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Automatic Placement of Genomic Research Results in Medical Records: Do Researchers Have a Duty? Should Participants Have a Choice?

Anya E.R. Prince, J.D., M.P.P,

Postdoctoral Research Associate at the Center for Genomics and Society at the University of North Carolina at Chapel Hill School of Medicine. Ms. Prince received her Juris Doctor and Masters of Public Policy from Georgetown University in Washington, D.C

John M. Conley, J.D., Ph.D,

William Rand Kenan, Jr. Professor of Law at the University of North Carolina, and an investigator in the university's Center for Genomics and Society. He received his A.B. from Harvard University in Cambridge, MA, and J.D. and Ph.D. (Anthropology) from Duke University in Durham, NC

Arlene M. Davis, J.D,

Research Associate Professor in the Department of Social Medicine at the University of North Carolina, core faculty in its Center for Bioethics, and Adjunct Associate Professor at the University of North Carolina School of Law. She received her Juris Doctor from the University of Washington School of Law, Seattle

Gabriel Lázaro-Muñoz, Ph.D., J.D., M.B.E, and

Postdoctoral Research Associate at the Center for Genomics and Society at the University of North Carolina School of Medicine. Dr. Lázaro-Muñoz received his Ph.D. in Neuroscience from New York University; his J.D. from the University of Pennsylvania School of Law; his Master of Bioethics degree from the Perelman School of Medicine at the University of Pennsylvania; and his B.A. from the University of Puerto Rico, Rio Piedras

R. Jean Cadigan, Ph.D

Research Assistant Professor in the Department of Social Medicine at the University of North Carolina. She received her Ph.D. in anthropology from the University of California, Los Angeles

I. Intro

The growing practice of returning individual results to research participants has revealed a variety of interpretations of the multiple and sometimes conflicting duties that researchers may owe to participants. One particularly difficult question is the nature and extent of a *researcher*'s duty to facilitate a participant's follow-up *clinical* care by placing research results in the participant's medical record. The question is especially difficult in the context of genomic research. Some recent genomic research studies — enrolling patients as participants — boldly address the question with protocols dictating that researchers place research results directly into study participants' existing medical records, without participant consent. Such privileging of researcher judgment over participant choice may be motivated by a desire to discharge a duty that researchers perceive themselves as owing to participants. However, the underlying ethical, professional, legal, and regulatory duties that would

compel or justify this action have not been fully explored. This paper is not an argument for or against including genomic information in an individual's medical record. Our purpose, rather, is to explore the specific question of who should decide whether to place genomic information generated in a research setting in a participant's medical record.

The medical record is often referred to as a singular entity, in effect giving the narratives, test results, measurements, and other documents that comprise it an elevated status and a life and agency of their own. However, there is no single medical record that travels with a person throughout his or her life and to all the various hospitals and facilities where he or she may receive care.[1] Instead, a medical record created in a particular setting — a clinic or hospital or other institution — will often be considered that provider's complete documentation regarding a patient under its care. It may include records from other institutions if the patient authorizes the transmittal. While there is increasing movement to create electronic medical records (EMRs) that are transferable between different facilities and systems, there is not yet any guarantee that patients' information will travel with them throughout their lives and on their various healthcare journeys. An overestimation of the uniformity, portability, and persistence of medical records may lead some researchers to also overestimate the legal and ethical duties surrounding the placement of information in those records.

In the body of this paper we explore what, if any, duties may justify a researcher's independent disclosure of the findings outside the research setting. Section II introduces the tensions between clinical and research ethics, especially in the context of the poorly described but currently ascendant field of research that "translates" genomic findings into clinical care and promotes the integration of results into medical records. Section III reviews past discourse regarding whether to return genomic research results and which results to return, as well as the still-evolving discussion regarding how to return results. Section IV presents ethical, professional, legal, and regulatory arguments for and against placement of results in medical records and brings these arguments to bear on researchers' perceptions of their duties to participants. We conclude that there is no clear ethical or legal duty for a researcher to place genomic research results in a medical record unless a participant requests its placement. On the contrary, we believe that providing participants with such a choice, while informing them of results and furnishing relevant medical recommendations and referral sources, will discharge any duty that researchers may owe.

II. Intersection of Clinical Care and Research Ethics

A. Ethics in Research and Clinical Care

Critical consideration of automatic placement of individual research results, both primary and incidental, in participants' medical records prompts an examination of the increasingly blurred line between clinical care and research. Individualized treatment is the fundamental difference between clinical care and the collection of generalizable data in the conduct of research. However, the general category of research with human subjects comprises a spectrum of possible interactions with participants, even if the intent to contribute to generalizable knowledge is the overarching goal. Consequently, the ethical duties that may arise in particular studies are highly context-sensitive.

Despite these complexities, clinicians and researchers have some common moral ground in their relationships with their respective patients and participants. First, while exceptions exist, both relationships are based upon consent. In addition, patient care and research share several guiding principles, such as respect for persons, beneficence, non-maleficence, and justice. Therefore, both realms seek to balance these principles by allowing autonomous individuals to govern their choices, while protecting vulnerable individuals; avoiding or mitigating harms; and ensuring fair treatment. These shared foundations are apparent to both clinicians and to researchers, though in slightly different ways. Clinicians are bound by ethical codes and their practice is overseen by state licensing boards. There is no similar state-regulated licensed practice of research, but researchers from widely different disciplines find related elements in their relevant ethical codes and in federal human subjects research regulations.

