Published in final edited form as:
Georgetown Law J. 2014 ; 102: 795–843.

Finding Fault? Exploring Legal Duties to Return Incidental Findings in Genomic Research

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Abstract

The use of whole-genome sequencing in biomedical research is expected to produce dramatic advances in human health. The increasing use of this powerful, data-rich new technology in research, however, will inevitably give rise to incidental findings (IFs)—findings with individual health or reproductive significance that are beyond the aims of the particular research—and the related questions of whether and to what extent researchers have an ethical obligation to return IFs. Many have concluded that researchers have an ethical obligation to return some findings in some circumstances but have provided vague or context-dependent approaches to determining which IFs must be returned and when. As a result, researchers have started returning IFs inconsistently, giving rise to concerns about legal liability in circumstances in which notification could have potentially prevented injury. Although it is clear that ethical guidance should not be automatically codified as law and that crafting ethical obligations around legal duties can be inappropriate, the ethical debate should not proceed unaware of the potential legal ramifications of advancing and implementing an ethical obligation to return IFs.

This Article assesses the legal claims that could be brought for a researcher's failure to return IFs. The potential for researchers to be held liable in tort is still uncertain and turns largely on a number of factors—including customary practice and guidance documents—that are still in flux. Unlike medical care, which has a well-defined duty into which evolving scientific knowledge about genetics and genomics can readily be incorporated, a researcher's duty to return IFs is less

well defined, making it difficult to determine at the outset whether and when legal liability will attach.

This Article advocates for a clearer, ethically sound standard of requiring that researchers disclose in the informed consent document which approach to offering IFs will be taken. This approach enables participants to know at the outset which findings, if any, will be returned, allows researchers to ascertain when their failure to appropriately return incidental findings will give rise to liability, and enables courts to make determinations that will produce more consistent legal guidance.

Introduction

A little over a decade ago, researchers first sequenced a rough draft of the human genome, the complete set of human genetic information.[1] Sequencing the human genome took over a decade and cost approximately $2.5 billion.[2] The hope and expectation was that delving further into the human genome would advance scientific knowledge and human health through genomic research. Few could have imagined the progress that would be made in the decade that followed.

Ten short years later, the estimated cost of sequencing an entire genome has dropped below $10,000, and the $1,000 genome is within sight.[3] Whole-genome sequencing has quickly been incorporated into research, with researchers in a wide variety of disciplines—from mental health to cancer research—incorporating whole-genome sequencing into their research in hopes of uncovering a genetic component to the diseases they study.[4]

With the incorporation of whole-genome sequencing into research comes concerns about incidental findings[5] (IFs)—genetic or genomic discoveries about individual research participants that are otherwise beyond the scope of research[6]—and the extent to which researchers have an ethical obligation to offer to return these results.[7] For example, does a researcher looking for the underlying genetic cause of heart disease, who discovers that a research participant's genetic sequence indicates a predisposition to an untreated condition, such as breast cancer, have an obligation to disclose that information? The references in this Article to the return of IFs are, in most cases, shorthand for an offer to return IFs which a participant can autonomously reject.

Those who have considered whether and to what extent researchers have an ethical obligation to offer to return IFs arising from genomic research have generally found there to be an ethical obligation to return some IFs in some contexts, but they have offered varying or context-specific standards or frameworks that are not sufficient to solve this difficult and controversial problem.[8] Perhaps because of this lack of unanimity, and in the absence of clear guidance, researchers have taken a variety of approaches to returning IFs in practice, and some researchers have chosen not to return IFs altogether.[9] This gap between the view that researchers have an ethical obligation to return at least some IFs, and the reality that some, but not all, researchers choose to return IFs has led many to worry about the potential for legal liability arising from inconsistent approaches to returning IFs.[10] Given that tort law duties are determined by the prevailing standard of care, recognition by scholars and the

research community of an ethical obligation to return IFs could ultimately lead to a legal obligation.[11]

We examine whether, and under what circumstances, there may be a *legal* obligation to offer to return IFs—an analysis that is currently lacking.[12] Although there is no law or case law directly on point,[13] this Article concludes that there is a small possibility that a failure to appropriately return IFs could result in legal liability under law as it stands today. Furthermore, there is a greater likelihood of legal liability as scholars and researchers continue to advocate for an ethical obligation, particularly if returning IFs becomes widespread practice.[14] We also recognize that fragmented and varying ethical guidance could give rise to uncertain and inconsistent legal duties—a result that would make it difficult for researchers, participants, and courts and that could cause gridlock in this emerging scientific arena.

For this reason, this Article argues that the research community should consider prospectively adopting a clearer approach to returning IFs that could give rise to a more definitive legal standard delineating when IFs should be returned. A clearer legal standard would tell researchers when they are expected to offer to return IFs, and when they will face liability for falling short of this standard; a clearer approach would also let participants know which IFs they can reasonably expect to have returned.[15]

Part I provides an overview of the issue of IFs in the context of whole genome sequencing research, including a discussion of the IFs that might arise in genomics research; the ethical principles that potentially underlie a researcher's ethical obligation to return IFs; and the different approaches setting forth whether, when, and which IFs ought to be returned. Part II reviews the possible tort law claims that could be brought alleging a failure to adequately return IFs and recognizes that there may only be a narrow set of circumstances in which researchers could be held liable today. As the research community increasingly recognizes an ethical obligation to return IFs, as guidance documents set forth which IFs should be returned and when, and as research custom moves toward routine return of IFs, researchers will be increasingly likely to face legal liability. Part III recommends that researchers develop clearer policies for when IFs will be returned and communicate to research participants whether, when, and which IFs will be returned. Research participants can thereby develop reasonable expectations about the IFs they can expect to receive. This Part sets forth and analyzes several approaches that would provide clear and consistent guidance and selects the approach that best allows researchers to make informed decisions about appropriate policies for returning IFs. This approach also makes clearest to research participants which IFs they can reasonably expect to have returned. Part IV suggests that courts that are faced with lawsuits alleging a researcher's failure to adequately return IFs adopt the proposed standard, bringing clarity to this uncertain terrain.

I. An Ethical Obligation to Return Incidental Findings from Genomic Research?

The high likelihood—or virtual certainty—that IFs will arise in genomic research has given rise to questions about a researcher's ethical obligation to return IFs. This Part notes that certain ethical principles—beneficence, respect for persons, a duty to rescue, reciprocity, and partial entrustment—could give rise to an obligation to return IFs; other notions,

however, including non-maleficence, concerns about the therapeutic misconception, and worries about burdening the research enterprise—caution against finding such an ethical obligation. This Part examines the guidance documents—documents that seek to establish best practices and that are often relied upon by practitioners—and frameworks that assess whether and when IFs should be returned.

A. INCIDENTAL FINDINGS IN GENOMIC RESEARCH—Over the past decade, biomedical research has increasingly incorporated whole-genome sequencing, whole-exome sequencing (a process of selectively sequencing the small portion of the genome that codes for proteins, which is believed to cover approximately eighty-five percent of the disease-causing regions in the genome), and other large-scale genomic methodologies into research in hopes of better understanding the genetic causes of disease.[16] With these new technologies, researchers are no longer limited to interrogating certain targeted portions of the genome; instead they can conduct genome-wide analyses, casting a wider net in the hopes of finding answers to their research questions.[17] Although a powerful research tool, this broader sequencing gives rise to a greater likelihood of finding IFs. Furthermore, as the cost of whole-genome sequencing falls, researchers who had heretofore used targeting sequencing (or who had not used genetic methodologies at all) will increasingly incorporate whole-genome sequencing into their research, increasing the number of studies in which IFs are likely to become a relevant issue.

The issue of IFs is not unique to genomic research; IFs can arise from a number of different types of tests.[18] What distinguishes the issue of IFs in genetic research from IFs in imaging and other research procedures is the likelihood and scope of potential IFs. In imaging research—research conducted using imaging techniques that include MRI, CT scans, and PET scans to examine particular parts of the body—the question is *whether* one of a limited handful of types of IFs will occur.[19] In the context of genetic research, the question is how to deal with the dozens or hundreds of disparate IFs that can potentially be uncovered in any individual research participant's genetic material.[20]

IFs can exhibit a wide range of usefulness.[21] For example, an IF can indicate an urgent, clinically actionable condition such as a predisposition to non-polyp-forming colon cancer—a cancer that is fatal and otherwise undetectable through standard screening.[22] An IF could predict a propensity to develop disease in the future, such as the possibility of developing breast cancer or Alzheimer's.[23] Even when the variant's meaning is known, "the probabilistic character of genetic information and the pleiotropic nature of genes make accurate interpretation … particularly challenging."[24] Some IFs will reveal information that is not clinically significant, such as information about ethnic or geographic heritage.[25] Yet other variants, perhaps even most variants, may instead be something the meaning and import of which is unknown.[26]

When the consequence of the variant is known and the finding has clinical significance, research participants may benefit from learning about IFs discovered during the course of research. A research participant who learns that she has a BRCA mutation, an indication of a predisposition to developing breast cancer, could take measures aimed at preventing undesirable future medical outcomes, including participation in regular mammogram

screening.[27] Even research participants who learn that they are predisposed to Alzheimer's disease—a disease that is currently unpreventable and untreatable—may decide to monitor more vigilantly scientific advances to obtain the benefit of any potential future treatments.[28]

Despite the potential benefits of learning about genetic predispositions, disclosing IFs—even IFs of known clinical significance—may nevertheless pose risks for individual research participants. Disclosing IFs that suggest genetic predisposition for disease can cause psychosocial harms and may raise concerns about loss of privacy or confidentiality.[29] Given the possibility that any IF could be a false positive, a research participant's decision to undergo medical treatment in response to an IF "could lead research participants down inappropriate or dangerous clinical pathways."[30] As noted in the article, *The Future of Incidental Findings: Should They Be Viewed as Benefits?*:

> The positive or negative outcome depends partly on one's circumstances (e.g., whether one has insurance to cover follow-up evaluation or must shoulder crippling costs and even job loss, whether discovery of the IF saves one's life or leads only to expensive and burdensome tests yielding no useful medical information) and one's values (e.g., whether a diagnosis of untreatable cancer prompts a clarification of one's priorities, provides the opportunity for salvific suffering, or lowers a black cloud of depression over one's final months).[31]

Disclosing IFs also has costs for the research enterprise. Before returning an IF, researchers must determine that an IF is analytically valid—that the IF was correctly identified by the sequencing process as a variant.[32] Determining analytic validity may require confirmation from a laboratory approved under the Clinical Laboratory Improvement Amendments (CLIA).[33] Researchers must also ensure that results are clinically valid—that the genetic variant identified is predictive of a propensity towards developing a specific disease,[34] which may require a time-consuming analysis of the current state of scientific knowledge.[35] Some guidelines also require that IFs be clinically actionable before they can be returned—a requirement that research participants be able to act upon the finding to avoid unwanted medical outcomes.[36] A requirement of actionability means that researchers must go through an additional analytic process to assess whether a particular variant should be returned, a process that could require additional time and expense. The process of validating IFs imposes additional burdens on the research enterprise, both in time and money.[37]

IFs in genomic research are therefore extremely common and likely to occur, with frequency increasing as one broadens the definition of what counts as an IF. IFs may indicate important, clinically actionable results or may instead be findings the meaning and importance of which are unknown. Returning IFs may benefit individual research participants, but it also risks harming individuals and burdening the research enterprise.

B. PRINCIPLES UNDERLYING AN ETHICAL OBLIGATION TO RETURN INCIDENTAL FINDINGS—Given the vast array of IFs that could be discovered in genomic research, the question arises as to whether and when researchers have an ethical obligation to return IFs to individual research participants. A number of principles support an ethical obligation to return IFs.[38] Beneficence, for example, requires that researchers take efforts to "maximize possible benefits and minimize possible harms."[39] With regard to IFs,

returning IFs could benefit participants if the information enabled participants to take additional precautions to prevent or minimize future medical harm.[40] To the extent particular IFs are likely to be valuable to research participants, beneficence suggests that the IF should be returned.[41]

Respect for persons—a recognition that individuals should be treated as autonomous agents, capable of making decisions and acting in accordance with their unique value systems—might also support an ethical obligation to return IFs.[42] Respect for persons suggests that when researchers have information that participants would find useful in making their own medical decisions, such information should be disclosed.[43] Respect for persons may even support returning IFs for which disclosure may be harmful, recognizing that individuals should be free to make autonomous decisions based upon this information.[44]

A third principle, and possible source of an ethical obligation to return IFs, is the duty to rescue, which obligates an individual to act when presented with an opportunity to alleviate the serious plight of another with minimal burden to oneself.[45] The extent of any duty to rescue turns on "the urgency of the situation, the severity of the outcome if nothing is done, the ability of the potential rescuer to prevent that outcome, and the fact that only modest effort or sacrifice on the rescuer's part is required."[46] The quintessential example of a general duty to rescue involves a passerby seeing a young child drowning in a shallow pool of water; with minimal inconvenience—perhaps a few minutes of time spent, or clothes that become wet—the passerby can save the life of a drowning child. The passerby is generally thought to have a moral obligation, even though not a legal duty, to rescue the drowning child.[47]

Under a duty-to-rescue-based argument, researchers would have an ethical obligation to return certain IFs to research participants if the level of effort required to return them is minimal and the possible benefit to participants is great.[48] Arguably, the current process for returning IFs is burdensome,[49] and few known findings rise to the level of alleviating a serious plight of another.[50] A duty to rescue would therefore be unlikely to attach under these circumstances.

A fourth principle, reciprocity, suggests that those who contribute to the research enterprise—either with time or by providing biological material—are owed something in return for their participation.[51] Though the exact contours of what the principle of reciprocity requires are subject to debate, a reasonable interpretation could include notifying those who contribute biological samples of relevant IFs.[52]

Finally, the partial-entrustment model—developed to assess when researchers are ethically obligated to provide care beyond that which is necessary to protect participants from the risks of research or for the scientific conduct of the research, otherwise known as ancillary care—sets forth a framework to assess whether researchers are ethically obligated to return IFs.[53] The partial-entrustment model recognizes that participants grant researchers access to otherwise private health information, creating a relationship of limited trust, but that research participants do not generally rely exclusively on researchers for their medical needs.[54] Under the partial-entrustment/ancillary-care model, once a condition is determined

to be within the scope of entrustment, the strength of any obligation turns on a variety of factors, including: (1) participants' vulnerability; (2) participants' uncompensated risks or burdens; (3) the depth, in intensity and duration, of the researcher–participant relationship; and, (4) participants' dependence on the researchers.[55]

Although several of the variables in the partial-entrustment model, including participant vulnerability and uncompensated risks, cannot be assessed in the abstract, analysis of the remaining variables suggest that researchers may not have a universal ethical obligation to return IFs.[56] For example, researchers conducting genomic research may have only a minimal, or nonexistent, relationship with research participants.[57] And participants in genomic research entrust their genetic information to researchers but do not generally entrust researchers with their medical care.[58]

Several principles caution *against* finding that researchers have an ethical obligation to return IFs. The first principle is that of non-maleficence, often stated as "do no harm."[59] As discussed in section I.A, returning IFs has the potential to cause harm, either by causing emotional unrest upon learning of upsetting information or by causing physical harm to the extent false positives result from unnecessary medical treatment.[60] Because IFs can cause harm, the principle of non-maleficence cautions against returning IFs in the absence of a plan to minimize the risks of harm.

Concerns about the therapeutic misconception may also counsel against an ethical obligation to return IFs.[61] Many research participants suffer from what is called the therapeutic misconception—the mistaken conflation of medical research with clinical care.[62] As a result, research participants often believe that researchers will provide treatment comparable to that provided by physicians and accordingly believe that researchers who come across information that can prevent future medical harm will disclose this information even absent a fiduciary relationship. As has been noted, however, though the primary goal of medicine is to treat individual patients, the primary goal of research is to produce generalizable knowledge.[63] Participants may rely on researchers in ways that were never intended. Researchers who choose to return IFs may therefore inappropriately contribute to the therapeutic misconception.[64]

A final concern counseling against finding an ethical obligation to return IFs is the burden that this obligation would place on the research enterprise.[65] Returning IFs requires outlays of time and money that must be diverted from other research objectives. Investing this time and money into returning IFs—information that primarily benefits individual research participants—detracts from the goal of creating generalizable knowledge in ways that some may argue is unethical.[66]

This section is merely intended to lay out the range of principled arguments that scholars have made for and against the idea that researchers have a duty to disclose IFs. Although it appears that these ethical principles may support some (possibly limited) duty to disclose incidental findings, the contours of any possible duty still remain unsettled. Appeal to ethical principles provides no clear answer as to whether researchers must, can, should, or should not return IFs.[67] As shown in the next section, this uncertainty carries into research practice.

