Society of Medical Education & Research

2023, Volume 3, Page No: 94-108
ISSN: 3108-5059

Asian Journal of Ethics in Health and Medicine

Biobank Participants and the Return of Genetic Findings: Results from a Mixed-Methods Study in Lithuania

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Abstract

The question of whether and how to return individual genetic findings (IGF) in biobank research continues to generate debate worldwide. Different return models are being considered, and practical frameworks for their use are gradually evolving. This study explores how both the general public and experts in Lithuania view the return of IGF and seeks to inform future strategies tailored to the Lithuanian biobank system. A mixed-methods design was applied, consisting of semi-structured interviews with experts and an online survey of 700 individuals representing the national population. Conducted in Lithuania in 2021, the study asked participants to reflect on four hypothetical cases of IGF: (1) Lynch syndrome, (2) a pathogenic variant associated with Huntington's disease, (3) a pathogenic variant linked to cystic fibrosis, and (4) elevated genetic susceptibility to type 2 diabetes. Among those willing to participate in biobank activities, a large majority (81–92%) indicated interest in receiving all types of IGF included in the study. Expert opinions, however, were more divided. While there was consensus that results revealing increased risk for preventable or treatable monogenic conditions (such as Lynch syndrome) should be disclosed, experts disagreed on the appropriateness of returning information related to untreatable or less actionable findings, including Huntington's disease, cystic fibrosis, and type 2 diabetes risk. For Lithuania, strengthening policies on the return of IGF without broadening the scope of what counts as clinically actionable information appears essential. Two possible routes may support this process: adopting curated lists of genes and conditions, such as those proposed by the American College of Medical Genetics, or applying structured frameworks (e.g., those developed by Berg and colleagues) that assess the actionability of specific findings.

Keywords: Biobanking, Genetic findings, Result disclosure, Ethics

Background

The number of empirical studies examining the return of individual genetic findings (IGF) to biobank participants has grown rapidly worldwide [1–4]. Evidence increasingly suggests strong public and participant support for an ethical obligation to share such results. Surveys from different countries consistently demonstrate that people wish to be informed of any health-related findings uncovered through biobank research [1–4]. International organizations, including the CIOMS guidelines [5] and the Global Alliance for Genomics and Health [6], also highlight the emerging ethical and legal consensus that certain findings should be returned.

In contrast, experts engaged in biobank-related work—such as clinicians, researchers, and ethics committee members—often hold divergent views, both across professional groups and even within them [7–11].

Access this article online https://smerpub.com/

Received: 21 June 2023; **Accepted:** 07 September 2023

How to cite this article: Musulas T, Gervickas A, Leketas M. Biobank Participants and the Return of Genetic Findings: Results from a Mixed-Methods Study in Lithuania. Asian J Ethics Health Med. 2023;3:94-108. https://doi.org/10.51847/YlWXNJWG1o

Biobank practices similarly reflect a wide range of return strategies [12].

In Lithuania, biobanking activities only became fully regulated in 2016, following an amendment to the Law on the Ethics of Biomedical Research. This legal update removed previous barriers to biobanking and created a clear framework for its operation. Among other provisions, it directly addressed the return of IGF, stipulating that results should be communicated to participants when findings indicate a serious condition for which effective interventions exist. Yet, what constitutes a "significant" finding in practice remains open to debate.

The purpose of this paper is to examine public and expert views on IGF return in Lithuania and to contribute to the broader discussion on selecting appropriate return strategies. To our knowledge, this is the first empirical study on the topic in Lithuania, with potential implications for other countries as well.

Methods

This research employed a mixed-methods design, combining qualitative interviews with a population-based survey conducted in 2021.

Expert interviews

Semi-structured interviews were used to gather expert perspectives. For the purposes of this study, "experts" included Lithuanian professionals involved in regulating, organizing, overseeing, or using biobanking, such as researchers working with human biological material, as well as specialists in ethics, data protection, and health law.

Participants were recruited using purposive and snowball sampling. Initial contacts were identified via online searches and the research team's professional network. Additional participants were suggested by interviewees, and recruitment continued until data saturation was achieved.

A total of 17 experts were interviewed: 11 with biomedical expertise (e.g., genetics, pathology, oncology, laboratory medicine, molecular biology, and related fields) and 6 with non-biomedical expertise (e.g., ethics, law, and data protection). On average, participants had 5.7 years of experience in biobanking. Interviews were conducted between September and November 2021, primarily online (via Microsoft Teams or Skype) due to pandemic restrictions, though in-person meetings were arranged when preferred. Further details of participant characteristics are presented in **Table 1**.

