japan) has policy that addresses this distinction.[87] The conditions required to override or forego obtaining consent from participants vary among countries.[88] The text of these conditions is listed in **Table 2**.

SEVERITY OF HARM

Magnitude of harm is mentioned frequently in policies permitting sharing of genetic research results with relatives (5 countries out of the 8 that envision some form of sharing genetic results with relatives without consent). Laws and policies in Australia, Canada, Israel, Japan, and Singapore are tied to the severity of the condition indicated by the result.[89] Australia and Canada reference "life-threatening" or "serious"

conditions as circumstances that would warrant sharing genetic information with relatives.[90] Israel similarly references conditions of severe magnitude, stating that sharing will be permitted for "the prevention of death, illness, or serious disability of such relative, including an unborn relative."[91] Japanese policy does not explicitly require severe harm, but rather states that sharing may occur when "genetic information is highly likely to have a serious impact on the life of the donor's blood relative."[92] Singapore's policy refers to risk of severe harm, but does so by noting that participants' results may not be kept confidential when researchers are legally obligated "to warn family members of genetically-based risks of severe harm."[93]

Not all circumstances that warrant sharing genetic information with relatives hinge on the severity of harm, however. Some countries permit sharing merely to benefit the health of a participant's relatives. New Zealand does not require a measure of severity to share results with relatives. Instead, New Zealand requires that participants must be told that "if the research generates information of relevance to the health of other family members, their consent will be sought to disclosing the information to those members of their family"[94] — suggesting that "relevance" apart from "severity" may warrant return to relatives. Israel's law also implies that sharing may occur when it "is required for the maintenance of the health of the relative or to improve such person's health," and to prevent "death, illness, or serious disability."[95] This suggests that sharing would be allowed even if only to maintain or improve the health of a relative, regardless of the severity of the condition involved.

ACTIONABILITY

Australia, Canada, Israel, and Japan condition sharing on the actionability of the participant's research results. Each country, however, defines actionability differently within its policy. Australia, for example, permits the sharing of life-threatening or serious results only when "treatment is available or pending."[96] In contrast, Canadian policy says "information about a life-threatening or serious condition" may be disclosed if the condition "can be prevented or treated through intervention."[97] The use of the term "intervention" and inclusion of "prevent[ion]" in addition to "treatment" implies that information about a broader range of conditions, including those without active "treatment," may be shared with relatives. The Israeli Genetic Information Law does not reference actionability specifically, but echoes Canadian policy by stating that sharing may only occur where required for "maintenance of the health of the relative or to improve such person's health," and for the "prevention of death, illness, or serious disability."[98] Here, as in Canadian policy, a specific "treatment" need not be available. Rather, the ability to maintain health or prevent disease in a relative is enough to warrant disclosure of a participant's results.

Japan takes differing approaches in its two separate guidance documents. In "Fundamental Principles of Research on the Human Genome,"[99] the Japanese Bioethics Committee states that sharing may occur without the participant's consent "only if preventive measures or treatment have already been established for the disease in question."[100] This requirement combines the above Australian, Canadian, and Israeli approaches by stating that either prevention or treatment of a condition must be feasible in order to share results with relatives. The Ministry of Education's "Ethical Guidelines for Human Genome/Gene Analysis Research," however, requires actionability only in some circumstances. A proxy consenter may obtain access when sharing of results is required for the "protection of the life, body or property of an individual" (implying protection as a type of actionability) and research directors may share results without participant consent if "there is an effective treatment protocol."[101] However, actionability is not required when results are shared with relatives after the death of the participant or when a minor's results are shared with a proxy.[102] The latter policies not requiring actionability are comparable to laws and policies from Austria, New Zealand, Singapore, and the United Kingdom that similarly do not require actionability in order to share results with relatives.

Discussion

Although laws and policies vary among the countries examined, these approaches provide lessons for U.S. policy makers and researchers addressing whether or how to share genetic and genomic research results with the relatives of study participants.

A. Relatives' Access Should Be Addressed in Research Protocols and Consent Forms

As the international community continues to address the issue of whether relatives should have access to an individual's genetic and genomic research results, researchers and policy makers within the United States should formulate best practices suited to the American context. Although the Privacy Act, HIPAA, and the Common Rule apply to sharing of genetic and genomic information, these rules do not provide researchers with specific and adequate guidance to design research protocols that address communicating such research information to relatives, including after death of the participant. The shared nature of genetic and genomic information, increased recogni-

tion of pathogenic variants, and the increased capacity to generate incidental findings using more powerful analytic technologies, however, suggest that issues of access to familial genetic and genomic information will only increase in the coming years.

