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# The Fiduciary Relationship Model for Managing Clinical Genomic "Incidental" Findings

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## I. Introduction

The physician-patient relationship has a long history and is rich in deeply held traditions, yet it is one of the principal destinations for many of society's most innovative technological advances. The implementation of scientific innovations, such as genomic sequencing, forces the physician-patient relationship to continuously confront difficult ethical and legal dilemmas. The way the physician-patient relationship responds to the implementation of genomics is a crucial aspect of the success of these technologies as catalysts for the improvement of human health. Therefore, it is important to identify frameworks that can guide the sustainable implementation of genomics in clinical care. One promising alternative is to apply legal fiduciary principles to guide the generation, use, and handling of genomic information in the clinic.

Courts, legislatures, scholars, and medical organizations have applied fiduciary principles to define or describe different aspects of the physician-patient relationship. Recently, the American College of Medical Genetics and Genomics (ACMG) and the Presidential Commission for the Study of Bioethical Issues (PCSBI) released reports that refer to clinicians as fiduciaries when ordering genomic sequencing tests in clinical care.[1] However, in these reports the implications of applying fiduciary principles were often not made explicit, which can lead to uncertainty about how clinicians should act or some fiduciary principles were applied without considering others, which led to recommendations that are actually in conflict with the principles of fiduciary law.

This article examines the concept of fiduciary relationships as a framework for defining clinicians' duties and patients' rights when ordering whole genome/exome sequencing (WGS/WES) in the clinic and managing potential genomic "incidental"[2] or secondary target findings. In this context, the application of fiduciary principles (e.g., duty of loyalty, duty of care, duty to inform, and the duty act within the scope of authority), which have their origins in trust and agency law, gives rise to at least four specific clinician fiduciary duties.

These clinician fiduciary duties include the duty to: (1) provide material pretest information about secondary target genomic conditions that may be analyzed and reported when WGS/WES is ordered; (2) give patients the opportunity to opt-out of the analysis and report of any secondary target genomic condition; (3) offer WGS/WES and the examination of secondary target conditions, even if patients do not want all secondary target conditions examined; (4) respect patients' "right not to know" secondary target genomic information.

## II. Background and Problem

In the coming years massively parallel DNA-sequencing technologies (MPS) will revolutionize health care, and become a factor in many important personal and business decisions. We are already witnessing a rapid expansion of the applications of genetics in our lives. Companies are marketing direct-to-consumer genetic testing claiming to provide information about health risks and drug responses.[3] Oncologists are sequencing tumors to personalize cancer treatments.[4] Clinicians are offering genetic testing to assess an individual's risk for developing numerous diseases including Alzheimer's disease, Huntington's disease, breast and ovarian cancer, colon cancer, and different types of heart disease.[5]

Moreover, recent advances in MPS or next-generation sequencing technologies have decreased the cost of sequencing an individual's genome and increased the level of detail at which individual genomes can be examined.[6] These sequencing technologies are powering the application of genomics to new areas.[7] For example, they are leading to pushes for the creation of population-based preventive genomic screening programs for asymptomatic individuals.[8] They are facilitating the development of pharmacogenomics, which allows clinicians to prescribe drugs to patient subgroups based on their genetic profiles.[9] Likewise, MPS is driving the field of epigenetics, which is helping understand how genetic expression is regulated and influenced by environmental factors that precipitate or prevent disease.[10] Finally, MPS is currently also applied to perform WGS/WES in the clinic in order to identify if a patient's symptoms have a genetic origin, which can help guide patient care.[11]

All of these efforts are aimed at improving human health by realizing the promise of genomics and personalized medicine. Yet, these new technologies generate major ethical, legal, and social dilemmas that must be addressed so genomic sequencing technologies can be implemented in sustainable ways that are consistent with patients' rights. One key problem involves what kind of control individuals should have over their genomic information. Specifically, what kind of control should patients have over the type and amount of health risk information analyzed, reported, and disclosed when a clinician orders genomic sequencing in the clinic.

Every cell in the human body contains a copy of an individual's genome. Therefore, whenever clinicians order WGS/WES the patient's sample can potentially yield information about almost every genomic risk known. However, there are numerous reasons why a patient may just want to learn about some, but not all, genomic health risks. For instance, according to the U.S. Preventive Services Task Force, the net benefit of testing for some genetic conditions such as hereditary breast and ovarian cancer ranges from minimal to

potentially harmful for asymptomatic individuals that do not have a medical or family history of the disease.[12] Part of the concern is that there is a lack of research about how potentially harmful mutations are expressed in this population, therefore, if potentially harmful mutations are found in asymptomatic individuals this could generate anxiety and defensive medicine that can lead to unnecessary medical procedures, overtreatment, and iatrogenic effects.[13] Furthermore, individuals may be concerned about the way genomic risk information could seriously impact their ability to get, or pay for, life, disability or long-term care insurance, which are not protected by the Genetic Information Nondiscrimination Act (GINA).[14] Other individuals may simply not want to undergo the psychological burden of learning about these genomic risks.

