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Guiding Ethical, Legal, and Social Practices in Genomic Medicine

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Abstract

Genetic and genomic testing (GGT) offer valuable tools for enhancing health outcomes and preventing disease. However, because GGT involves sensitive personal information that can significantly affect patients and their families, it is crucial to address its Ethical, Legal, and Social Implications (ELSI). ELSI research seeks to identify and mitigate potential risks posed by genomic studies to individuals, families, and society. Existing literature, however, shows both quantitative and qualitative inconsistencies in defining the components of ELSI, which may lead to patient misinformation and adverse decisions. We reviewed major international documents published by global organizations to clarify the parameters defining ELSI and the recognized standards for GGT. This review is intended to provide guidance for researchers, healthcare professionals, and policymakers. First, we established clear definitions for the ethical, legal, and social dimensions of GGT to reduce ambiguity when using the ELSI framework. Next, from 44 relevant publications on genomic medicine, we selected nine key documents for detailed analysis. From these documents, we identified 29 ELSI sub-criteria related to GGT, which we grouped under 10 core criteria: two ethical, four legal, and four social. An additional analysis of the frequency of these sub-criteria across documents enabled us to prioritize seven key criteria for initiating evaluation and developing national regulations for GGT. The ELSI criteria identified in this study offer a structured foundation for developing national policies on personalized genomic medicine, ensuring alignment with international bioethical standards.

Keywords: Genomic testing, Ethical, Legal and Social Implications, Genetic testing, Bioethics, ELSI criteria, Genomic medicine, Patient rights, Policy-making, Healthcare

Background

Genetic and genomic testing (GGT) are complementary tools used to improve health outcomes and prevent disease. Genetic testing identifies specific mutations in a patient's genome to detect monogenic disorders, whereas genomic testing evaluates multiple genes to assess disease risk and predisposition [1]. GGT can reveal DNA features that impact a patient's health, enabling physicians to (a) prevent or delay disease onset, (b) estimate risks for family members, and (c) reduce the likelihood of transmitting these risks to offspring [2, 3]. Because GGT involves highly sensitive personal information with significant implications for patients and their families, it is critical to address ethical, legal, and social considerations in its practice [4]. However, key aspects of these considerations remain incompletely defined.

Ethical, Legal, and Social Implications (ELSI) research formally began in 1990 as part of the Human Genome Project, aiming to identify and address potential risks arising from genomic research to individuals, families, and society. Over the past 30 years, ELSI has evolved into a broad interdisciplinary field that integrates ethical, legal, and social concerns rather than treating them as separate domains [5]. This integration has led to conceptual ambiguity, and existing literature shows both quantitative and qualitative inconsistencies in defining

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the specific elements within each ELSI domain, particularly in the context of genetic and genomic testing and public health genomics [4, 6, 7].

International documents from major organizations reflect this inconsistency: in some cases, elements are broadly labeled as ELSI [8–10], while in others, ethical principles are cited even when legal or social aspects are included [11, 12]. Furthermore, the number and scope of ELSI criteria vary across sources [8, 13]. This lack of consensus complicates policy-making and regulation, potentially undermining patient rights—for example, in newborn screening programs [14] or cases like the Havasupai Indian Tribe, where informed consent and privacy were violated [15]. It may also lead to harmful health choices, such as patients misinterpreting direct-to-consumer BRCA testing results [16], or to breaches of privacy and misuse of genetic data with economic, health, or discriminatory consequences [6, 17, 18].

Despite significant efforts to address these challenges [10, 19–22], many initiatives have focused primarily on clinical research, neglecting other crucial aspects of ELSI in GGT, such as commercialization and regulatory considerations. Consequently, discrepancies persist in the literature, hindering a consistent framework for defining ELSI elements and criteria.

In this study, we aim to define ethical, legal, and social implications for GGT by first clarifying the parameters of each ELSI domain. We then analyzed major international documents on genomic medicine to synthesize an unbiased, comprehensive view of relevant ELSI topics. The resulting framework may support researchers, healthcare professionals, and policymakers in making informed, consistent decisions regarding GGT.

Methods

This study focused on the ethical, legal, and social implications (ELSI) associated with genetic and genomic testing (GGT) for disease detection or risk assessment in adults capable of providing informed consent. To clarify the parameters defining ELSI criteria in GGT, we reviewed international documents using a modified systematic review approach based on Strech and Sofaer's methodology for ethical reasoning [23] **(Figure 1)**. As noted by Boyle (1999), international documents often provide guidance for national regulation; non-binding recommendations, or "soft law," can inform legally enforceable policies [24]. In this study, "documents" refers broadly to binding instruments, non-binding guidance, and expert panel recommendations issued by international organizations.