C. INCONSISTENCY IN PRACTICE—Given the inconclusive guidance provided by an analysis of the relevant ethical principles, scholars and practitioners have sought to resolve the issues of when, whether, and which IFs ought to be returned through practical guidance. Researchers can choose to take a range of actions with regard to returning IFs, from returning nothing to returning everything (such as a comprehensively annotated analysis of the subject's entire genome). Most of those who have studied this issue conclude that neither of these extremes is practicable or appropriate.[68] Rather, they generally conclude that there is an ethical obligation to return at least some IFs in some circumstances[69] but offer a variety of sometimes inconsistent approaches about which IFs must be returned and when.[70]

A majority view is beginning to emerge that IFs should be returned only when they are analytically valid,[71] have significant health implications, and are clinically actionable.[72] A number of institutional efforts to promulgate guidance on this issue, and on the related issue of when individual research results should be returned, have reiterated these factors.[73] The consistency of these criteria belies the vagueness in how these terms are defined.[74] For example, what constitutes a "significant" health implication? Must the consequences be life or death? Or is an IF that, once revealed, leads to actions that can lower one's chance of contracting an unpleasant disease sufficiently significant? Must the IF have individual significance, or is reproductive significance—significance to offspring—sufficient?[75]

The same definitional uncertainty applies to the requirement that findings be clinically actionable. One group, the 2010 National Heart, Lung, and Blood Institute (NHLBI) Working Group, defined "clinically actionable" as follows:

> Actionable means that disclosure has the potential to lead to an improved health outcome; there must be established therapeutic or preventive interventions available or other available actions that may change the course of disease. Actionable may include surveillance and interventions to improve clinical course, such as by delaying onset, leading to earlier diagnosis, increasing likelihood of less burdensome disease, or expanding treatment options.[76]

This definition seems to foreclose returning IFs that are not clinically actionable now but may become clinically actionable in the future.[77] And still other approaches have been suggested for defining clinical actionability.[78]

In addition to vagueness in the definitions, there is inconsistency in how these factors are to be applied. For example, the National Bioethics Advisory Commission concluded that IFs should *only* be returned if they satisfy the criteria, whereas in 2004, the NHLBI Working Group concluded that IFs *should not be withheld* if they satisfied the criteria.[79]

The uncertainty in the way the factors are defined and applied has led some to conclude that determinations about whether to return results should be made on a case-by-case basis.[80] The uncertainty has also led to ongoing efforts by a number of advisory bodies to promulgate lists of which IFs ought to be returned.[81] Although preliminary data suggested that there may be a great deal of consensus about the limited set of particular results that should be returned,[82] as guidance documents have begun to take more concrete positions about what should constitute an appropriate standard of care, the pushback has been intense.

For example, in 2013, the American College of Medical Genetics and Genomics recommended that for *clinical* whole-genome sequencing, a limited set of IFs should always be returned, without deference to individual patient or clinician preferences or to patient age.[83] This guidance document generated a flurry of positive and negative responses, with critiques focusing on the move away from a "right not to know" and the abandonment of seemingly settled thoughts about the inappropriateness of testing minors for adult-onset conditions.[84] A contemporaneous publication from the European Society of Human Genetics covered similar ground, although it offered a different set of recommendations.[85]

By and large, scholars, practitioners, and advisory bodies agree that researchers have an ethical obligation to offer to return some IFs. The various frameworks that have been offered to assess IFs are starting to converge around three variables: validity, a significant health impact, and clinical actionability. But this seeming consensus belies the vagueness and inconsistency in how these variables are defined and applied. The current thinking about when IFs ought to be returned provides little practicable guidance to researchers.

D. CONCERNS ABOUT LEGAL LIABILITY—Despite the emerging majority view that researchers have an ethical obligation to return at least some IFs arising from genomic research, the practice of returning IFs has developed more slowly and in a highly variable manner. Rather than adopting comprehensive policies to determine whether, when, or which IFs should be returned, some researchers have chosen to avoid the problem, stating in informed consent documents that no individual results, incidental or otherwise, will be returned.[86] Others have not precluded the possibility of return but have set forth policies indicating that IFs will be returned under extraordinarily narrow circumstances. Many others have remained silent in their consent forms about the entire concept of IFs. Even researchers who conscientiously choose to return IFs often do not clearly define the circumstances under which they will do so.[87]

This gap between the emerging majority view that some IFs ought to be returned and the reality that IFs often are not returned—or are returned under a variety of narrowly or ill-defined plans—has led to growing concern about potential legal liability arising from a researcher's failure to return IFs.[88] Consider, for example, a heart disease researcher conducting whole-genome sequencing who accidentally stumbles upon a finding that a participant has a propensity to develop otherwise difficult-to-detect non-polyp-forming colon cancer. Because the consent form clearly states that only results related to heart disease will be returned (or perhaps because the consent form states that no individual results will be returned whatsoever), the researcher does not disclose the individual's heightened risk of developing colon cancer. When that individual later goes on to develop the disease and learns that she could have had a better treatment prognosis with earlier notification, she could bring a lawsuit against the researcher for failing to disclose the potentially lifesaving information.

Although there is, as yet, no law on point,[89] there is a growing sense that we may be standing at the precipice of legal liability for failing to adequately return IFs.[90] Liability could arise from three situations: (1) failing to return IFs at all; (2) returning some but not the ones that could prove critical; or (3) returning IFs that turn out to be false positives that

give rise to harms as a result of attempting treatment. To the extent there continues to be a push towards an ethical obligation to return at least some IFs, and to the extent offering to return IFs develops into a research standard or custom, the ethical obligation to return IFs could give rise to a legal duty.[91] Although it is clear that ethics is not the law[92] and that deriving the parameters of ethical obligations from concerns about potential legal obligations can be inappropriate, the ethical debate should not proceed unaware of the potential legal ramifications of advancing and implementing an ethical obligation to return IFs.

II. Potential Tort Law Claims for Failure to Return Incidental Findings in Genomic Research

The discrepancy between the emerging ethical view that at least some IFs should be returned and the reality that IFs are being returned inconsistently has given rise to concerns about legal liability.[93] There is growing concern that research participants who later develop a disease that could have been predicted may bring suit against the researcher who knew about the potential harm but did not disclose it. Injured research participants could allege that, had they been notified about their propensity to develop a disease, they would have taken additional precautions to prevent or minimize the consequences.[94]

Because there is no case law directly addressing researchers' legal obligations to return IFs,[95] plaintiffs bringing suit—and the courts hearing these cases—will have to reason analogically to areas in which courts have considered liability for failure to disclose. The discussion below examines possible tort law claims for failing to return IFs.[96] As a general rule, injured research participants will almost always have difficulty recovering in tort. This is so, in part, because informed consent documents have been viewed by courts as means by which participants assume the risks of research, because the duties that researchers owe are uncertain and have been held to be limited to compliance with federal regulations, and because research interventions can result in injury even if no one was at fault.[97] Nevertheless, as additional voices call for an *ethical* obligation to return IFs, and as this emerging ethical obligation increasingly becomes standard or customary practice in research, the emerging ethical obligation could give rise to a legal obligation to return IFs, the failure of which could result in legal liability.

A few illustrative examples of possible scenarios are set forth here and analyzed throughout the section that follows. These examples set forth a number of factors that courts would likely consider under the current tort law regime. Most notably for our analysis, we will discuss: (1) the extent of any researcher–participant relationship; (2) the foreseeability and proximity of any harm; and (3) the extent to which the harm uncovered is preventable.

Example 1 (Anesthesia Death): Having suffered a heart attack once before, Arnold Adams is altruistically motivated to enroll in research to contribute to a deeper understanding of the genetic causes of heart disease. Arnold is referred by his heart specialist to Dr. Ames, a physician specializing in heart disease research, for enrollment in Dr. Ames's non-therapeutic research protocol. Dr. Ames meets with Arnold and sequences Arnold's entire genome. Dr. Ames learns that Arnold has a rare variant that causes a potentially fatal outcome should Arnold be exposed to a particular anesthesia that can be used in heart

surgery. Dr. Ames does not tell Arnold of this genetic variant. One month later, Arnold goes into surgery for his heart condition, is given the anesthesia, and dies.

Example 2 (De-Identified Data): Betsy Banks donates blood and agrees that her blood can be used in research so long as no other identifying information is provided. Dr. Bell, a Ph.D. scientist, is conducting research using de-identified samples and notes that the blood marked Specimen X, Betsy's blood, contains a genetic marker for a predisposition to breast cancer. Unaware of her predisposition to breast cancer, and in accordance with clinical guidelines for those with no predisposition to breast cancer, Betsy gets regular mammograms every two years. The guidelines for those with a predisposition to breast cancer suggest getting mammograms every year. In the second year following her mammogram, Betsy develops breast cancer and ultimately succumbs to it.

Example 3 (Large-Scale Research): Cal Crawford decides to enroll in a research study as a healthy research participant. Dr. Cruz, an oncologist, is sequencing the whole genome of both healthy and sick research participants to ascertain the underlying genetic causes of a particular cancer. The study is a large-scale study with thousands of participants, none of whom Dr. Cruz meets personally. In sequencing Cal's whole genome, Dr. Cruz discovers that Cal's genome contains the ApoE gene, indicating a predisposition to Alzheimer's disease. Dr. Cruz does not return this result to Cal. Fifteen years later, Cal developes Alzheimer's disease. Had Cal been told about his predisposition, he would have monitored scientific developments about emerging ways to stave off Alzheimer's disease and might have made a different set of life choices.

The claim most likely to be brought by a participant in one of the above scenarios is a tort law claim alleging negligence.[98] To prove negligence, a research participant must show: (1) that a researcher owed a duty to participants to return IFs arising from research; (2) that the researcher breached the duty; (3) that the breached duty was the "but for" and proximate cause of the participant's injury; and (4) that the participant suffered measurable harm.[99] An analysis of each of these elements is set forth below.

A. A LEGAL DUTY TO RETURN INCIDENTAL FINDINGS?—As a general rule, individuals owe a duty of reasonable care under the circumstances.[100] Absent particular circumstances, tort law imposes no affirmative duties to act for another's benefit,[101] and individuals are not required to warn others of impending harm.[102] A number of factors can overcome this general tort law notion that individuals do not owe others affirmative duties, including: (1) special relationships;[103] (2) contractual agreements to act in ways that differ from common law presumptions;[104] (3) particular undertakings by either party;[105] and (4) particular skills, training, and ability.[106] Analysis of each of these factors, and the extent to which they give rise to tort law duties to warn, is context specific.

1. The Fiduciary Duty of Physicians to Return Findings: The medical profession with the most clearly articulated and legally recognized duties is that of physicians providing medical care to patients.[107] The heightened duty owed by physicians is a duty to comply with medical customs or standards.[108] In other words, physicians have an obligation to act using the same skill, knowledge, and care possessed and exercised by comparable physicians.[109]

Physicians providing medical care owe a fiduciary duty to their patients, which entails a duty to act in the patient's best interest.[110] As articulated by Professors Thomas L. Hafemeister and Selina Spinos:

> Because physicians have superior medical knowledge and skill and are the gatekeepers to medical services, patients are dependent on them. Patients lack the knowledge or skill to assess their own health conditions. Instead, they must depend on their physicians to provide critical information about their medical well-being. … Because patients are so vulnerable and dependent on their physicians, the law imposes a "trust" on doctors—a fiduciary responsibility stemming from the dependence and vulnerability of the patient, and from the disparity between a patient's and a physician's knowledge and ability to act.[111]

A fiduciary duty to act in the patient's best interest means that physicians must disclose unexpected findings that indicate potential future harm, even if these findings fall outside of the physician's particular area of expertise.[112] Failure to properly disclose unexpected findings can lead to tort liability and damage awards to patients.[113]

Were a researcher to be treated like a physician, a researcher—like a physician—would have a duty to return IFs. But researchers qua researchers are not generally thought to owe fiduciary duties, despite often having similar knowledge, skills, and abilities as physicians. In critically important ways, a researcher is not given the flexibility to act in a participant's best interest[114] and thus cannot be a fiduciary.[115] Researchers, therefore, owe participants something less than a fiduciary duty. Courts assessing claims that researchers failed to appropriately return IFs should not find a treating physician's duty to disclose dispositive unless a researcher was actually or effectively acting as a treating physician in addition to acting as a researcher.

2. Third-Party Physicians' Duty to Return Findings: The area of established case law that more closely resembles the researcher-participant relationship is the body of case law dealing with third-party physicians. Third-party physicians are physicians hired by employers or insurance companies to conduct physical examinations to determine whether an individual has any disqualifying or costly health problems.[116] Because, like researchers, third-party physicians do not provide clinical care to patients, they are similarly thought not to owe fiduciary duties to examinees.

Nevertheless, third-party physicians have the knowledge, skills, and ability to make medical assessments; are privy to private health information about the examinee; are uniquely positioned to discover preventable harms; and may develop a special relationship with the examinee.[117] A number of courts have therefore held that third-party physicians have a duty to return unexpected findings to the individuals being examined, even absent a fiduciary relationship.[118]

For example, in *Stanley v. McCarver*, a third-party physician evaluated a chest x-ray of Ms. Stanley as part of a pre-employment tuberculosis screening.[119] Dr. McCarver recognized that the x-ray showed particular abnormalities, yet these abnormalities were not disclosed to Ms. Stanley by her prospective employer, in violation of their company policy.[120]

Approximately ten months later, Ms. Stanley was diagnosed with lung cancer and brought suit against Dr. McCarver, his employer, and her prospective employer alleging a negligent failure to "timely and adequately diagnose and/or communicate to [her] the abnormality evident on her chest x-ray."[121] The court noted that "Dr. McCarver did agree, for consideration, to interpret Ms. Stanley's confidential medical record" and that "[b]y doing so, he undertook a professional obligation with respect to Ms. Stanley's physical well being."[122] The Court concluded that "Dr. McCarver placed himself in a unique position to prevent future harm to Ms. Stanley" and that Ms. Stanley could have "reasonably expect[ed] the physician to sound the alarm if any serious abnormality [was] discovered."[123]

In the case of *Reed v. Bojarski*, the New Jersey Supreme Court also decided that third-party physicians can owe duties to their examinees even outside a traditional physician–patient relationship.[124] As part of a pre-employment physical conducted by Dr. Bojarski, Arnold Reed underwent a chest x-ray that revealed a widened mediastinum, known to be a potential indicator of Hodgkin's Lymphoma.[125] In violation of the terms of the contract, Dr. Bojarski never notified Reed's potential employer about his potentially dangerous condition, and Reed's potential employer responded to Reed that he was in good health.[126] About six months later, Reed returned for another examination, having already lost twenty-five pounds and suffering from flu-like symptoms.[127] A month following that, Reed was admitted to the hospital and diagnosed with Stage IIB Hodgkin's disease.[128] Reed died eight months after his initial examination at the age of twenty-eight.[129] The New Jersey Supreme Court concluded that Dr. Bojarski owed Reed a duty of reasonable care and that in light of the evaluative purpose of the exam, Reed "had an absolute right to expect that he would be told if something was wrong."[130]

Like the third-party physicians in *Stanley* and *Reed*, researchers will also have access to a patient's confidential medical record and may also be in a unique position to prevent harm. Although a researcher does not accept monetary consideration from research participants, a court could conclude that researchers have a similar duty to "sound the alarm" if any serious abnormality is discovered.

3. A Researcher's Duty to Return Findings?: As a general rule, researchers are not fiduciaries of participants, so they do not owe fiduciary duties to act in a participant's best interest.[131] Courts that have considered the duties that researchers owe to participants have generally found that researchers have a legal duty to comply with the federal regulations governing research.[132] The regulations are silent about how researchers must handle IFs.[133]

The question then is what level of responsiveness to an IF would satisfy a researcher's duty of care. Is a researcher's duty discharged merely by returning results that the researcher stumbles upon? Or is a researcher obligated to look for IFs?[134] Is a researcher's duty time limited? That is, must a researcher report only those IFs that are known or validated by today's science? Or is a researcher obligated to continually reexamine the whole-genome-sequence data in light of new, emerging science—an approach that would undoubtedly be burdensome? Existing legal doctrine provides no clear answers.

Ultimately, a researcher's duty to return IFs will turn on whether researchers are treated more like physicians, who have a duty to comply with medical customs and standards,[135] or more like third-party physicians, who have a duty of reasonable care under the circumstances taking into account a number of factors.

If a researcher owes a duty comparable to that owed by a physician—a duty to act in accordance with the customs and standards of comparable researchers—a court would be unlikely to conclude that researchers owe a duty of care to return IFs.[136] At present, there is too much inconsistency among researchers concerning the return of IFs for any custom to develop.[137] Similarly, although courts can use guidance documents as evidence of a duty owed,[138] the current guidance as to which IFs should be returned in which circumstances is too varied and has yet to reach a level of consensus. Accordingly, it is too soon for these guidance documents to give rise to a researcher's duty.[139] Once a consensus does emerge, courts in some states would look to these guidance documents as evidence of a standard of care.[140]

To the extent that a researcher's duty of care is determined like that of a third-party physician, a court would look to a number of factors to determine whether a researcher acted reasonably under the circumstances. For example, a court may consider: (1) whether the researcher was in a unique position to prevent harm, (2) the burden of preventing harm, (3) whether the plaintiff relied upon the researcher's diagnosis or interpretation, (4) the closeness of the connection between the defendant's conduct and the injury suffered, (5) the degree of certainty that the plaintiff has suffered or will suffer harm, (6) the skill or special reputation of the actors, (7) the scope of any agreement, and (8) public policy.[141]

Our Example 1 (Anesthesia Death) presents a strong case for a researcher having a duty to return the particular IF. In Example 1, Dr. Ames was one of the few people who knew or could have known about Arnold's vulnerability to a particular anesthesia and was therefore in a unique position to prevent harm; the burden of preventing the harm through notification was likely to be low given that the Dr. Ames and Arnold had already met, and there was a high degree of certainty that Arnold would suffer harm. Without more information, however, we cannot determine the extent to which Arnold relied on Dr. Ames's offer to return IFs.