Table 1. Interview participants

Expert Identification Code	Institution Type	Professional Field	Experience Profile in Biobanking (BB)	Experience
Experts with a Biomedical Background				
P2bio	University	Laboratory Medicine	Research and development of biobanks	7 years
P4bio	Healthcare Institution	Medical Biology	Research and administration of biobanks	2 years
P5bio	Healthcare Institution	Oncology	Research, regulation, creation, and management of biobanks	8 years
P7bio	University	Genetics	Research and establishment of biobanks	3 years
P8bio	Healthcare Institution	Genetics	Research and development of biobanks	10 years
P9bio	Healthcare Institution	Pathology	Research, regulation, creation, and management of biobanks	10 years
P11bio	Healthcare Institution	Biochemistry	Research and administration of biobanks	1 year
P12bio	Other Research Organization	Molecular Biology	Research organization for biobanking	1 year
P13bio	University	Medical Genetics	Development of biobanks	>1 year
P15bio	Other Research Organization	Biology	Research and creation of biobanks	15 years
P17bio	Healthcare Institution	Biology	Administration of biobanks	1.5 years

Experts without a Biomedical Background				
P1law	Regulatory Institution	Law	Regulation of biobanks	4 years
P3et	Regulatory Institution	Ethics	Oversight and regulation of biobanks	10 years
P6data	Regulatory Institution	Data Protection	Oversight and regulation of biobanks	10 years
P10et	University	Ethics	Oversight of biobanks	2 years
P14data	Private Consulting Organization (Regulatory)	Data Protection	Regulation of biobanks	6 years
P16law	Private Consulting Organization (Regulatory)	Law	Regulation of biobanks	5 years

Informed consent

All participating experts provided informed consent prior to the study. Before agreeing, they were informed about the study's purpose, the intended use of their data, and the conditions of anonymity. While names would not appear in any publications, experts were cautioned that, given the small professional community in this field, complete confidentiality could not be guaranteed, as certain statements might allow indirect identification.

Expert interviews

Semi-structured interviews were guided by a protocol developed by the research team after a comprehensive literature review on IGF and consultations with specialists in genetics and research ethics. The English translation of the interview guide is available as supplementary material (Additional Files 1 and 2).

Experts were asked to share their views on whether IGF discovered in the course of biobank research should be returned, and under what circumstances. To facilitate discussion, they were presented with four hypothetical cases:

1. Lynch syndrome
2. Pathogenic variant associated with Huntington's disease
3. Pathogenic variant associated with cystic fibrosis
4. Increased genetic predisposition to type 2 diabetes

These scenarios were designed to reflect three conceptual approaches to defining the scope of IGF in genetic testing [13]: (i) the *medically actionable genes (MAG)* approach (Lynch syndrome), (ii) the *patient actionable genes (PAG)* approach (Huntington's disease and cystic fibrosis), and (iii) the *direct-to-consumer genetic testing (DTC-GT)* approach, which includes complex, multifactorial diseases (type 2 diabetes). Following the presentation of each case, experts were asked whether, in their view, such findings should be communicated to biobank participants.

All interviews were audio-recorded, transcribed verbatim, and analyzed using thematic analysis. Coding was performed with MAXQDA software, and emerging themes were reviewed and refined through team discussions.

Survey

To assess public attitudes, a representative online survey of the Lithuanian population was conducted in collaboration with the market research company TNS LT. A total of 700 respondents completed the survey between August and September 2021. The survey specifically examined the willingness of individuals to collaborate with biobanks and their preferences regarding the return of different categories of IGF. Respondents' socio-demographic details are provided in **Table 2**.

Table 2. Characteristics of respondents (n = 700)

Absolute No.		%
Gender		
Male	319	45,6%
Woman	381	54,4%
Age		
18–25	78	11,1%
26–35	143	20,4%
36–45	130	18,6%
46–55	143	20,4%
56–65	138	19,7%
65+	68	9,7%
Education		
Primary	12	1,7%

Secondary	195	27,9%
Professional (technical colleges, upper secondary schools) (ex-specialised secondary schools)	114	16,3%
Higher (university, college)	379	54,1%
Education (combined)		
Lower than university graduate	321	45,9%
University graduate	379	54,1%
Place of residence		
Major 5 cities (Vilnius, Kaunas, Klaipėda, Šiauliai, Panevėžys)	313	44,7%
Another city or district centre	251	35,9%
Town or rural area (up to 2 000 inhabitants)	136	19,4%
Marital status		
Married	377	53,9%
Living with partner	113	16,1%
Single	104	14,9%
Divorced	73	10,4%
Widowed	33	4,7%
Income (average salary per month per person in the family)		
Less than €300	52	7,4%
301–600 Eur	226	32,3%
601–900 Eur	145	20,7%
More than €900	165	23,6%
I have no income	7*	1,0%
I don't want to specify	105	15,0%
Health status		
Bad	222	31,7%
Fair	348	49,7%
Good	130	18,6%
***Small** sample		

Survey

To assess which types of IGF the public considered important to receive from a biobank, respondents were presented with the same four scenarios used in the non-biomedical expert interviews. They were asked whether they would want each type of finding returned (an English translation of the questionnaire is provided in Supplementary Information – Additional File 3).

To improve clarity and reliability, a pilot survey was carried out before the main study. Feedback from the pilot informed adjustments to the wording of scenarios and questions.