When a study is squarely aimed at generalizable knowledge, both clinician and non-clinician researchers may be comfortable with the idea that any responsibilities toward the participant can be discharged within the research relationship. This comfort may be reinforced by the emphasis on subject choice and voluntary participation in research relationships. For example, researchers have historically disclosed clinically relevant results and provided referrals directly to participants without breaching the confidentiality of the research relationship by directly informing clinicians of results.[2]

Research guidance, such as the Belmont Report and the Common Rule, does not mandate confidentiality, yet many researchers promise confidentiality in order to respect participants and minimize harms that might result from disclosure of sensitive or personal information.[3] Some studies go so far as to secure a Certificate of Confidentiality, which provides assurances to participants that researchers will not have to disclose identifiable research information in response to legal demands.[4] If researchers have promised confidentiality to participants, then disclosure of research information to those outside of the study, including by placing information in a medical record, could be a violation of this promise. Although the clinical and medical records realms have privacy protections under the Health Insurance Portability and Accountability Act (HIPAA), these protections allow for many more disclosures of health information than the typical research consent.[5]

But when the research involves the prospect of direct health benefit to an individual who is both a subject and a patient, both clinician and non-clinician researchers may decide that further steps are necessary to discharge their respective duties. In such a context, a clinician-researcher may subordinate his or her research role to that of clinician. Given the potential involvement of professional obligations, a clinician-researcher's perceived duty to include research data in the medical record may be accorded great weight. However, *all* decisions to breach the confidentiality of the research data — in this case by placement of the results outside the protections of the study — must still be interrogated under the core principles fundamental to the conduct of all human subjects research. While arguments for particular actions by researchers may grow stronger when research results could have direct benefit to the participant, it is not clear that those arguments should ever overcome the preferences of the participant.

The blurring of research and clinical care also raises concerns of therapeutic misconception. Therapeutic misconception occurs when research participants inaccurately understand the distinctions between research and clinical care and believe that researchers are acting in the participant's best medical interests rather than seeking generalizable knowledge.[6] Therapeutic misconception is a threat not only to participants, but to investigators as well.[7] If returning results in and of itself may lead to therapeutic misconception, placing the results directly into a medical record can only add to this confusion. While it may be possible to clearly explain the demarcation between receiving results *in research* that may need to be followed-up *in clinical care*,[8] it is much more difficult to explain the distinction when the *research* team is reaching across the boundary and placing results in a *clinical* medical record.

B. Translational Genomic Research

The National Human Genome Research Institute (NHGRI) has recently shifted its focus toward translational genomics research. In 2011, Eric Green and Mark Guyer mapped the goals of genomic research for NHGRI, with a strong focus on translating basic genomic research to clinical care — from bench to bedside.[9] Accordingly, many recent studies have been designed as research with clinically beneficial elements, and therefore implicate some of the tensions between clinical and research ethics discussed above.

NHGRI recently established two broad grant funding categories that specifically focus on the clinical applications of genomics. Announced in 2007, the Electronic Medical Records and Genomics (eMERGE) Network is comprised of nine funded studies aimed at merging DNA biorepositories with EMRs.[10] A primary goal of the eMERGE project is to "explore the best avenues to incorporate genetic variants into EMR for use in clinical care such as improvement of genetic risk assessment, prevention, diagnosis, treatment, and/or accessibility of genomic medicine."[11] A second NHGRI grant program, the Clinical Sequencing Exploratory Research (CSER) program, began in 2010 with the goal of supporting "both the methods development needed to integrate sequencing into the clinic and the ethical, legal, and psychosocial research required to responsibly apply personal genomic sequence data to medical care."[12] There are currently eight funded CSER projects and nine funded sub-projects within the CSER grant program that explore ethical, legal, and social implications of return of results.[13]

The eMERGE and CSER projects blur the lines between clinical care and research, with both consortiums heavily focused on patients, medical records, and genomics. The eMERGE Network research compares genomic variants with existing phenotypic information in individual medical records to understand the genetic bases of disease and analyzes how to incorporate the genetic variants back into a patient's EMR.[14] The 2010 CSER application instructions specifically called for a detailed plan of how individual genomic research results generated in studies of patients as participants could be incorporated into their medical records.[15] The funded projects have varied in their approach to this mandate, although only the CSER at University of North Carolina at Chapel Hill permits participants to decide whether or not their results are placed into their medical records.[16] Given the size and broad scope of the eMERGE and CSER networks, future

research projects of all kinds may look to these studies for research standards, especially regarding medical records. Their prominence may prove problematic unless careful attention is given to the trend toward automatic placement and the implications this may bring.

II. Historical Arc of Return of Genomic Research Results

A. Whether to Return Results and Which to Return

Historically, prevailing research standards barred participant access to either individual or aggregate research findings;[17] however, over the past two decades, this strong stance has softened. There is now a consensus that *aggregate* results should be made available to participants in all research.[18] The position on return of *individual* research results has also evolved, from non-return to a return only in exceptional circumstances[19] to, in the case of genomic research, a consensus on return of clinically valid and medically actionable results that could develop into a standard of care.[20]

Once a consensus emerged that some research results should be returned, or at least offered, to participants, considerations turned to determining which results to return. Whole-exome sequencing provides data for over 20,000 genes, leading to an overwhelming amount of potential returnable information.[21] This information can range from raw genomic data to interpreted results. The interpreted results can provide information about variants associated with serious diseases, such as cancer and Alzheimer's, or with innocuous traits, such as the ability to roll one's tongue. Sequencing analysis can also identify variants of uncertain significance (VUS), alterations that are not yet known to be deleterious or benign, in genes associated with specific diseases. A genomics study may be designed to explore a very specific problem or genetic variant — the primary finding — but sequencing can produce additional findings not related to the object of the study but discovered during the course of the research — incidental findings.[22] In many cases, the determination of whether a variant is pathogenic, of unknown significance, or benign cannot be adjudicated solely by computer analytics, but requires human interpretation of how a novel variant fits into evolving genotypic and phenotypic knowledge.[23]

The decision to return particular research findings to participants typically hinges on three interpretive factors: analytic validity, clinical validity, and medical actionability.[24] Analytic and clinical validity refer, respectively, to the accuracy of the test — that is, does it accurately report the DNA sequence — and the ability of the sequencing to identify a clinical condition or predisposition.[25] Medical actionability, or clinical utility, generally is dependent upon whether the genetic test result can inform treatment decisions or provide opportunities for disease prevention.[26] A growing consensus argues that medically actionable results should be offered to participants and that researchers have discretion to offer a broader range of results, such as those without clinical utility or VUSs.[27]