Example 2 (De-Identified Data) or Example 3 (Large-Scale Research) present much weaker cases. In neither of the cases was the researcher in a position to prevent harm. In Example 2, this is because Betsy's data was shared without identifying information, and in Example 3, this is because Alzheimer's disease is currently unpreventable and untreatable. In both examples, the burden of preventing harm through notification could be quite high given that these examples both involve research with large numbers of participants.

Nevertheless, it is not entirely clear how a court would rule given the context-specific nature of this analysis. Although this context-specific approach is a fundamental aspect of tort law, it provides very limited guidance to researchers about when they can expect tort law duties to attach. And a fact- and context-specific approach is particularly problematic in cases in which the ethical and scientific analysis is evolving and uncertain. Though it is not clear that

a court today would find a researcher's duty of reasonable care to include a duty to notify participants about IFs, a continuing push for an ethical obligation to return IFs, guidance documents that advocate returning IFs in particular circumstances,[142] and movement towards returning more IFs in practice could foreseeably give rise to a legal duty to return IFs in the future.[143]

B. WAS THE DUTY BREACHED?—Assuming courts find that researchers owe participants a duty to return some IFs, assessing whether the duty has been breached is no simple matter and may, in fact, raise more questions than answers.[144] Merely concluding that individuals have a duty to return particular findings does not, however, mean that the duty has been breached.[145] The issue of whether a duty was breached is in most cases a question for a jury.[146]

The Court of Appeals for the Tenth Circuit has addressed the issue of when a third-party physician's failure to notify examinees should be considered a breach of a duty owed. In *Pehle v. Farm Bureau Life Insurance Co.*, a husband and wife applied to Farm Bureau for life insurance.[147] Blood tests conducted in 1999 revealed that both husband and wife were HIV positive.[148] The laboratory testing company notified both Farm Bureau and the state department of health, as required by law.[149] Farm Bureau notified the couple that their application for insurance was being denied based on the results of their blood test and offered to send the blood-test results to their physician upon written authorization.[150] The couple made no such request until the wife developed symptoms of AIDS in 2001.[151]

The Court of Appeals for the Tenth Circuit held that "the trust and confidence that the [couple] put in Farm Bureau was sufficient to create a relationship giving rise to a limited duty"[152] and that "if an insurance company, through independent investigation by it or a third party for purposes of determining policy eligibility, discovers that an applicant is infected with HIV, the company has a duty to disclose to the applicant information sufficient to cause a reasonable applicant to inquire further."[153] Despite this heightened duty, the Tenth Circuit affirmed summary judgment in favor of the laboratory, while concluding that whether Farm Bureau satisfied its duty was a genuine issue of material fact.[154]

In the context of researchers who conduct whole-genome sequencing, adopting a standard that researchers have a duty to disclose to the participant "information sufficient to cause a reasonable [participant] to inquire further" would not settle the issue.[155] Unlike researchers, third-party physicians have a duty to thoroughly investigate the examinee and are tasked with discovering health problems that are well-characterized and understood. Researchers, by contrast, can potentially find thousands of IFs of which the meaning and import could be unknown. Even those IFs that are well-characterized and understood often only indicate a probability of developing disease and are much less definitive than a clear diagnosis of HIV.

C. DID THE BREACHED DUTY CAUSE INJURY?—A successful tort lawsuit generally requires that the defendant's conduct be both the "but for" and proximate cause of the plaintiff's harm.[156] Under a conventional causation analysis, participants alleging a researcher's failure to appropriately return IFs will have difficulty showing that the researcher's failure to return IFs was the direct cause of their injury; the but-for cause will

always be the disease resulting from the underlying variant.[157] Courts have nevertheless recognized the legal doctrine "loss of a chance," which acknowledges that the possibility of preventing a medical misfortune is itself a valuable thing[158] and that the diminution of a chance to prevent or minimize future harm should be compensated if it results from a medical professional's failure.[159]

Loss-of-a-chance doctrine speaks to both the causation and injury elements of a tort law claim. Although causation and injury are generally considered separately,[160] loss-of-a-chance redefines the interest that was injured (the chance of recovering or preventing injury rather than the ultimate outcome)[161] and then considers whether the medical professional's action was the but-for cause of the lost chance.[162]

Although loss-of-a-chance is a relatively recent doctrine, it has started to make inroads in state courts and has been adopted in nearly half of all states.[163] The loss-of-a-chance doctrine is viewed as being more in accord with the ideals of tort law generally. Without loss of a chance, any situation in which an individual had less than a fifty percent chance of recovering would be wholly immunized from tort liability.[164]

Thus far, loss-of-a-chance has been applied primarily in the context of medical malpractice,[165] but the doctrine could be applied more broadly.[166] One reason that the loss-of-a-chance doctrine has been used in medical malpractice is that "reliable expert evidence establishing loss of chance is more likely to be available in a medical malpractice case than in some other domains of tort law."[167] Second, "it is not uncommon for patients to have a less than even chance of survival or of achieving a better outcome when they present themselves for diagnosis, so the shortcomings of the all or nothing rule are particularly widespread."[168] Third, the "failure to recognize loss of chance in medical malpractice actions forces the party who is the least capable of preventing the harm to bear the consequences of the more capable party's negligence."[169]

Some of the factors that justify application of loss-of-a-chance to medical malpractice also support applying the doctrine to research. First, the same reliable expert evidence about the chances of succumbing to, for example, undisclosed breast cancer in a medical malpractice case could also be provided in the research context. Second, the same diseases for which individuals may have a less-than-even chance of survival could occur in both the medical and research contexts. Third, as with medical malpractice, the failure to recognize loss-of-a-chance in the research context forces the party who may be the least capable of preventing the harm to bear its consequences.

Some reasons used to justify loss-of-a-chance in the context of medical malpractice are not similarly applicable in research. Courts have looked to the specific physician–patient relationship—particularly the expectation that "the physician will take every reasonable measure to obtain an optimal outcome for the patient"—as warranting these additional protections.[170] Such expectations are generally not justifiable in research, and courts should be cautious before imposing additional burdens on researchers that were specifically disclaimed during the informed consent process. Moreover, courts have justified loss-of-a-chance in the context of medical malpractice because "reasonably good empirical evidence

is often available about the general statistical probability of the lost opportunity."[171] In research, where so much is unknown, this simply may not be true. Certain IFs, such as those unlikely to be uncovered by other means, would be more likely to lead to recovery under loss-of-a-chance principles than would others. Example 1, introduced at the outset of this section, presents just such a case. Other IFs, such as the possibility of developing breast cancer or Alzheimer's disease in the future (Examples 2 and 3), may be less likely to satisfy this criterion.[172]

A research participant must also show that the researcher's conduct was the proximate cause of the participant's harm—"that the harm was the general kind that was unreasonably risked by the defendant, the kind of harm the defendant should have been more careful to avoid."[173] Whether harm is foreseeable turns "on what facts the defendant actually knew or those he should have known."[174] Regardless of whether the other elements, including but-for causation, have been satisfied, one could argue that in each of the examples set forth at the outset, the harm that materialized was precisely the harm predicted by the IF: Arnold's reaction to the particular anesthesia, Betsy developing breast cancer, and Cal developing Alzheimer's disease were all probabilistically foretold by the particular variants discovered. But these cases may be among the easiest examples. In other cases, the proximate cause analysis is far less straightforward.

In many, if not most, cases, the IF will be of unknown significance so that any harm that occurs would not be foreseeable. In other cases, the risk could foreseeably be discovered through routine medical tests, and thus the harm would not be foreseeably likely to occur. In all cases, an IF arising from genomic research only gives rise to a probabilistic chance of harm occurring that may or may not be sufficiently proximate.

For the reasons discussed above, even a research participant able to prove negligence will have a difficult time proving causation. An injured participant could only succeed in a state that has adopted the loss-of-a-chance doctrine, and in a court that is willing to extend the doctrine from medical malpractice to research. Even then, an injured research participant could recover only if the researcher's failure to disclose was the but-for and proximate cause of the participant's injury—a claim that, in most circumstances, will be quite difficult to prove.

D. IS THE PARTICIPANT'S INJURY COMPENSABLE?—A final requirement for a successful tort lawsuit is that a plaintiff suffer actual, compensable harm.[175] In the context of loss-of-a-chance, the plaintiff is entitled to recover only the value of the chance that was destroyed.[176] An injured participant's damages are determined "by subtracting the decedent's postnegligence chance of survival from the prenegligence chance of survival."[177] Thus, if an injured research participant had only a forty percent chance of surviving a potentially disclosed IF and the researcher's negligence deprived the participant of that chance entirely, the researcher would be liable for forty percent of the total damages suffered.[178]

In Example 3, Cal's recovery for loss-of-a-chance would approach zero percent because given today's treatment options, Cal would have had no chance of preventing his

Alzheimer's disease regardless of what Dr. Cruz disclosed. In Example 1, Arnold's recovery would be close to one hundred percent because Dr. Ames's failure to notify Arnold wholly removed his chance to use a different anesthesia during surgery. Betsy's recovery in Example 2 would fall somewhere between these two extremes because she would have had a better chance had she obtained more frequent mammograms, but she still would have had a risk of contracting, and succumbing to, breast cancer.

The foregoing analysis suggests that a researcher will have a duty to act with reasonable care under the circumstances, although it is unclear, at present, the parameters of the duty given the highly contextual analysis. A continued push for an ethical obligation, guidance documents that set forth the IFs that should be returned in particular circumstances, and an emerging research custom of returning IFs could lead a court to conclude that researchers have a legal duty to return IFs. Whether any such duty has been breached, however, raises questions about which IFs must be returned, how hard a researcher must look for IFs, how researchers should handle probabilistic information, and whether a researcher's duty is time limited or requires continued reexamination. Once negligence is established—a difficult proposition in and of itself—to succeed with a legal claim, participants would have to rely on the loss-of-a-chance doctrine to show that researchers were the but-for cause of their inability to avoid succumbing to a subsequent adverse medical outcome and that the researcher's failure to disclose was the proximate cause of the participant's injury—claims that would be difficult to prove. In the unlikely circumstance that a participant satisfies these criteria, a participant would then have to demonstrate a compensable injury, the value of which would be reduced proportionately under the loss-of-a-chance calculations.

Research participants would also have to show that had they known about the particular information, they would have acted differently in courts adopting a subjective standard, or that a reasonable person would have done so if the objective standard is used.[179] Arnold would have to show that, had he or a reasonable person known about his potential reaction to anesthesia, he or a reasonable person would have used a different one during his surgery. Betsy would have to show that she or a reasonable person would have gotten more frequent mammograms. Cal would be unable to show any actions that would have prevented his Alzheimer's.

Although this analysis describes the complexities and uncertainties inherent in describing whether tort liability will attach, it does not answer the broader question of whether tort liability should attach. The broader goals of tort law include compensating those who are injured;[180] deterring undesirable behaviors;[181] notions of corrective justice, or righting wrongs;[182] distributive justice, or addressing equitable distribution of goods in society;[183] and policy and utility, or assessing what is good for society as a whole.[184] Tort law is also fundamentally concerned with fault.[185]

In the context of a researcher's liability for failure to return IFs, these considerations lead to different conclusions. Considerations of policy and utility counsel against tort liability because potential liability could hamper socially beneficial research. Notions of distributive justice similarly counsel against liability because it is not clear that particular research participants have a stronger claim to funds that would otherwise be used for socially

beneficial research. Considerations of compensating those injured and corrective justice weakly support liability to ensure that those who are injured are adequately protected. Ultimately, however, the analysis comes down to fault and the idea that researchers should not be held accountable or found to be at fault for a duty so broadly conceived. As set forth in Part III, a duty more narrowly conceived could more reasonably give rise to fault-based liability.

III. Potential Standards for Disclosing Incidental Findings

Under current law, the questions of when and whether a researcher can be held liable for failure to return IFs are still uncertain. As a result of this confusion, researchers are left with little guidance about when liability for failure to return IFs will attach, participants lack meaningful guidance about which IFs they can reasonably expect to have returned and when, and courts are left to make complicated determinations about researchers' legal duties in light of uncertain and evolving scientific knowledge and customary practice, potentially giving rise to an inconsistent body of case law. A clearer legal standard would address each of these concerns.

One challenge in adopting an appropriate standard is that many of the ethical, scientific, and legal issues regarding a researcher's duty to return IFs are still in flux.[186] Waiting until these areas settle, however, is an untenable solution. Courts will be asked to weigh in on this issue and, absent clearer legal standards, could decide cases inconsistently—an approach that could bring confusion and gridlock to an emerging scientific arena.[187]

To avert confusion and gridlock, this Article proposes adopting a clearer standard that provides ethically sound, consistent guidance about when IFs ought to be returned and when the failure to return IFs can and should give rise to legal liability.[188] This Part argues that biomedical researchers should adopt one of several possible standards for disclosing which IFs will be offered that are appropriately transparent. We then advocate that courts recognize the proposed standard and grant researchers that select one of these options the benefit of accepting the terms of that selection, and then in Part IV, explore some of the nuanced interpretations courts will have to make when adopting our proposal.

A. DISCLOSING THE PROCESS OF OFFERING INCIDENTAL FINDINGS IN THE INFORMED CONSENT DOCUMENT—

A clear and appropriate rule would require that researchers disclose in the informed consent document the extent to which IFs will be returned to participants, with a corresponding legal duty to act in a manner consistent with the terms set forth in the informed consent document.[189] The approach to returning IFs must be understandable to research participants and must set forth clear guidelines that allow participants to ascertain which IFs will be returned to them and the extent to which a researcher's silence can be interpreted to indicate good health. Negligence could be found when researchers act in ways that are inconsistent with the policy set forth in the informed consent document.[190]

This approach recognizes the value of both informing research participants about what to expect throughout the informed consent process and meeting those expectations.[191] This approach is also consistent with established case law holding that clinicians[192] and third-

party physicians[193] can establish the parameters of which results will be returned and can be held liable in tort for failing to comply with these terms—terms upon which a recipient could reasonably be expected to rely. This approach also recognizes, as many scholars have, that there are many ethically permissible approaches to returning IFs.[194]

The next three sections outline three possible approaches that can be articulated clearly enough to satisfy our goal of adequately informing research participants. These approaches are: no return of IFs, returning all genomic data without interpretation, and returning results consistent with a compendium. Although they each have strengths and weaknesses, and they might not be universally embraced as ethically optimal, we believe that they are at least prima facie ethically defensible and provide the clearest articulation of the IFs that will be offered to research participants. After outlining these three options, we then articulate a framework that explores why researchers should generally be on safer legal footing if they select from one of these options and explain why other common, possible return paradigms are inappropriate.

1. No Return of Incidental Findings: The first proposed standard is that researchers not return IFs to participants regardless of the seriousness of their findings. This approach acknowledges the difficulties inherent in tracking down and locating large numbers of participants and recognizes that a large amount of resources—both time and money—may be needed to analyze, return, and provide counseling for the thousands of variants that could arise in any given research participant's whole-genome-sequence data.[195] Under this approach, no liability would attach for failing to return IFs, but liability could attach once a researcher chooses to return IFs but does so improperly.

An advantage of this approach is that it appropriately recognizes the distinctions between research and clinical care and does not contribute to the therapeutic misconception.[196] This approach also respects an arguably proper allocation of research resources. Research is funded to create generalizable knowledge that advances the public good.[197] Returning IFs can be costly, diverting funds from research that benefits the general public to the process of returning IFs, which generally benefits particular individuals.[198]

This approach does, however, have a number of disadvantages. First, given the emerging ethical guidance encouraging the return of certain results in certain circumstances, and given that some researchers have already started returning IFs, a court may be unwilling to conclude that researchers have no duty to return IFs, particularly in a case with a serious IF, a substantial researcher–participant relationship, and a sympathetic plaintiff.[199] Second, the reason that some researchers started returning IFs is because they felt morally bound to return IFs with significant health implications. Creating a standard whereby researchers are not expected to return IFs, and in which researchers may be penalized for doing so, may lead researchers to compromise their moral conviction. Third, this approach does not address research participants' reasonable expectations that someone with particularized knowledge and skills who is granted privileged access to otherwise private health information would inform them of any significant health findings.

For these reasons, scholars have argued that not returning IFs regardless of their severity is unethical,[200] and very few have advocated for this approach.[201] Given that some researchers feel a moral obligation to return certain IFs—and that many researchers have begun returning IFs, thereby fostering a reasonable expectation among participants that particular IFs will be returned—setting a threshold legal standard at no return is not an appropriate bright-line rule in all cases, though it may be appropriate in certain circumstances (for example, secondary research using stored specimens, or research using de-identified samples).[202]

2. Return All Genomic Data Without Interpretation: An approach that has been suggested but rarely seriously considered is an obligation to return all genetic sequence data —the nucleotide base pairs of As, Ts, Cs, and Gs—without interpretation or annotation.[203] This approach is generally only considered before settling on a more "reasonable" position somewhere between the extremes of not returning anything and returning everything.[204] Nevertheless, a bright-line rule suggesting the return of all whole-genome-sequence data without interpretation does have some advantages.

