

Genomics and Infectious Diseases: *Expert Perspectives on Public Health Considerations regarding Actionability and Privacy*

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ABSTRACT There is growing evidence that human genetics plays a significant role in shaping human responses to infectious diseases. For instance, individuals' genetic susceptibility or resistance to infectious disease is likely to affect disease transmission. Yet little attention has been paid to the ethical, legal, and social implications of research in genomics and infectious disease, despite the unique ethical issues that arise in this arena. This article presents results from a pilot study exploring ethics in research on human genetics and response to HIV and other infectious diseases and is focused on perspectives from expert stakeholders. Whereas chairs of institutional review boards, biobank directors, and researchers in genomics and infectious disease expressed similar views about research privacy in the context of a public health emergency, they expressed different perspectives about the role that public health considerations ought to play in the return of individual results to research participants. These perspectives highlight the need to emphasize the importance of broad dialogue for helping various parties navigate the ethically complex current and future challenges of genomics and infectious disease research.

KEYWORDS human research ethics, genomic research, infectious diseases, Certificate of Confidentiality, return of results, genetic privacy

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Mounting evidence shows that human genetics—in addition to pathogen genetics—plays a significant role in shaping the human body's response to infectious diseases, including susceptibility to infection and disease progression and severity, and to treatments for those diseases.¹ Yet little attention has been paid to the ethical, legal, and social implications (ELSI) of research in genomics and infectious disease, despite the unique ethical issues that arise in this arena. Individuals' genetic susceptibility or resistance to infectious disease is likely to affect disease transmission, and this type of information may be relevant to public health. When public health and individual interests do not align, ethical issues may arise that have not yet been part of investigations of ethics

and genetics in the context of public health and non-communicable disease.²

Two of the primary ethical, legal, and social concerns in genetics and genomics have been the return of research results to participants and privacy.³ Ethicists and health care providers have been concerned about the behavioral and psychosocial effects that genetic information might have on research participants (which are also concerns in clinical contexts),⁴ and they have also been concerned about the validity of genetic research results, including the question of whether results of tests not conducted in labs that comply with the Clinical Laboratory Improvement Amendments (CLIA) of 1988 ought to be given to research participants.⁵ In practice, whether to provide genetic research

results to research participants has been determined primarily on the basis of clinical actionability or utility of the results, usually defined based on level of risk, disease severity, and the existence of proven interventions.⁶ However, experts disagree on what level of treatment efficacy is required for a result to be considered actionable and what level of penetrance a disease-associated gene would have to have to justify giving test results to research participants.⁷ In light of broader understanding about individuals' right to their health information and research participants' desire to have access to their genetic information, there have been increasing calls to expand the criteria for determining when results should be provided to research participants.⁸

Guidelines developed for assessing actionability of incidental findings in a clinical context, such as those developed by the American College of Medical Genetics and Genomics, have in some cases been applied in research contexts and have provided a basis for developing guidelines specifically aimed at research contexts, taking into account the ways that risks and responsibilities differ between such contexts.⁹ Berg and colleagues have proposed a “semiquantitative” metric of actionability based on disease severity, the likelihood of the disease outcome, the efficacy and burden of the intervention, and the relevant knowledge base—allowing for a weighing of these factors such that genetic variants with low scores on one variable, such as penetrance, might still be deemed actionable based on more positive scores in other areas, such as the efficacy and burden of the intervention.¹⁰ Lázaro-Muñoz and colleagues have described the process by which the Gene Selection Committee for the research project GeneScreen used these variables to determine which variants would be considered actionable. For example, experts determined that research results regarding the *HFE* gene, which is associated with hereditary hemochromatosis, should be considered actionable in spite of the gene's low penetrance and its association with only medium severity of the disease because therapeutic phlebotomy is available as a safe and effective treatment intervention.¹¹