Data analysis was conducted using IBM SPSS Statistics 24.0. Descriptive, inferential, and advanced statistical techniques were applied. In preparation for analysis, some variables were recoded: responses on the 5-point Likert scale (ranging from "definitely yes" to "definitely no") were collapsed into three categories—"yes" (combining "definitely yes" and "more likely yes"), "no" (combining "definitely no" and "more likely no"), and "don't know."

Results

Expert interviews

Before discussing specific findings, it is important to note that experts emphasized the requirement of *clinical validity* for all IGF. The results below are therefore presented under the assumption that findings are validated. Although participants were initially grouped into biomedical and non-biomedical backgrounds, this distinction did not produce meaningful differences in opinions. Thus, results are presented collectively.

Finding No. 1: Lynch syndrome

Experts strongly supported informing biobank participants about Lynch syndrome, highlighting that awareness of cancer risk enables preventive actions and early detection, which can significantly improve prognosis.

- "With preventive measures, it is possible to allow a person to live a quality life and to have a life expectancy that would be the same without this change." (P7bio)
- "Obviously it's just a possibility, but it's also a risk group, you know you are at risk and you can detect it in the early stages if it does occur." (P10et)

Experts pointed to the high (around 80%) cancer risk and the seriousness of the condition as the main criteria for disclosure. At the same time, they raised concerns about the difficulty of defining what qualifies as a "serious disease":

- "What qualifies as a serious disease? For example, is rheumatoid arthritis considered a serious disease? … Diabetes is also a serious disease. Or does 'serious' only refer to fatal diseases?" (P15bio)

While preventive measures may be invasive, experts generally considered risk level and the availability of effective interventions to be more important. Some emphasized the need to consider all criteria together when making disclosure decisions.

When asked whether such findings should be disclosed without seeking prior consent from participants, experts expressed mixed views **(Table 3)**.

Table 3. Informing biobank participant on Lynch syndrome

Lynch Syndrome	Inform Without Asking for Consent	Inform Only With Consent
	✓ Disease severity (cancer risk)	
	✓ Availability of effective preventive and treatment options	
	✓ Obligation to protect human life	
	✓ Risk that a biobank participant's consent choice may not reflect their true intentions (e.g., misunderstanding or changing preferences over time)	
		✓ Respecting personal and religious beliefs
		✓ Opportunity for biobank participants to prevent illness
		✓ Potential to cause emotional distress
		✓ Some individuals, such as older adults, may prefer not to be informed
		✓ The right not to know is protected under Lithuanian law

Some interviewees argued that findings related to Lynch syndrome should be disclosed even without explicit consent. For them, the seriousness of the condition and the possibility of prevention outweighed the principle of choice. A few noted that when the researcher also serves as a physician, the duty to protect life and health becomes paramount. Others added that advance consent may not capture a person's genuine preference, since it is difficult to imagine how one would react before being confronted with such information.

"When people tick yes or no in a consent form, it doesn't necessarily reflect what they truly think. It's an almost impossible decision until you are actually in the situation … but once the risk is explained and preventive measures are possible, it becomes easier." (P17bio)

Those in favor of this approach still emphasized the need for transparency: consent documents, they argued, should clearly explain that clinically significant findings like Lynch syndrome could be returned, and outline the process of notification.

Other experts disagreed, stressing that disclosure should only happen if participants explicitly opted in. They pointed out that preferences may be shaped by personal or religious beliefs and reminded that a predisposition is not the same as a diagnosis—some people with the variant may never develop the disease. Concerns were also raised about the psychological burden of knowing, particularly the potential for anxiety, fear, or constant worry. Several noted that some individuals, including older participants, may prefer ignorance, and emphasized that Lithuanian law protects a person's right not to know.

Finding No. 2: Pathogenic variant for huntington's disease

On Huntington's disease, opinions were even more divided (see Table 4). Many experts leaned against disclosure, arguing that no preventive or therapeutic measures exist and that the knowledge could cause serious harm. They highlighted risks of unnecessary worry, depression, or even suicide in vulnerable individuals.

- "This only creates needless anxiety for the person." (P3et)
- "In my opinion, only very strong and resilient people could handle such information … I don't think feedback should be provided." (P17bio)
- "For some, it could push them into depression or even suicide." (P2bio)

Table 4. Informing a biobank participant on a pathogenic variant associated with Huntington's disease

A Pathogenic Variant Associated with Huntington's Disease	Not Inform	Inform Only With Consent
	✓ Absence of preventive measures	
	✓ Potential to cause significant emotional distress	
	✓ Possible adverse social impacts (e.g., increased insurance premiums, denial of coverage, or restricted job opportunities)	
		✓ Opportunity to reassess life priorities based on potential health changes
		✓ Potential for effective preventive or treatment options in the future

In Lithuania, clinical protocols already require a psychological evaluation before genetic testing for Huntington's disease, underscoring the gravity of receiving such information. Experts also pointed out possible social consequences, such as higher insurance premiums, denial of coverage, or barriers to employment. Still, not all respondents opposed disclosure. Some argued that participants should have the right to decide, even if the condition is untreatable. From this perspective, awareness could provide time to reorient life goals, prepare emotionally, or make practical arrangements for the future.