However, while many agree that medically actionable results should be returned, the definition of medical actionability is not universally agreed-upon.[28] Additionally, results pertaining to non-treatable diseases may be relevant to some people or important for reproductive decision-making.[29] Studies have documented that individuals may be interested in receiving research results for reasons beyond medical actionability, such as

personal or reproductive utility.[30] Some researchers have agreed that participants should be able to receive research results that are personally meaningful, even if not clinically relevant,[31] and that keeping non-clinically useful results from participants may disrespect their right to decide for themselves what information they want to learn.[32] Nonetheless, the majority of recommendations regarding returning research results currently focus only on medical actionability, narrowly defined in terms of utility in treatment or prevention.[33]

Generally, variants are described dichotomously as medically actionable or not. This characterization is typically based on broad variant and population information, not on an individualized assessment of age, circumstances, and values. Some studies do take individual factors into account when determining which results to return,[34] but others may decide to return a certain set of "medically actionable" variants to the entire research population regardless of individual characteristics. However, these characteristics will often alter the practical utility of the available interventions. Although a genetic variant may be associated with a medically actionable condition, the condition will not have the same temporality for all individuals tested. For example, a child or young adult tested for a variant associated with an adult-onset condition or an elderly adult tested for a variant associated with phenotypes that typically appear in a person's forties or fifties may not have any appropriate clinical actions available, even though the condition is medically actionable in the abstract.

C. How to Return Results

Although there has been much discussion regarding the *whether* and *which* questions of returning individual research results to participants, the discussion regarding *how* to return the results has been more limited. Past genomic studies have varied greatly in the design of return of results. Along the continuum from providing research results without counseling to providing clinical care as part of the research design, there are many points where one could potentially draw the boundary of the researcher's duty. As part of answering the *how* question, researchers must also decide *who* should give results (specifically, whether they should be delivered by a genetic counselor or other genetics professional) and *to whom* the information should be given (that is, whether family members should also receive information about or be tested for potentially clinically relevant variants).

In the most limited view of a researcher's duty, a researcher can simply provide the participant with results in the form of a letter. However, commentators have argued that this approach may be both ethically and legally inadequate and that researchers are obligated to make some effort to convey the clinical importance of the results and to refer for appropriate follow-up care.[35] That raises the further question of what researchers must do to satisfy this obligation. The possibilities include providing a list of resources for a participant's own follow up, giving a referral to a provider, actually securing a follow-up appointment for the participant with that provider, or even paying for or providing follow-up care through the researcher's study.[36] The translational goals of current genomic research, the prospect of benefit to research participants, and the involvement of clinician-researchers inform much of the ongoing discussions about offering results, making appropriate referrals, and extending a

study design beyond the research relationship. What, however, is the appropriate limit of the researcher's duty? We turn next to the various dimensions of this question.

IV. Is There a Duty to Place Research Results in Medical Records?

If a researcher has a duty to refer participants to follow-up care that is medically recommended given certain genomic research findings, at what point has the researcher successfully discharged this duty? Specifically, does the discharge of this duty necessarily entail a medical record entry? If a participant, upon return of results from the researcher, objects to further disclosure of the results — such as by entry into a medical record — is there a duty that supports disregarding that preference? Would such a practice benefit research participants? Could it cause undue harms? And could anyone but a licensed clinician place a finding into a medical record? In this section, we explore the ethical, professional, legal, and regulatory duties that are at work when determining whether researchers should place study results in participants' medical records.

A. Ethical Duties

There are three guiding ethical principles in research that must be balanced in the determination of whether to place genomic research results in a participant's medical record without consent: respect for persons, of which respect for autonomy is a part, beneficence, and non-maleficence. A researcher may desire to place results, especially medically actionable results, in a medical record in order to discharge duties of beneficence and non-maleficence. Under this view, a researcher should promote medically advised interventions to prevent or mitigate potential disease and placement in the medical records will ostensibly help ensure this goal. However, respect for participant autonomy argues in favor of a research participant deciding whether research results are entered into their medical record. If a researcher decides that he or she knows what is best for the participant, disregarding the autonomous participant's preferences, then the resulting paternalistic placement of results in the medical record requires strong justification. Researchers may appeal to the importance of the results and the danger of possible participant inaction as justification. That is, they may believe that the importance of the research result cannot otherwise be conveyed sufficiently to propel the participant to seek follow-up care that the researcher views as essential.

Allowing participants to decide what to do with their research results may be alarming to researchers who believe that there is a single proper response for participants who receive medically actionable findings. While it is foreseeable that many participants will opt to place genomic research results in their medical record and choose to discuss the results with their physicians in order to begin the recommended follow-up, there are rational reasons why individuals may not do so. For example, some people may have concerns about how such information can affect eligibility for life, long-term care, or disability insurance;[37] they may be years or decades away from the point when clinical preventive measures would begin and wish to bring genomic information into the clinical realm only when clearly relevant; or they may wish to process the information or inform family members before devoting energy to deciding whether and how their clinical care should be affected.

Respect for autonomy is also the ethical principle underlying both a participant's right not to know research results and to withdraw from research. The implications of both of these rights argue against automatic placement of results in a medical record. A recent consensus statement by several researchers involved in the eMERGE and CSER projects — projects that, on the whole, automatically place research results into medical records — noted that "participants have a right to decline to receive genomic results, even when doing so may be viewed as a threat to the participant's health."[38] If respecting autonomy permits participants to opt out of receiving results, then a natural extension of that respect is allowing them to decide whether results are placed in the medical record, even if the researcher believes that not doing so may cause harm.

Participants also typically have a right to withdraw from research. Researchers must explain before participation begins how a participant could withdraw as well as any limitations on that right. The transfer of research findings into a medical record makes understanding the rights associated with withdrawal particularly important. Once the findings are entered into the record, the confidentiality of research data has been breached. These data now have their own life in a separate, clinical world, making *complete* withdrawal from the initial research difficult, if not impossible.[39]

Automatic placement of results into the medical record in order to discharge the researchers' duties of beneficence and non-maleficence is problematic for several reasons. First, participants' preferences about how to manage this information are ignored in favor of increasing the chances that an unknown physician will have access to the information in the future. In this way, the unknown physician is treated as a more reliable agent than the participant, presumably because of physicians' medical knowledge. However, a patient's physician may lack the knowledge needed to interpret genomic findings or provide appropriate follow-up care or may disagree with the findings' rele-vance.[40] Moreover, research results and their management impact not only participants' medical interests but also their familial, economic, emotional, and social interests.[41] Participants, not physicians, are in a better position to take all of these interests into account when determining how to manage their research findings. If participants were deemed competent enough to weigh the risks and benefits and provide informed consent to participate in the research study, they should be trusted to make determinations about how to manage the information that is generated about them.