Debates about privacy and confidentiality in the ELSI literature on genetics and genomics have focused primarily on the possibility that deidentified genetic information can be linked to the specific individuals whose DNA was analyzed. In recent years, research-

ers have demonstrated that individuals can often be identified through triangulation with publicly accessible genetic databases, leading to substantial concerns about the confidentiality of individuals' genetic data.¹² Widespread public participation in direct-to-consumer genetic testing notwithstanding, adults in the United States report substantial concerns about privacy in genetic research. For instance, results from a nationally representative survey published in 2009 showed that 90% of respondents stated a concern with privacy in genetic research. Respondents indicated concern about “the type(s) of information being collected and shared, the degree of control that participants have over access

With regard to privacy and infectious disease research, expert stakeholders expressed a great deal of concern that genetic privacy protections may be undervalued in the context of outbreaks or epidemics.

to their information, the types of researchers (and other parties) that may have access, as well as what, besides research, could be done with the personal information for harm or exploitation of study participants.”¹³

Within these discussions about privacy and about giving individual genetic research results to participants, a focus on infectious disease raises novel questions about how effects on public health might figure into such concerns and issues.¹⁴ We conducted an exploratory pilot study to identify perspectives from a variety of expert stakeholders regarding the ethics of research on genetic variants related to susceptibility to and transmission of infectious diseases, with a focus on HIV. We used HIV as a starting point to enable comparisons with other infectious diseases, including influenza, severe acute respiratory syndrome (SARS), and Ebola—diseases that vary on ethically relevant features such as ease of transmission, severity, preventability, and treatability. In this article, we describe the results of the pilot study, highlighting unique issues in genom-

ics and infectious disease research and their relevance to current debates about both the ethics of returning results and privacy.

STUDY METHODS

We conducted the exploratory pilot study with three focus groups of experts between May 2017 and May 2018. The groups consisted of investigators running cohort studies related to infectious disease ($n = 5$), members of institutional review boards (IRBs) ($n = 5$), and directors of research biobanks ($n = 6$). The cohort studies included are prospective studies in which both genetic and infectious disease information is collected and analyzed. Biobanks are repositories and resources that provide human biospecimens and data for research on genetics and infectious disease.¹⁵ We designed this sampling of stakeholders in order to map the range of perspectives across relevant expert groups. The IRB at Johns Hopkins University approved the study.

For recruitment, current chairs of IRBs in the study region were identified through publicly available sources and recruited via email. Additional IRB members with expertise relevant to the research questions were recruited via email based on referral from IRB administrators in the region. Investigators running long-term cohort studies across the United States were also identified through publicly available sources and recruited via email to participate in a focus group held at the 2018 meeting of the Conference on Retroviruses and Opportunistic Infections. Directors of biobanks operating globally were recruited to participate in a focus group held at the 2017 Annual Meeting of the International Society for Biological and Environmental Repositories.

We used a semistructured format to explore a broad range of emerging themes. We designed our moderator guides to use the genetics of HIV as an anchor for broader discussions of ELSI in genomics and infectious disease. We asked all stakeholder groups to imagine research that would identify people with decreased or increased genetic susceptibility to HIV relative to the general population, as well as people with increased genetic likelihood of transmitting HIV, noting that the latter two cases are as yet hypothetical. We then asked them to identify major ethical issues of concern, initially without prompting of specific issues. In all groups,

participants introduced issues relating to return of results, and several participants introduced comparisons with other infectious diseases, such as hepatitis C. The moderators further introduced questions related to privacy and about comparisons with infectious diseases including influenza, SARS, and Ebola, as well as about comparisons to issues in noncommunicable disease.

Focus group participants granted oral consent before the group discussion was initiated, and each session was recorded and transcribed for coding. Each focus group discussion lasted approximately 90 minutes. As compensation for their participation, participants were provided with a meal and \$20.

