



## How Geisinger made the case for an institutional duty to return genomic results to biobank participants



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*To return or not to return the results of genomics research:* that has been the question at the crux of an ongoing debate spawned by the increasingly rapid evolution of genomics.<sup>1</sup> Like many debates, this one arises from conflicting perspectives on broader concerns: for example, the purported distinction between research and patient care, the relationship between health care institutions and the communities they serve, and the role of patient- and research-participant-engagement in such debates (and in their resolution).

In 2012, Geisinger began to lay the groundwork for a significant expansion of the *MyCode Community Health Initiative*, a research platform comprised not only of a biobank established five years earlier but also of the clinical data collected in the electronic health records of the biobank's patient-participants and of the investigations made possible by these resources. Advances in genomic knowledge, coupled with steady decreases in sequencing costs, supplied the immediate context for this effort, which also entailed extensive internal discussion and patient-participant engagement focused on the ethical question, *should Geisinger return clinically actionable results of genomics research to MyCode's patient-participants whose sequenced genomes yield such results?*

In convening the internal discussions, the aim was to enlist organizational leaders, clinicians, and investigators in a process of ethical analysis and reflection for the purpose of identifying what obligations, if any, Geisinger has toward its patient-participants with regard to the return of results. Through engagement with the patient-participants, nearly 100 of whom were convened through focus groups described below, the aim was to solicit their views on the very same question.<sup>2</sup>

After the focus groups, the views of the engaged participants were clear: they overwhelmingly favored the return of results. Additional discussions were then held with leadership, researchers and Geisinger's

Institutional Review Board (IRB) and ultimately, Geisinger did indeed decide to return genomic results to that subset of MyCode participants whose sequenced genomes are found to contain one or more of the genetic variants on a defined list (based in part on the March 2013 clinical testing recommendations of the American College of Medical Genetics and Genomics<sup>3</sup>) and to integrate those clinically actionable results in genetically informed plans of care for these patient-participants.

Soon after this decision, in early 2014, Geisinger announced an ambitious collaboration in genomics discovery with the Tarrytown, NY-based Regeneron Pharmaceuticals and embarked upon the anticipated expansion of MyCode—the current goal of which is to increase the ranks of patient-participants to at least 250,000 over five years. Against the backdrop of President Obama's recently announced Precision Medicine Initiative (PMI), which calls for the development of a one-million-participant cohort, Geisinger hopes to become a funded member of the PMI consortium and is considering a many-fold increase in the size of MyCode, inspired, in large measure, by rapid growth in the number of consented participants.<sup>4</sup>

Here we describe the development of the ethical rationale for returning genomic results to patient-participants in the MyCode Community Health Initiative with special attention to the aforementioned internal discussions, reflections and focus groups through which the institution sought to engage patient-participants.

### 1. "Make my hospital right—Make it the best"

The Geisinger Health System encompasses more than 30,000 employees, a 1100-member multi-specialty group practice, nine hospital campuses, two research centers and a 467,000-member health plan. Now one of the nation's largest rural health care systems, Geisinger is the outgrowth of the vision of Abigail Geisinger, a widow who committed her late husband's fortune to the establishment of a hospital to serve the health care needs of the thriving community of Danville, Pennsylvania. To the Mayo-trained Harold Foss, M.D., the surgeon-architect who Abigail entrusted with the realization of her vision, she issued the mandate that has resonated throughout the subsequent decades with successive generations of Geisinger leaders,

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<sup>1</sup> The literature emanating from this debate is now quite extensive and has grown significantly following the 2013 publication of the ACMG recommendations for reporting of incidental findings in clinical exome and genome sequencing. For a representative critique of the ACMG's recommendations, see Susan M Wolf, George J Annas, and Sherman Elias, "Respecting Patient Autonomy in Clinical Genomics: New Recommendations on Incidental Findings Go Astray," *Science*. 2013 May 31; 340(613b): 1049–1050. For a defense of the recommendations, see Amy L McGuire et al., "Ethics and Genomic Incidental Findings," *Science*. 2013 May 31; 340(6136): 1047–1048.

<sup>2</sup> David J Carey et al., "The Geisinger MyCode Community Health Initiative: An Electronic Health Record-Linked Biobank for Precision Medicine Research," *Genetics in Medicine*. In press. [doi: 10.1038/gim.2015.187].

<sup>3</sup> Robert C. Green et al., "ACMG Recommendations for Reporting of Incidental Findings in Clinical Exome and Genome Sequencing." 2013; 15(7): 565–574.