Second, the EMR infrastructure is currently not configured to adequately sort and present the vast amounts of genomic data produced by whole genome and whole exome sequencing.[42] Many commentators are concerned that genomic research results that lack clinical validity or utility will end up in the medical record and cause misunderstanding and anxiety for the participants, or be misinterpreted by general practitioners not properly trained in genomic analysis.[43] Although many genomic research studies only return results with clinical validity and utility, this is not always the case and the situation may change in the future. Also, when sequencing is done in research, the lab may convey all information in a single report that mixes clinically valid with non-clinically valid results and contains VUSs. Therefore, it may be difficult in practice to prevent non-clinically actionable information from ending up in the medical record.

Finally, placement alone has no guaranteed impact on health. It is widely recognized that many physicians lack sufficient training to understand the clinical relevance of and properly interpret genomic information that may be in the medical record.[44] Placing research findings in a participant's medical record at the clinical institution where the research was conducted may be futile if the participant's physician is not associated with that institution or the participant does not intend to seek follow-up medical care there. Additionally, even if the individual desires follow-up care, there is no guarantee that an insurance company will reimburse the costs for preventive interventions, leaving some unable to pay for the recommended medical actions. Given the lack of a single medical record and limited physician training, it is problematic to rely heavily on the power of medical records as a repository for genetic risk and a guarantor of proper follow-up care.

A researcher's decision to place a *participant's* research results into a *patient's* medical record certainly does "translate" research into clinical care.[45] However, it does so dangerously, taking away the participant's ability to decide whether and when to move this information from the research to clinical realm. Even if most participants would likely agree with the researcher's views of appropriate next steps in clinical care, ethical considerations argue strongly for providing participants the choice for whether a researcher places results into the medical records.[46] Without such an option, researchers who are placing results in medical records are weighing beneficence over participant autonomy, but with little assurance of the beneficent results.

B. Professional Duties

The professional ethics guidelines of those who conduct genomic research might provide another source of relevant authority. In this context we mean "profession" in the narrow sense of an occupation that requires a high level of skill and, in consequence, is granted special privileges by the government, most importantly the power to control entry through licensing and the right and duty of self-regulation.[47] Professional self-regulation usually involves written ethical codes or rules, the violation of which can lead to discipline and even loss of license. Scientific researchers in general do not comprise a profession in this sense. However, members of other professions often participate in research, and are potentially bound by their respective professions' ethical rules when doing so. This is particularly true when, as in the case of genomic research, a project may have elements of both pure scientific research and clinical practice.

We analyzed the professional ethical codes of two licensed professions whose members regularly participate in genomic research: medicine and genetic counseling. These two groups of professionals often participate in ways that may put them in relationships with research participants that the professionals or the participants may perceive as clinical. In each case, we examined whether the respective profession's ethical rules impose or suggest an ethical duty to place genomic research results in the participant's medical record. If so, then these professionals would presumably have to draw a clearly defined line: I must put the results in the medical record, or risk professional sanctions. The consequence would be that these professionals could not participate in research unless the results were put in the medical record.

We find, however, that neither medicine nor genetic counseling appears to have a rule that deals with this question. In medicine, we began with the example of the rules prescribed in our own state of North Carolina by the state licensing agency, the North Carolina Medical Board.[48] These rules, which are incorporated into the North Carolina Administrative Code and thus have the force of law, do not mention anything related to either medical records or research; they deal for the most part with procedural and administrative issues. The Board also issues advisory "Position Statements" on a range of topics, including one on "Medical Record Documentation."[49] Position Statements such as this purport to "reflect commonly accepted standards" and "encourage" new developments — in this case "the trend towards the use of electronic medical records."[50] However, as with the North Carolina rules, this position statement says nothing that sheds any light on the question that this paper addresses.

In addition to mandatory rules issued by state medical boards, the American Medical Association's Code of Medical Ethics has, since the mid-1800s, provided a set of voluntary guidelines. The Code takes the form of an Introduction followed by sets of Opinions on nine general topics. Here again, nothing addresses, even indirectly, the question of a professional duty to place genomic research results in a medical record.

Opinion 2.07, "Clinical Investigation," does support the general premise that physicians participating in research are bound by medical ethics: "In conducting clinical investigation, the investigator should demonstrate the same concern and caution for the welfare, safety, and comfort of the person involved as is required of a physician who is furnishing medical care to a patient independent of any clinical investigation."[51] In the case of "clinical investigation primarily for treatment," "[t]he physician must recognize that the patient-physician relationship exists and that professional judgment and skill must be exercised in the best interest of the patient."[52] In a clinical investigation, primarily for treatment, then, there is no doubt that the research participant is a patient in a professional relationship with the physician-researcher. Even though the Opinion is silent on the point, it is possible that the physician-researcher would interpret his or her duty to the participant-patient as including a duty to place results in the medical record, especially if the rules of the physician's hospital or practice so required.

However, "[i]n clinical investigation primarily for the accumulation of scientific knowledge," — the principal focus of this paper — there is no reference to the existence of a physician-patient relationship, and the Opinion offers only a general statement of the applicable ethical standard:

> Adequate safeguards must be provided for the welfare, safety, and comfort of the subject. It is fundamental social policy that the advancement of scientific knowledge must always be secondary to primary concern for the individual.[53]

There is no suggestion about how to apply these general principles to the present question.