There is a growing tradition of respect for patient autonomy that supports patients' right to refuse testing, analysis, report, and disclosure of medical information, and to control the information that is obtained from their bodies.[15] Nevertheless, protecting patients' autonomy rights can be a struggle amidst the enthusiasm to realize the promise of genomics. The influential ACMG has been at the forefront in attempting to regulate the implementation of genomic sequencing in the clinic. In 2013, the ACMG released recommendations that had important implications for defining the kind of control patients should have over what genomic information is analyzed and reported to their clinician when WGS/WES is ordered in the clinical care setting.

The 2013 ACMG report stated that regardless of patient preference, or the reasons for requesting the test, whenever WGS/WES is ordered for adults or children, the laboratory should report to the ordering clinician mutations found in 56 genes associated with 24 severe diseases for which "intervention may be possible."[16] This mandatory extended search recommendation for the ACMG's 56-gene panel would reveal risks for severe conditions such as: Romano-Ward Long QT syndrome and hypertrophic cardiomyopathy (both associated with risk of sudden death due to arrhythmia), familial hypercholesterolemia, hereditary breast and ovarian cancer, and colon cancer.[17] Furthermore, the ACMG report stated that regardless of patient preference, or the indication for which clinical sequencing was ordered, additional genes may be analyzed and reported if the laboratory deems it appropriate.[18]

The mandatory extended search recommendation was met with criticism. Commentators argued it transgressed patient autonomy rights and could be potentially harmful, particularly for asymptomatic individuals with no family history of the diseases associated with the ACMG's 56-gene panel.[19] The ACMG recognized that their recommendations "may be seen to violate existing ethical norms regarding the patient's autonomy and "right not to know" genetic risk information."[20] However, the ACMG argued that "clinicians and laboratory personnel have a *fiduciary duty to prevent harm* by warning patients and their families about certain incidental findings and that this principle supersedes concerns about autonomy."[21] Therefore, the ACMG used fiduciary principles (i.e., duty of care) to support its determination about clinicians' responsibilities towards patients in the clinical genomic sequencing context. Nevertheless, the ACMG did not address the role of other relevant fiduciary principles (e.g., duty of loyalty to the interests of the patient, duty to act within the scope of authority).

In 2014, the ACMG announced that it had changed its recommendation. It stated that patients should get the opportunity to decide whether they want all or none of the 24 secondary target genomic conditions on the ACMG 56-gene panel analyzed and reported (complete opt-out).[22] As discussed below, an alternative approach, more consistent with fiduciary principles, would have been to recommend that patients get the opportunity to selectively opt-out of the analysis and report of specific secondary target genomic conditions that are part of the ACMG 56-gene panel.[23] The ACMG did not elaborate on why it recommended a complete opt-out instead of a selective opt-out approach nor the role that their perspective on clinicians' fiduciary duties to patients played in this decision.

Similar to the ACMG's 2013 report, recently the PCSBI also used the idea of clinicians as fiduciaries to define clinicians' duties when managing genomic "incidental" or secondary findings. The PCSBI specifically stated that "[c]linicians should respect a patient's preference not to know about incidental or secondary findings to the extent consistent with the *clinician's fiduciary duty*."[24] However, the PCSBI report did not address in detail the implications of the clinician's fiduciary duty in this context.

If the idea of the clinician as a fiduciary of the patient is to be used to define clinician duties in the management of genomic information, it is important to examine the origin and implications of all relevant fiduciary principles. The following sections argue that a proper application of the principles of fiduciary law gives rise to at least four clinician fiduciary duties that apply to the management of potential "incidental" or secondary target findings when WGS/WES is ordered in the clinic.

## III. Clinicians as Fiduciaries

The term fiduciary relationship has evolved through the years.[25] Originally, the term was applied to describe the duties that trustees held towards beneficiaries. Generally, in a trust one party (the "settlor") creates a relationship with another (the "trustee") in which they agree that the trustee will manage a property for the benefit of a third party (the "beneficiary").[26] For example, an ill mother can establish a trust and agree to have a trustee manage her estate for the benefit of her children until they become adults. Given that the trustee has the authority to manage the property there is always the potential for abuse.[27] To avoid abuses of power, the law imposes on trustees a number of duties: be loyal, keep the settlor and beneficiary informed, act within the scope of authority, act "in good faith, with prudence," act "consistent with the purpose of the trust and the interests of the beneficiaries," and avoid acting based on self-interest.[28]

Courts, legislatures, and academics have found the concept of fiduciary relationships useful for defining the duties and responsibilities between parties in other contexts. Thus, the application of the term has expanded. Today, this term is applied to define the relationship between trustees and beneficiaries, agents and principals, attorneys and clients, physicians and patients, parents and children, employers and employees, executors and heirs, and directors and shareholders.[29] This has major legal implications for these relationships. Fiduciary relationships have common general principles, but the particular interests and

characteristics of the parties involved dictate the specific fiduciary duties that arise from each relationship.[30]

When determining the fiduciary duties between clinicians and patients, courts, legislatures, and the medical community have used the fiduciary laws of trust and agency as a model.[31] "Agency is the fiduciary relationship that arises when one person (a 'principal') manifests assent to another person (an 'agent') that the agent shall act on the principal's behalf and subject to the principal's control, and the agent manifests assent or otherwise consents so to act."[32] Some commentators argue that agency law, not trust law, is more directly applicable for determining clinicians' fiduciary duties to patients.[33] However, regardless of which body of law, trust or agency, is used to define clinicians' fiduciary duties the principles of fiduciary law establish that a clinician has a duty to respect a patient's self-determination in a way that precludes the unconsented analysis, report, and disclosure of secondary target genomic conditions.