Policies requiring researchers to educate participants prior to participation on whether and how their genetic and genomic information will be shared ensure that researchers anticipate these issues in research design and that participants are able to make informed decisions on participation in such research. Of the countries examined, Australia, New Zealand, and Canada offer the best examples of providing participants with advance warning of how sharing results with relatives will be handled. The Australian approach requires researchers to tell participants that results may be shared in the event of a treatable, serious condition, even if the participant does not agree to this.[103] This approach clarifies that researchers have a responsibility to alert participants to the possibility that their genomic information may be shared, in some cases even without their consent. New Zealand takes a less aggressive approach to sharing with relatives and requires that participants be notified that, in the event that results relevant to the health of relatives are discovered, the participant's consent to disclosure will be sought.[104] Like the Australian policy, the New Zealand policy provides participants with advance notice of the potential for sharing research results with relatives, but then goes on to say that participant consent to sharing will be sought. Canada requires that preferences for sharing be solicited from participants.

American research protocols should also alert prospective participants to the research project's approach to sharing results with relatives and should elicit participants' preferences on sharing. Participants can then decline to participate if the approach to sharing results with relatives is unacceptable to them and can exercise choice on sharing research results. Consent documents should also address the research project's approach to sharing results after a participant's death and should permit participants to express preferences about posthumous sharing with relatives. Establishing expectations prior to participation will clarify roles, rights, and duties for researchers, participants, and relatives. Even in research protocols that do not easily lend themselves to sharing research results with participants or relatives (for example, studies with de-identified samples), providing participants with information on whether, how, and when results might be returned to relatives will create clearer expectations.

B. American Policy Should Protect the Confidentiality of Participants' Genetic Research Results, Permitting Access by Relatives Only with Consent or in Exceptional Circumstances

PRESUMPTION OF CONFIDENTIALITY

Of the 10 countries' laws and policies examined, only 2 countries (France and Sweden) require consent for all disclosures of genetic information to relatives. All other approaches (8 countries out of 10) create a presumption of confidentiality coupled with exceptions that may depend on the seriousness and actionability of the results to be shared. Like these approaches, American law and regulation create a presumption of confidentiality, but may permit disclosure of genetic information in some circumstances. These include "compelling circumstances affecting the health or safety of an individual,"[105] situations in which one health care practitioner requests results from another to treat a relative, or cases in which caretakers or personal representatives seek access. Although the Privacy Act also permits an individual's information to be shared in "compelling circumstances affecting the health or safety of an individual,"[106] whether genetic or genomic information would qualify as creating such a "compelling circumstance" is unclear. HIPAA provisions controlling access to genetic information do not explicitly consider the severity or nature of the information to be shared; rather, information can be shared when a personal representative has gained access to the information and chooses to share, or when a practitioner decides to share genetic information for treatment of an individual's relative.[107] As noted above, the latter provision has been criticized for failing to protect individual privacy adequately.[108]

EXCEPTION TO CONFIDENTIALITY ENVISIONED IN MOST POLICIES

Although all of the policies examined appear to start from a presumption of confidentiality, 8 out of 10 envision some sort of exception to that confidentiality through which a relative could access an individual's genetic information or research results. Austria, New Zealand, Singapore, and the United Kingdom provide little detail on how the exception applies. Australia, Canada, Israel, and Japan provide more detail — Australia removes the presumption of confidentiality for results that are serious and treatable, Canada and Israel provide an exception when results are serious and treatable or preventable, and Japan creates exceptions for varying circumstances — when a result is "connected to the [etiology] of a disease" and the disease is preventable or treatable, and when results may have a serious impact and are treatable.

HIPAA and the Privacy Act provide extensive protections for genetic and genomic information in most circumstances, but American law and policy also create exceptions to the presumption of confidentiality. The Privacy Act permits disclosure without consent upon a "showing of compelling circumstances affecting the health or safety of an individual," and HIPAA permits disclosure to personal representatives and caretakers, as well as between practitioners for the treatment of a participant's relatives.

None of these policies, however, provides the high level of privacy protections and explicit guidance contained in the 1998 ASHG guidance. The 1998 ASHG policy provides a narrow exception to confidentiality when an individual declines to warn relatives, and harm is likely, serious, foreseeable, and preventable or treatable.[109] Similar to the ASHG policy, five countries — Australia, Austria, Canada, Japan, and Singapore — create an exception to the confidentiality of genetic information only in exceptional circumstances or where harm to the relative is serious, life-threatening, or severe.

By requiring harm to be likely, serious, foreseeable, preventable, and treatable, ASHG policy protects privacy while recognizing that in only a few, clearly defined circumstances would harm be imminent and severe enough to warrant overriding the requirements of confidentiality and the need for consent of the participant.[110] Federal statutes and regulations are more permissive than these ASHG guidelines. The Privacy Act and HIPAA both provide relatives with ways to gain access to research results prior to the death of the participant.[111] These routes of access, however, do not depend on the likelihood, seriousness, foreseeability, preventability, and treatability of the condition. Rather, the Privacy Act permits disclosure after a showing "compelling circumstances affecting the health or safety," with no statutory requirement that the compelling circumstances necessarily be likely, foreseeable, preventable, and treatable. HIPAA also does not limit disclosure to these five requirements, but rather permits access based on whether an individual is a caretaker or personal representative, or if a health care provider elects to share information to treat a relative. Because the approaches in the Privacy Act and HIPAA do not fully consider whether harm is likely, serious, foreseeable, preventable, and treatable, these policies permit the disclosure of results to relatives and intrusion into participant privacy when this may not be required for the health or safety of relatives. The 1998 ASHG guidelines provide more protection for the privacy of participants. Both policy makers and researchers should consider utilizing these guidelines instead, particularly when determining whether to share results over a participant's stated objection.