First, this approach allows researchers to fulfill their moral convictions about returning information to participants while minimizing the burden of doing so. Returning all genomic information without interpretation allows researchers to bypass the requirements of additional confirmatory testing in a CLIA-approved laboratory, additional searching, interpreting, seeking out genetic counselors, and making decisions about which results to return on the basis of shifting criteria of clinical utility or actionability. And as more websites and services allow individuals to input their whole-genome-sequence data to obtain reasonably priced interpretations, participants can take control over when and whether they learn more about their genetic information.[205] This approach is responsive to data that suggest that participants prefer to receive significantly more information than has generally been returned, even if the information is not clinically actionable.[206] This approach also does away with a potential obligation to reexamine and re-notify participants with updated analyses because participants have access to their own genomic sequence data and can seek out their own reexaminations in light of evolving science.

This approach, like the others before it, also has some downsides. First, this approach may not satisfy researchers' moral conviction about alerting research participants to IFs that may have significant health consequences. The actual genetic information returned—the As, Ts, Cs, and Gs—does not itself alert participants to any actionable anomalies. Second, handing genetic information to research participants without any interpretation may overwhelm those who do not know where to turn for interpretation or who may get their genomic data interpreted without appropriate counseling or guidance about what the information means.[207] Finally, this approach may be technologically and logistically difficult and expensive, particularly with regard to large genomic studies that involve thousands of participants.

3. Return Results Consistent with a Compendium: A third proposed standard would require that researchers return IFs that are listed in a compendium of consensus returnable IFs, as determined by a body of expert medical geneticists. Legal liability would attach if

researchers fail to return such results. There are currently several ongoing efforts to determine which results rise to the level of a returnable genomic findings.[208] These groups would be expected to reexamine and modify these compendia over time, consistent with evolving science.[209] Though the exact number of variants will depend on the criteria used, one notably (and arguably conservative) early effort resulted in a list containing fifty-six possible variants.[210]

One advantage of this approach is that results will be returned consistently across all types of research and in accordance with the most rigorous determination of what ought to be returned.[211] Although this approach establishes a limited obligation on the part of the researchers to hunt for findings beyond those that are stumbled upon, the obligation is narrow and confined to those specific variants that are well-characterized and understood.[212] This approach minimizes the more costly elements of returning IFs. Because there would be a known universe of IFs that must be returned, deciding which results to return and how to return them could become standardized and less costly.[213] This approach also likely satisfies a researcher's moral convictions about returning IFs that may have important health implications.

This approach also has some disadvantages. First, as mentioned above, there is not yet one standardized compendium, but several emerging ones.[214] And although there is some common ground among geneticists about the IFs that merit routine return, there is not absolute agreement, which could result in differences among the compendia.[215] Second, as mentioned above, these compendia evolve over time, raising questions about when a researcher's duty to examine a participant's data attaches and whether researchers have an ongoing obligation to reexamine participant data in light of changes to the compendium.[216] Third, some compendia may be geared to the IFs that should be returned in the clinic; it is unclear whether the same guidelines should apply in research.[217] Finally, an argument could be made that even this level of return contributes to the therapeutic misconception and causes research participants to rely on researchers and the research process in a way that was not intended.[218]

B. A PROPOSED FRAMEWORK FOR RETURNING INCIDENTAL FINDINGS—As applied, researchers would be able to choose their approach to returning IFs from the options set forth above—no return of IFs, offering to return consistent with a specified compendium, or offering full return of data without interpretation or annotation. Researchers who select and comply with one of these approaches should be found to have satisfied their legal duty under tort law. Allowing researchers to choose a justifiable approach to returning IFs from among these options and subjecting that chosen approach to Institutional Review Board (IRB)[219] review permits researchers to choose an option that is consistent with their moral convictions about returning IFs, sets reasonable expectations among research participants about the results that they should expect to receive, and is consistent with the oft-made argument that the appropriateness of returning IFs turns on a variety of factors.[220] Although this approach potentially protects researchers who choose not to return any IFs from liability, it only does so in cases for which a researcher's determination not to return IFs has been reviewed and approved by an IRB. An IRB presumably would only accept a

researcher's proposal to not return any IFs when accompanied by well-articulated and compelling scientific or practical justifications.

Researchers who take a different approach—including a more subjective promise to return all findings that, for example, have "significant health implications" or that are "clinically actionable" or a promise to comply with participant preferences, regardless of the clarity with which participants express those preferences—are setting themselves up to comply with a heightened legal duty. Because these researchers will have begun an undertaking that they now have a duty to satisfy responsibly,[221] and because these researchers have made a promise that can induce reliance,[222] these researchers have taken upon themselves a duty to comply with the heightened fiduciary duty generally applied to physicians.[223]

Similarly, some researchers might want to return IFs consistent with a complex solicitation of participant preferences.[224] To the extent that return consistent with participant preferences hinges on terms that are difficult to define, like "actionability" and "clinical significance," this approach would not bring clarity to participants about the IFs that they can reasonably expect to have returned and should not be one of the options for researchers. Although this approach may lead to an *ethically* sound policy for returning results, it would remove researchers from the safety of a clearly stated and articulable approach to returning IFs.

We acknowledge that our proposal could be controversial in that it would allow researchers to escape legal liability in some cases where people will have a strong moral intuition that they should have returned patently life-saving medical information. For instance, in Example 1, in a circumstance where an approach of not returning IFs was approved by an IRB, Dr. Ames would be insulated from suit for failing to disclose his participant's risk of being exposed to certain anesthetic agents. As is often noted, however, law and ethics can frequently diverge, and this seems to be a case in point. We believe that the value of a clearly articulated legal rule in this complicated and important research field outweighs the moral distress that some people will feel regarding very difficult marginal cases.

IV. Guidance for Courts

Courts that are faced with legal challenges brought by research participants who allege inadequate or improper disclosure of IFs will almost certainly find themselves faced with a variety of confounding fact patterns. This Part provides guidance to courts to help navigate this difficult terrain. We address (1) the implications of inadequate or silent consent-form language, (2) factors relevant to determine the scope of a researcher's duty, and (3) how to assess whether adequate disclosure has been made.

A. INTERPRETING CONSENT-FORM LANGUAGE—In Part III, we proposed a paradigm in which researchers could choose from a menu of ethically justifiable options (subject to IRB review) and would have to clearly articulate their plan for managing IFs during the informed consent process. This does not, however, account for cases in which the informed consent is silent about—or inadequately addresses—the issue of returning IFs. The question for courts, then, is how to assess informed consent documents that do not explicitly or sufficiently address IFs.

As set forth above, because genomic sequencing generates so much data, researchers are expected to explicitly disclose a number of pieces of information, including: (1) that the subject's entire genome will be sequenced; (2) that there is a high likelihood that IFs will arise; and (3) the plan for managing any IFs that do arise.[225] To the extent researchers set forth an IRB-approved approach to returning IFs, that should be the standard by which researchers are judged for purposes of assessing legal liability. For informed consent that is silent, or that inadequately addresses the return of IFs, the general assumption should not be that researchers are therefore protected from legal liability. Rather, courts should look carefully and skeptically at inadequate consent documents.

There are, however, two circumstances in which a silent or inadequate informed consent document might be justified. The first justification for inadequate consent language relates to the evolving nature and adoption of new sequencing technologies. As genomic-sequencing technologies became available, they were first adopted by a handful of researchers with significant genetic-research expertise.[226] During this period of early adoption when there was no clear ethical guidance, researchers and IRBs were understandably unsure about how to address the IFs arising from genomic sequencing during the consent process. As a result, informed consent disclosure about the possibility of IFs was varied, less evolved, and perhaps—if judged by today's standards—inadequate. Courts should therefore be sympathetic to a researcher with an inadequate consent document if the relevant document originated when there was no established practice regarding the informed consent disclosure of IFs. Similarly, a researcher might have a justifiably insufficient informed consent form if she can demonstrate that the specific language was consistent with the IRB's practices or institutional policies during this early adoption period.[227]

This early stage has given way, however, to much more widespread adoption as the price of sequencing has dropped and a wider range of researchers have become intrigued by the power of whole-genome sequencing. The increased uptake has been accompanied by a proliferation of debate and discussion in the research ethics literature,[228] such that no researcher today could reasonably claim ignorance about the need for clear language about IFs in the informed consent document. Reasonable researchers should be expected to have a well-articulated plan as soon as they should have been made aware of the contours of this ethical controversy.

A second justification for inadequate informed consent language is that for certain kinds of research, the relationship between the researcher and the individual participant might be sufficiently distant so as to obviate the need for language about IFs. Under this line of reasoning, certain kinds of research would effectively exempt researchers from a duty of having to offer IFs, and from a corresponding duty to include informed consent language about IFs. This category might include researchers whose valid methodological choices make it extraordinarily difficult (or even impossible) to recontact participants (such as biobanks or studies involving de-identified samples) or where the inherent characteristics of the research mean that offering to return IFs would be prohibitively resource intensive (such as large-scale public-health studies).

If an informed consent document is silent or inadequate and neither of the justifications have been met, the scope of a researcher's legal duty will be defined not by the silent or inadequate informed consent language but instead will turn on a number of factors set forth below. Allowing researchers to establish the parameters of potential legal liability through appropriate informed consent disclosure is part of recognizing the importance of adequate disclosure. A researcher's failure to adequately set forth an IF disclosure policy results in legal liability that hinges on the multifactored analysis set forth below, thereby introducing an element of uncertainty to a researcher's defense against liability.

B. FACTORS IMPORTANT FOR DETERMINING THE SCOPE OF A RESEARCHER'S LEGAL DUTY TO RETURN INCIDENTAL FINDINGS—Under our proposed framework, if plaintiffs can demonstrate that the informed consent language was inadequate and there is no justification for that inadequacy, the analysis then shifts to the difficult task of determining the extent of a researcher's legal duty concerning the return of IFs. As discussed in Part II, because of differences in clinical care and research, we disagree with the notion that courts should use the stricter fiduciary standard typically applied to physicians. Rather, we suggest that courts should use a more general, multifactored test often associated with third-party physicians. Under this test, researchers have a reasonable duty of care, taking into account a range of contextual factors and circumstances, including the factors described in section II.A.3.

Not all of the factors to be considered are equal, however, and some might carry more weight than others. One critical factor is whether and to what extent a research participant reasonably relied on a researcher to return IFs. This factor could be satisfied by showing that the researcher (by word or action) explicitly took on a duty of disclosure on which it was reasonable for the participant to rely. Evidence demonstrating that a participant reasonably relied on the researcher to disclose important IFs would strongly weigh in favor of a researcher's legal duty to return IFs. Absent evidence of an explicit promise, such an argument would, in large part, be a function of the depth of relationship between a researcher and participant and the extent to which the relationship resembled a typical doctor–patient relationship.

Courts might look to a number of other factors to evaluate a claim that the researcher–participant relationship gave rise to justifiable reliance. One potentially important factor is the nature or design of the research. Late-stage clinical trials would be most likely to give rise to justifiable reliance, given that participants generally receive clinical interventions with a prospect of direct individual benefit. Studies in which there is a long-term relationship between the researcher and participant (such as natural-history protocols) might similarly be convincing. This would be particularly true when that relationship has an explicitly clinical component, like if the study team provides standard-of-care treatment as a component of the research. Studies on samples from biobanks, particularly when there is minimal or no contact between the research team and the participant, are less likely to give rise to circumstances that justify reliance.

Other study characteristics might also provide evidence of justifiable reliance. The existence of study resources (such as genetic counselors) for returning certain genetic information

might support a plaintiff's claim. Conversely, the complete absence of any infrastructure for returning results would suggest the opposite. Researcher expertise in genomic science (or lack thereof) would follow a similar line of reasoning: clinicians—and medical geneticists in particular—would be more likely to lead participants to justifiable reliance; basic scientists and non-clinicians are presumably much less likely to do so.

C. ASSESSING WHETHER ADEQUATE DISCLOSURE HAS BEEN MADE—Even if a court concludes that researchers have a duty to return IFs, questions will remain about whether and when researchers have adequately satisfied their disclosure obligations. This question will be complicated by the fact that, as sequencing technology improves and is increasingly incorporated into research protocols, a growing number of professional societies and governmental agencies will weigh in with their thoughts about the contours of researchers' obligations to return IFs. To the extent that these guidance documents point towards returning IFs, they have the potential to give rise to a corresponding legal duty to return IFs in genomic research, thus increasing the chances that participants will successfully be able to win liability suits. This analysis will likely be far from straightforward; much of this guidance is divergent and evolving, and many of these documents make self-limiting disclaimers about how they should be used by the courts.

As with all questions of fact about medical practice, courts will have to weigh a variety of kinds of evidence. In this case, professional association and government guidance documents are just one part of the picture. It is arguably even more important to determine the extent to which certain categories of researchers (such as clinical researchers) as a group have begun implementing this guidance to determine whether any standard of care has developed. The challenge will be to determine how to draw appropriate boundaries around each relevant professional group. Courts must consider whether they should establish a prevailing standard of care by looking to the entire population of researchers, to the set of clinical researchers, or to some more limited subset. We endorse the view that courts should draw the line broadly as an initial starting point but suggest they carefully consider contextual factors that suggest excluding certain groups for whom imposing a duty would be unduly burdensome—such as biobanks or basic science researchers working with de-identified samples.

Another question remains: to what lengths will researchers reasonably be required to go to inform participants of IFs? One circumstance in which this question could arise is when researchers no longer have a participant's updated contact information. In most cases, researchers ask participants to provide contact information during initial intake, but participants retain the responsibility of updating their information over time. If a participant fails to do so and later sues, a defendant researcher will presumably argue that the failure to provide updated contact information releases the researcher from an obligation to disclose. As a complete defense, this seems unconvincing because it places all of the responsibility for maintaining contact on the participants and because conducting some basic inquiries about an individual's whereabouts is not terribly burdensome in the modern digital age. With that said, courts must recognize that there are limits on a researcher's ability and obligation to actively seek out lost participants. As discussed above, researchers are not clinicians and do not have the same clear obligation to act in the best interest of their

participants.[229] Research is undertaken with the goal of producing socially beneficial, generalizable knowledge,[230] so it is unreasonable to expect researchers to devote resources to tracking down participants to the extent that doing so undermines their ability to answer important research questions.

The manner of disclosure might also be subject to dispute. For example, can a researcher discharge his or her duty by returning the information in a letter or phone conversation? Or are researchers instead required to provide robust genetic counseling to ensure that participants fully understand the clinical meaning of the incidental finding? We argue that although researchers are not necessarily *obligated* to provide genetic counseling, they must responsibly convey information in a way that is readily understandable. The manner of disclosure should be tied to the importance and urgency of the information being disclosed or the complexity or nuance of a particular finding.

Conclusion

The increasing use of whole-genome sequencing in research is likely to give rise to a wide range of potential IFs—from indications of a propensity to develop breast cancer to findings about which the meaning and importance are still unknown. Though the extent of any ethical obligation is still unsettled, a number of scholars, researchers, and institutional groups have promulgated guidance documents that attempt to set forth the IFs that should be returned and when they should be returned, or that have advanced criteria to be used in making these determinations. Researchers have responded by implementing their own piecemeal approaches to returning IFs. This push toward an ethical obligation to return particular IFs, coupled with a move among researchers towards returning IFs, has given rise to concerns about tort liability for failure to offer to return these results.

The extent to which a researcher could be held liable for inadequately returning IFs is uncertain. The extent of a researcher's legal duty to return IFs turns on a number of factors, including the extent of any researcher–participant relationship, research customs or standards with regard to returning IFs, and guidance documents addressing when IFs should be returned. The last two factors are still very much in flux. A researcher's liability will also turn on a court's willingness to import the loss-of-a-chance causation analysis into research. But the researcher would be unable to ascertain at the outset when the failure to return IFs will give rise to liability.

Accordingly, this Article advocates adoption of a transparent standard that makes clear to participants which IFs, if any, will be returned to them. A researcher should decide at the outset which of several explainable approaches to returning IFs will be taken. The approach chosen, reviewable by an IRB, must be set forth in the informed consent document and will form the basis of a tort law duty—a researcher's failure to comply with the terms in the informed consent document could lead to a finding of negligence.

This framework gives deference to a researcher's considered judgment about the best approach to returning IFs given the particular circumstances of a research protocol, while allowing participants to know from the outset about which IFs will be returned and when,

and it provides guidance to courts about whether liability should attach, given the evolving ethical, legal, and scientific considerations.