## How Have Fiduciary Principles Been Applied to the Physician-Patient Relationship?

The defining characteristics of a fiduciary relationship are difficult to establish. However, fiduciary relationships are generally found to exist when one party allocates on another (the "fiduciary") the discretion to act on behalf of the party with respect to some critical resource, and there is an expectation that the fiduciary will be loyal to the interests of the party that allocated the discretion.[34]

The physician-patient relationship is fiduciary because when it is established, patients, implicitly or explicitly, allocate on clinicians discretion to act on patients' behalf with respect to their health. Furthermore, the asymmetry of power and medical knowledge between patients and clinicians places patients in a vulnerable position. This unequal condition, often exacerbated by patient anxiety, generates the potential for clinicians' misuse or abuse of their power.[35] Consequently, in order to protect patients there is a heightened ethical and legal expectation that clinicians should: be loyal to patients' interests, avoid acting in self-interest, keep patients informed, and act in good faith, within the scope of authority, and with utmost care in patients' best interest.[36]

The fiduciary nature of the physician-patient relationship is widely recognized by courts.[37] For instance, courts have stated that "[t]he relationship of patient and physician is a fiduciary one of the highest degree. It involves every element of trust, confidence and good faith."[38] Furthermore, "[t]he patient's reliance upon the physician is a trust of the kind which traditionally has exacted obligations beyond those associated with arms-length transactions. His dependence upon the physician for information affecting his well-being, in terms of contemplated treatment, is well-nigh abject."[39]

Courts have recognized that physicians owe a fiduciary duty to patients in specific aspects of the physician-patient relationship.[40] For example, in informed consent cases, courts have stated that there is a fiduciary "duty of reasonable disclosure of the choices with respect to proposed therapy and the dangers inherently and potentially involved."[41] In informed refusal cases courts have held: "the need for disclosure is not lessened because patients reject a recommended procedure. Such a decision does not alter what has been termed the 'fiducial

qualities' of the physician-patient relationship, since patients who reject a procedure are as unskilled in the medical sciences as those who consent."[42] Moreover, in confidentiality cases, courts have held that a breach of confidentiality is "not merely a broken contractual promise but a violation of a fiduciary responsibility to [the patient] implicit in and essential to the doctor-patient relation."[43] Lastly, disclosure of physicians' conflict of interests cases have held that "(1) a physician must disclose personal interests unrelated to the patient's health, whether research or economic, that may affect the physician's professional judgment; and (2) a physician's failure to disclose such interests may give rise to a cause of action for performing medical procedures without informed consent or breach of fiduciary duty."[44]

Finally, physicians themselves recognize that they are in a fiduciary relationship with patients. The American Medical Association refers to the physician-patient relationship as one that has the core characteristics of a fiduciary relationship: "[t]he relationship between patient and physician is based on trust and gives rise to physicians' ethical obligations to place patients' welfare above their own self-interest and above obligations to other groups, and to advocate for their patients' welfare …. Within the patient-physician relationship, a physician is ethically required to use sound medical judgment, holding the best interests of the patient as paramount."[45]

## IV. Implications of the Fiduciary Relationship Model for the Management of Genomic Secondary Targets

### (1) Clinicians have a fiduciary duty to provide material pretest information about the secondary target genomic conditions that may be analyzed and reported when WGS/WES is ordered

The 2013 ACMG report is not clear about what clinicians need to disclose concerning the secondary target conditions on the ACMG 56-gene panel. The ACMG report suggests that it is enough that clinicians discuss the possibility that genomic sequencing may yield "incidental" findings and make the patient aware that analyses will be performed to examine these.[46] A different ACMG report about informed consent in genomic sequencing also recommends that patients be informed of the "likelihood and type of incidental results that may be generated" and the "potential benefits and risks of [W]GS/[W]ES, the limitations of such testing, potential implications for family members, and alternatives to such testing."[47] However, the ACMG does not make clear recommendations about what information should be disclosed regarding the 24 secondary target conditions on the ACMG 56-gene panel during the informed consent process.

The ACMG report does argue that it would be impractical to obtain the same level of informed consent for primary and secondary target tests because it would require too much genetic counseling for patients.[48] Primary targets are genes related to the clinical purpose for ordering WGS/WES, while secondary targets are genes that are unrelated to the purpose for ordering WGS/WES, but the laboratory may still examine, such as the genes and conditions that are part of the ACMG 56-gene panel. Despite the logistical difficulties, fiduciary principles, ethical, and legal precedents of respect for patient autonomy suggest that patients should receive sufficient material information about all of the secondary target conditions or

about representative categories of the secondary target conditions that the laboratory will potentially analyze and report when WGS/WES is ordered. Patients need to know what they are being tested for in order to provide meaningful informed consent. Otherwise, clinicians would be breaching their fiduciary duty to inform patients.