The same is true of Opinion 2.079, "Safeguards in the Use of DNA Databanks in Genomic Research." To the extent that this opinion is relevant at all, it might be read as according primacy to the privacy interest of the participant. Paragraph 3(a) provides: "Special emphasis should be placed on disclosing the specific standards of privacy contained in the

study: whether the material will be coded (ie: encrypted so that only the investigator can trace materials back to specific individuals) or be completely de-identified (ie: stripped of identifiers).”[54] This is complemented by paragraph (4), which provides: “To strengthen the protection of confidentiality, genomic research should not be conducted using information and samples that identify the individuals from whom they were obtained (ie: by name or social security number).”[55] Opinion 2.139, “Multiplex Genetic Testing,” also stresses potential harms to the patient from test results: “Multiplex testing and its resultant information may also have widespread societal implications that include discriminatory practices against not only individuals but specific ethnic groups that have been designated ‘at risk’ populations.”[56] Finally, Opinion 7.05, “Retention of Medical Records,” deals with several issues relating to the retention of records, but says or implies nothing about what should go into them.[57]

According to the National Society of Genetic Counselors, 15 states currently license genetic counseling as a profession, while licensure provisions are pending in four others.[58] By its own account, the NCGS is a voluntary organization that, among other activities, advocates for professional licensing; toward this end, it provides model legislation for state governments. The NCGS has issued a Code of Ethics.[59] Aside from being voluntary, it is purely aspirational, as each of its four sections begins, “genetic counselors strive to…” None of its provisions deal in any way with medical records. The only conceivably relevant provision, section II.4, stresses well-informed decisions by clients: “Enable their clients to make informed decisions, free of coercion, by providing or illuminating the necessary facts, and clarifying the alternatives and anticipated consequences.”[60] In fact, the very use of the word “client” suggests that a recipient of genetic counseling is something other than a traditional medical patient.

To summarize, the question of whether to place genomic research results into a participant’s medical record cannot be resolved by recourse to binding standards of professional responsibility. Such standards appear not to address this question at all, nor do they imply the correctness of any particular answer.

C. Legal Duties

Clinician-researchers are concerned not only with their ethical and professional duties, but also with whether they are opening themselves up to legal claims by failing to place research results in medical records. This concern leads to the question of whether the law creates a duty to place research results in a participant’s medical record. The current answer to that question is clearly *no:* at present, there is no statutory, regulatory, or case law that imposes such a duty on researchers. In fact, there is little or no scholarly writing that even debates the desirability or feasibility of such a duty on a theoretical level. However, as we discuss in this section, there is a substantial literature that addresses the related question of whether researchers have a legal duty to disclose medically actionable information to research participants, particularly incidental findings.

The putative duties to disclose to the participant and then to record in the medical record are related in that both would require a researcher first to recognize and then to respond to a research finding that could have significant health implications for the participant. The first

part of each duty — to *recognize* the finding — seems identical in the two instances. But the second or *response* part, the conduct that is sufficient and necessary to discharge the duty to recognize, is different. In the instance of a duty to disclose, the researcher must explain the finding to the participant; in the instance of a duty to record, the required response is to put a note in the medical record. Logically, a duty to place a finding in the medical record would strongly imply a duty to tell the participant. It would make little sense to record something that is material to the participant's current and future healthcare but not to tell the participant. This logic is less compelling in the opposite direction, however. As we have noted, there are many reasons that participants would desire disclosed results not to be recorded. Thus, the two formulations of the duty to respond will overlap in many cases, but by no means all. Nonetheless, the overlap is substantial enough that the duty to disclose literature, read against the background of some established principles of medical malpractice law, can inform how a duty to place research results in the medical record might evolve in the future.

It is already common practice to return primary research findings, so most literature discussing legal duties regarding return of results focus primarily on incidental findings. The literature on the return of incidental findings is, and has long been, unanimous on one point: there is "no explicit legal duty to disclose in the United States."[61] In fact, as one very recent review concludes, "There is no law or case law directly on point."[62]

Despite this lack of law, researchers continue to worry about the possibility of legal liability.[63] Those who worry about possible legal liability tend to start, as we do, with a presumed ethical consensus to offer to return some findings.[64] The effort to translate this presumed ethical duty into an impending legal duty quickly bogs down in a tangle of attenuated analogies, to which we turn next.

Most of the concern about possible legal liability for failure to return research findings is rooted in tort law, and in particular the law of negligence, of which professional malpractice is a branch. A negligence case requires proof that the defendant owed a duty to the plaintiff, that the defendant breached that duty, and that the breach caused compensable harm to the plaintiff. Where the conduct in question is that of a professional such as a physician or lawyer, a special duty is created by the professional relationship (as between doctor and patient) and the conduct must meet the standard of care required of similar professionals in similar circumstances. This higher duty is often characterized as a fiduciary duty, a duty to act always in the best interest of a patient who is assumed to be at a significant knowledge disadvantage and thus inherently vulnerable and dependent. As we will explore shortly, whether *researchers* have a fiduciary or other special duty to research participants is a vexing question.

Under most circumstances "tort law imposes no affirmative duties to act for another's benefit, and individuals are not required to warn others of impending harm."[65] Put somewhat differently, while they must avoid doing harm, ordinary people generally have no legal duty to take action to help or even rescue others. However, there are exceptional situations where the law might disregard the general rule and impose liability. These situations include special relationships, the presence of contractual agreements that

supersede the general rule, the voluntary assumption of a higher duty, and a party's possession of superior skills, training, and ability.[66] In other words, "legal obligations are generally role specific."[67]

There is no doubt that medical professionals in a clinical setting can have a duty to notice, disclose, and sometimes act upon findings that they are not looking for. Thus, several cases have recognized that clinical radiologists may have an affirmative duty to discover and disclose incidental findings.[68] The existence of such a duty derives from several of the exceptional circumstances noted above: the special fiduciary relationship between a physician and patient — even a physician like a radiologist whom the patient neither selects nor consults directly; the physician's assumption of a duty toward the patient; and the physician's superior skill, training, and ability.