"For some, it can be an incentive to get their lives in order and live a productive and good life for a while." (P2bio)

"It should be reported for social reasons, so the person can make arrangements with relatives, find care when needed, and decide for themselves how to plan their future." (P1law)

Several experts emphasized that the severity and inevitability of the disease must be central in disclosure decisions. Even if current treatments are unavailable, future medical advances could change the picture. They also stressed that, should such findings be returned, genetic counseling and ongoing psychological support must accompany disclosure to help participants and their families cope with the information.

Finding No. 3: Pathogenic variant associated with cystic fibrosis

Opinions on returning cystic fibrosis findings were also divided **(Table 5)**. Some experts viewed disclosure as beneficial, given the potential reproductive implications and the importance of early diagnosis in affected children. Others were more cautious, questioning whether such results should be reported when the participant may remain a healthy carrier.

Possession of a Pathogenic Variant Associated with Cystic Fibrosis	Not Inform	Inform Only With Consent
	✓ Conditional relevance of the finding (e.g., dependent on whether the biobank participant's partner carries the cystic fibrosis pathogenic variant)	
	✓ Low likelihood of the biobank participant's offspring developing the condition	
	✓ Potential to cause emotional distress	
	✓ Risk of disrupting personal life (e.g., potential family conflict arising from this information)	
	✓ Lack of relevance for biobank participants beyond reproductive age	
		✓ Some individuals may wish to be informed about this finding

		✓ Enabling better-informed reproductive choices
		✓ Possibility of reducing emotional distress after testing the partner
		✓ Potential benefits of awareness for future generations

Finding No. 3: Pathogenic variant associated with cystic fibrosis

Some experts argued against routinely disclosing cystic fibrosis carrier status. They emphasized that the information is only meaningful if the participant's partner also carries the variant, in which case the couple would face a 25% chance of having a child affected by the condition.

"Cystic fibrosis is a recessively inherited disease, which means I have to meet a partner who has the gene, and then there is a 25% chance of having a child with cystic fibrosis." (P13bio)

For some, this probability was too low to justify disclosure. Others worried that carrier status could trigger anxiety or disrupt personal relationships, for example by influencing partner choice. They also questioned its relevance for individuals beyond reproductive age:

"If I am a biobank participant and they find something at the age of 50, there is no point for me to get it, because I won't have any more children." (P3et)

In contrast, supporters of disclosure maintained that such findings should at least be offered to participants. Carrier information, when combined with a partner's genetic status, could either provide reassurance or allow for informed reproductive planning through options such as preimplantation genetic testing, assisted reproduction, or embryo donation. Early knowledge could also help prepare for a child's medical needs, allowing timely interventions that improve prognosis and quality of life.

"Cystic fibrosis is one of those diseases where, if you know in advance, treatment can start immediately after birth … symptoms are less severe, attacks are less frequent, and both lifespan and quality of life improve." (P2bio)

Some added that even participants who are past reproductive age might consider this knowledge valuable for their children or future generations. From a public health perspective, disclosure was also viewed as potentially cost-saving, since identifying carriers early could streamline reproductive decision-making and reduce healthcare burdens. A final consideration was population prevalence: the higher the frequency of the pathogenic variant in the community, the stronger the case for disclosure.

Finding No. 4: Increased genetic risk of type 2 diabetes

As with Huntington's disease and cystic fibrosis, experts disagreed on whether participants should be informed about genetic susceptibility to type 2 diabetes **(Table 6)**.

Table 6. Informing a biobank participant about the increase in genetic risk of type 2 diabetes

Increased Genetic Risk of Type 2 Diabetes	Not Informed	Inform Only With Consent
	✓ Absence of effective measures to manage genetic risks	
	✓ Low probability of the biobank participant developing the condition	
	✓ Not classified as a life-threatening asymptomatic condition	
	✓ No significant new health information provided to the biobank participant	

✓ Potential to cause emotional distress	
✓ Risk of social stigma	
✓ Limited, absent, or only temporary boost in motivation for lifestyle changes	
✓ Insufficient scientific evidence on the health impact of such findings	
✓ Prevention programs already address these risks	
	✓ Extra motivation to manage non-genetic risk factors
	✓ Interest from some individuals in receiving such information (indicating minor additional disease risk; growing use of direct-to-consumer genetic tests for multifactorial diseases)
	✓ Some biobanks provide this type of information
	✓ Value of educating individuals about healthy lifestyle choices

Finding No. 4: Increased genetic risk of type 2 diabetes

Many experts, particularly medical geneticists, natural scientists, and ethicists, argued against disclosing this type of finding. They noted that a modest increase in genetic risk offers little meaningful information and could be misleading:

"This type of information is like astrology… it's not enough information." (P10et)

"To me, 5% is nothing, there's no need to make a person nervous." (P15bio)

They further emphasized the lack of targeted preventive measures and the fact that type 2 diabetes is neither fatal nor silent, making the genetic risk less clinically relevant. Some also cautioned that disclosure could trigger anxiety, hypochondria, or stigma.