Legal fiduciary principles suggest that a clinician has a duty to keep patients informed about material information that can affect their interests. Trust law states that trustees have the duty to disclose "material information needed by beneficiaries for the protection of their interests."[49] Meanwhile, agency law states that the fiduciary has the duty to disclose information the "agent knows, has reason to know, or should know … the principal would wish to have the facts or the facts are material to the agent's duties to the principal."[50]

The ACMG 56-gene panel would provide risk information about severe conditions such as hereditary breast and ovarian cancer, colon cancer, Romano-Ward Long QT syndrome, and familial hypercholesterolemia.[51] Predictive genes for these and other conditions are on the ACMG 56-gene panel because these are severe conditions for which, the ACMG argues, "penetrance may be high and intervention may be possible."[52] However, regardless of the potential benefits, finding and disclosing a potentially harmful mutation on any of the ACMG's proposed secondary targets could have substantial implications for patients' health, psychological, and economic interests. Therefore, it is essential that clinicians provide sufficient material information about these secondary targets so that patients can protect their interests by knowingly and intelligently consenting or refusing the examination of these genomic risks.

Information about secondary targets is highly material to protect patients' interests for three main reasons. First, patients need sufficient information about secondary targets to make an informed decision about whether the health benefits of testing outweigh the possible health-related harms. There are many potential benefits of testing for the ACMG 56-gene panel such as identifying and potentially preventing the development of a severe disease. However, there are also significant risks in consenting to the examination of the ACMG 56-gene panel. Many important questions remain about the potential harms of screening asymptomatic patients with no family history for the conditions on the ACMG 56-gene panel. For example, little is known about the penetrance (likelihood that potentially harmful mutations will lead to severe outcomes), the natural course from gene to disease, or the protective factors[53] that may shield an asymptomatic patient with a potentially harmful mutation in one of these 56 genes from developing the disease.[54] Because of these questions, commentators argue that examining the ACMG's list of 56 genes as secondary targets in patients that are asymptomatic or have no family history for the conditions associated with these genes can potentially lead to unnecessary medical procedures, overtreatment, and iatrogenic effects.[55]

Second, pretest information about secondary targets is material to allow patients' to protect their emotional interests. Patients need to make an informed decision about the possible psychological harms versus the health benefits of testing.[56] For example, it is material for patients' emotional interests to know that they will be tested for genomic mutations that can

predispose them to sudden death due to arrhythmia so that patients can determine if they believe it is in their best emotional interest to potentially learn about these genomic risks.[57]

Another key issue regarding patients' emotional interests is that many individuals will not have the economic resources, or health insurance, to cover the interventions available to prevent or minimize the poor health outcomes associated with secondary target conditions. Therefore, even if effective interventions are available, these patients will need sufficient material information about the risks and benefits of examining secondary target conditions to determine if the potential benefits of testing are worth the psychological burden of becoming a kind of "patient-in-waiting;"[58] knowing they have a potentially harmful mutation that has a high probability of a severe health outcome, but not having access to potentially beneficial interventions.

Third, patients should receive sufficient material pretest information about secondary targets to make an informed decision as to whether the benefits of testing outweigh the potential economic risks of a secondary target finding. Patients cannot control whether information about potentially harmful mutations found in secondary target genes is included in their medical record, and this can have a substantial impact on patients' economic interets.[59] It is generally up to clinicians to decide what is included in the medical record and their decisions are restricted by numerous ethical and legal obligations.[60]

Secondary target genomic risk information found in a patient's medical record can severely compromise a patient's ability to get life, disability, and long-term care insurance because GINA does not protect against genetic discrimination in these areas.[61] Most states do not offer such protection either.[62] This means that in most states, insurance companies can use secondary target genomic information found in patients' medical records to make determinations about eligibility, coverage, and rates for disability, life, and long-term care insurance. To try to mitigate this problem some commentators advocate that "[p]hysicians….consider suggesting that patients contemplate obtaining disability, life, or long-term care insurance before testing."[63] However, this may not be feasible for many patients who lack the economic means or those who urgently need their genomic sequencing results. Furthermore, GINA and state statutes, generally, do not offer protection against genetic discrimination for mortgages, commercial transactions and other uses of genomic information.[64] As the uses of genomic information continue to expand, inside and outside of the clinic, secondary target findings may also affect other aspects of patients' lives.[65]

Together, these arguments support the idea that pretest information about secondary targets is highly material to protect patients' health, emotional, and economic interests. Therefore, when clinicians order WGS/WES in the clinic they have a fiduciary duty to disclose material information about the risks and benefits of examining the secondary target conditions on the ACMG 56-gene panel.

**What Needs to Be Disclosed?—**A detailed analysis of what information should be disclosed to obtain legally valid informed consent that is consistent with fiduciary principles is beyond the scope of this article, but the reasonable patient standard of informed consent can offer guidance. The parameters of the reasonable patient standard of informed consent

closely resemble the fiduciary law's duty to inform. They both emphasize the materiality of information to the patient/beneficiary/principal. As stated above, from a trust and agency law perspective, a clinician, as a fiduciary, would have a duty to disclose "material information needed by [patients] for the protection of their interests"[66] or information the "[physician] knows, has reason to know, or should know … the [patient] would wish to have the facts or the facts are material to the [physician's] duties to the [patient]."[67] Similarly, under the reasonable patient standard, a risk is material and thus must be disclosed "when a reasonable person, in what the physician knows or should know to be the patient's position, would be likely to attach significance to the risk or cluster of risks in deciding whether or not to forego the proposed therapy."[68]