What are the implications of these legal doctrines for the return of research findings? A researcher who *does* disclose research findings but does so negligently could potentially be held liable under principles of ordinary negligence.[69] It might even be argued that if a researcher did disclose, but then did not record, this would be negligent completion of an act — returning results — already undertaken. However, in order to succeed on such a claim, a participant plaintiff would have to prove that the researcher's failure to place the results in the medical records caused harm, such as the occurrence of a preventable illness. Assuming that the researcher told the plaintiff of the results and their clinical significance, it would be difficult for the plaintiff to prove that it was not his or her lack of action in response to such a disclosure, rather than the researcher's lack of action, that caused the harm. Thus, our primary concern is with a failure to return potentially actionable findings, which, for legal purposes, would be a failure to act as opposed to an act undertaken but negligently executed.

Transposed into the research context, the no-affirmative-duty-to-help rule would imply that researchers are generally under no affirmative duty to act for their subjects' benefit, and thus have no duty to warn subjects of findings that might portend harm. But could the failure to disclose research findings fall under one of the exceptions to the no-affirmative-duty-to-help rule?

There is currently no legal authority for the proposition that a researcher has a fiduciary duty to a participant.[70] This has been the case notwithstanding widespread documentation of the "therapeutic misconception," meaning that research participants often believe that they will receive clinical medical care, regardless of any disclaimers they are given. If a fiduciary duty were found, the literature speculates, it would probably be as a result of some special features of the researcher's profile or the research project that made the therapeutic misconception even more plausible to participants.[71] For example, a researcher who was also the participant-patient's clinical physician might conceivably be held to have a fiduciary duty even with respect to the research aspects of the relationship. More generally, researchers who are also clinicians might be somewhat more likely to be held to a fiduciary duty, especially if participants knew that status. A research project in which participation "looked" more like clinical care — for example, with lengthy in-person consultations rather than mere submission of a saliva sample — might also incline a court toward finding a fiduciary duty.

It has also been suggested that "immediately actionable findings" might trigger a "common law duty to rescue" even in the absence of a fiduciary duty, but this argument finds — at best — only attenuated support in current law.[72] Finally, if an informed consent document were treated as a contract, it could possibly create a contractual duty to disclose. On their face, they have some of the attributes of contracts. The typical contract involves an exchange of promises: I agree to do this, and in return you agree to do that. An informed consent document might be read as an exchange of the participant's promise to participate in return for the various commitments made by the researcher. However, researchers make every effort to ensure that such documents are *not* treated as contracts, courts have usually not treated them as contracts, and they are also written so as to minimize any duties owed to subjects.[73]

In any event, all of this is mere theorizing. There is currently no legal authority for the proposition that a researcher must disclose incidental findings to a participant. Although, as with all case law, this could change at any time, there is no reason to suspect that such a change is imminent. As we argued above, it is all but impossible to envision a duty to enter research findings into the medical record absent an underlying duty to disclose. We therefore conclude that — at least for now — researchers do not face legal liability if they fail to put research findings in a participant's medical records.

D. Regulatory Duties

Another important issue is whether there are any government regulations that require or prohibit the inclusion of research findings in participants' medical records. There are two regulatory frameworks that provide guidance for return of results in genom-ics research: the Clinical Laboratory Improvement Amendments of 1988 (CLIA) and the Common Rule. Neither requires that results be placed in medical records; on the contrary, the Common Rule would likely support non-placement in the medical records given its requirement to minimize risk to research participants. Although regulatory guidance for research conducted under the purview of the Food and Drug Administration (FDA) is not identical to the Common Rule, it does require similar efforts to minimize participant risk.[74]

CLIA contains several provisions that are relevant to this discussion. Broadly, CLIA regulates laboratories that perform analysis for clinical care to ensure that they meet specified quality standards.[75] Several genomic research studies have returned research results directly to participants. This means that subjects receive results generated in a research laboratory (research grade) that are not confirmed by repeating the testing in a CLIA-compliant clinical laboratory (clinical grade).[76] For example, the Familial Dilated Cardiomyopathy Research Project searched for gene variants through a research laboratory. When results showed suspected meaningful results, participants were notified and encouraged to pursue genetic counseling and undertake confirmatory testing in a clinical lab.[77] The participants were notified by a letter, written by a genetic counselor, and were given comprehensive information and referrals for clinical genetic counselors and laboratories.[78] However, the return of research-grade results directly to research participants without additional clinical-grade testing may be a violation of CLIA.[79]

Research laboratories are exempt from CLIA's requirements unless they "report patient specific results for the diagnosis, prevention or treatment of any disease or impairment of, or the assessment of the health of individual patients."[80] Because the CLIA regulations do not define diagnosis, prevention, or treatment, interpretations of what rises to this level vary.[81] Some argue that any research result returned to an individual requires certification by a CLIA laboratory,[82] but this position has been criticized as too extreme because it would require CLIA certification of results returned for all purposes, not just for diagnosis, prevention, or treatment.[83] Others have argued that the return of research results is not clinical care and thus cannot be within the scope of CLIA.[84] Under this conception of return, there may not be a CLIA violation if results are given directly to participants for informational purposes only, with the advice that clinical confirmation and follow-up should be sought.[85] However, Wolf and colleagues note that if individuals' results may be used to "assess health or trigger such assessment," CLIA confirmation may be necessary before results are returned.[86] Researchers currently have no concrete best practice guidelines on the issue.[87]

Whether CLIA confirmation is legally required remains an open question. However, given that a violation of CLIA requirements can result in criminal penalties and that certain journals may not accept publication of study findings in research returned without CLIA certification, it is likely that many researchers will opt to undergo CLIA confirmation before returning results to participants.[88] If researchers adopt CLIA confirmation as a usual practice, the practical effect will be that the presumed ethical duty to return results will include a further duty to seek CLIA confirmation — even though CLIA does not mandate return of results in the first place.

Must CLIA-confirmed results be entered into a medical record? Even assuming that one must confirm research results in a CLIA-certified laboratory before returning them, it does not inevitably follow that CLIA results must be placed into medical records. Under CLIA, laboratories are permitted to release results only to "authorized persons," as defined by federal regulations and state law,[89] and are required to keep detailed records of the lab request, analysis, and results. Authorized persons are defined with reference to state law,[90] although recent federal regulations clarify that individual patients are authorized to receive laboratory results under HIPAA even if they are not considered authorized users under state law.[91] While CLIA allows laboratories to transfer results to medical records upon the request of an authorized person, it does not mandate this transfer.