The review process followed four steps:

Defining the review question and inclusion criteria,

Identifying and selecting relevant documents,

Extracting and synthesizing key information,

Summarizing findings to answer the review question.

Our review question was: *"Which ELSI criteria have international organizations recommended for GGT over the past three decades?"* Eligible documents were those published in the last 30 years by international organizations and addressing GGT for disease detection or risk assessment in adults with full consent capacity.

To identify relevant documents, we conducted a systematic search of the databases of leading international organizations involved in genomic medicine, prioritizing guidelines intended for broad international applicability rather than country-specific regulations. Search terms included "genomic medicine," "genetic testing," and "human rights and health." This selection was refined through iterative testing to ensure comprehensive coverage and reduce the likelihood of excluding relevant documents.

Finally, we screened documents published in the past 30 years that focused on GGT for health purposes in adults with the capacity to consent. Figure 1 presents the flow diagram detailing the literature identification process, adapted from Page *et al.* [25].

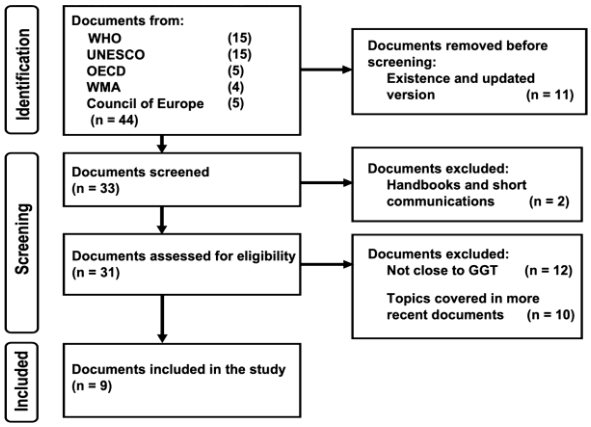

Figure 1. Flow diagram for selecting GGT-related content in databases of major international ELSI documents

Data extraction and synthesis

For the third step—data extraction and synthesis—we conducted a thorough, systematic review of all identified documents. Each document was read in full to pinpoint core concepts relevant to the eligibility criteria. These core concepts were then reviewed and confirmed by all authors, with disagreements resolved by majority vote. The final set of core concepts included: informed consent, non-discrimination, counseling, privacy and confidentiality, regulation, equity and accessibility, quality, and trained medical personnel.

Following this, we screened each document to extract specific ideas or statements associated with these core concepts. Each extracted idea was recorded as a "criterion" in a master list. In the fourth step, these criteria were organized into thematic groups to define overarching criteria and sub-criteria. All criteria and sub-criteria were then categorized into ETHICAL, LEGAL, or SOCIAL fields through consensus among the authors, guided by the definitions outlined below.

From this organization, primary criteria were identified based on their coverage and relevance, particularly those that should guide regulations to protect personal genetic information and patient rights. Finally, these findings were interpreted in light of both current practice and future regulatory considerations.

Defining ELSI parameters

Clarifying the boundaries of the ethical, legal, and social fields is crucial to avoid ambiguity when using the term ELSI. To define criteria for GGT, we first established clear distinctions among these fields. While several approaches exist to differentiate ELSI components [20, 26], we adopted the framework proposed by Chameau *et al.* [27], which clearly separates ethical, legal, and social considerations. Additionally, human rights principles provide a baseline for ethical standards and patient rights [28]. Key bioethical principles—beneficence, non-maleficence, autonomy, and justice—established by Beauchamp and Childress [29] have become widely accepted as a foundational framework for medical practice [30]. The World Health Organization's guidelines for GGT services were also considered to adapt these principles specifically to genomic medicine [11].

Based on this framework:

ETHICAL criteria were defined as those grounded in beneficence, non-maleficence, and respect for autonomy, including human rights and dignity.

LEGAL criteria encompass regulatory measures governing GGT, including authority, limits, and decision-making procedures to safeguard the rights of individuals involved.

SOCIAL criteria relate to distributive justice, focusing on equitable access to genomic medicine services, communication, and dissemination of information throughout society.

The complete schema illustrating the ELSI fields and their interconnections is presented in **Figure 2**.