In order to obtain informed consent that is consistent with fiduciary principles, the clinician has the duty to inform those risks that a reasonable patient would consider material in making a decision about whether to consent to the sequencing, analysis, report, and disclosure of secondary targets. According to the reasonable patient standard the clinician has no duty to disclose risks that are remote, a person of average sophistication knows, or a patient has already discovered.[69] Furthermore, a clinician "need not make disclosure of risks when the patient requests that he not be so informed."[70]

Under a reasonable patient informed consent approach, an explanation of concepts such as incidental findings, secondary targets, penetrance, and actionability would likely constitute material information. Patients should also be informed that the examination of the ACMG 56-gene panel is unrelated to the clinical purpose for ordering WGS/WES and the clinician's policy as to whether to include any positive secondary target finding in the medical record. Information about alternatives to the examination of secondary targets and the implications of such examination for relatives would likely also be considered material to allow patients to make an informed decision.

Given the amount of conditions on the ACMG 56-gene panel and the time constraints that clinicians face in everyday practice, it may not be feasible to disclose material information about the risks and benefits for each of the 24 secondary target conditions. Nevertheless, there are ways to facilitate the informed consent process and still obtain consent that is consistent with fiduciary principles.[71] For example, the physician or a genetic counselor may disclose the material risks and benefits of examining representative categories of the 24 genomic conditions that compose the ACMG 56-gene panel. Under this approach clinicians would need to disclose the material risk and benefits of testing for each category. The disclosure process should include a description of each category and illustrative examples of the conditions that are part of each category. If feasible, clinicians should also provide written material information about each of the 24 genomic conditions. The representative category approach would facilitate the informed consent process, but still provide the patient with sufficient material information about the secondary target genomic conditions that may be examined. Finally, in order to facilitate the informed consent process and ease time pressures, clinicians could use decision aids as was recommended by the PCSBI,[72] and the medical community should look for ways to increase patient access to genetic counselors who could take care of the informed consent process and likely deliver this information in more effective ways given their expertise.

### (2) Clinicians have a fiduciary duty to give patients the opportunity to opt-out of the analysis and report of any secondary target genomic condition

One of the principal problems that fiduciary law tries to prevent is the misuse or abuse of power by the fiduciary.[73] Fiduciaries must have sufficient authority to help beneficiaries/principals, but they cannot misuse or abuse this power.[74] This is of concern particularly in fiduciary relationships such as the physician-patient relationship, in which the beneficiary/principal is at a marked disadvantage in terms of knowledge and power compared to the fiduciary. To promote the benefits of fiduciary relationships and minimize the possible misuses and abuses of power, the law creates a heightened expectation that the fiduciary, in this case the clinician, will act with utmost care, but also be loyal to the interests of their patients, and act within the scope of authority.[75]

Some could argue, as the ACMG suggests, that clinicians' fiduciary duty of care means that when ordering WGS/WES clinicians should also order the analysis and report of secondary target conditions that are believed to be in the best medical interest of the patient.[76] Nevertheless, to avoid potential misuses or abuses of power, fiduciary principles should not be considered in isolation. If the fiduciary duty of care is used to support a clinician's action, it is essential to consider the role of other fiduciary principles that apply in that context. In this case it is essential to also consider the role of the fiduciary duty of loyalty to the interests of the patient and the duty to act within the scope of authority.

In both trust and agency law, the fiduciary duty of loyalty implies that the fiduciary must not act in self-interest or in the interest of a party other than the beneficiary or principal.[77] The fiduciary duty of care and the duty of loyalty to the interests of the patient generally support the same course of action (e.g., the clinician believes that taking a particular medication is in the best interest of the patient and the patient agrees). However, loyalty to the interests of the patient may, at times, require acting in a way that is not consistent with what the clinician believes is in the best medical interest of the patient. Even if a clinician believes that examining secondary targets is in the best interest of the patient, for any number of reasons, patients may believe that examining particular secondary target conditions is not consistent with their interests. Competent patients have a broad legal right to decide for themselves whether they want to undergo particular medical interventions including tests, taking into account not just their medical interests, but also their values and overall interests (e.g., personal and familial medical, emotional, economic, and social interests).[78] As courts have stated, "If a right exists, it matters not what 'motivates' its exercise. We find nothing in the law to suggest the right to refuse medical treatment may be exercised only if the patient's motives meet someone else's approval."[79] Therefore, even if a clinician does not believe that the patient's determination is the best medical course of action, competent patients have a right to make determinations about which medical interventions they wish to undergo and loyalty to the interests of the patient would mean acting in a way that is respectful of these patients' expressed interests and determinations.