The research team used a structural coding approach for analysis of focus group data, implemented using the qualitative data analysis software Atlas.ti 8.0. Questions from the moderator guide formed the basis for codes used to index topics across groups and to guide development of thematic codes therein.¹⁶ AW served as the primary coder of transcripts from expert stakeholder groups based on a codebook previously developed and validated by our research group through multiple rounds of coding and refining of the codebook, including detailed review of codes by each author for a full focus group transcript. The codebook included four major code families and 64 codes, based around three types of gene variants (susceptibility, transmissibility, protective) and broader concerns in human genetic research related to infectious disease. Expert groups were treated as a single unit of analysis, with the goal of mapping the range of perspectives, rather than producing comparisons across expert groups.

Two key themes emerged as most central to expert discussions of ethical and social concerns in genomics and infectious disease research: the proving of individual results to research participants and the disclosure of results to third parties, which raises privacy concerns. In all three focus groups, concern about return of results arose spontaneously without prompting from moderators. Privacy issues that might arise from disclosure of results to third parties came up spontaneously in only one group; in the other groups, these privacy concerns became a major focus of discussion after being introduced by moderators.

RETURN OF INDIVIDUAL RESULTS TO RESEARCH PARTICIPANTS

In all groups, stakeholders emphasized the importance of considering the kinds of results that should be returned to individual participants in research on genomics and infectious disease. Past studies have described concerns of such expert groups regarding the validity of results and the importance of giving results to individual research participants only if the work has been conducted in a CLIA-approved lab.¹⁷ The responses from our focus groups were consistent with the literature on this topic.¹⁸ However, our research also revealed several issues specific to the growing field of research in genomics and infectious disease, including issues related to predictive values in genomics and infectious diseases, the impact that information in this area might have on the transmission of disease based on its effects on people's behavior, and the nature of actionability in infectious disease.

Predictive values in infectious disease. Research on the ethics of returning research results to individual participants has often drawn attention to the predictive value of a trait, including a trait's effect size.¹⁹ In the case of infectious disease, several expert stakeholders noted that effect sizes tend to be small. One IRB chair, for example, spoke about the effect of genotype for the human leukocyte antigen (HLA) on HIV progression, in order to speak more broadly about the return of results in this area. This IRB chair emphasized that it is standard practice to “only inform people of the results a) if they request them; b) if it's going to affect their health. And I think with the HLA data, the differentials are so small that I don't know what you would say to somebody if this is a protective variant” (IRB Chair 1). This IRB chair argued that when predictive values of genetic variants are low, research participants need not be alerted of individual research findings. The quotation from this chair also speaks to possible behavior changes associated with receiving information regarding a protective variant as opposed to a variant associated with greater risk in relation to the broader population, and to the nature of actionability, including how predictive values ought to be weighed against other factors such as disease severity and the existence of acceptable treatments—as discussed below.

Public health impacts and behavior change. Expert stakeholders felt that public health considerations play a significant role in shaping ethical issues in the return of genetic results regarding infectious disease. Several expressed more concern about sharing information with participants regarding genetic variants that would make a person less susceptible to infectious disease (protective) than variants that would make individuals more susceptible, noting that the former could result in riskier behaviors. As one IRB chair pointed out,

I guess the concern I would have would be . . . whether or not, and if so, how to communicate that in a consent form. Particularly in the direction of a genetic predisposition to make you less susceptible. Because . . . one worry would be how might that affect their behavior? And might it affect behavior in the direction of them taking more risk? In some ways, I would feel a little more comfortable about disclosing if they had a susceptibility that put them in the direction of being at increased risk, because I could see that that might influence them to take more precaution. (IRB Chair 2)

This IRB chair expressed a viewpoint common across stakeholder groups: that information about genetic protection could lead to riskier behaviors. For this focus group member, that tendency could be relevant for the return of results, leading to a greater imperative to return results on variants conferring susceptibility than those conferring greater immunity.