References

1. *See, e.g.*, Collins, Francis S.; Morgan, Michael; Patrinos, Aristides. The Human Genome Project: Lessons from Large-Scale Biology. Sci. 2003; 300:286, 287.
2. *See* International Consortium Completes Human Genome Project. Nat'l Human Genome Res Inst. Apr 14.2003 http://www.genome.gov/11006929
3. *See, e.g.*, Donley, Greer; Hull, Sara Chandros; Berkman, Benjamin E. Prenatal Whole Genome Sequencing: Just Because We Can, Should We? Hastings Center Rep. Jul-Aug;2012 :28, 28, 31.
4. *See, e.g.*, Collins, Francis S.; Green, Eric D.; Guttmacher, Alan E.; Guyer, Mark S. A Vision for the Future of Genomics Research. Nature. 2003; 422:835, 836. [PubMed: 12695777] Morozova, Olena; Marra, Marco A. Applications of Next-Generation Sequencing Technologies in Functional Genomics. Genomics. 2008; 92:255, 257–58. [PubMed: 18703132] Tran, Ben, et al. Cancer Genomics: Technology, Discovery, and Translation. J Clinical Oncology. 2012; 30:647, 647.
5. "Incidental findings" can also be called "secondary findings" or "incidentalomes."
6. *See* Wolf, Susan M., et al. The Law of Incidental Findings in Human Subjects Research: Establishing Researchers' Duties. JL Med & Ethics. 2008; 36:361, 363. (defining IFs as "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").
7. *See infra* section I.B.
8. *See infra* section I.C.
9. *See, e.g.*, Cho, Mildred K. Understanding Incidental Findings in the Context of Genetics and Genomics. JL Med & Ethics. 2008; 36:280, 280. (noting the "common practice among researchers to notify participants during the informed consent process that no individual results will be disclosed, 'incidental' or otherwise"); Wolf et al., *supra* note 6, at 362 ("Despite the potential to generate IFs during the course of research, researchers, Institutional Review Boards (IRBs), and universities have been conducting research with no agreement that they have any responsibility to address and report IFs.").
10. *See infra* section I.D.
11. *See infra* Part II.
12. *See, e.g.*, Wolf, Susan M. The Role of Law in the Debate over Return of Research Results and Incidental Findings: The Challenge of Developing Law for Translational Science. Minn JL Sci & Tech. 2012; 13:435, 439. (calling work on the legal implications of IFs "surely needed"); Clayton, Ellen Wright; McGuire, Amy L. The Legal Risks of Returning Results of Genomics Research. Genetics Med. 2012; 14:473, 475. [PubMed: 22323070] (noting that "the possibility of exposing researchers to legal liability for negligence if results are not offered and returned deserves careful analysis").
13. *See, e.g.*, Furman, Richard L, Jr. Genetic Test Results and the Duty to Disclose: Can Medical Researchers Control Liability? Seattle U L Rev. 1999; 23:391, 404. ("No court has yet been faced with deciding whether a nonphysician medical researcher has an affirmative duty to disclose genetic test results to a research subject or other third party."); Wolf, *supra* note 12, at 436 ("There is no law directly on point. . . . To date, no reported legal case has been discovered that addresses return of results or incidental findings in the domain of research.").
14. *See infra* Part II.
15. *See infra* Part III.
16. *See, e.g.*, Presidential Comm'n for the Study of Bioethical Issues. Privacy and Progress in Whole Genome Sequencing. 2012; 17:106, 116–17. [hereinafter Presidential Comm'n]; Collins et al., *supra* note 4, at 836; Morozova & Marra, *supra* note 4, at 840.
17. *See* Presidential Comm'n, *supra* note 16, at 9.

18. *See, e.g.*, Wolf et al., *supra* note 6, at 361 (noting that the "technologies used in research to generate images, scans, and data can now produce so much information that there is significant potential for incidental findings").
19. *See, e.g.*, Orme, Nicholas M., et al. Incidental Findings in Imaging Research: Evaluating Incidence, Benefit, and Burden. Archives Internal Med. 2010; 170:1525, 1528. (finding that approximately forty percent of imaging examinations had at least one IF).
20. Some have even argued that IFs could be in the thousands. For example, applying a set of criteria developed in 2010 by the National Heart, Lung, and Blood Institute (NHLBI), researchers analyzed whole-genome-sequence data from asymptomatic individuals and concluded that each had approximately 2,000 of the most serious category of variants; any or all of these variants could show up as IFs in research. *See* Cassa, Christopher A., et al. Disclosing Pathogenic Genetic Variants to Research Participants: Quantifying an Emerging Ethical Responsibility. Genome Res. 2012; 22:421, 423. [PubMed: 22147367] ; s*ee also* Gliwa, Catherine; Berkman, Benjamin E. Do Researchers Have an Obligation to Actively Look for Genetic Incidental Findings? Am J Bioethics. Feb.2013 :32, 37. ("Before any filtering, each exome typically has around 80,000 variants; each genome, 3 to 4 million . . . . Thus, the first step in identifying *significant* mutations is filtering the results to leave only those variants most likely to cause disease . . . This reduces the number of relevant exome variants to around 10,000–15,000.") (internal citations omitted).
21. *See, e.g.*, Gordon, Matthew P. A Legal Duty to Disclose Individual Research Findings to Research Subjects? Food & Drug LJ. 2009; 64:225, 228. (noting that "data will vary regarding predictive value, with a range from highly predictive of health outcomes to negligibly so"); Wolf et al., *supra* note 6, at 363 (noting that IFs range from "those that have clear clinical significance and reveal conditions that can be treated . . . to those whose clinical meaning is unknown").
22. *See, e.g.*, Henning, Brodersen N., et al. Anticipated Reactions to Genetic Testing for Hereditary Non-Polyposis Colorectal Cancer Susceptibility. Clinical Genetics. 2004; 66:437, 437–38. [PubMed: 15479189]
23. *See, e.g.*, Nat'l Inst. on Aging, U.S. Dep't of Health & Human Servs. Alzheimer's Disease Genetics Fact Sheet. 2011; 4 available at http://www.nia.nih.gov/alzheimers/publication/alzheimers-disease-genetics-fact-sheet.
24. Ravitsky, Vardit; Wilfond, Benjamin S. Disclosing Individual Genetic Results to Research Participants. Am J Bioethics. Nov-Dec;2006 8:8.
25. *See, e.g.*, Wolf et al., *supra* note 6, at 362 ("Genetic family studies are estimated to reveal misattributed paternity in about 10 percent of research participants in the general population . . . .").
26. *See, e.g.*, Gliwa & Berkman, *supra* note 20, at 36 ("Genomic science is still in its infancy, and the amount we know about the relationship between genomic data and human disease is dwarfed by the amount we do not yet know.").
27. *See, e.g.*, Nat'l Inst. on Aging, *supra* note 23, at 4.
28. *See, e.g.*, Parker, Lisa S. The Future of Incidental Findings: Should They be Viewed as Benefits? JL Med & Ethics. 2008; 36:341, 344. ("Nevertheless, one must guard against assessing benefit solely in medical terms. Health risk information has enabled people to engage in reproductive and other life planning and has afforded many individuals psychological benefit, even when nothing could be done medically.").
29. *See, e.g.*, Beskow, Laura M.; Burke, Wylie. Offering Individual Genetic Research Results: Context Matters. Sci Translational Med. Jun 30.2010 :1, 1. ("Genetic research typically involves informational risk, including the potential for psychosocial harm and for the loss of privacy or confidentiality."); Bredenoord, Annelien L., et al. Disclosure of Individual Genetic Data to Research Participants: The Debate Reconsidered. Trends in Genetics. 2011; 27:41, 43–44. [PubMed: 21190750] (noting that "[t]he information disclosed to research participants could be harmful in several ways," including "adverse social and financial consequences, such as affecting someone's opportunity to obtain or maintain health insurance[,] and could potentially be stigmatizing"); Miller, Franklin G.; Mello, Michelle M.; Joffe, Steven. Incidental Findings In Human Subjects Research: What Do Investigators Owe Research Participants? JL Med & Ethics. 2008; 36:271, 277. ("Disclosing incidental findings carries the risk of distress in the subject, the

risk of a false-positive finding, and the risk of physical harm from procedures to diagnose and (in some cases) treat the putative problem.").

30. Kaufman, David, et al. Subjects Matter: A Survey of Public Opinions About a Large Genetic Cohort Study. Genetics Med. 2008; 10:831, 837. [PubMed: 19011407]
31. *See* Parker, *supra* note 28, at 343.
32. *See, e.g.*, Wolf, Susan M., et al. Managing Incidental Findings in Human Subjects Research: Analysis and Recommendations. JL Med & Ethics. 2008; 36:219, 222.; Wolf et al., *supra* note 6, at 376 ("Before researchers offer to disclose certain IFs to their research participants, they have a duty to verify and evaluate those IFs.").
33. *See, e.g.*, Bredenoord et al., *supra* note 29, at 43 ("[I]f results are obtained in a research laboratory, feedback could also imply re-testing of the genetic data in an accredited clinical laboratory . . . ."); Clayton & McGuire, *supra* note 12, at 474 ("Research testing typically does not meet the laboratory requirements of the clinic. There are reasons why tests whose results may be used to alter clinical care must be obtained in clinically approved laboratories . . . and interpreted by appropriately qualified clinicians."). There is some disagreement about whether this confirmation is, in fact, necessary. *See, e.g.*, Fabsitz, Richard R., et al. Ethical and Practical Guidelines for Reporting Genetic Research Results to Study Participants: Updated Guidelines from a National Heart, Lung, and Blood Institute Working Group. Circulation: Cardiovascular Genetics. 2010; 10:574, 576. [PubMed: 21156933] ("Working Group members disagreed on the interpretation of what constitutes compliance with the CLIA regulations for the return of research results in genetics studies.").
34. *See, e.g.*, Wolf et al., *supra* note 6, at 376 ("The researcher must confirm the existence of an IF, determine whether the IF has likely clinical or reproductive significance and whether the level of significance warrants offering the IF to the research participant, and consult a clinical expert, if necessary, to make these determinations.").
35. Although databases are beginning to emerge that specify the IFs that ought to be returned, these databases are still somewhat flawed. *See, e.g.*, Gliwa & Berkman, *supra* note 20, at 37 ("Although the curators of some databases may make a recommendation as to whether there is sufficient published evidence to suggest that the variant has been proven pathogenic or not, the irregular quality of these data means that currently, for every variant examined, a researcher still has to read all of the primary literature and assess for her- or himself the chances that the variant has a significant chance of causing disease in that individual.").
36. *See, e.g.*, Wolf et al., *supra* note 6, at 378.
37. *See, e.g.*, Wolf et al., *supra* note 6, at 364 (noting that "an IF discovered during the course of research can increase the cost and burden to the research enterprise and institutions supporting medical research").
38. *See, e.g.*, Ravitsky & Wilfond, *supra* note 24, at 8 (noting that "ethical principles of beneficence, respect, reciprocity, and justice provide justification for routinely offering certain results to research participants").
39. Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research, Report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 44 Fed. Reg. 23,192, 23,194 (Apr. 18, 1979) (codified at 45 C.F.R. pt. 46 (2010)) [hereinafter Belmont Report].
40. *See, e.g.*, Miller, Mello & Joffe, *supra* note 29, at 277 ("[D]isclosing incidental findings also carries the potential benefit of obtaining medical intervention to correct a health problem that may be dangerous or adjusting life plans in light of an untreatable condition.").
41. *See, e.g.*, Bredenoord et al., *supra* note 29, at 44; Green, Robert C., et al. ACMG Recommendations for Reporting of Incidental Findings in Clinical Exome and Genome Sequencing. Genetics Med. 2013; 15:565, 571. [PubMed: 23788249] (selecting variants to return that maximize benefits and minimize harms); Ravitsky & Wilfond, *supra* note 24, at 9 ("Beneficence requires that investigators offer results that are clinically useful, which means results are expected to be valuable to participants' physical or psychological well being, to their reproductive decision making or to their life planning.").

42. *See, e.g.*, Belmont Report, *supra* note 39, at 23,193 ("To respect autonomy is to give weight to autonomous persons' considered opinions and choices while refraining from obstructing their actions unless they are clearly detrimental to others.").
43. *See, e.g.*, Bredenoord et al., *supra* note 29, at 44 ("[I]f participants assign personal value to results they should, out of respect for the participant's autonomy, be disclosed."); Ravitsky & Wilfond, *supra* note 24, at 9 ("Respect for participants requires that investigators provide results that may be of interest to participants and that have been acquired based on their participation.").
44. *See, e.g.*, Bredenoord et al., *supra* note 29, at 44 ("Even if there are risks or potential harmful consequences, participants should decide themselves if they want to run those risks by requesting results."). Nevertheless, respect for persons may also encompass an individual's right *not* to know. *See* Ravitsky & Wilfond, *supra* note 24, at 9 ("Respect also requires that investigators respond to participants' preferences to receive, or not receive, a certain result.").
45. *See, e.g.*, Belsky, Leah; Richardson, Henry S. Medical Researchers' Ancillary Clinical Care Responsibilities. British Med J. 2004; 328:1494, 1494. (arguing that "everyone arguably has a duty to rescue those in need, at least when they can do so at minimal cost to themselves"); Beskow & Burke, *supra* note 29, at 1 ("A duty to rescue is based on the premise that, when confronted with a clear and immediate need, an individual who is in a position to help must take action to try to prevent serious harm when the cost or risk to self is minimal."); Miller, Mello & Joffe, *supra* note 29, at 273 (noting that "presented with a situation in which you can prevent something very bad from happening, or alleviate someone's dire plight, by making only a slight (or even moderate) sacrifice, then it would be wrong not to do so").
46. Miller, Mello & Joffe, *supra* note 29, at 273.
47. *See, e.g.*, Singer, Peter. The Drowning Child and the Expanding Circle. New Internationalist Mag. Apr 5.1997 www.newint.org/features/1997/04/05/drowning/
48. *See, e.g.*, Beskow & Burke, *supra* note 29, at 1–2 (noting that the duty to rescue "is met when, in the course of research, an investigator discovers genetic information that clearly indicates a high probability of a serious condition for which an effective intervention is readily available").
49. Although certain whole-genome-sequencing techniques and an understanding of the significance of newly identified IFs currently remain within the exclusive province of research, *see, e.g.*, Gliwa & Berkman, *supra* note 20, at 33 ("At least at present and likely in the near future, WGS and genomic analysis will be primarily available through research, giving researchers unique access to benefits that only they can provide to their participants."); Gordon, *supra* note 21, at 247 ("For example, when genetic researchers make an initial discovery that a particular gene is linked with a higher incidence of a disease, they alone possess that knowledge, at least prior to sharing or publication. In such a circumstance, a subject with the relevant genotype could not possibly learn the salient information from any source other than the researcher."), the current process of identifying which IFs should be returned is too burdensome for it to rise to the level of an ethical obligation, *see, e.g.*, Gliwa & Berkman, *supra* note 20, at 37 ("[D]etermining precisely whether a specific variant is likely to cause disease (pathogenicity), however, must be done manually, and requires considerable time and diligence.").
50. *See, e.g.*, Gliwa & Berkman, *supra* note 20, at 36. Recent recommendations promulgated by the American College of Medical Genetics and Genomics set forth twenty-four phenotypic outcomes that a working group considered to be sufficiently serious that it recommended that return of those findings be mandatory in the clinic. *See* Green, *supra* note 41, at 569–71.
51. *See, e.g.*, Bredenoord et al., *supra* note 29, at 44 (noting that "some argue that people tend to expect an element of reciprocity when contributing to research, particularly in the context of biobank research").
52. Reciprocity can also be criticized, however, because the benefits of returning IFs can be arbitrarily and unevenly distributed to participants, even though all participants arguably have an equal claim.
53. *See, e.g.*, Henry S. Richardson & Leah Belsky, *The Ancillary-Care Responsibilities of Medical Researchers: An Ethical Framework for Thinking About the Clinical Care That Researchers Owe Their Subjects*, Hastings Center Rep., Jan.–Feb. 2004, at 25, 26 ("Ancillary care is that which goes beyond the requirements of scientific validity, safety, keeping promises, or rectifying injuries.").
54. *See id.* at 30 ("The scope of entrustment is not set by what subjects hope or expect, nor by what they think they are entrusting to researchers. Rather, the initial scope of entrustment is fixed by the

subset of the permissions obtained during the consent process that are required for the research team to carry out the study validly and safely.").

55. Belsky & Richardson, *supra* note 45, at 1495; *see also* Richardson & Belsky, *supra* note 53, at 30–31 (discussing factors).
56. *See, e.g.*, Miller, Mello & Joffe, *supra* note 29, at 275 ("[T]he professional's privileged access to private information in the context of a consensual, professional relationship, together with his or her competence to identify the potential significance of this information, trigger and give shape to obligations to respond to incidental findings.").
57. Beskow & Burke, *supra* note 29, at 3 ("With the advent of large-scale repositories that facilitate unprecedented sharing, a rapidly increasing amount of genomic research can occur with no interaction at all between researchers and the individuals who contributed the specimens and/or data under study.").
58. *Id.* at 2–3 ("[P]articipants in most genomic research entrust their information to researchers—not aspects of their health care, as may be the case with the clinical research initially contemplated under ancillary care frameworks.").
59. *See, e.g.*, Bredenoord et al., *supra* note 29, at 43 ("A final argument supporting a restrictive disclosure policy is based on the principle of nonmaleficence.").
60. *See, e.g.*, Miller, Mello & Joffe, *supra* note 29, at 277 ("Disclosing incidental findings carries the risk of distress in the subject, the risk of a false-positive finding, and the risk of physical harm from procedures to diagnose and (in some cases) treat the putative problem."); *see also* Bredenoord et al., *supra* note 29, at 43 ("The information disclosed to research participants could be harmful in several ways.").
61. *See, e.g.*, Bredenoord et al., *supra* note 29, at 42 ("The most prominent argument supporting a restrictive disclosure policy contends that blurring the distinction between research and clinical care has the potential to lead to the therapeutic misconception . . . ."); Gliwa & Berkman, *supra* note 20, at 32 (noting that "others see an obligation to disclose incidental findings as inappropriately emphasizing benefit to individual participants over the production of generalizable knowledge, and worry about the risks associated with conflating research and clinical care"); Kaufman et al., *supra* note 30, at 837 ("Some critics of returning individual genetic research results to research participants cite a version of the problem of 'therapeutic misconception'—that participants will confuse researchers and research data with clinicians and clinical data—and that individual results generally should not be returned."); Wolf et al., *supra* note 6, at 364 ("[R]esearchers are performing research, not clinical care, and thus are not obligated to return information of potential clinical importance; indeed, returning such information may encourage the therapeutic misconception.").
62. *See, e.g.*, Kohane, Isaac S.; Taylor, Patrick L. Multidimensional Results Reporting to Participants in Genomic Studies: Getting It Right. Sci Translational Med. Jun 23.2010 :1, 1. ("Participants believe that researchers are obligated to provide useful personal results.").
63. *See, e.g.*, Belmont Report, *supra* note 39, at 23,193 ("'[R]esearch' designates an activity designed to test an hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge."); *see also* Grimes v. Kennedy Krieger Inst., Inc., 782 A.2d 807, 838 (Md. 2001) ("The experiment is driven by the investigator's dedication to the advancement of knowledge . . . ; it is also driven by society's interest in future benefits that will flow from medical discoveries.").
64. In response to concerns about the therapeutic misconception, one could argue that the solution is simply to ensure that the informed consent process more clearly and explicitly details what participants can (and cannot) expect from the research team. Although this critique has some merit, it ignores that general understanding of even the best informed consent documents is dismal and that clinical-type relationships can induce therapeutic misconception, independent of the text in the informed consent document. Furthermore, the practical reality is that informed consent documents will often be far from ideal, as we discuss in detail in Parts III and IV.
65. *See, e.g.*, Belsky & Richardson, *supra* note 45, at 1494 (noting that "offering ancillary care this broadly may drain limited human and financial resources"); Ossorio, Pilar N. Letting the Gene Out of the Bottle: A Comment on Returning Individual Research Results to Participants. Am J

Bioethics. Nov-Dec;2006 :24, 25. ("[T]he practicalities of returning results may impose untenable burdens on the existing research infrastructure.").