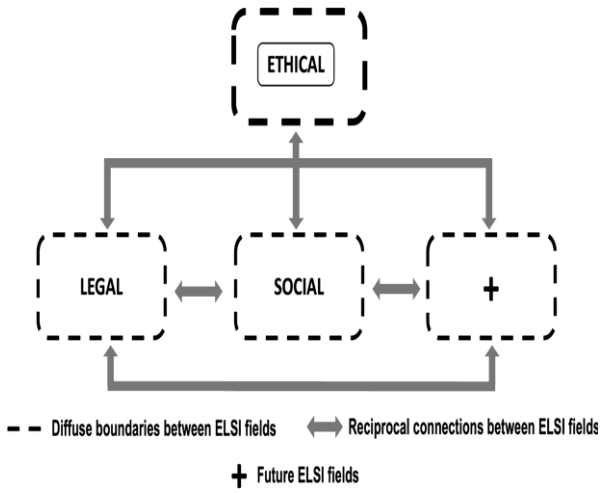

Figure 2. ELSI concept fields and their interconnections. The ETHICAL field is located at the top as mainstay for the rest of the fields—LEGAL, SOCIAL and future (+)—, which are placed in a lower hierarchical order. The interconnections between fields and the fuzzy limits among them are also represented

Conceptualizing ELSI fields

In developing the framework illustrated in Figure 2, we conceptualized the ETHICAL field as the foundational pillar of ELSI. It encompasses respect for human rights and takes precedence over scientific or economic interests, connecting both vertically and horizontally with the other fields. For this reason, it is positioned at the top of the scheme and enclosed within a continuous-line box. This placement reflects that the core principles of GGT are rooted in universal rights inherent to every patient.

Beneath the ETHICAL field, the LEGAL and SOCIAL fields are positioned hierarchically, alongside an additional, unnamed field marked with a "+" sign to anticipate the potential inclusion of new dimensions in future ELSI studies. Each of these fields is enclosed in

dotted-line boxes to indicate that their boundaries are not rigid, reflecting the frequent overlap in their areas of concern. Bidirectional arrows illustrate the reciprocal connections between fields, recognizing that individual criteria often span multiple domains and cannot be considered in isolation.

As shown in Figure 2, the components of ELSI operate synergistically. At the same time, the framework allows each field—ETHICAL, LEGAL, and SOCIAL—to be analyzed individually, providing clear parameters while accommodating the orderly addition of future elements. This structured approach facilitated the subsequent steps of our study.

Results and Discussion

ELSI criteria in genetic and genomic testing from international bioethical documents

An initial review covering the past 30 years identified 44 potentially relevant sources. After further screening for recent publication dates and close relevance to GGT in terms of ethical, legal, and social issues, nine documents were selected for in-depth analysis **(Table 1)**.

Table 1. International ELSI documents analyzed

Document	Agency	Year	Identification
Universal Declaration on the Human Genome and Human Rights	United Nations Educational, Scientific and Cultural Organization (UNESCO)	1997	UDHG
Convention on Human Rights and Biomedicine: Protecting Human Rights and Dignity in the Application of Biology and Medicine	Council of Europe	1997	OC
Review of Ethical Considerations in Medical Genetics	World Health Organization (WHO)	2003	REI
International Declaration on Human Genetic Data	United Nations Educational, Scientific and Cultural Organization (UNESCO)	2003	HGD
Reykjavik Declaration: Ethical Principles for the Use of Genetics in Healthcare	World Medical Association (WMA)	2019	DR
Medical Genetic Services in Developing Nations: Ethical, Legal, and Social Implications of Genetic Testing and Screening	World Health Organization (WHO)	2006	MGS
Guidelines for Ensuring Quality in Molecular Genetic Testing	Organization for Economic Co-operation and Development (OECD)	2007	GQA
Additional Protocol to the Convention on Human Rights and Biomedicine Concerning Genetic Testing for Health Purposes	Council of Europe	2008	APOC
Report of the International Bioethics Committee on Revisiting Reflections on the Human Genome and Human Rights	United Nations Educational, Scientific and Cultural Organization (UNESCO)	2015	IBC

[a] Better known as "Oviedo Convention". To date signed by 29 countries

[b] Adopted in October 2005 and subsequently revised in 2009 and 2019 by the WMA General Assembly

[c] To date signed by 6 countries

applied to GGT and in the level of detail provided. Notable documents, in chronological order, include:

UNESCO 1997 Universal Declaration on the Human Genome and Human Rights (UDHG) [39]: Considered a cornerstone of international legal frameworks in genomic medicine, this declaration prioritizes human rights, dignity, and fundamental freedoms over other interests.

Oviedo Convention (OC, 1997) [40]: The first internationally binding treaty for countries that ratify it (currently 29 signatories) expands on UDHG principles, specifying requirements for research, informed consent, and genetic counseling, while promoting the use of genetic testing strictly for health purposes [41].

WHO Review of Ethical Aspects in Genetic Medicine (REI, 2003) [11]: Based on Beauchamp and Childress's four principles of bioethics—autonomy, beneficence, non-maleficence, and justice—this report applies these principles to genetic health services, emphasizing informed consent, genetic counseling, public education, and social considerations to support equitable and responsible use of GGT.