<sup>4</sup> Francis S. Collins and Harold Varmus, "A New Initiative on Precision Medicine," *New England Journal of Medicine*. 2015; 372(9): 793–795.

clinicians, and, more recently, investigators: *Make my hospital right, make it the best.*

In the 1950s, the pursuit of Abigail's original mandate began to extend beyond the provision of clinical care to the residents of the surrounding community to include the conduct of research. In the mid-2000s, Geisinger's research leaders became keenly interested in the potential establishment of a biobank as a resource for basic studies into heart disease, obesity, and other problems of concern to the surrounding community. Because such a resource would depend upon biospecimens voluntarily donated by patients, those same leaders thought it essential to proceed by first surveying Geisinger's patients in order to gauge their understanding of and attitudes toward biomedical research in general and genomics/genetics in particular. At stake was the trust that had developed between the institution and its surrounding community over the course of nearly a century. In order to maintain that trust, it would be important to determine if Geisinger's patients were inclined to support a venture that would be fundamentally dependent on their good will. As the results of the survey and of subsequent focus groups showed, a clear majority supported the development of a biobank with a focus on genetics, although Geisinger leadership, researchers, and the patient participants themselves did evince concerns about the potential for discrimination based on genetic information.

In 2007, Geisinger's biobank, MyCode, was officially launched. Research and institutional leadership predicted that at some point in the future the cost of sequencing would drop and that the National Institutes of Health (NIH) or another government agency would fund the development of a large biobank for population-based sequencing. With its stable multi-generational population, willing participants and early adoption of an electronic medical record, Geisinger wanted to make sure that it was ready for such a government funded project. Consistent with the expressed preferences of the survey and focus group participants, a broad, general consent was developed for the purposes of recruiting Geisinger patients and obtaining their biospecimens and their permission to use the information stored in their electronic health records, both for broad data sharing and future unspecified research.<sup>5</sup> Although the original consent left the door open to returning results, it stated results would not be deposited in the electronic health record due to the concern about potential discrimination. From 2007 to 2013, Geisinger's practices with regard to returning results reflected the then-dominant view—that is, that results should *not* be returned.

## 2. The research/clinical care distinction and the patient/participant perspective

The initial survey and the focus groups, the results of which were instrumental in the founding of MyCode, were efforts to engage Geisinger's patients in research and discovery. As such, they reflected the growing awareness of the value of engagement—of *patient, participant, and community* engagement—in all phases of the scientific process, from the design of investigations to the dissemination of their findings.

Moreover, both the initial survey and the focus groups yielded an understanding of Geisinger that was (and remains) at odds with a decades-old tradition of bioethics dogma concerning patient care and

<sup>5</sup> The ethical requirements for consent to biobank-based research have also been a focus of considerable discussion and debate, although it is arguable that a consensus now affirms the ethical validity of a broad consent for this purpose. Questions and concerns about broad consents for biobank research are explored in B Hofmann, "Broadening Consent—Diluting Ethics?" *Journal of Medical Ethics*. 2009 February; 35(2):125–129. For a defense of broad consent, see Mats G Hansson et al., "Should Donors Be Allowed to Give Broad Consent to Future Biobank Research?" *Lancet Oncology*. 2006; 7: 266–269. Participants in a 2013 workshop convened by the Department of Bioethics at the Clinical Center, National Institutes of Health also affirmed the ethical validity of broad consents; for a summary of that discussion, see Christine Grady et al., "Broad Consent for Research with Biological Samples: Workshop Conclusions." *American Journal of Bioethics*. 2015; 15(9): 34–42.

research, that is, the idea that the two activities are—and must be kept—ethically and conceptually distinct, even if, in reality, the line between them is blurred. This idea was originally articulated and enshrined in the *Belmont Report* of 1979, which set forth the ethical principles for regulating human subjects research in the United States. According to *Belmont*, caring for patients and conducting research are ethically distinct because the former is focused on the needs of an individual, while the latter is oriented to the advancement of a social or public good, i.e., the good of new knowledge in the biomedical sciences.<sup>6</sup> Given that alleged distinction, some have argued that researchers have no obligation to cross the divide and, for example, return clinically relevant ("actionable") genomic results to biobank participants. Others have reached a similar conclusion for different reasons, arguing that the return of such results could or would be potentially more harmful than beneficial to the participants in such research.<sup>7</sup>

For the participants in the initial survey and the focus groups, however, there was no such divide, no clear distinction, between the Geisinger that cared for them as patients and the Geisinger that seeks to use their biospecimens and their clinical data in research, with the ultimate aim of improving their care. This dual commitment to improving care for the local and broader community and, at the same time, giving excellent care to individuals was (and has been repeatedly) endorsed by Geisinger's patient-participants, just as it was embraced as an institutional obligation by the system's leaders, clinicians, and investigators.