"People just don't think every day that they might get a disease … findings like this come from the hypochondria series." (P3et)

Others argued that risk information might fail to motivate lasting lifestyle changes—or could even reduce personal responsibility:

"If I know that I have a genetically determined predisposition, then I will no longer feel an inner obligation to try to live, say, a good life." (P10et)

On the other hand, a smaller group of experts, especially from law and data protection fields, supported disclosure if participants wished to know. They suggested that awareness, even without clinical actionability, might encourage healthier lifestyles:

"For someone, it can be a very good stimulus to start exercising or eating healthy." (P1law)

Some also pointed out that younger people in particular express strong interest in multifactorial disease risk, as reflected in the popularity of direct-to-consumer genetic testing. They noted that national biobanks, such as Estonia's, have already begun incorporating multifactorial disease risk assessments. In this view, providing information on diabetes risk could serve as a public health tool, especially if framed within broader prevention programs and supported by individualized health assessments and guidance.

Survey results

Survey findings showed that most Lithuanians favored disclosure of all four hypothetical findings. The proportion of respondents who wished to be informed ranged from 80.7% for cystic fibrosis carrier status to 92.2% for Lynch syndrome **(Figure 1)**. Notably, sociodemographic characteristics did not significantly influence these preferences **(Table 7)**.

When asked about the factors guiding their decisions, respondents cited the severity of the disease, the probability of developing it, and the availability, effectiveness, and invasiveness of preventive measures. Multiple factors could be selected, reflecting the complex reasoning behind individuals' choices.

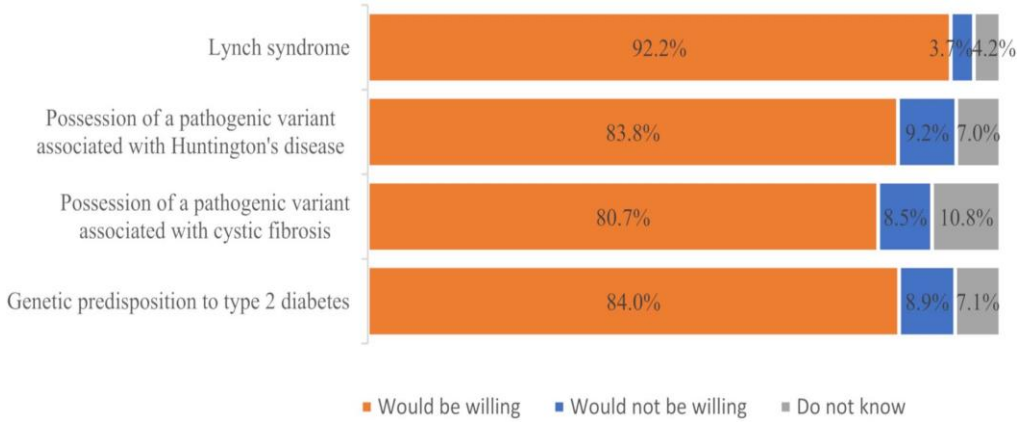

Figure 1. Respondents' willingness to know different findings (*n*=575)

Table 7. Results of binary logistic regression analysis (ref. Would prefer to be informed about the four findings)

Would prefer to be informed about all four findings:	**Lynch syndrome**			**Possession of a pathogenic variant associated with Huntington's disease**			**Possession of a pathogenic variant associated with cystic fibrosis**			**Increase in genetic risk of type 2 diabetes**		
Sociodemographic characteristics	B	S.E.	Sig.	B	S.E.	Sig.	B	S.E.	Sig.	B	S.E.	Sig.
Age	-0,006	0,006	0,323	-0,001	0,006	0,930	0,000	0,006	0,954	0,008	0,006	0,213
Gender (ref. male)	-0,191	0,186	0,305	-0,181	0,173	0,294	-0,242	0,171	0,155	-0,119	0,177	0,500
Education (ref. tertiary)												
primary	-0,011	0,288	0,970	0,025	0,264	0,925	-0,121	0,261	0,643	0,402	0,273	0,141
secondary	-0,082	0,237	0,728	0,067	0,219	0,762	-0,045	0,219	0,836	0,109	0,223	0,625
Place of residence (ref. rural arear)												
city	0,359	0,252	0,153	0,351	0,231	0,128	0,617	0,227	0,007	0,461	0,235	0,050
medium/small size town	-0,260	0,243	0,284	0,035	0,229	0,878	0,037	0,222	0,867	0,032	0,232	0,889
Married (ref. yes)	0,119	0,197	0,545	0,062	0,184	0,737	-0,084	0,183	0,646	-0,006	0,189	0,974
Income (ref. more than 900 euro per month)												
No answer	-0,616	0,318	0,053	-0,420	0,299	0,160	-0,554	0,301	0,065	-0,595	0,303	0,049
Less than 300 eur	-0,667	0,369	0,071	-0,207	0,355	0,560	-0,346	0,354	0,328	-0,573	0,357	0,109
301–600 eur	0,224	0,272	0,409	0,226	0,250	0,366	0,045	0,250	0,857	0,125	0,256	0,626
601–900 eur	0,420	0,327	0,198	0,277	0,293	0,344	0,250	0,295	0,397	0,480	0,310	0,122
Constant	1,439	0,511	0,005	0,670	0,466	0,151	0,771	0,464	0,096	0,276	0,474	0,560
N	700			700			700			700		
Nagelkerke R2	0.059			0.029			0.050			0.051		
Model Chi Square	p = 0,02			p = 0,325			p = 0,03			p = 0,09		