Expert stakeholders also highlighted the public health context of disease burden as relevant to the ethics of return of results. The group of biobank directors, whose participants work across the world, focused on the importance of returning results based on a high infectious disease burden in some locations. A biobank director said, “This [host] genomic information on ID is really important to participants in our biobank. In Vietnam we have many infectious diseases and outbreaks a year. When we see any abnormality in participants, we try to find out the reasons why and tell people” (Biobank Director 1). For this focus group member, the public health context of infectious disease in Southeast Asia demands sharing with people any information about their genetics related to infectious disease traits. This sentiment is similar to viewpoints expressed by IRB chairs, several of whom noted that there would be more impetus to return results about genetic susceptibility or

proclivity to spreading infectious diseases in contexts of high prevalence, such as with HIV in parts of West Africa, where, as one IRB chair noted, its prevalence rate is 42%.

Experts saw genetic variants related to proclivity to transmit as especially relevant to public health and felt that this information would be particularly important to provide to individual research participants, in some cases even more so than information about individual susceptibility. For example, members of one focus group expressed much less concern with effect sizes when discussing genetic predisposition to transmitting a pathogen than when discussing genetic susceptibility to infection. Most members of this group felt information about genetic predisposition to pathogen transmission would constitute actionable information. Discussing so-called super-spreaders with such genetic proclivity, two focus group members had the following exchange:

IRB Chair 3: [Y]ou would consider someone knowing that they are a super-spreader to constitute actionability. The expectation is that they would somehow quarantine themselves or severely limit—

IRB Chair 5: Take precautions, whatever they may be. But I think from a public health perspective, you would have some obligation to minimize the transmission that person might engage in.

Moderator: And would that look different at all based on disease, Ebola versus SARS versus flu versus HIV?

IRB Chair 5: Well, I think, with potentially lethal diseases, there's a greater imperative.

These focus group members discussed how, in the case of some infectious diseases, sharing information with research participants about a small effect size of a genetic variant could nonetheless have major impact on health outcomes because of the ability of that individual to change their behavior to control subsequent exposures; if a person takes preventative measures based on the information, that can have a large effect even if the genetic risk is small.

However, in other focus groups, discussion of transmission variants turned to the story of how Mary Mallon, known as Typhoid Mary, was forcibly placed in solitary confinement by the New York Health Department because it suspected that her poor handwashing as a cook had helped spread the disease. This action resulted

in debate at the time and thereafter about the relationship between the need to protect the public's health and individual rights. One cohort study principal investigator (PI) who participated in our focus groups argued that the effect size (the magnitude of the phenomenon) is essential in considering the real risks presented by anyone with an increased genetic likelihood of transmission:

I think it depends on the magnitude, right? Are we talking about there's a statistically significant but miniscule increased risk, like a five or ten percent increased risk that in a huge cohort comes out with a P value that's meaningful? And is there something that can be done about that information? So, do you always wear a mask, or do you use mupirocin or something? Again, it gets back to what's the risk to the patient and the people around them, and then how good a job are you doing educating. (PI 1)

For this focus group member, the effect size was still crucial to the ethics of returning results about a transmission variant, as well as the kinds of information offered alongside those results.

Actionability and the rapid pace of research. Across the expert groups, concerns about the return of results were largely based on the issue of actionability. However, participants understood actionability in diverging ways. At a general level, most participants understood actionability as rooted in the ability to improve health based on the information. According to one of the PIs in the study, actionability “has to do with the probability and it has to do with the severity of what you're telling them that they have, and whether you can do anything about it” (PI 2). For this member, disease severity is significant to actionability, as is the predictive value of a trait.

Similarly, one IRB member linked disease severity and effect size with means of prevention as key elements: “HIV and flu may be two different examples. [If you have a genetic variant that] creates susceptibility by twenty or thirty percent to the flu, is that something which really would drive you to notify or not, something that's so common . . . with influenza, outside vaccination, it's very limited in what we can do to control your exposure, whereas [with HIV] . . . I think they're going to have more agency over it” (IRB Member 6). This focus group member emphasized the ethical relevance of disease severity and ability to control exposure in considerations about return of results, noting

that the latter is a key variable in whether information is really actionable—whether there are steps an individual can take based on the information that will affect health outcomes.