66. *See, e.g.*, Bredenoord et al., *supra* note 29, at 43 ("Disclosure can be resource intensive, and some argue that it would be unethical to use those resources for feedback when they could have been used for research.").
67. *See, e.g.*, Ossorio, *supra* note 65, at 24 ("The authors note that returning certain types of individual results is consistent with principles of beneficence, respect for persons, reciprocity, and justice, but they never state why returning results rises to the level of an obligation for researchers. An act may be consistent with many principles and still be superogatory or even wrong, all things considered.").
68. *See, e.g.*, Wolf, *supra* note 12, at 444–45 ("[I]t has become hard to find participants in the return of results debate who maintain that no individual results or findings should ever be returned, no matter how clinically urgent the information. . . . [I]t is also increasingly difficult to find commentators who argue for conveying all information derived in the research sphere, at least at this juncture. Too much of that information still remains uncertain and even mistaken, to dump it all on research participants."); *see also* Bredenoord et al., *supra* note 29, at 42 ("At one end of the spectrum it is argued that no individual genetic research results should be disclosed whatsoever. This, however, is an exceptional position, because only one publication adhered strictly to a 'no disclosure at all' policy, even of life-saving information—and this article was restricted to biobank research.").
69. *See, e.g.*, Clayton & McGuire, *supra* note 12, at 473 ("There is substantial consensus that people should be offered results that could trigger interventions that are lifesaving or that could avert serious adverse health outcomes; there is somewhat less consensus about whether people should be offered results that may have reproductive implications or that could be personally meaningful."); Gliwa & Berkman, *supra* note 20, at 33 ("[O]pinion seems to be moving toward the idea that there is some obligation to offer to disclose a limited set of findings . . . ."); Gordon, *supra* note 21, at 235 ("Commentators generally support the notion that there is a *moral* duty to disclose medically important information.").
70. *See, e.g.*, Clayton & McGuire, *supra* note 12, at 473 ("[T]he debate quickly turns to issues of mechanics (e.g., which results? who discloses? for how long does the obligation exist?)."); Fabsitz et al., *supra* note 33, at 575 (concluding that "debate continues over when, how, and who should return individual results to participants"); Ossorio, *supra* note 65, at 25 ("I believe that we will identify a miniscule number of cases in which researchers have obligations to offer individual genetic research results and a very large number of cases in which it may be ethically permissible to do so. There will also be a few cases in which it will be impermissible to return results.").
71. A commonly accepted definition of "analytic validity" is how accurately and reliably the test measures the genetic variant of interest. *See, e.g.*, Genomic Testing: ACCE Model Process for Evaluating Genetic Tests. Centers for Disease Control & Preventionhttp://www.cdc.gov/genomics/gtesting/ACCE/ (last updated Jan. 3, 2010).
72. *See, e.g.*, Gliwa & Berkman, *supra* note 20, at 33 (noting that the consensus is moving toward disclosure when findings "meet an exacting standard of validity, severity, and actionability"); Wolf et al., *supra* note 6, at 373 ("[P]articipants are entitled to information regarding IFs of likely clinical or reproductive significance . . . .").Other scholars have set forth other factors, including communicability, the closeness of the researcher–participant relationship, the subjective interests of the participants, and the type of study. These positions have not reached a comparable level of consensus. *See, e.g.*, Kohane & Taylor, *supra* note 62, at 3 (focusing on communicability); McGuire, Amy L.; Caulfield, Timothy; Cho, Mildred K. Research Ethics and the Challenge of Whole-Genome Sequencing. Nature Rev Genetics. 2008; 9:152, 153. [PubMed: 18087293] (focusing on "the type of study, the clinical significance and reliability of the information, and whether the study involves patients . . . or healthy volunteers"); Ravitsky & Wilfond, *supra* note 24, at 14–15 (focusing on the researcher–participant relationship); Rothstein, Mark A. Tiered Disclosure Options Promote the Autonomy and Well-Being of Research Subjects. Am J Bioethics. Nov-Dec;2006 :20, 20. (focusing on the subjective interests of research participants).
73. *See, e.g.*, Wolf, *supra* note 12, at 440–41 (summarizing the positions of the institutions that have considered the issue); *see also* Nat'l Bioethics Advisory Comm'n. Research Involving Human Biological Materials: Ethical Issues and Policy Guidance. :72.1999available at http://

bioethics.georgetown.edu/nbac/hbm.pdf (relying on these factors); Fabsitz et al., *supra* note 33 (same); NHLBI Working Group on Reporting Genetic Results in Research Studies. Meeting Summary. Nat'l Heart, Lung, & Blood Inst. Jul 12.2004 #x0005B;hereinafter NHLBI Working Group], http://www.nhlbi.nih.gov/meetings/workshops/gene-results.htm (same).

74. *See, e.g.*, Gordon, *supra* note 21, at 254 ("These guidelines, however, lack answers to important questions, such as how the determination of clinical utility should be made.").
75. *See, e.g.*, Rothstein, *supra* note 72, at 21 ("Some options for disclosure would be that the results have reproductive significance, diagnostic significance, or treatment significance.").
76. Fabsitz et al., *supra* note 33, at 575–76.
77. *See, e.g.*, Gordon, *supra* note 21, at 229 ("[O]ne would plausibly be more motivated to actively seek out or monitor information related to the disease such that, should future research determine that certain behaviors or medications reduce the risk of contracting the disease, one would be better positioned to take advantage of the new information.").
78. *See, e.g.*, Beskow & Burke, *supra* note 29, at 1 ("Although many agree that results should be offered only when they have utility, opinions vary as to whether the line should be drawn at clinical utility (that is, a proven therapeutic or preventive intervention is available), at personal utility (such as for reproductive decision-making or life planning), or in recognition that some individuals will find the information useful in and of itself (for example, through an enhanced sense of personal identity)."); Bredenoord et al., *supra* note 29, at 45 ("The concept of clinical utility is also debated, because the clinical utility of testing varies widely, depending on the magnitude of the risk, the accuracy of the risk prediction, the potential for risk reduction, the efficacy of available interventions, and the implications for the capacity of the individuals concerned to obtain health insurance.").
79. NHLBI Working Group, *supra* note 73.
80. *See, e.g.*, Beskow & Burke, *supra* note 29, at 1; Ravitsky & Wilfond, *supra* note 24, at 15 ("[T]he same result can therefore be handled differently in different studies.").
81. *See, e.g.*, Gliwa & Berkman, *supra* note 20, at 33 ("A number of groups have recently discussed the possibility of building standard lists of variants that could or should be disclosed as incidental findings . . . ."); Green et al., *supra* note 41, at 569 (providing a list of variants that must be disclosed in the clinical context).
82. *See, e.g.*, Gliwa & Berkman, *supra* note 20, at 36 ("Based on recent surveys, experts can agree on only a handful of variants that should be routinely disclosed. One study found that 100% of genetic specialists were in agreement in favor of disclosing to adults 21 conditions or genes classified as 'known pathogenic mutations' (more than 80% agreed on 64 conditions or genes).").
83. *See, e.g.*, *id.*
84. *See, e.g.*, Wolf, Susan M.; Annas, George J.; Elias, Sherman. Patient Autonomy and Incidental Findings in Clinical Genomics. Sci. 2013; 340:1049, 1049–50.Burke, Wylie, et al. Recommendations for Returning Genomic Incidental Findings? We Need to Talk! Genetics Med. Aug 1.2013 15:854. http://www.nature.com/gim/journal/vaop/ncurrent/pdf/gim2013113a.pdf. [PubMed: 23907645] .
85. *See generally* van El, Carla G., et al. Whole-Genome Sequencing in Health Care. Eur J Hum Genetics. 2013; 21:580. [PubMed: 23676617]
86. *See, e.g.*, Cho, *supra* note 9, at 280 (noting the "common practice among researchers to notify participants during the informed consent process that no individual results will be disclosed, 'incidental' or otherwise"); Wolf et al., *supra* note 6, at 362 (noting that "researchers, Institutional Review Boards (IRBs), and universities have been conducting research with no agreement that they have any responsibility to address and report IFs").
87. Klitzman, Robert, et al. Processes and Factors Involved in Decisions Regarding Return of Incidental Genomic Findings in Research. Genetics Med. Sep 26. 2013 http://www.nature.com/gim/journal/vaop/ncurrent/full/gim2013140a.html
88. *See, e.g.*, Gordon, *supra* note 21, at 226 ("Although the bulk of the literature asserts that researchers have a moral duty to disclose medically useful results, the question remains whether there ought to be a corresponding legal duty.").

89. *See, e.g.*, *id.* at 231 ("The Common Rule does not, however, directly address the provision of results to subjects."); Wolf, *supra* note 12, at 436 ("There is no law directly on point. . . . To date, no reported legal case has been discovered that addresses return of results or incidental findings in the domain of research."); Wolf et al., *supra* note 6, at 362 ("Current law and federal regulations offer no direct guidance on how to deal with IFs in research . . . .").
90. *See, e.g.*, Clayton & McGuire, *supra* note 12, at 476 ("One thing is certain—if these practices become routine, they *will* be legally required. This is the way tort law has worked for decades."); Wolf, *supra* note 12, at 437 ("Yet already, we see views expressed that researchers must navigate between legal threats on both sides—liability for failure to return findings on one side, and liability for wrongly returning on the other."); Wolf et al., *supra* note 6, at 365 ("Some recent case law suggests that a legal trend may be emerging toward recognizing an obligation on the part of a researcher to provide a research participant with information acquired from a study, when that information has clinical implications for the participant.").
91. *See, e.g.*, Clayton & McGuire, *supra* note 12, at 473 ("Although commentators are careful to distinguish this as an ethical rather than legal obligation, we worry that return of results may unjustifiably become standard of care based on this growing 'consensus,' which could quickly lead to a legal (negligence-based) duty to offer and return individualized genetic research results."); Gordon, *supra* note 21, at 260 ("But the common law has advanced such that the imposition of a researcher duty to disclose individual research findings that are clinically useful to subjects appears to be a logical next step.").
92. *See, e.g.*, Wolf, *supra* note 12, at 441 ("All of these papers present ethics recommendations. And to date, not a single one of them appears to have been cited in any legal decision or used to impose liability. There is a very good reason for this: ethics is not the same as law.").
93. *See supra* section I.D.
94. There is also the possibility that research participants could bring suit alleging that a researcher violated the "right not to know." In other words, a researcher told them about a genetic predisposition that they specifically disclaimed any interest in knowing more about. A claim alleging a violation of a right not to know could proceed if a participant suffered injury, either emotional or physical, upon learning information that a researcher had reason to know a participant would not want disclosed.
95. *See, e.g.*, sources cited *supra* note 13.
96. Although a more detailed analysis is beyond the scope of this Article, a participant who was not told of an IF and who subsequently suffered injury would have even less of a chance of succeeding in a lawsuit upon bringing a breach of contract or property claim. A research participant bringing a breach of contract claim against a researcher for failing to return IFs could only succeed if the informed consent document were treated as a contract and the informed consent document made clear that IFs would be returned. Courts and scholars are divided about whether an informed consent document should be treated as a contract. *See, e.g.*, Dahl v. HEM Pharm. Corp., 7 F.3d 1399, 1404–05 (9th Cir. 1993) (interpreting participation in a medical trial as a contract); Grimes v. Kennedy Krieger Inst., Inc., 782 A.2d 807, 843–44 (Md. 2001) (finding that the consent form created a bilateral contract between parties); Gordon, *supra* note 21, at 255 ("Informed consent documents have previously been treated as binding contracts by courts . . . ."); Meyer, Michelle N. The Subject–Researcher Relationship: In Defense of Contracting Around Default Rules. Am J Bioethics. Apr.2011 :27, 28. ("Courts have increasingly held . . . that the research consent form constitutes a contract . . . ."). *But see, e.g.*, Wash. Univ. v. Catalona, 490 F.3d 667, 674–77 (8th Cir. 2007) (holding that the signed consent forms demonstrated the donors' intent to make a gift); Ram, Natalie. Assigning Rights and Protecting Interests: Constructing Ethical and Efficient Legal Rights in Human Tissue Research. Harv JL & Tech. 2009; 23:119, 163. ("Despite their frequent similarity in form to contracts, however, informed consent documents, whether tiered or otherwise, are generally not considered to be contractual documents."); Saver, Richard S. At the End of the Clinical Trial: Does Access to Investigational Technology End As Well? W New Eng L Rev. 2009; 31:411, 428. (observing that some courts have "treat[ed] the informed consent documents as merely notice of the subjects' consent rather than an enforceable contract"); Wolf et al., *supra* note 6, at 372 ("[C]ourts have generally been reluctant to find binding contractual obligations in the research setting.").Research participants who are unsuccessful in bringing claims either in tort or for breach of contract may try to bring claims alleging a property right in their genetic-research

results. Individuals claiming that they have a property right to information about themselves uncovered during research would require courts to find that individuals retain ownership interests in the biological material that they have contributed to research and the results derived there from —claims that courts have been unwilling to recognize. *See, e.g.*, Bregman-Eschet, Yael. Genetic Databases and Biobanks: Who Controls Our Genetic Privacy? Santa Clara Computer & High Tech LJ. 2006; 23:1, 22–26. (noting that, in a number of cases, courts have not recognized an individual's property rights in biological specimens donated to research); Rao, Radhika. Genes and Spleens: Property, Contract, or Privacy Rights in the Human Body? JL Med & Ethics. 2007; 35:371, 372. ("There are three important cases in which individuals have claimed ownership of their own bodies in the context of biomedical research. In all three cases, the courts refused to accord property rights to those who supply body parts for medical research . . . ."); Wolf et al., *supra* note 6, at 372 ("In *Ande v. Rock*, researchers conducted a cystic fibrosis study on samples from newborns and did not inform parents of a newborn who tested positive of the results. The parents claimed a property right to these test results and argued that if this information had been disclosed, they could have avoided harm in two ways: they would have been able to accept treatment for their child to lessen the severity and progression of her disease, and they would have chosen not to have a second child who was also diagnosed with cystic fibrosis. None of their claims to this information succeeded."). It is therefore extremely unlikely that a research participant can succeed in claiming that she has a property right in her genomic information that includes a derivative right to obtain IFs.

97. *See, e.g.*, Pike, Elizabeth R. Recovering from Research: A No-Fault Proposal to Compensate Injured Research Participants. Am JL & Med. 2012; 38(7):27–29. (articulating the many reasons that injured research participants will always have difficulty recovering in tort).
98. *See, e.g.*, Ram, *supra* note 96, at 156–57 ("In most cases, however, medical professionals who fail to adequately disclose information material to decision making may be subject only to tort liability under negligence.").
99. *See, e.g.*, Dan B. Dobbs, Paul T. Hayden & Ellen M. Bublick, The Law of Torts § 124 (2d ed. 2011) (setting forth the elements of a tort law negligence claim); Ram, *supra* note 96, at 156–57 (same).
100. *See, e.g.*, Dobbs, Hayden & Bublick, *supra* note 99, § 125 ("The duty or standard imposed in most cases is the duty of reasonable care under the circumstances, no more, no less.").
101. *See, e.g.*, *id.* ("It sounds surprising, but there are cases in which the defendant literally owes the plaintiff no duty to exercise care to prevent the harm suffered by the plaintiff."); Hoffmann, Diane E.; Rothenberg, Karen H. Whose Duty Is It Anyway?: The Kennedy Krieger Opinion and Its Implications for Public Health Research. J Health Care L & Pol'y. 2002; 6:109. 111–12. ("[T]he law provides that there is 'no duty to act affirmatively for the benefit of others in the absence of some special relationship.'").
102. *See, e.g.*, Furman, *supra* note 13, at 400 ("Under common law, a person owes no duty to control the conduct of another or to warn others of anticipated conduct."). One such exception may occur in cases where an individual *created* the risk of physical or emotional harm. *See, e.g.*, Restatement (Third) of Torts § 18 (2010); Hoffmann & Rothenberg, *supra* note 101, at 111–12 ("In general, the law holds that one has a duty to act reasonably to prevent physical harms to others that might result from one's affirmative acts. . . .").
103. *See, e.g.*, Pehle v. Farm Bureau Life Ins. Co., Inc., 397 F.3d 897, 902 (10th Cir. 2005) ("A duty arises when 'a relation exists between the parties [such] that the community will impose a legal obligation upon one for the benefit of the other . . . .'"); Stanley v. McCarver, 92 P.3d 849, 851 (Ariz. 2004) ("Duties may also arise from a special relationship between the parties . . . ."); Dobbs, Hayden & Bublick, *supra* note 99, § 405 ("The exceptional circumstances in which a defendant may owe a duty of reasonable assistance to a plaintiff include: . . . (2) the defendant is in a special relationship to the plaintiff . . . ."); Furman, *supra* note 13, at 401 ("An exception to the common law rule exists when the defendant has some special relationship with the person whose conduct needs to be controlled or is in a relationship with a foreseeable victim of the conduct."); Hoffmann & Rothenberg, *supra* note 101, at 113 ("However, when individuals are in a special relationship, courts have often imposed a different level of duty.").