The results indicated that respondents considered all of the provided factors important when deciding whether they wished to receive information, though the relative weight of each varied slightly across findings. For the first three scenarios, the likelihood of developing the disease, its severity, and the availability and effectiveness of preventive measures were most influential. In contrast, for the fourth scenario—an increased genetic risk of type 2 diabetes—the severity of the disease emerged as the most decisive factor **(Figure 2)**.

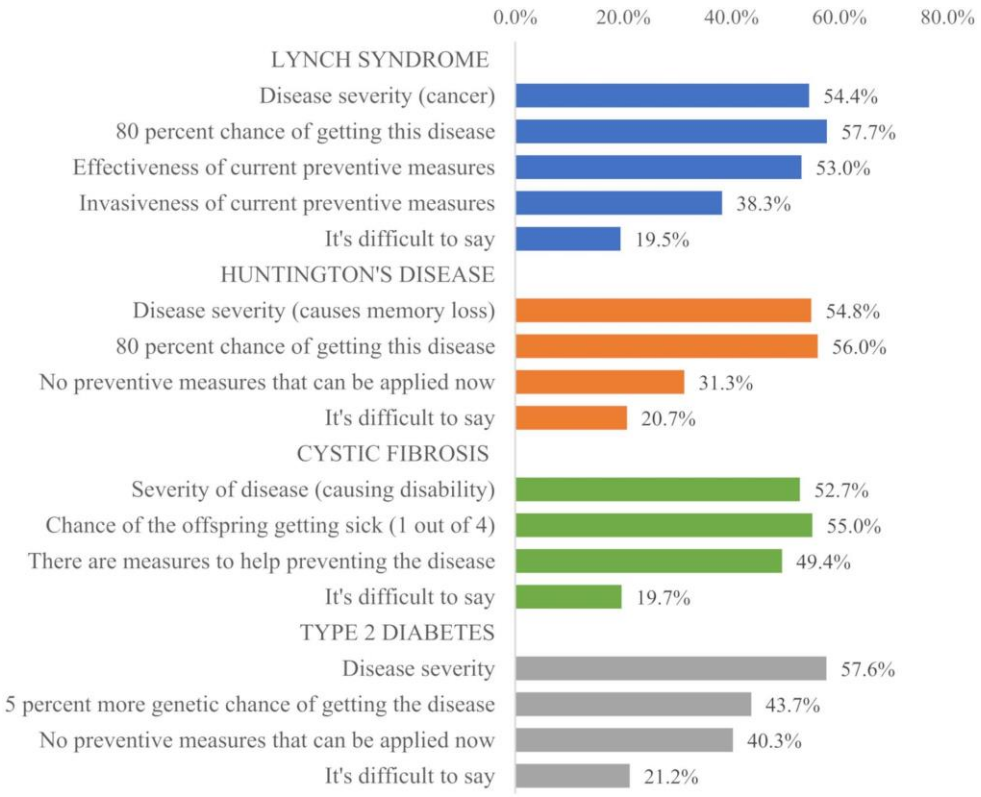

Figure 2. "Which information was important to you in your decision to know or not to know about the finding"? (n=575)

Attitudes of the lithuanian public and experts towards the return of IGF

The quantitative survey demonstrated a strong interest among the Lithuanian public in receiving health-related information from biobanks. These findings are consistent with international studies, which also show high levels of support for the return of individual genetic findings (IGF) [14]. Importantly, the public expressed interest not only in medically actionable conditions but also in information about untreatable monogenic diseases (e.g., Huntington's disease), carrier status for recessive conditions (e.g., cystic fibrosis), and even modest increases in genetic risk for multifactorial diseases such as type 2 diabetes [1,3]. For example, in a U.S. survey, 95% of respondents wanted information about treatable conditions (e.g., asthma), and 90% expressed interest in untreatable conditions (e.g., Alzheimer's disease) [3]. Similarly, in Japan, more than 80% of biobank participants wanted lifestyle-related risk information, a higher proportion than those who prioritized clinically significant findings (over 50%) [1].