Some participants linked actionability closely with clinical significance, as described by this IRB focus group member:

If [researchers] stumble upon something they think would be of clinical significance, in the sense that it's actionable, then there's a provision to come back to the IRB . . . present that to us and have us decide whether or not it should be disclosed and how it should be done. And typically, I think we like to see the test repeated in a CLIA-approved lab, if that's possible. And then go from there. So, we will sometimes allow that door to be opened downstream if we think there's something that's clinically significant. (IRB Member 3)

Likewise, another IRB member argued that information shouldn't be shared with participants before research has made clear the significance of that information. This member noted that studies commonly

do not return any genetic information to people, for the simple reason that it's research . . . so there was some linkage on chromosome 10, right? Well, that's meaningless to the individual person. . . . [T]hat's a finding from a large set of markers. . . . [Y]ou wouldn't know what to tell someone because, at that moment, its predictive value is totally unknown. And next year there'll be a study which doesn't replicate it . . . but there is guidance. . . . [F]indings should be disclosed to people if they are actionable. (IRB Member 2)

For this IRB member, research results should not be returned to participants unless they are clearly actionable, as laid out in official guidelines and regulations, in part because these results may not be validated in the future.

This perspective differed substantially from those voiced by other focus group members, who noted that it is nearly impossible to know how people will respond to genetic information, making it important to share all information with research participants, even if the information does not meet the standards for current clinical significance. For example, as one of the PIs contended,

I really think it's hard in such a rapidly changing field to predict what you [as a patient or research participant] would do with the genomic information. . . . But I still feel strongly that the family has the right to the infor-

mation in real time. . . . I think it's hard for us to say actionability today is the same as actionability tomorrow. . . . [B]ecause the field changes, a year later . . . the field has changed so much that what was not actionable then became actionable so completely differently now. (PI 3)

This focus group member stressed that the rapid pace of research in genomics and infectious disease makes it difficult to anticipate what research results might mean to participants now or in the future and that this calls for erring on the side of sharing information with participants so that they can have the power to make use of it in light of the changing state of the science.

Another cohort study PI drew a parallel to the history of HIV surveillance studies, arguing that situations change and alter the meaning of research results:

When we did large-scale testing of people in countries where they didn't have access to therapy or there wasn't therapy, a lot of the countries opted to not provide that information, but I remember in particular in a couple countries they decided . . . that was actually very helpful information, and a lot of places opted to say, "At least you should know, because someday therapy may be available," and fortunately for some of those people, it did become available . . . and they were more likely to get in line then and do it, and access to testing was less. (PI 4)

For this individual, experience has shown that research results can take on new meaning in light of shifting circumstances for treatment or other factors, making it important to share results with an eye toward the future. The rapid pace of research in genomics and infectious disease makes these issues especially pressing.

In spite of these differences in understanding of actionability, the expert stakeholders in our study generally agreed that information about genetics and infectious disease is uniquely actionable because of the strong link between behavior and health outcome, at least in the case of HIV. One PI stressed that, even in the absence of treatment options, based on personal genetic information regarding infectious disease, "you could still choose to alter your behavior to minimize risk to your partners, right? So that by itself is actionable" (PI 2). Another PI noted that "it's the behavioral piece that makes it—I mean, that's the problem with a BRCA gene or any of these others. . . . There's no known risk behavior—or protective behaviors that you can adopt to prevent you from getting the breast cancer . . . and so because there's

this behavioral piece [for HIV], I think that makes it even more compelling with the susceptibility to make that information available.” For this PI and other expert stakeholders, the behavioral component of many infectious diseases makes susceptibility information particularly actionable as compared to the case of noncommunicable diseases.