104. *See, e.g.*, Hoffmann & Rothenberg, *supra* note 101, at 112 ("As regards a contractual agreement, an individual may be liable for harms based on actions he or she promised via contract to perform but failed to carry out.").
105. *See, e.g.*, *id.* § 410 ("The general rule that undertakings can create a duty of care is often expressed by saying one who voluntarily assumes a duty must then perform that duty with reasonable care.").
106. *See, e.g.*, *id.* § 127 ("The defendant's conduct can thus be compared to the conduct we would expect of a reasonable person having, say, certain knowledge and ability.").
107. *See, e.g.*, *id.* § 284 ("Under traditional rules, physicians owe a duty of care set by the custom of their profession rather than a duty of reasonable care under the circumstances.").
108. *See, e.g.*, *id.* § 283 ("The duty to patients under the traditional legal rule is not the familiar duty of reasonable care but the duty to comply with medical customs or medical standards that supposedly dictate the exact methods by which a medical procedure is carried out.").
109. *See, e.g.*, *id.* § 292 ("The medical standard is sometimes stated by saying that physicians must exercise at least the skill, knowledge, and care normally possessed and exercised by other members of their profession in the same school of practice in the relevant medical community.").
110. *See, e.g.*, Meltzer, Leslie A. Undesirable Implications of Disclosing Individual Genetic Results to Research Participants. Am J Bioethics. Nov-Dec;2006 :28, 29. ("[P]hysicians are fiduciaries to their patients. This means that physicians have not only an ethical, but also a legal duty to act solely for the benefit of their patients."); Meyer, *supra* note 96, at 28 ("Generally, a fiduciary is someone who voluntarily agrees to promote the best interests of another; who is given considerable discretion in so acting since what will best promote the beneficiary's interests cannot be spelled out in advance . . . .").
111. Hafemeister, Thomas L.; Spinos, Selina. Lean on Me: A Physician's Fiduciary Duty to Disclose an Emergent Medical Risk to the Patient 86. Wash U L Rev. 2009; 1167:1186–87.
112. *See, e.g.*, Furman, *supra* note 13, at 409 ("To recover for a failure to disclose under the rules of professional malpractice, the plaintiff must show that the physician violated his or her duty to inform. In addition, the plaintiff must show that the physician's nondisclosure caused a recognizable harm under the law of negligence."); Hafemeister & Spinos, *supra* note 111, at 1169–70; Miller, Mello & Joffe, *supra* note 29, at 279 ("Whereas failure to look for incidental findings would constitute malpractice for radiologists engaged in medical practice, we contend that the duty of investigators is more limited, owing to the nature of clinical research as distinct from medical care.").Doctors have even been found to owe a duty to relatives of the patients who would be affected by the findings. *See, e.g.*, Pate v. Threlkel, 661 So.2d 278, 281–82 (Fla. 1995) (finding that a physician owed a duty to warn patient of genetic condition that could be passed on to child); Safer v. Estate of Pack, 677 A.2d 1188, 1192 (N.J. Super. 1996) (same). The implications of *Safer* were subsequently overturned by a genetic-privacy statute in New Jersey.
113. *See, e.g.*, Hafemeister & Spinos, *supra* note 111, at 1198 ("A patient who has not received adequate disclosure . . . merits both equitable relief and compensatory damages for resulting economic and noneconomic injuries."); Meltzer, *supra* note 110, at 29 ("In the personal context of the physician–patient relationship, fundamental ethical principles compel physicians to share individual genetic results with patients. In fact, failure to share such information in all but the most exceptional circumstances is legally actionable . . . .").
114. *See, e.g.*, Pike, Elizabeth R. Recovering from Research: A No-Fault Proposal to Compensate Injured Research Participants. Am JL & Med. 2012; 38:7, 12. ("In fact, many elements of research—placebo-controlled trials, random assignment to treatment arms, restricted flexibility in adjusting dosages, restrictions on using concomitant medications—are contrary to good medical care.").
115. *See, e.g.*, Gordon, *supra* note 21, at 245 ("Others, however, posit that the relationship cannot be fiduciary because the researcher's primary loyalty is to his protocol rather than to any one subject.").
116. *See* Dobbs, Hayden & Bublick, *supra* note 99, § 286 (defining a third party doctor as a "physician or other professional [who] may be employed to examine prospective employees, prospective insureds, or litigation claimants").

117. *See, e.g.*, *id.* § 286 ("[S]ome authority has expressly held that a doctor who actually examines a patient or reads his X-rays owes a duty of reasonable care which may require both care in making a diagnosis and reasonable care in notifying the patient of serious medical conditions within the scope of the examination he has undertaken. If the physician has undertaken to provide care to a person or created a reasonable expectation that he would do so, then delivery of such care to should be the order of the day, whether that person is characterized as a patient or not."); Gordon, *supra* note 21, at 239 ("Numerous courts have now held that, despite the traditional rule, physicians conducting employment-related physical examinations of employees (prospective or current) at the behest of employers have a duty to reveal important medical information discovered during the course of the examination to the examinee.").
118. *See, e.g.*, Stanley v. McCarver, 92 P.3d 849, 853 (Ariz. 2004) ("[I]n placing oneself in the hands of a medical professional, even at the request of one's employer or insurer, one may have a reasonable expectation that the expert will warn of any incidental dangers of which he is cognizant due to his peculiar knowledge of his specialization.") (internal quotation marks omitted); Reed v. Bojarski, 764 A.2d 433, 443 (N.J. 2001) ("[T]he patient is entitled to rely on the physician to tell him of a potential serious illness if it is discovered. Any reasonable person would expect that and the duty to communicate with a patient who is found to be ill is non-delegable."); Meinze v. Holmes, 532 N.E.2d 170, 173–74 (Oh. Ct. App. 1987) (holding that third-party doctors had a duty to communicate a significant risk of danger to the plaintiff, even in the absence of a doctor–patient relationship).
119. *Stanley*, 92 P.3d at 849.
120. *Id.* at 851.
121. *Id.* (alteration in original)
122. *Id.* at 853.
123. *Id.*
124. Reed v. Bojarski, 764 A.2d 433, 441 (N.J. 2001).
125. *Id.* at 435.
126. *Id.*
127. Id.
128. *Id.*
129. Id.
130. *Id.* at 445.
131. *See, e.g.*, Meltzer, *supra* note 110, at 29 ("Investigators are not fiduciaries of research participants, and as such, do not presently have a legal obligation to act in the best interests of participants.").
132. *See, e.g.*, Whitlock v. Duke Univ., 637 F. Supp. 1463, 1471 (M.D.N.C. 1986) (holding that the federal research regulations provided the standard of care), *aff'd*, 829 F.2d 1340 (4th Cir. 1987); Daum v. SpineCare Med. Grp., 61 Cal. Rptr. 2d 260, 273 (Cal. Ct. App. 1997) (same); Vodopest v. MacGregor, 913 P.2d 779, 787 (Wash. 1996) (same); Jansson, Roger L. Researcher Liability for Negligence in Human Subject Research: Informed Consent and Researcher Malpractice Actions. Wash L Rev. 2003; 78:229, 247. ("[T]here appears to be an emerging trend among courts to use the federal regulations as the standard of care for informed consent in human subject research.").At least one leading case, *Grimes v. Kennedy Krieger Inst., Inc.,* has concluded that a researcher's obligations may extend significantly beyond the federal regulations. 782 A.2d 807 (Md. 2001). The Supreme Court of Maryland noted that research can, and normally will, give rise to special relationships that obligate researchers beyond the general tort law duty not to cause injury. *Id.* at 834–35. This special relationship arises, in part, because "investigators are in a better position to anticipate, discover, and understand the potential risks to the health of their subjects." *Id.* at 851. Several scholars have expressed concern about the implication of *Grimes* in the context of IFs—that *Grimes* indicates "that a legal trend may be emerging toward recognizing an obligation on the part of a researcher to provide a research participant with information acquired from a study, when that information has clinical implications for the participant." Wolf et al., *supra* note 6, at 365. To the extent *Grimes* is extended or followed in other courts, a court could conclude that researchers have a legal duty to return IFs in certain circumstances. *See, e.g.*, Gordon, *supra* note 21, at 234. But courts that have

considered similar fact patterns have generally refused to extend the holding of *Grimes*, and *Grimes* has been the subject of significant scholarly criticism. *See, e.g.*, Hoffmann & Rothenberg, *supra* note 101, at 147.

133. *See, e.g.*, Dobbs, Hayden & Bublick, *supra* note 99, § 249 ("Most statutes and even regulations are relatively permanent and relatively abstract; they cannot take into account the particular concerns of individual cases. They aim at minimum standards but are not meant to establish the outer limits of the defendant's safety responsibilities.").

134. Assuming that there is an obligation to disclose findings that have been discovered during research, some may question whether researchers have an obligation to purposefully investigate sequence data in search of IFs. *See, e.g.*, Gliwa & Berkman, *supra* note 20, at 33. It is unreasonable to expect that researchers will spend excessive resources—measured both in time and money—looking extensively for all manner of IFs. If there is an obligation to look, then it must be only for information that is extremely well-validated and useful for mitigating serious disease. *Id.* Furthermore, the process of looking for IFs cannot be so difficult as to seriously undermine a researcher's ability to produce generalizable knowledge that can lead to social benefit.

135. *See, e.g.*, Dobbs, Hayden & Bublick, *supra* note 99, § 283 ("The duty to patients under the traditional legal rule is not the familiar duty of reasonable care but the duty to comply with medical customs or medical standards that supposedly dictate the exact methods by which a medical procedure is carried out.").

136. *See, e.g.*, *id.* § 292 ("The medical standard is often understood to be the medical custom or practice with respect to the particular act of diagnosis or treatment. . . . Practically speaking, the standard can be the custom or practice of the relevant medical community, or it can be a qualified expert's opinion that does not refer to custom or practice at all and may not even refer to any source.").

137. *See, e.g.*, Wolf, *supra* note 12, at 442 ("We would all be kidding ourselves to believe that we had already generated such consensus across the research community about return of results and incidental findings and such specificity about what return should look like that courts would find an established standard of care. The reality is that debate, research, and specification are very obviously works in progress.").

138. *See, e.g.*, Stanley v. McCarver, 92 P.3d 849, 854 n.6 (Ariz. 2004). ("While rules of professional conduct may provide evidence of how a professional would act, they do not create a duty or establish a standard of care as a matter of law."); Dobbs, Hayden & Bublick, *supra* note 99, § 295 ("Quite apart from statute, some courts have accepted evidence of such guidelines as sufficient to establish the standard of care in favor of the plaintiff.").

139. *See supra* section I.C.

140. *See, e.g.*, Stanley v. McCarver, 92 P.3d 849, 854 n.6 (Ariz. 2004) ("We continue to believe, however, that while such rules may illuminate the standard of care, they do not serve as a basis on which to impose a duty."); Dobbs, Hayden & Bublick, *supra* note 99, § 295 ("In addition, the reasons to say that compliance with statutes and regulations should not be taken to show conclusively that the defendant exercised due care apply as well to compliance with medical protocols. There is room . . . for healthy scepticism about their value as ultimate tests of liability or non-liability.").

141. *See Stanley*, 92 P.3d at 853; *see also* Dobbs, Hayden & Bublick, *supra* note 99, § 410 ("A person who undertakes actions that would increase physical safety for the plaintiff is under a duty to use reasonable care to carry out his undertaking, but only if one of two conditions [are] met . . . (1) that the defendant's failure to exercise reasonable care increased the risk of harm . . . or (2) that the plaintiff relied on the undertaking."); Miller, Mello & Joffe, *supra* note 29, at 272–73 ("[T]he patient likely expects that the physician will disclose all health-related findings, an expectation that might lead to 'reliance' behaviors on the patient's part—that is, the patient may rely, to his detriment, on the physician's decision to remain silent.").

142. *See, e.g.*, Green, *supra* note 41, at 569.

143. *See, e.g.*, Clayton & McGuire, *supra* note 12, at 475 ("However, if guidelines suggest there is an ethical obligation to offer results and investigators adopt this practice widely, both could be used as evidence of what is the standard of care for investigators.").

144. *See, e.g.*, Dobbs, Hayden & Bublick, *supra* note 99, § 253 ("The duty issue is whether there is a standard the defendant must meet in his conduct; the breach issue is whether the defendant violated that standard.").
145. *See, e.g.*, *id.* § 286 ("Given a duty of care, however, the question remains whether, in any given case, he has breached that duty.").
146. *See, e.g.*, *id.* § 125 ("Juries, not judges, decide whether the defendant was negligent unless the question is too clear to permit different evaluations by reasonable people.").
147. 397 F.3d 897, 899 (10th Cir. 2005).
148. *Id.*
149. *Id.*
150. *Id.*
151. *Id.*
152. *Id.* at 904.
153. *Id.*
154. *Id.* at 905.
155. *Id.* at 904.
156. *See, e.g.*, Dobbs, Hayden & Bublick, *supra* note 99, § 125 ("The traditional view is that the plaintiff's injury is caused by the defendant's conduct if, but for the defendant's conduct, the plaintiff would have escaped the injury.").
157. *See, e.g.*, Sawlani v. Mills, 830 N.E.2d 932, 938 (Ind. Ct. App. 2005) ("No matter how negligent the doctor's performance, it can never be the proximate cause of the patient's death. Since the evidence establishes that it is more likely than not that the medical problem will kill the patient, the disease or injury would always be the cause-in-fact." (quoting Mayhue v. Sparkman, 653 N.E.2d 1384, 1387 (Ind. 1995))); King, Joseph H, Jr. Causation, Valuation, and Chance in Personal Injury Torts Involving Preexisting Conditions and Future Consequences. Yale LJ. 1981; 90:1353, 1358. ("The disease was obviously a cause of the harm. The doctor's negligence in allowing the disease to progress may also have caused harm.").
158. *See, e.g.*, Matsuyama v. Birnbaum, 890 N.E.2d 819, 823 (Mass. 2008) ("[T]he loss of chance doctrine views a person's prospects for surviving a serious medical condition as something of value, even if the possibility of recovery was less than even prior to the physician's tortious conduct."); Dobbs, Hayden & Bublick, *supra* note 99, § 196 ("The idea is that the plaintiff's chance of survival itself has value for which compensation is due."); King, *supra* note 157, at 1354 ("[T]he loss of a chance of achieving a favorable outcome or of avoiding an adverse consequence should be compensable and should be valued appropriately.").
159. *See, e.g.*, *Matsuyama*, 890 N.E.2d at 823 ("Where a physician's negligence reduces or eliminates the patient's prospects for achieving a more favorable medical outcome, the physician has harmed the patient and is liable for damages."); King, *supra* note 157, at 1354 (noting that when "preexisting conditions have not absolutely preordained an adverse outcome, however, the chance of avoiding it should be appropriately compensated even if that chance is not better than even").
160. *See, e.g.*, King, *supra* note 157, at 1363 ("*What* caused a loss, however, should be a separate question from what the *nature and extent* of the loss are.").
161. *See, e.g.*, *Matsuyama*, 890 N.E.2d at 832 (noting that injury "consists of the diminished likelihood of achieving a more favorable medical outcome").
162. *See, e.g.*, *Matsuyama*, 890 N.E.2d at 832 ("[W]e recognize loss of chance not as a theory of causation, but as a theory of injury. . . . In order to prove loss of chance, a plaintiff must prove by a preponderance of the evidence that the physician's negligence caused the plaintiff's likelihood of achieving a more favorable outcome to be diminished."); *Sawlani*, 830 N.E.2d at 939 ("We think that loss of chance is better understood as a description of the injury . . . ."); King, *supra* note 157, at 1360 (arguing that the medical professional should be liable to the extent that he "contributed to the harm by allowing a preexisting condition to progress").
163. *See, e.g.*, *Matsuyama*, 890 N.E.2d at 828 ("[A] substantial and growing majority of the States that have considered the question have indorsed the loss of chance doctrine, in one form or another, in medical malpractice actions."); Dobbs, Hayden & Bublick, *supra* note 99, § 196 ("Although a

significant number of states have specifically rejected the lost chance approach, an even larger number has embraced it. A recent article places the count at 16 states against the doctrine and 22 in favor.").