In contrast, Lithuanian experts expressed a more cautious and diverse set of views. While there was consensus that findings indicating a high risk of a treatable monogenic disease such as Lynch syndrome (MAG approach) should be returned, opinions diverged on other types of findings. Experts were divided on whether biobank participants should be informed about Huntington's disease variants or cystic fibrosis carrier status (PAG approach). Views also varied on returning multifactorial risk findings such as type 2 diabetes (DTC GT approach). Here, disciplinary differences were most pronounced: medical geneticists, natural scientists, and ethicists generally opposed disclosure due to concerns about limited predictive value, misunderstanding, and possible distress, whereas legal and data protection experts tended to support disclosure, reflecting positions closer to public opinion.

This divergence between public expectations and expert caution mirrors findings from other contexts. For instance, a Danish study on clinical genome sequencing showed that public preferences often prioritize PAG-type results, including severe but non-actionable conditions, whereas professionals follow ACMG recommendations

that emphasize MAG findings [15]. Such evidence points to the need for hybrid policies that balance professional standards with public expectations.

Nevertheless, the alignment between experts and the public in supporting the return of Lynch syndrome findings is noteworthy. It should be emphasized, however, that our case example involved a high-penetrance pathogenic variant. The interpretation of lower-penetrance variants may be more complex, raising risks of false positives, over-diagnosis, unnecessary surveillance, and distress [16]. Future research should examine how both publics and professionals weigh such scenarios.

Finally, Lithuanian experts highlighted the importance of validating all findings in accredited laboratories before return. Although this issue was not raised in the interview guide, it reflects a critical practical challenge: the significant resources required to confirm the clinical validity of potentially returnable variants in a biobank context.

Both issues—the consensus on returning high-penetrance, serious monogenic disease findings and the emphasis on clinical validity—are already partially reflected in Lithuania's current strategy for disclosing health-related findings to biobank participants. However, our analysis of the empirical data highlights several areas for improvement.

First, disagreements among experts in interpreting specific findings under the existing strategy reveal challenges in consistent application. For biobank participants, this complexity is even greater: they may not fully understand what type of health information can be returned, and in some cases, they may feel surprised or unprepared when confronted with findings they had previously agreed to receive.

Second, both experts and citizens in Lithuania identified additional factors—such as the invasiveness of preventive measures—that are not currently addressed in national legislation but strongly influence decisions about disclosure.

Third, while criteria such as disease severity, likelihood of disease, effectiveness of preventive measures, and invasiveness were all acknowledged as relevant, their relative weight differed depending on the specific finding. This underscores the need to consider not just individual criteria but also their interplay when determining whether a particular result should be returned or known.

Measures to improve the IGF strategy in Lithuania

Drawing on the results of this study, we suggest that the primary goal for improving Lithuania's IGF return strategy should be **to refine and specify the existing framework**, while remaining anchored in the medically actionable genes (MAG) approach. Two main directions can support this refinement:

Development and use of a gene–disease list

A curated list of genes and diseases should be developed, based on criteria considered important by both Lithuanian experts and the public. This would provide clarity and consistency for researchers and participants alike. The potential benefits and challenges of introducing such a list into biobank practice are summarized in **Table 8**.

Table 8. Advantages and challenges of using a gene and disease list

Advantages	Challenges
✓ Decreases the likelihood that biobank participants will have unrealistic expectations about the information they might receive.	✓ Lists from other biobanks may not be appropriate for a specific biobank due to differences in operational context or other factors.
✓ Facilitates managing the volume of findings returned to biobank participants.	✓ Restricted ability of researchers to curate and interpret findings effectively.
✓ Streamlines the estimation and allocation of human and financial resources for implementing the return-of-findings strategy for biobank operators and funders.	✓ Limited clinical expertise among genomics researchers.
✓ Requires few modifications to existing legal frameworks.	✓ Potential ethical dilemmas for researchers or biobanks when additional incidental genetic findings (IGF) about a participant are discovered.
✓ Leverages insights from the use of similar lists in other scientific initiatives.	

The use of a **gene–disease list** has already been recommended and applied in several scientific and clinical projects across Europe that aim to integrate genome sequencing into clinical practice [17, 18]. In recent years, this method has also been adopted in biobank settings [19, 20].

One of its main advantages is that it provides clarity for all stakeholders involved in biobank activities—administrators, participants, and funders—by clearly defining which findings may be detected and potentially returned. For participants, reviewing such a list helps to manage expectations and avoid misconceptions (e.g., assuming that the absence of results equates to being in good health). For biobank administrators and researchers, the list serves as a practical tool to narrow down which findings should be considered for return, while funders and managers can use it to plan and allocate resources more effectively [21]. Importantly, adopting a gene–disease list would require only minimal changes to Lithuania's current legal framework.