PRIVACY AND CONFIDENTIALITY

In addition to concerns about actionability, IRB chairs, biobank directors, and cohort study PIs all expressed concern about privacy in genomics and infectious disease research. And while these expert stakeholders expressed some ideas that have been well described in the ELSI literature, for example, regarding consent and concerns about repercussions for insurance coverage,²⁰ they also expressed concerns that are unique to the public health dimensions of genomics and infectious disease and the shifting approaches to research.

One focus group, for example, discussed the Certificate of Confidentiality that the U.S. National Institutes of Health (NIH) provides to researchers to limit disclosure of identifiable, sensitive research information, even if compelled to do so by a court subpoena. However, there are instances when disclosure of identifiable information is permitted, for example, if states have laws requiring the reporting of communicable diseases to state and local health departments.²¹ Indeed, several focus group members expressed doubt as to whether a Certificate of Confidentiality would provide sufficient privacy protection in a public health emergency. As one focus group member noted, “We have [an IRB] board member who isn’t very enthusiastic about Certificates of Confidentiality. He feels like it’s sort of an empty promise,” suggesting that this certificate adds little above and beyond other existing protections for health data.

Continuing that conversation, two focus group members had the following exchange with a focus group moderator:

Moderator: In the case of a public health crisis, if we did have an outbreak of Ebola or a major influenza, and some IRB had control over . . . relevant information . . . that a public health authority would consider helpful if it were subpoenaed, how much protection would a Certificate of Confidentiality give in that case?

Participant 5: Not much . . . I mean, look at that nurse that came back from [West Africa after working with an Ebola outbreak], and they put her in isolation. You know, I thought that was a terrible breach of confidentiality and—

Participant 4: —and liberty.

Participant 5: —human rights, yeah.

These IRB chairs argued that the balance between individual liberty and the protection of public health had erred too far in the latter direction in the case of the response of U.S. public health authorities to the Ebola outbreak in West Africa in 2014 and 2015, and suggested that this was likely to happen again in the future in the case of public health emergencies, including with regard to genomic data.

Multiple cohort study investigators noted problems they personally had with public health authorities attempting to compel them to disclose their research data, for example, in the following discussion between two investigators:

Investigator 1: In our study we guarantee [our research participants’] confidentiality, and I almost went to jail because I wouldn’t reveal it, and the university initially wouldn’t back me up.

Investigator 2: We had the same experience [with contact tracing data].

The first of these two investigators referred specifically to human genetic data, while the second described an earlier experience with contact tracing data, in other words, data that helps identify individuals who may have been in contact with a person who has an infectious disease. Both these investigators emphasized that they felt unsupported by their universities and had faced very serious legal ramifications for protecting the privacy of their research participants.

DISCUSSION

The results of the pilot focus group study emphasize important ethical dynamics that arise in genomics and infectious disease research based on their public health implications. Expert stakeholders—cohort study PIs, IRB chairs, and biobank directors—emphasize concerns regarding the ways that public health dynamics could or should shape the return of individual re-

search results, the unique dynamics of actionability in infectious disease, and privacy protections in the context of public health demands.

With regard to actionability, a focus on genomics and infectious disease draws attention to behavioral aspects beyond clinical utility. Across stakeholder groups, experts suggested that behavioral change is particularly salient in this area, especially because even genetic factors with small effect sizes can have large impacts on health outcomes by influencing health behavior. The ability to eliminate infectious disease exposure through behavior differs in important ways from the noncommunicable disease context, although the line between the two is being increasingly blurred as diseases that have previously been understood as genetic are shown to have an infectious element and vice versa.²² Here the question of what constitutes an impactful exposure becomes ever more complex, as do understandings about the thresholds of effect that make information actionable. This is a crucial question in the return of results, as seen in our focus groups, where the notion of what counts as a *low* predictive value was essential to understanding of actionability and return of results. While some experts may see effect sizes in infectious disease as generally low, experts in the genomics of infectious disease emphasize that effects in this area are high, with some variants multiplying the likelihood of a specific outcome two to three times.²³ The idea expressed among focus group members that a 20% to 30% increase in risk of influenza would not drive a researcher to return results might be shocking to some, who would consider this to be an extremely large increase in risk. Such diverging ideas call for dialogue and consensus building to determine directions for the future.