164. *See, e.g.*, *Matsuyama*, 890 N.E.2d at 829–30 ("[T]he all or nothing rule provides a 'blanket release from liability for doctors and hospitals any time there was less than a 50 percent chance of survival, regardless of how flagrant the negligence.'"); Dobbs, Hayden & Bublick, *supra* note 99, § 196 ("In such cases, however, the evidence may show that even if diagnosis and treatment had been timely, the patient might have had only a 40% chance of living. On those facts, the plaintiff definitely could not prove by a preponderance of the evidence that the defendant caused the patient's death."); Fischer, David A. Tort Recovery for Loss of a Chance. Wake Forest L Rev. 2001; 36:605, 611. ("Loss of a chance is often justified in these cases because the physician breached a duty to protect the patient from the preexisting condition, and the patient would have placed high value on the chance of a cure even if it was less than 50 percent.").
165. *See, e.g.*, *Matsuyama*, 890 N.E.2d at 823 ("Permitting recovery for loss of chance is particularly appropriate in the area of medical negligence. Our decision today is limited to such claims."); Restatement (Third) of Torts § 26 cmt. n (2010) ("To date, the courts that have accepted lost opportunity as cognizable harm have almost universally limited its recognition to medical-malpractice cases."); Fischer, *supra* note 164, at 610 ("These courts typically apply the doctrine in medical malpractice cases where the physician improperly diagnoses or treats a disease."); Wolf et al., *supra* note 6, at 371–72 ("Many state courts allow recovery for 'loss of a chance,' especially in medical contexts.").
166. *See, e.g.*, Dobbs, Hayden & Bublick, *supra* note 99, § 196 ("Although most cases debating lost chance recovery are patterned on the physician example, where a preexisting condition plays a major role, the legal issues could occur in any kind of case where evidence fails to show causation more probably than not."); Wolf et al., *supra* note 6, at 371–72 (noting that loss of a chance "can be applied more broadly" and that "[a] number of courts have used the doctrine to allow recovery for 'failure to protect a person from a pre-existing condition'" (quoting Restatement (Third) of Torts § 26 (2005); Fischer, *supra* note 164, at 610)).
167. *Matsuyama*, 890 N.E.2d at 834–35.
168. *See id.* at 835.
169. *See id.*
170. *See id.*
171. Restatement (Third) of Torts § 26 cmt. n (2010).
172. *See, e.g.*, *Matsuyama*, 890 N.E.2d at 826 ("Finkel told the jury that if Birnbaum had ordered the appropriate testing on Matsuyama in 1995, the cancer 'would have been diagnosed' and 'treated in a timely fashion when it might still have been curable.' As a result of Birnbaum's failure to make a timely diagnosis, Finkel opined, the cancer metastasized to an advanced, inoperable phase, resulting in Matsuyama's premature death.").
173. *See* Dobbs, Hayden & Bublick, *supra* note 99, § 125.
174. *See, e.g.*, *id.* § 159.
175. *See, e.g.*, *id.* § 120 ("A third characteristic of negligence cases can be seen in the rule that no claim for negligence will be recognized unless the plaintiff suffers actual harm.").
176. *See, e.g.*, Pipe v. Hamilton, 56 P.3d 823, 827 (Kan. 2002) ("The proportional damage approach ensures that a plaintiff recovers only the loss attributable to the loss of chance and not for an arbitrary amount awarded by the jury or for the total damages sustained."); Dobbs, Hayden & Bublick, *supra* note 99, § 196 ("Under the value of the chance rule, the plaintiff recovers, but only an amount representing the value of the chance destroyed by the defendant's negligence.").
177. *See* Sawlani v. Mills, 830 N.E.2d 932, 947 (Ind. Ct. App. 2005). An interesting caveat in the research context is that had the participant never enrolled in research and never had his whole genome sequenced, he would be unlikely to have learned about his predisposition, potentially negating a claim that he lost a chance to prevent a harm.
178. *See* Dobbs, Hayden & Bublick, *supra* note 99, § 196; King, *supra* note 157, at 1356 ("Valuation is animated by a premise similar to that underlying causation: that a tortfeasor should be charged only with the value of the interest he destroyed. In determining what that value is, the preinjury condition of the victim should be taken into account.").

179. *See, e.g.*, *id.* § 190 ("The specific act of negligence claimed by the plaintiff largely determines the hypothetical alternative conduct to be compared. If the plaintiff alleges that the defendant failed to keep a proper lookout, the hypothetical alternative case to be considered is one in which the defendant does keep a proper lookout and the question becomes whether, had he done so, he would have avoided injuring the plaintiff.").
180. *See, e.g.*, *id.* § 10.
181. *See, e.g.*, *id.* § 10.
182. *See, e.g.*, *id.* § 11.
183. *See, e.g.*, *id.* § 11.
184. *See, e.g.*, *id.* § 11.
185. *See, e.g.*, *id.* § 10 ("The first bases tort law on moral responsibility or at least on some idea that the defendant has in some important way wronged the plaintiff.").
186. *See, e.g.*, Wolf, *supra* note 12, at 439 ("[N]either the law of research nor the law of clinical care is fully adequate to govern what is in essence a problem about the translational process of moving research-derived information into the domain of clinical care. We need to develop law that is appropriate for this translational science process. This is a substantial challenge. We need to seize the opportunity afforded by these early days of debate to shape and develop law in a way that will support sound and sustainable answers.").
187. *See, e.g.*, Wolf, *supra* note 12, at 439 ("Where law threatens to derail sound research or clinical practice or the translational process between them, it offers answers that are difficult to defend and sustain. Law should ultimately support sound resolution of the issues surrounding return of results and incidental findings.").
188. This Article is not the first to suggest a clearer, more consistent standard. *See, e.g.*, Sharp, Richard R.; Foster, Morris W. Clinical Utility and Full Disclosure of Genetic Results to Research Participants. Am J Bioethics. Nov-Dec;2006 :42, 43. (proposing several approaches to standardize the return of IFs, including making "determinations on a case-by-case basis according to the researcher's assessment of the pertinent values at stake (the current default position)").
189. *See, e.g.*, Fabsitz et al., *supra* note 33, at 576 ("Researchers should consider prospectively whether their study has potential to yield individual research results of clinical importance and describe plans for [returning results] in consent forms and processes."); Parker, *supra* note 28, at 348 ("The nature and probability of generating these types of findings should be disclosed to prospective subjects during informed consent, along with plans for their management, including plans for disclosure or nondisclosure, recording, and privacy protection."); Rothstein, *supra* note 72, at 21 ("Disclosure options should be selected by research subjects before the research begins, rather than by investigators after a research finding."); Wolf et al., *supra* note 6, at 378 ("The pathway for handling IFs, including expert consultation when needed, should be explained in the informed consent process. Researchers should clarify for participants the level of review that IFs will receive, so that participants do not mistakenly rely on the belief that more work-up will be provided than the research protocol actually calls for.").
190. Some have suggested that delineating at the outset which IFs will be returned is a means of contracting around liability that may violate the federal regulations governing research—regulations that specify that research participants not be made to waive liability. *See* Gordon, *supra* note 21, at 255 ("One plausible approach to the threat of liability is to attempt to contract around the duty to disclose. In practice, this could be accomplished by inserting language into the informed consent document stipulating that individual research findings will not be returned to subjects under any circumstances."); Wolf et al., *supra* note 6, at 367–68 ("This would seem to raise questions about consent forms that disclaim any researcher or institutional responsibility for managing IFs and include language claiming to immunize researchers or their institution from any legal consequences or liability for failing to warn research participants of IFs with serious clinical implications."). Still others have expressed the idea that such disclaimers may be struck down as unconscionable or void as against public policy. *See, e.g.*, Gordon, *supra* note 21, at 257 ("The point is not that courts will necessarily choose, on a regular basis, to invalidate or disregard provisions in informed consent forms that purport to relieve an investigator of the duty to disclose clinically useful individual research findings to her subjects. It is merely that there are

plausible reasons why some courts might choose to do so."); Ram, *supra* note 96, at 164–65 ("Even if a court were willing to recognize an informed consent document as some form of a contract, this contract might be unenforceable or invalid . . . as against public policy."). These concerns about unconscionability and waivers of liability are particularly pertinent with regard to contract claims, but are less so in the realm of tort law where these statements provide evidence of the duty owed rather than of liability more generally.

191. *See, e.g.*, Meltzer, *supra* note 110, at 28 ("Investigators best respect participants as persons when they disclose the terms of the research and allow people to choose whether to enroll.").
192. *See, e.g.*, Parker, *supra* note 28, at 342 ("In clinical care, for example, genetic counselors and clinics have established policies regarding the management of misattributed parentage and other IFs. Prior to testing, as part of the informed consent process, they typically disclose the possibility of discovering such an IF and state—or negotiate—whether and to whom such findings will be disclosed, as well as whether and where they will be recorded.").
193. *See, e.g.*, Stanley v. McCarver, 92 P.3d 849, 855 (Ariz. 2004) ("Finally, we note that doctors may deal with this issue as a matter of contract. They may, for example, require x-ray subjects to consent to having the results reported only to the employers.").
194. *See generally* Beskow & Burke, *supra* note 29.
195. *See, e.g.*, Cho, *supra* note 9, at 282 ("In genomic and genetic research, it is common for scientists to conduct research on samples from human subjects with whom the researchers have had no contact."); Wolf et al., *supra* note 6, at 364 ("In large-scale research on big datasets (whether those datasets aggregate genomic or imaging data), many commentators argue that researchers cannot track huge numbers of participants, cannot locate them reliably over time, and have no budget to report information back to participants, much less offer genetic counseling or follow-up.").
196. *See* sources cited *supra* note 61.
197. *See* sources cited *supra* note 61.
198. *See, e.g.*, Bredenoord et al., *supra* note 29, at 43.
199. *See supra* Part II.
200. *See, e.g.*, Beskow & Burke, *supra* note 29, at 2 (noting that some have suggested that "the failure to return clinically meaningful research results to individuals 'seems, at least in extreme situations, immoral, possibly illegal, and certainly unwise'" (quoting Henry T. Greely, *The Uneasy Ethical and Legal Underpinnings of Large-Scale Genomic Biobanks*, 8 Ann. Rev. Genomics & Hum. Genetics 343, 359 (2007))); Bredenoord et al., *supra* note 29, at 42 ("At one end of the spectrum it is argued that no individual genetic research results should be disclosed whatsoever. This, however, is an exceptional position, because only one publication adhered strictly to a 'no disclosure at all' policy, even of life-saving information—and this article was restricted to biobank research."); Sharp & Foster, *supra* note 188, at 43 (calling an approach of not returning any results "the default position of many studies" and "deficient for several reasons").
201. *See, e.g.*, Wolf, *supra* note 12, at 444 ("Indeed, it has become hard to find participants in the return of results debate who maintain that no individual results or findings should ever be returned, no matter how clinically urgent the information.").
202. *See, e.g.*, Cho, *supra* note 9, at 282 ("In genomic and genetic research, it is common for scientists to conduct research on samples from human subjects with whom the researchers have had no contact."); Wolf et al., *supra* note 6, at 364 ("In addition, researchers analyzing archived data may, in fact, be secondary users who did not collect the data and never had direct contact with the research participants, but retrieved the data from a databank or data repository.").
203. *See, e.g.*, McGuire, Caulfield & Cho, *supra* note 72, at 153 ("First, what kind of data should be provided to research participants? Should participants simply be given their raw sequence data? For most individuals, this form will be meaningless.").
204. *See, e.g.*, Wolf, *supra* note 12, at 445 (noting that "it is also increasingly difficult to find commentators who argue for conveying all information derived in the research sphere, at least at this juncture").
205. *See, e.g.*, Presidential Comm'n, *supra* note 16, at 59; Kayte Spector-Bagdady & Elizabeth R. Pike, *Consuming Genomics: Regulating Direct-to-Consumer Genetic and Genomic Information*,

92 Neb. L. Rev. (forthcoming Jan. 2014), *available at* http://papers.ssrn.com/sol3/papers.cfm?abstract_id=2343723 (discussing the emergence and significance of genomic interpretation services).

206. *See, e.g.*, Beskow & Burke, *supra* note 29, at 1 ("Adding to the policy debate is a growing body of evidence documenting participants' interest in receiving results."); Kaufman et al., *supra* note 30, at 835 (finding that over ninety percent of participants wanted their individual research results about health risks "even if there was nothing [they] could do about them") (alteration in original).
207. *See, e.g.*, Wolf, *supra* note 12, at 445 ("Too much of that information still remains uncertain and even mistaken, to dump it all on research participants.").
208. *See, e.g.*, Gliwa & Berkman, *supra* note 20, at 33 ("A number of groups have recently discussed the possibility of building standard lists of variants that could or should be disclosed as incidental findings."); Green et al., *supra* note 41, at 569.
209. *See, e.g.*, Gliwa & Berkman, *supra* note 20, at 40 ("[R]esearchers are regularly discovering new variants—one estimate puts the number of total known variants growing from around 120,000 in 2012 to 150,000 in 2015—and it is likely that a significant portion of these will meet a threshold for disclosure."); Ravitsky & Wilfond, *supra* note 24, at 11("[M]any reported associations are not robust: a comprehensive review showed that of 166 putative associations that have been studied three or more times, only six have been consistently replicated.").
210. *See* Green et al., *supra* note 41, at 570–71 tbl.1.
211. *See, e.g.*, Fabsitz et al., *supra* note 33, at 577 ("Having a central body generate guidance on what is reportable in genetic studies would provide an opportunity for broad stakeholder input, allow a more consistent approach across research studies, and provide credible guidance for researchers and IRBs.").
212. *See, e.g.*, Gliwa & Berkman, *supra* note 20, at 32–33.
213. *See id.* at 38 ("[L]ooking for the variants on the list *could* be as easy as pushing a button to activate a standardized analytic tool. In this case, the burden of looking would be significantly reduced . . . . ") (internal quotation marks omitted).
214. *See id.* at 38 ("[S]ome experts have recently been discussing the possibility of creating an authoritative list of variants that should be disclosed. There are active processes moving toward this goal, including conferences and surveys of experts seeking agreement.").
215. *See id.* at 36 ("[E]xperts can agree on only a handful of variants that should be routinely disclosed. One study found that 100% of genetic specialists were in agreement in favor of disclosing to adults 21 conditions or genes classified as 'known pathogenic mutations' . . . .").
216. *See, e.g.*, Cho, *supra* note 9, at 283 ("Reanalysis . . . raises the issue of how long the duty persists to report findings after samples are collected or data are generated. DNA data may be analyzed long after they are collected, and as our understanding of pleiotropy, gene-gene, and gene-environment interaction grows, the same data may have different meaning with time.").
217. Green, *supra* note 41, at 569 ("There is an active debate about the return of incidental findings in genomic research, and recommendations for this setting are evolving. Although we hope that investigators find our process and these recommendations useful in their attempts to design thresholds and lists for the return of genomic findings to research participants, we did not design this list for that purpose.").
218. *See supra* section I.B.
219. *See* 45 C.F.R. § 46.107 (2012). The Common Rule specifies the composition of IRBs and the criteria that must be used in reviewing research protocols.
220. *See supra* section I.B.
221. *See, e.g.*, Dobbs, Hayden & Bublick, *supra* note 99, § 410 ("The general rule that undertakings can create a duty of care is often expressed by saying one who voluntarily assumes a duty must then perform that duty with reasonable care.").
222. *See, e.g.*, *id.* § 410 ("[T]he plaintiff must show reliance upon the defendant's undertaking or assumed duty. Reliance shows that the defendant's failure to live up to his undertaking was a cause in fact of the plaintiff's harm.").
223. *See supra* section II.A.1.

224. One ethically permissible way that researchers could provide more than is strictly required is to have researchers return IFs consistent with participant preferences. This could be accomplished either through a process of informed disclosure of potential IFs or through ascertaining participant preferences at the outset. The process of informed disclosure entails notifying all research participants of the range of IFs—from a predisposition to Alzheimer's disease to a propensity for developing breast cancer—that were discovered among all research participants and inviting participants to get in touch with the researchers if they would like to have their individual IFs returned to them. A second approach would involve obtaining participant preferences at the outset of research, allowing participants to make known to researchers the particular types of results they would like to have returned to them. Under this approach, participants would be able to specify, for example, that they would like to learn about a predisposition to harm from certain kinds of anesthesia but would not like to know about a predisposition to Alzheimer's disease. Although these approaches may lead to an ethically sound policy for returning results, they remove researchers from the safety of a clearly stated and articulable approach to returning IFs.

225. *See supra* Part III.

226. *See, e.g.*, Collins et al., *supra* note 4, at 841–42; Morozova & Marra, *supra* note 4, at 257–58.

227. We acknowledge that open questions remain about the possibility of IRB exposure to liability. Nothing discussed here is meant to suggest an argument for such an outcome, but a full discussion of this topic is beyond the scope of this Article.

228. *See supra* Part I.

229. *See supra* Part II.

230. *See, e.g.*, Grimes v. Kennedy Krieger Inst., Inc., 782 A.2d 807, 838 (Md. 2001) ("The experiment is driven by the investigator's dedication to the advancement of knowledge . . . ; it is also driven by society's interest in future benefits that will flow from medical discoveries."); Belmont Report, *supra* note 39, at 23,193 ("'[R]esearch' designates an activity designed to test an hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge.").