Nor does CLIA mandate in any other way that research results, even those clinically confirmed, be placed in the medical records. For example, researchers can obtain results from CLIA-certified laboratories by submitting samples with unique identifiers for analysis and, as authorized persons, receiving the results linked to the identifiers. The researchers could then link the research participants' identities to the identifiers and return the CLIA-based results directly to the participants.

A second important regulation, the Common Rule,[92] may argue against placement. The pressure on clinicians to place information in medical records has begun to pervade the research setting. However, as discussed above, the duties and potential liabilities of

researchers are very different from those of clinicians. Additionally, researchers have a duty to minimize unnecessary exposure of participants to risk, specifically in the context of the Genetic Information Nondiscrimination Act (GINA) and potential genetic discrimination.[93]

In the clinical context, physicians face difficult decisions about which genetic information to include in medical records and many feel legal and ethical pressure to ensure that all genetic information is documented.[94] Clinicians' concerns range from fear of medical malpractice, either from the patient or a patient's family member, to the belief that it is unethical or illegal to "hide" genetic information from insurers or employers.[95] GINA greatly limits the ability of covered employers and health insurance companies to collect genetic information from medical records.[96] For example, health insurers can only request genetic information from medical records for limited research purposes or to determine whether to pay for a procedure such as prophylactic surgery.[97] Other insurance companies, such as life, long-term care, or disability insurers, are permitted to collect and use genetic information housed in medical records when patients provide permission — a necessary condition of any insurance application.

Under GINA, if an employer or health insurer makes a medical records request that does not fall under one of GINA's exceptions for the collection of genetic information, the requesting entity must state that genetic information, including family medical history, should not be included in the information that the healthcare facility provides.[98] The burden is on the healthcare facility to redact genetic information from the copy of the record that is sent — a practice that is probably far from universal. By placing genomic research results into the medical record, researchers are increasing the chances that employers and health insurance companies will get genetic information, which the individual has a legal right to keep from them. This inclusion thus increases the risk of harms to the participant. Allowing participants to decide whether to place their results in their medical records would align with the goals of the Common Rule by providing participants the opportunity to minimize harms.

VI. Conclusion

There is an emerging consensus that researchers have a duty to return clinically useful results to individual participants; however, the boundaries of this duty are not well defined. This uncertainty generates situations that may put research participants' interests at risk. Specifically, in an effort to meet their duty to return results, numerous genomics research projects have decided not only to disclose clinically useful findings to their subjects, but to enter the clinical realm by actions such as clinician conversations or automatic placement in the participants' clinical medical record.

This practice can cause harm to participants on many levels, however. Automatic placement in the medical record denies participants the opportunity to take the time they believe is necessary to process their results, both practically and emotionally, and perhaps discussing it with their relatives, before determining what course of action is best for them, constraining their autonomy without sufficient justification. Not only may placement in the medical record fail to result in a benefit to the individual, it may also negatively impact research participants in a number of tangible ways. If included in the medical record, research results

related to genomic health risks can affect a participant's ability to obtain life, disability, and long-term care insurance, which are not protected under GINA. It may also jeopardize participants' privacy interests and put them at risk for employment discrimination by increasing the chances that their employers gain access to their genomic risk information. Moreover, once this information is placed in their medical record, there is little they can do to remove it.

Given the number of potential negative consequences associated with this practice, we sought to examine if there are any ethical, professional, legal, or regulatory obstacles that may prevent researchers from giving participants a choice about whether to include individual research results in their medical record. We find that there are no such obstacles.

From a research ethics perspective, the principle of beneficence suggests that researchers should act in a way that promotes the well-being of participants. Some may argue that this means that researchers should automatically place individual research findings in participants' medical record to increase the chances that participants' clinicians will have access to genomic risk information in order to help prevent or minimize health-related risks. However, giving participants a choice about this issue will not jeopardize the care of those participants who wish to seek preventive measures. First, many participants may choose to include clinically useful research findings in their medical records. Second, those participants who choose not to immediately place this information in their medical record may still do so in the future, authorizing their clinician to add it to their medical record in the course of seeking guidance about available preventive measures.

Even if most participants would choose to place research findings in their medical records, giving them a choice respects their autonomy. If they were capable of consenting to the research study, it seems to follow that they have the capacity to make determinations about how to manage the results that emerge from that study. In addition, giving participants a choice allows them to make a more comprehensive calculation of the risks and benefits of including this information in their medical record, considering not just their health interests, but also their familial, economic, emotional, and social interests.

We also argue that there are no professional, legal, or regulatory duties that preclude researchers from giving participants a choice about the inclusion of research findings in the medical record. Physicians and genetic counselors often participate as researchers in genomics studies; however, the professional ethics guidelines that apply to these professionals do not address this question, let alone specify a duty to preempt the participant's choice. Furthermore, from a legal perspective, researchers are not in a fiduciary relationship with participants and they do not have an affirmative duty-to-help that requires them even to disclose individual research findings to participants. Absent an underlying duty to disclose, a duty to place findings in a medical record is inconceivable. Finally, from a regulatory perspective, there is no requirement that researchers automatically place research findings in medical records. CLIA may require that research findings be verified in a CLIA-certified laboratory before they are returned to participants, but it does not mandate the placement of these findings in participants' medical records.

We find neither ethical, legal, professional, or regulatory duties that require placement of genomic research results in medical records nor any duties that prohibit such a practice. Therefore, researchers have discretion to decide whether to do so. However, while the automatic placement of participants' research findings in medical records is driven by an interest in helping participants minimize or prevent the risk of health-related harms, this practice could also have a number of negative consequences. We believe that the best policy is to give participants a choice about the placement of research findings in their medical records so that they can weigh the risks and benefits of such action by taking into account all of their relevant personal interests. The clinical utility of genomic information generated in the course of research makes it difficult to distinguish between the research and the clinical worlds, but researchers must not fall into the trap of therapeutic misconception. Medically relevant information generated in the context of a research study should not be automatically transferred into the clinical realm. Participants should have the opportunity to decide whether they want their research findings to be a part of their medical records.