In time, that understanding of Geisinger, on the part of MyCode's first patient-participants, and that institutional obligation, on the part of Geisinger's leaders, clinicians, and investigators, set the stage for an additional round of ethical reflections, spurred by some salient realities *and* by some pressing questions. The realities included the fact that the individuals recruited to participate in MyCode were (and are) Geisinger patients: a condition of participation is that one must be a patient receiving care somewhere within the system. Another fact is that investigations in genomic discovery made possible by the gift of their biospecimens routinely yield information of potential benefit to those same patients. Would withholding that information from patients, in deference to the dogma about the distinction between research and patient care or out of concerns almost solely focused on risk, be an ethically defensible posture for Geisinger to assume? What about the time- and resource-intensive nature of returning that information to MyCode's patients-participants? Could that be a legitimate reason for withholding, rather than disclosing potentially beneficial information to these individuals and the clinicians who care for them? And, what would those same patient-participants say about this question of whether to withhold or return potentially beneficial genomic information?

In early 2013, answers to these questions about returning genomic results were supplied through a series of focus groups with MyCode participants, conducted under the auspices of the NHGRI-funded eMERGE consortium, which Geisinger joined in 2011 to spur progress in the integration of genomic data into electronic health records—and thus in clinical care. At Geisinger's flagship hospital and at local primary care clinics, six focus groups were held with a total of ninety-three MyCode participants. (The participants were 57% female and 43% male. The age distribution matched the MyCode population with the majority being over age 50. Nearly half of the participants had been Geisinger patients for twenty years or more and 85% reported receiving the majority of their medical care in the Geisinger Health System.) Five types of genomic research results were discussed, including: (1) pharmacogenomics; (2) recessive carrier status; (3) increased risk

<sup>6</sup> National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, "The Belmont Report: Ethical Principles for the Protection of Human Subjects of Research," April 18, 1979, <<http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.html>> (2 November 2015).

<sup>7</sup> Gail P. Jarvik et al., "Return of Genomic Results to Research Participants: The Floor, the Ceiling, and the Choices in Between," *The American Journal of Human Genetics*. 2014; 94: 818–826.

for preventable or treatable conditions (BRCA or colon cancer); (4) increased risk for non-treatable or non-preventable condition (Alzheimer's); and (5) genetic changes that we currently do not understand.

A large majority of the participants favored the return of *all* five types of results, with nothing withheld due to concerns about psychological harm or clinical actionability. A few participants were hesitant about the value of the results for their own health care but were convinced that their results could be of value to their children and grandchildren. They were also interested in learning their results if they could provide additional information that might increase their value for research. Altruism—the desire to help others—was the major motivation cited by participants to explain their willingness to be recruited for the biobank and to participate in the focus groups. They also favored returning results to both biobank participants and their health care providers and recommended that education and medical support should be provided for patients and providers. And they wanted clinically actionable results to be placed in their medical records and thereby to be made available to all of their healthcare providers.

As mentioned, the results of this second round of focus groups generated yet another round of intense discussion and reflection among Geisinger's research and institutional leaders. Some were hesitant to return results, but in time, a majority coalesced around the moral conviction that the institution actually has a duty to do so—a duty to care by making every effort to use clinically actionable genomic results for the clinical benefit of any patient–participant. With its original position on returning results (“we may do so but we will not deposit the results in the electronic health record”), crafted a year before the passage of the Genetic Information Non-Discrimination Act,

Geisinger sought to signal its respect for concerns about privacy and confidentiality on the part of MyCode's first participants. In revising its original position, Geisinger sought to respect the overwhelming support—even demand—for returning results on the part of the participants in the 2013 focus groups, and, at the same time, make good on this duty to care for these participants as patients, as individuals whose care might benefit from the return of results.

Thus, in late summer 2013, the decision was made to move forward and begin to develop a process to return clinically actionable results from the MyCode Community Health Initiative. The original broad consent form was modified to discuss—and seek the participant's permission to—return of results and the deposition of those results in the electronic health record. Due to the potential for therapeutic misconception, a related decision was made to return only clinically actionable results, a provision that is also explained in the consent form. In addition, the consent form also assures patient–participants that they are free to opt out at any point in the process without incurring any penalties or any other changes to their rights or healthcare services. In October 2013, Geisinger's institutional review board approved these revisions in the MyCode consent. This approval that was the outcome of two interrelated processes: one of patient–participant engagement and the other of internal discussion and ethical reflection.

Geisinger has just begun the process of returning clinically actionable results to patient–participants. And in so doing, it has begun to grapple with the very real practical challenge of returning these results in a way that benefits individual patient–participants and, through both internally and externally funded studies, answers research questions of critical importance to the effective integration of genomics in health care.