In fiduciary law, the fiduciary also has a duty to act within the scope of the authority provided by the settlor/principal. For example, agency law states that "[a]n agent has a duty to take action only within the scope of the agent's actual authority" and "to comply with all lawful instructions received from the principal and persons designated by the principal

concerning the agent's actions on behalf of the principal."[80] In trust law "[t]he trustee has a duty to administer the trust, diligently and in good faith, in accordance with the terms of the trust and applicable law."[81] This means that if clinicians are seen as fiduciaries, they must act within the scope of the authority and terms established by a competent patient. Although not always invoking fiduciary principles, the idea that clinicians must act within the scope of authority, has been reasserted many times in informed consent and right to refuse medical treatment cases.[82]

In sum, if only the clinicians' fiduciary duty of care is considered clinicians should, in theory, order the analysis of every secondary target condition they believe is in the best interest of the patient to examine, perhaps the entire ACMG 56-gene panel. However, when other relevant fiduciary principles are taken into account the analysis changes. Loyalty to the interest of the patient requires ordering the analysis and report of only those secondary target conditions that the patient judged to be in his or her best interest to examine. Furthermore, if a clinician were to order the analysis and report of secondary target conditions that the patient refused, this would constitute a misuse of power and a breach of the duty to act within the scope of authority. Therefore, fiduciary principles suggest that when clinicians recommend WGS/WES patients should have the opportunity to selectively opt-out of the analysis and report of any secondary target genomic condition that they judge not to be in their best interest to examine.

**Conflicting Fiduciary Principles—**As fiduciaries, clinicians owe patients a duty of care which encompasses a duty to prevent harm.[83] Consequently, even if there are other conflicting fiduciary principles, some may believe that refraining from ordering the analysis and report of actionable secondary target conditions would constitute a breach of clinicians' fiduciary duty to prevent harm.[84] Fiduciary law contemplates situations similar to this one in which there are conflicting applicable fiduciary duties (e.g., duty of care vs duty of loyalty and the duty to act within the scope of authority). Fiduciary law suggests that it is not a breach of fiduciary duty if a fiduciary acts according to a capable patient's wishes even if the act would otherwise constitute a breach of fiduciary duty.

For example, in trust law, if the settlor has capacity to act: "[t]he trustee has a duty to comply with a direction of the settlor even though the direction is contrary to … the trustee's normal fiduciary duties …."[85] Furthermore, in agency law the general fiduciary principle states that "[a]n agent has a fiduciary duty to act loyally for the principal's benefit in all maters connected with the agency relationship."[86] Yet, "[c]onduct by an agent that would otherwise constitute a breach of duty as stated … [in the general fiduciary principle] … does not constitute a breach of duty if the principal consents to the conduct."[87] Therefore, under fiduciary law, it is not a breach of the fiduciary duty to prevent harm to refrain from examining actionable secondary target genes if a competent patient validly refused the examination of these genes. It is important to note that valid refusal, like valid consent, requires that clinicians offer adequate disclosures, consistent with the doctrine of informed consent.[88]

### (3) Clinicians have a fiduciary duty to offer WGS/WES and the examination of actionable secondary target conditions, even if patients do not want all secondary target conditions examined

As stated above, the fiduciary has a duty of loyalty and care.[89] In trust law this means that "a trustee has a duty to administer the trust solely in the interest of the beneficiaries"[90] and "a duty to administer the trust, diligently and in good faith …."[91] In agency law "[a]n agent has a fiduciary duty to act loyally for the principal's benefit in all matters connected with the agency relationship"[92] and "a duty … to refrain from conduct that is likely to damage the principal's enterprise."[93] In both trust and agency law the duty of loyalty implies that the fiduciary must not act in the interest of a party other than the beneficiary or principal.[94] The American Medical Association's Code of Ethics also recognizes clinicians' duties of loyalty and care in the physician-patient relationship.[95]

Under the ACMG's mandatory extended search recommendation, patients for whom WGS/WES was medically indicated needed to agree to the analysis and report of the secondary targets on the ACMG 56-gene panel if they wanted to undergo WGS/WES.[96] This "all or nothing" recommendation was criticized by a number of commentators, including some who suggested it jeopardized the medical care of some patients.[97] The ACMG's mandatory extended search recommendation was inconsistent with the fiduciary duty of care because, in theory, it denied access to tests (WGS/WES) that were medically indicated to manage a patient's symptoms or disease, if the patient did not agree to the examination of potential genomic risks for secondary target conditions that were unrelated to the patient's medical needs. This recommendation was also in conflict with the clinician fiduciary duty of loyalty to those patients who believed that the analysis and report of WGS/WES primary targets, but not secondary targets, was consistent with their interests.

The ACMG's updated recommendation, the complete opt-out approach, is still not consistent with fiduciary principles because it offers another "all or nothing" choice that can be detrimental and against the overall interests of some patients. Under the ACMG's complete opt-out approach the ACMG recommends that clinicians offer patients the opportunity to opt-out of the entire ACMG 56-gene panel, the ACMG does not recommend that patients get to opt-out of specific secondary target conditions. This approach is inconsistent with the fiduciary duty of care because it would potentially deny—those patients who want to opt-out of the examination of some of the secondary target conditions on the ACMG 56-gene panel—the opportunity to examine other secondary targets on the ACMG 56-gene panel that the ACMG itself has recognized are likely to benefit patients and their relatives.[98] Furthermore, the complete opt-out recommendation is also inconsistent with the fiduciary duty of loyalty to the interests of the patient. If patients decide that for any number of personal reasons it is in their interest to examine some, but not all, of the secondary target conditions, then loyalty to the interests of the patients would demand that clinicians order the analysis and report of those secondary targets that are consistent with the expressed interests of the patients.