These focus groups drew attention to differential calculations that may affect ethical considerations in the return of results regarding different kinds of variants: protective variants versus those conferring greater disease risk, as well as variants related to likelihood of transmission. Expert stakeholders expressed a desire for more caution in returning individual research results related to disease protection due to the possible risky behavior that this could drive. And while concerns about such “risk compensation” have been present in the ELSI literature on noncommunicable disease,²⁴ they have been especially central to infectious disease, given the

link between behavior, exposure, and disease in these contexts.²⁵ As noted above, scholars have attempted to develop systems for weighing the many factors relevant to decisions about return of individual genetic research results, including disease severity, likelihood of the disease outcome, efficacy and burden of intervention, and relevant knowledge base.²⁶ While the expert stakeholders participating in this study echoed these perspectives, noting that concerns about returning results with a low predictive value might be tempered in the case of lethal diseases, many of these experts also saw public health impact as a significant factor in the return of results. This concern for public health impact includes a responsibility for researchers to guard against widespread transmission motivating return of results to “super-spreaders” over return of results to particularly susceptible individuals, and the return of susceptibility results over those related to protective variants.

With regard to privacy and infectious disease research, expert stakeholders expressed a great deal of concern that genetic privacy protections may be undervalued in the context of outbreaks or epidemics. And while they noted that popular perceptions of privacy may be shifting, experts underlined the importance of ongoing protections.

This pilot study was designed to map the range of ethical concerns, rather than to reach saturation in any one of the stakeholder groups in a way that permits robust group comparisons. However, some initial tendencies observed here deserve future attention. For example, while the focus group of IRB chairs concentrated on the importance of research validity, predictive values, and the severity of the relevant condition in shaping decisions about the return of results, biobank directors focused largely on concerns about consent. Cohort study investigators, by contrast, presented ideas much more in line with those observed in previous research among cohort study participants.²⁷ Like research participants, cohort study investigators concentrated on the value of genetic information regarding infectious disease beyond current clinical utility, as well as the limited ability of researchers to predict how any one individual might make use of their genetic information and the need to err on the side of sharing information based on the rapid pace of research in genomics and infectious disease. Further

research could investigate the factors contributing to divergent perspectives among expert stakeholders.

In light of the increasing movement toward return of research results in recent years,²⁸ it is especially significant to tease out the variables affecting how the return of results should be handled. Infectious disease research provides a crucial window for examining fundamental ethical issues in privacy and the return of results, as it generates unique calculations related to public health relevance. At the same time, the rapid pace of genomics and infectious disease research makes it a prime case study for lessons that also apply more broadly in ethics and genomics research. The disagreement among our study's expert stakeholders about whether the changing interpretation of genomic findings supports the return of results provides an excellent example of a broader phenomenon. This issue has not been settled in the ELSI literature for noncommunicable disease either.²⁹ The infectious disease context could provide a novel perspective for advancing the debate more generally.

The differing perspectives observed in this study regarding ethics in research on genomics and infectious disease emphasize the importance of broad dialogue for helping various parties navigate the ethically complex decisions in this domain. At the same time, converging ideas among experts about the unique privacy concerns in genomics in the face of public health emergencies point to a need for efforts to develop improved policy solutions.

As to study limitations, the small number of focus groups we assembled did not allow for robust intergroup comparison. However, methodological research has demonstrated that over 80% of themes are discoverable with just three focus groups.³⁰ The international perspectives introduced by biobank directors from around the world reinforce international experience of many investigators and IRB chairs with expertise in genomics and infectious disease but are not representative of U.S.-based expert groups, which the other two focus groups were. ♦

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