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research project" and defining incidental findings as "finding[s] 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."). In this paper, when we refer to research findings as it relates to placement in the medical records, we are referring to both primary and , if any, incidental findings since both raise similar concerns as it relates to transferring information from the research to clinical realm.

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39.
While individuals can request an amendment to their medical records under the Health Insurance Portability and Accountability Act (HIPAA), a health care provider can deny the request if the information is "accurate and complete," so it is highly unlikely that an individual could remove research results from a medical record after they were placed there. 45 C.F.R. § 164.526.

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60. *Id.*, at § II.4.

61. McGuire et al., *supra* note 20, at 719.

62.

Pike, Rothenberg, and Berkman, *supra* note 20, at 813. A 2002 case from an intermediate Wisconsin appellate court has been suggested to us as a counter-example, but the case did not actually decide the issue of duty to disclose. *Ande v. Rock*, 256 Wis. 2d. 265, 647 N.W. 2d 265 (Wisc. App. 2002). The plaintiffs were parents of two children born with cystic fibrosis. As newborns, the children had been screened for the condition as part of an ongoing research project. Because they were assigned to a control group, neither their parents nor their physicians were told that they had tested positive. In reviewing the dismissal of medical practice claims against various physician researchers, the court found that there was "no allegation in the complaint of any relationships between the Andes and any of the researchers from which one could conclude that [the alleged duties to disclose] arose from a physician-patient relationship," which foreclosed the malpractice claims.

63.
McGuire et al., *supra* note 20, at 719-723.

64.
Pike, Rothenberg, and Berkman, *supra* note 20, at 811; see also McGuire et al., *supra* note 20, at 719.

65.
Pike, Rothenberg, and Berkman, *supra* note 20, at 816.

66.
Id., at 816–817.

67.
McGuire et al., *supra* note 20, at 719.

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Id., at 719; Tovino SA. Incidental Findings: A Common Law Approach. Accountability in Research. 2008; 15(4):242–261. [PubMed: 18972265]

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In *Ande*, *supra* note 62, the court suggested that an ordinary negligence claim might be available against researchers who failed to disclose results, even in the absence of a physician-patient relationship that would support a malpractice claim. However, it did not rule on this issue since the plaintiffs had not raised it on appeal.

70.
Pike, Rothenberg, and Berkman, *supra* note 20, at 820; Tovino, *supra* note 68, at 251.

71.
E.g., Tovino, *supra* note 68, at 251-254; McGuire et al., *supra* note 20, at 720.

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74.
Criteria for IRB Approval of Research. 21 C.F.R. § 56.111.

75.
Clinical Laboratory Improvement Amendments of 1988 (CLIA), Pub. L. No. 100–578, 102 Stat. 2903 (codified as amended in scattered sections of 42 U.S.C. § 263a).

76. Siegfried JD, et al. Return of Genetic Results in the Familial Dilated Cardiomyopathy Research Project. Journal of Genetic Counseling. 2013; 22(2):164–174. at 165. [PubMed: 22886719]

77.
Id.

78.
Id., at 166.

79.
Clinical Laboratory Improvement Amendments of 1988 (CLIA), Pub. L. No. 100-578, 102 Stat. 2903 (codified as amended at 42 U.S.C § 263a (2006); Burke W, Evans BJ, Jarvik GP. Return of Results: Ethical and Legal Distinctions between Research and Clinical Care. American Journal of Medical Genetics. 2008; 166C(1):105–111. [PubMed: 24616381] Wolf SM, et al. Managing Incidental Findings in Human Subjects Research: Analysis and Recommendations. Journal of Law, Medicine & Ethics. 2008; 36(2):219–248.

80.
42 C.F.R. § 493.3(b)(2) (2013).

81.
Burke, Evans, and Jarvik, *supra* note 79.

82. Secretary's Advisory Committee on Genetics, Health and Society (SACGHS). U.S. System of Oversight of Genetic Testing: A Response to the Charge of the Secretary of Health and Human Services. 2008. at 128, *available at* <http://osp.od.nih.gov/sites/default/files/SACGHS_oversight_report.pdf> (last visited November 23, 2015)

83.
Burke, Evans, and Jarvik, *supra* note 79, at 108.

84.
Id.

85.
Id.

86.
Wolf et al., *supra* note 79, at n. 81, but see Evans BJ. The First Amendment Right to Speak about the Human Genome. University of Pennsylvania Journal of Constitutional Law. 2014; 16:549–636. [PubMed: 25473380] at 565 ("While it seems unlikely that a court would hold that urging a person to seek a health assessment is itself a health assessment, the sheer vagueness of CLIA's research exception does invite such speculation.").

87.
Wolf, *supra* note 19, at 371.

88.
Evans, *supra* note 86, at 567-568.

89.
42 C.F.R. § 493.1291(f) (2013).

90.
42 C.F.R. § 493.2 (2014).

91.
CLIA Program and HIPAA Privacy Rule: Patients' Access to Test Reports, 79 Fed. Reg. 7290 (Feb. 6, 2014) (to be codified at 42 C.F.R. Part 493 and 45 C.F.R. Part 164).

92.
Common Rule, 45 C.F.R. § part 46

93.
Id.; Office for Human Research Protections, Department of Health and Human Services (OHRP), *Guidance on the Genetic Information Nondiscrimination Act: Implications for Investigators and Institutional Review Boards* (March 24, 2009), *available at* <http://www.hhs.gov/ohrp/policy/gina.pdf> (last visited November 23, 2015).

94. Klitzman R. Exclusion of Genetic Information from the Medical Record: Ethical and Medical Dilemmas. JAMA. 2010; 304(10):1120–1121. [PubMed: 20823439]

95.
Id.

96.
Genetic Information Nondiscrimination Act of 2008 (GINA), Pub. L. No. 110–233, 122 Stat. 881 (codified as amended in scattered sections of 26, 29, and 42 U.S.C).

97.
26 C.F.R. § 54.9802-3T(c) (2009) (Interim Final Rules).

98.
29 C.F.R. § 1635.8(b)(1)(i) (2014); 26 C.F.R. § 54.9802-3T(d) (2)(ii)(B).