As suggested in the previous section, a selective opt-out approach would be more consistent with fiduciary principles. Under a selective opt-out approach clinicians would order the examination of those secondary target conditions that a competent patient determined to be

in line with his or her overall interests. A selective opt-out approach would not deny access to the examination of secondary target genomic information that the ACMG and clinicians may judge to be in the best medical interest of the patient. Furthermore, this approach helps prevent acts beyond the scope of authority because it would recommend that clinicians simply order the examination of those secondary target conditions for which the patient provided voluntary informed consent.

### (4) Clinicians have a fiduciary duty to respect patients' "right not to know" secondary target genomic information

The "right not to know" genomic information has been widely recognized.[99] UNESCO's Universal Declaration of Human Genome and Human Rights states that "[t]he right of each individual to decide whether or not to be informed of the results of genetic examination and the resulting consequences should be respected."[100] The "right not to know" genomic information is based on respect for patient autonomy and the notion that knowledge about genomic risks can significantly influence a person's acts and reproductive decisions.[101]

In the United States, a recent PCSBI report stated that "[c]linicians should respect a patient's preference not to know about incidental or secondary findings to the extent consistent with the *clinician's fiduciary duty*."[102] Fiduciary principles suggest that clinicians should respect patients' "right not to know" genomic information. Disclosing genomic information that the patient stated to not want to know would be an act beyond the scope of authority and contrary to the expressed interest of the patient, thus, also a violation of the duty of loyalty to the interests of the patient. In addition, these disclosures may be a violation of the duty of care because the patient may have decided he or she did not want to know this information to avoid some medical, psychological, economic, or social harm. Therefore, if fiduciary principles are applied to determine clinicians' duties in the clinical genomic sequencing context, clinicians have a fiduciary duty to respect patients' "right not to know" genomic information.

The ACMG's complete opt-out recommendation is more protective of patients' "right not to know" than the previous mandatory extended search recommendation. However, the complete opt-out approach is still not consistent with fiduciary principles and the "right not to know" in important scenarios. The complete opt-out approach offers sufficient protection for those patients that do not want to know the results of any secondary target condition because it allows them to opt-out of the analysis and report of the entire ACMG 56-gene panel. Nevertheless, the complete opt-out approach offers less protection for those patients who do not want to know the result of one or more particular secondary target conditions.

Under a complete opt-out approach, if patients do not want to know the result of a particular secondary target condition, they can consent to the analysis and report of the entire ACMG 56-gene panel, but request that their clinician does not disclose the result of that specific secondary target condition and thus, in theory, protect their "right not to know." This is the same argument that was used by supporters of the mandatory extended search recommendation to maintain that the analysis and report of the ACMG 56-gene panel, whenever a laboratory performs clinical WGS/WES, was consistent with patients' "right not to know."[103] The problem with this argument, as those critics of the mandatory extended

search maintained, is that it is "unrealistic" to "believe that a physician would or could withhold [genomic risk] information from a patient" once it is reported by the laboratory and included in the medical record.[104] Some clinicians may feel overwhelming psychological pressure to inform the patient given that secondary target findings could potentially help prevent or minimize health-related harms. Moreover, clinicians may feel legally obliged to disclose these findings, regardless of patients' preferences. For example, clinicians may be concerned about future malpractice claims for not warning patients about clinically useful findings that could help patients prevent or minimize the risk of poor health outcomes.[105]

Some could argue that clinicians can typically avoid any liability based on duty to warn by obtaining legally valid informed refusal for the disclosure of secondary target findings and ensuring that they have evidence to prove that the patient validly refused the disclosure.[106] However, even if clinicians follow all the proper procedures, this may not dissuade some patients, who later develop symptoms or disease associated with the undisclosed secondary target finding, from suing. Consequently, many clinicians may feel that, under the complete opt-out approach, once they receive a laboratory report with secondary target findings, in legal terms, the safest course of action is to disclose these findings to the patient, regardless of the patient's preference. In fact, medical commentators maintain that some physicians often "cite a legal canard that [n]o one has ever been successfully sued for erring on the side of preserving life, even in the face of patient refusal."[107] Additionally, some commentators and cases suggest that clinicians may have a legal duty to take "reasonable steps" to warn third parties, such as patients' relatives, about genetic disorders that could be a threat to them.[108] If this duty was recognized, patients' "right not to know" would be even more at risk under the complete opt-out recommendation because of how difficult it would be to keep a secondary target finding secret once patients' relatives are informed of their potential risk.

These complications suggest that a complete opt-out approach does not offer sufficient protection for the "right not to know." On the other hand, a selective opt-out approach would be more protective of patients' "right not to know," and it would be consistent with fiduciary principles (e.g., duty of loyalty, duty of care, and the duty to act within the scope of authority). Under the selective opt-out approach the laboratory would never analyze or report to the clinician the results of those secondary target genomic conditions that the patients refused to have examined after consulting with their clinician and considering their overall interests. This means that the secondary target genomic risk information the patient refused to have examined will never be reported to the clinician and the clinician would not have to face the emotional, ethical, and legal pressure of not disclosing this information. Likewise, because the secondary target genomic information the patient refused would never be analyzed or go into the medical record the selective opt-out approach eliminates the possibility of inadvertent disclosures by other health care providers who will have access to the medical records or if patients request access to their medical record for reasons unrelated to these secondary target findings.