C. American Research Policy Should Demonstrate a Reluctance to Share Participants' Results with Relatives in the Absence of Consent or Over the Objection of the Participant

None of the analyzed laws and policies — including those in the United States — explicitly differentiates between sharing without the consent of a participant and sharing over the objections or refusal of a participant. The policy closest to addressing this distinction is the Japanese policy, "Ethical Guidelines for Human Genome/Gene Analysis Research."[112] In one section the policy allows the research director to consider sharing with relatives when "it is difficult to obtain the consent of donors," and in another allows the director to consider posthumous return to relatives. In both cases, seeking contemporaneous donor consent appears difficult or impossible. However, when the donor is a living minor, "the research director shall check the intention of the minor and respect that intention." Moreover, the final relevant section considers cases in which the relative's need for the information is strong, but nonetheless calls for the research director to "seek[] the understanding of the donor again." Thus, when the donor's consent can be sought or their intention ascertained, researchers should do so. The emphasis on re-contacting participants and ascertaining their understanding implies a reluctance to share results without participant guidance and a reluctance to override the wishes of participants.

Researchers should be reluctant to share results without the guidance of the participant. When a researcher does not have consent to share the participant's genetic or genomic information, the researcher may be able to contact the participant to seek consent. If the participant is deceased, the researcher may direct relatives to the participant's personal representative, who will have the opportunity to express preferences on behalf of the participant. In either situation, the researcher will not be overriding the specific request of the participant, and instead will be deferring to the decision of the participant or personal representative. Deferring to such preferences demonstrates respect for participants by ensuring that the results obtained from an individual's participation in research are protected from unwanted intrusion.

The Japanese policy also requires research directors to evaluate the "[d]etails of the explanation on the disclosure of research results given at the time of the informed consent" when deciding whether to share with relatives the results of a participant who has not

consented to return.[113] By requiring researchers to consider what assurances or policies were made available to the participant prior to participation, the Japanese policy emphasizes the importance of maintaining trust between researchers and participants. Trust is maintained by not straying from the terms of the consent and proceeding with great caution if sharing with relatives goes against assurances made or preferences expressed by the participant.

Researchers should be especially reluctant to override the participant's explicit refusal of consent to share results with relatives. Participants may refuse for a number of reasons, including knowledge of misattributed paternity, undisclosed adoption, or non-relatedness of which others in the family are unaware. Researchers may not be privy to complex family dynamics that may make some participants reluctant to share genetic or genomic information with relatives. Participants may also simply regard their genetic or genomic information as private and agree to participate in research only when that privacy is protected. For all of these reasons, a participant's refusal to share, including after death, should be respected. Only in the most severe and actionable circumstances should sharing over the objection of a participant be considered.[114]

Conclusion

Although sharing genetic research results with relatives is in the early stages of ethical and legal analysis, the international approaches outlined here offer lessons for U.S. policy. Multiple countries address the difficult question of whether and when a research participant's genetic results may be shared with relatives. Some countries recognize the need to ask research participants their preferences for sharing their genetic results with relatives. Genetic information is generally treated as confidential, yet many countries recognize exceptional circumstances under which participants' information may be shared with relatives absent participant consent. One country's policy begins to differentiate sharing without participant consent from sharing over participant objection, and countries are addressing the question of sharing genetic results after the death of the participant.

U.S. policymakers and researchers can learn from the policy options being explored in other countries. To ensure that participants know what to expect prior to entering research and understand what information is truly confidential, consent documents should inform participants of what results may be shared under what circumstances. Researchers should ask participants whether they consent to sharing this information with relatives, asking both about pre-mortem sharing and post-mortem sharing, as participant preferences may be different in those two scenarios. Researchers should clarify for prospective participants whether there are circumstances under which the participant's decisions on sharing may be overridden.

All of this requires researcher planning and IRB oversight. Research protocols should anticipate whether and how research results might be shared with relatives if the research is anticipated to generate results of importance to participants and their relatives. The research protocol should specify how participants will be informed of the policy on sharing results with relatives, whether participants' sharing preferences will be elicited and then followed both before and after death, and how requests from relatives and their physicians will be handled.

Finally, researchers and policymakers should develop approaches that differentiate between situations in which consent cannot be obtained and sharing may be considered without consent from situations in which results may be considered for return over the participant's objection. Return over participant objection should be strictly limited to exceptional cases in which the seriousness and actionability of the finding make return highly likely to avert harm to the relative. Although the American context differs from those of the countries examined in this paper, the law and policies analyzed provide lessons on how to create an approach that anticipates and addresses the needs of researchers, participants, and their families, while recognizing that participant trust is essential to genomic research.

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