Despite these advantages, several challenges exist. First, **developing and maintaining an updated list** demands expert knowledge, time, and financial resources—all of which are limited in Lithuania. A potential solution is to adopt an existing resource, as done by the Estonian Biobank, which applies the American College of Medical Genetics and Genomics (ACMG) gene–disease list [22–26]. However, while the ACMG list is becoming a widely used reference, it may not perfectly match the specific goals, participant profile, communication practices, or available resources of every biobank. In some cases, a narrower or broader list may be more appropriate [21].

Second, even with a list in place, **curating and interpreting findings** remains a challenge. Gene lists signal which results deserve consideration but do not prescribe policies on how to act. Some policies may require active screening of all listed genes for pathogenic variants—an approach that is often impractical in research contexts—while others only mandate reporting if variants are incidentally discovered, which may be more feasible.

Third, there are questions about **clinical responsibility**. Many genomics researchers are not clinicians and have no direct relationship with participants, meaning they do not bear the same professional duties as healthcare providers. Applying clinical norms in research settings is therefore complex. One possible solution is to include clinical experts within research teams to ensure that appropriate expertise and responsibilities are clearly defined.

Finally, researchers may encounter **clinically relevant findings outside the established list**. To address this, biobanks could establish an advisory body tasked with reviewing novel or unexpected cases and deciding whether they warrant disclosure.

Use of guidelines for evaluating return criteria

Guidelines can either serve as an alternative to a gene–disease list or complement it by helping determine which genes and conditions should be included. A notable example is the **five-criteria scale** developed by Berg and colleagues for assessing the clinical significance of genetic findings. This interdisciplinary framework—created with input from geneticists, clinicians from various specialties, laboratory professionals, and ethicists—evaluates findings against five dimensions:

1. Severity of disease outcomes
2. Likelihood of disease occurrence
3. Effectiveness of interventions
4. Burden of interventions
5. Strength of evidence

Each dimension is scored, with a maximum total of 15 points; higher scores indicate greater clinical significance [27].

The appeal of this tool lies in its ability to provide a transparent and consistent rationale for why certain findings are returned while others are not (see Table 9). It can also be adapted flexibly to different contexts. For example, although Berg and colleagues originally applied the scale to genes linked with monogenic disorders, it could also be extended to complex diseases if needed. As with the gene–disease list, incorporating this tool into Lithuania's biobank strategy would require only minor adjustments to existing legal regulations.

Table 9. Advantages and challenges of using Berg and colleagues' scale for determining the clinical significance of findings

Advantages	Challenges

✓ Incorporates diverse expert perspectives on the return of biobank findings.	✓ The guidelines' evaluative nature may lead to differing opinions among experts, even within the same field.
✓ Simplifies the rationale for deciding whether a specific finding from biobank activities should be shared with a participant.	
✓ Promotes greater transparency and consistency in the evaluation of findings.	
✓ Adaptable to various strategies and contexts for returning findings.	
✓ Requires minimal adjustments to existing legal frameworks.	

A persistent difficulty in applying the Berg scale is the potential for inconsistent interpretation of its criteria. Experts from different fields may assign divergent scores, which risks undermining comparability across cases. To reduce such variation, the establishment of an interdisciplinary advisory group within the biobank would be valuable. Such a body could bring together expertise from genetics, clinical medicine, ethics, and law to guide the evaluation of specific findings.

The divergent opinions of Lithuanian experts on the return of non-clinically actionable information, contrasted with the strong public demand for such results, highlight the need for ongoing debate and further empirical investigation. In particular, greater attention should be paid to the motivations behind the public's interest in non-clinically actionable findings and to the psychological consequences of disclosing them. These questions extend beyond biobank governance and should be considered in the wider context of healthcare communication and patient autonomy.

Study limitations

This study is not without limitations. In the qualitative component, many interviewees held overlapping roles as biobank researchers, founders, or administrators. Their views may therefore reflect institutional commitments as well as personal expertise, which could differ from perspectives of researchers with no direct ties to the biobank. Including this latter group in future work would provide a fuller picture.

The survey data also warrant cautious interpretation. Participation was voluntary, and the overall response rate was modest (22.7%), leaving open the possibility of non-response bias. Moreover, the scenarios presented were hypothetical; actual decisions about receiving genetic information may be shaped by situational factors such as prior experiences with the health system or the nature of biobank recruitment. Since most respondents reported good or fair health and were drawn from the general population rather than biobank participants, the findings are more applicable to population-based than disease-specific biobanks. Finally, despite efforts to design a representative sample, older adults (65+) and people with lower levels of education were underrepresented, largely due to digital access barriers. Data weighting did not fully correct this imbalance.

Conclusions

Improving the Lithuanian framework for returning IGF requires refining, rather than broadening, the definition of clinically actionable information. Two complementary strategies could advance this aim: (1) the adoption of a curated list of genes and diseases, drawing on international models such as the ACMG recommendations, and (2) the application of structured evaluation tools, such as the Berg scale, to guide case-by-case decisions. Together, these approaches would make the return process more predictable and transparent while upholding ethical standards.

Acknowledgments: None

Conflict of Interest: None

Financial Support: None

Ethics Statement: None

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