## V. Conclusion

Advances in biotechnology will continue to generate numerous challenges for the physician-patient relationship. Identifying frameworks to guide the sustainable implementation of these technologies can help avoid endangering patients' rights and extemporaneous applications of technological innovations.[109] The fiduciary relationship model offers a promising framework for defining clinicians' duties in the genomic sequencing era.

The application of legal fiduciary principles (i.e., duty to inform) supports an informed consent process that is more comprehensive and patient-centered than what current proposals recommend for the examination of secondary target genomic conditions.[110] The fiduciary duty to inform suggests that before obtaining consent for the examination of secondary genomic targets, clinicians have a fiduciary duty to disclose any information about secondary targets that is material for the protection of patients' interests. As proposed above, one way to obtain informed consent that is consistent with fiduciary principles would be to apply the reasonable patient standard. Under this standard physicians or genetic counselors would have to disclose the risks and benefits that a reasonable patient would consider material when making a determination about whether to consent to the examination of secondary target conditions. If feasible, the material risks and benefits should be disclosed for each secondary target condition, but a representative category approach may be easier to implement and still allow for meaningful informed consent that is consistent with the fiduciary duty to inform.

Fiduciary principles (i.e., duty of care, duty of loyalty, the duty to act within the scope of authority, and the duty to comply with lawful directions of a competent patient even though it may be contrary to other fiduciary principles) support three other specific clinician fiduciary duties in the genomic sequencing context.[111] These specific clinician fiduciary duties include the duty to: give patients the opportunity to selectively opt-out of the examination of secondary target genomic conditions; offer patients WGS/WES and the analysis of actionable secondary targets, even if patients refuse the examination of some secondary target conditions and; respect patients' "right not to know" their genomic risk for particular secondary target conditions.

One way to promote that clinicians act in accordance with these specific clinician fiduciary duties would be to recommend a selective opt-out approach for the management of potential "incidental" or secondary target findings in genomic sequencing. Under a selective opt-out approach patients would be able to decide, in consultation with their clinician, and upon considering all of their relevant values, personal and familial interests, the examination of which, if any, genomic secondary target conditions would be in their best overall interest. Because the selective opt-out approach would recommend that clinicians order the analysis and report of those secondary targets that patients determined to be in their best interest, it would promote that clinicians act in a way that is loyal to the interests of their patients and within the scope of authority. Furthermore, under the selective opt-out approach clinicians would not deny access to potentially beneficial genomic risk information to patients who would like to exert their right to refuse the examination of a particular secondary target condition, therefore, clinicians would uphold their fiduciary duty of care.

In sum, the application of legal fiduciary principles yields recommendations for managing secondary target genomic information that, compared to current ACMG recommendations, are more consistent with patients' recognized rights to self-determination and control of information in the medical care context. The merits of the fiduciary relationship model should continue to be explored as a framework for the sustainable implementation of medical biotechnology into clinical care.

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92. Restatement (Third) Of Agency § 8.01 (2006).
93. Restatement (Third) Of Agency § 8.10 (2006).
94. Restatement (Third) Of Agency § 8.05 (2006); Restatement (Third) of Trusts § 78 (2007).

95. See AMA Ethics Opinion 10.015, *supra* note 45; American Medical Association Council on Ethical and Judicial Affairs. Code of Medical Ethics: Opinion 10.01: Fundamental Elements of the Patient-Physician Relationship. <http://www.ama-assn.org/ama/pub/physician-resources/medical-ethics/code-medical-ethics/opinion1001.page?> (last visited June 23, 2014)
96. See ACMG Report, *supra* note 1, at 568; Green et al., *supra* note 55; McGuire et al., *supra* note 55.
97. See Wolf et al., *supra* note 15, at 1049; Allyse and Michie, *supra* note 15, at 440.
98. See ACMG Report, *supra* note 1, at 567.
99. Universal Declaration Article 5, *supra* note 15; U.S. Task Force on Genetic Testing, *supra* note 15; PCSBI Report, *supra* note 1, at 64; Wolf et al., *supra* note 15, at 1049; Austl. Law Reform Comm'n, . Essentially Yours: The Protection of Human Genetic Information in Australia. ALRC Report 96. 2003; 360 available at <http://www.alrc.gov.au.libproxy.lib.unc.edu/sites/default/files/pdfs/publications/ALRC96_vol1.pdf> (last visited November 25, 2014). Andorno R. The Right Not to Know: An Autonomy-Based Approach. Journal of Medical Ethics. 2004; 30(5):435–439. [PubMed: 15467071]
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102. See PCSBI Report, *supra* note 1, at 64 (emphasis added).
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108. See *Safer v. Estate of Pack*, 677 A.2d 1188, 1192 (N.J. Super. Ct. App. Div. 1996); *Tarasoff v. Regents of the University of California*, 551 P.2d. 334 (Cal. 1976); Offit K, et al. The 'Duty to Warn' a Patient's Family Members About Hereditary Disease Risks. JAMA. 2004; 292(12): 1469–1473. [PubMed: 15383518] Clayton EW. Ethical, Legal, and Social Implications of Genomic Medicine. New England Journal of Medicine. 2003; 349(6):562–569. [PubMed: 12904522] , at 566.
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110. See Part IV, Section 1.
111. See Part IV, Sections 2–4.