UNESCO International Declaration on Human Genetic Data (HGD, 2003) [42]: Establishes principles for the collection, use, storage, and destruction of human genetic and proteomic data, including biological samples. It promotes international cooperation, equitable access to data, and regulatory frameworks for cross-border transfers, extending principles beyond research to clinical genomic services.

World Medical Association Declaration of Reykjavik (DR, 2005; updated 2019) [12]: Addresses ethical responsibilities of physicians in interpreting genetic results, including management of unexpected findings. It details standards for genetic counseling and professional training to ensure comprehensive informed consent in clinical practice.

WHO Report on Medical Genetic Services in Developing Countries (MGS, 2006) [8]: Highlights ethical, legal, and social challenges in genetic testing and screening, particularly in resource-limited settings. Emphasizes distributive justice, privacy, confidentiality, patient education, counseling, quality assurance, and regulatory improvements to promote equitable access and safe, effective genetic services.

Guidelines and Key international documents on ELSI in Genetic/Genomic testing

The OECD's *Guidelines for Quality Assurance in Molecular Genetic Testing* (GQA, 2007) [43] establish international standards to ensure high-quality practices in molecular genetic laboratories. These guidelines emphasize compliance with ISO 17025 [44] for laboratory accreditation, testing, and calibration, and ISO 15189 [45] for medical laboratory standards. GQA also promotes international cooperation, transparency, and public confidence in genetic testing, covering laboratory oversight, traceability, reporting quality, and cross-border exchanges of samples and information.

The 2008 *Additional Protocol to the Oviedo Convention on Genetic Testing for Health Purposes* (APOC) [22] expands the original convention's ethical and social principles. It addresses sample handling, communication of genetic risk to family members, non-directive genetic counseling, quality of services, consent for individuals unable to provide it themselves, and privacy protection. To date, only six countries have ratified APOC [46].

The UNESCO *International Bioethics Committee (IBC) Reflections on Human Genome and Human Rights* (2015) [21] is currently the most comprehensive document on the bioethics of genomic medicine. It identifies five key principles and challenges: (a) autonomy and privacy, (b) justice and solidarity, (c) understanding health and disease, (d) consideration of cultural, social, and economic contexts, and (e) responsibility toward future generations. The IBC addresses emerging applications of genomic medicine, including direct-to-consumer testing and precision medicine, and clarifies the responsibilities of stakeholders—countries, researchers, physicians, regulators, private companies, and media—while emphasizing distributive justice and international collaboration.

While these nine core documents vary in scope and approach, common themes emerge: (a) clinical care and doctor-patient relationships (OC, REI, DR); (b) safeguarding patient rights through quality services (HGD, GQA); and (c) interdisciplinary reviews of ELSI concerns (MGS, IBC). The earliest documents, such as UDHG and OC (1997), focus primarily on the ETHICAL domain—protecting patient rights in research contexts—with only limited attention to LEGAL and SOCIAL considerations. By contrast, the 2015 IBC document expands coverage to include legal responsibilities and social considerations, such as equitable access to services and information dissemination, reflecting a progressive development in ELSI frameworks from basic ethical protections toward broader concerns including technology applications and commercialization.

This evolution is also evident in transnational ELSI programs. Early initiatives, like the U.S. National Human Genome Research Institute's program (1990) [47], focused primarily on ethical and legal issues in research. Later programs broadened the scope: the GE3LS program in Canada (2000) [48] and McGill University's P3G2 program (2004) [49] supported public policy development; ELSI2.0 (2012) [50] emphasized international scientific collaboration; and GA4GH (2013) [51] focused on data sharing. Together, these initiatives illustrate a shift from individual and family rights toward comprehensive management of genomic technologies, emphasizing regulation, data protection, and global cooperation.

Because no single document covers all ELSI criteria for GGT, multiple documents were selected for in-depth analysis to provide a complete view of the relevant ethical, legal, and social criteria.

ELSI criteria for genetic/Genomic testing

From this analysis, 29 ELSI sub-criteria were identified for GGT. These sub-criteria were subsequently organized into ten primary criteria: two in the ETHICAL domain, four in the LEGAL domain, and four in the SOCIAL domain **(Table 2)**.

Table 2. Ethical-legal-social criteria and sub-criteria for genetic/genomic testing

	Criteria	Sub-criteria	Reference
Ethical	Patient rights	Right to health	1, 3, 6, 8, 9
		Free and informed consent	1, 2, 3, 4, 5, 6, 7, 8, 9
		Knowing or not knowing results and implications	1, 2, 3, 4, 5, 7, 8
		Respect for privacy and confidentiality	1, 2, 3, 4, 5, 6, 7, 8, 9
		Respect for human dignity	1, 2, 4, 8, 9
	Non-discrimination	Avoid genetic reductionism	1, 2, 3, 4, 5, 8, 9
		Genetic exceptionalism	1, 2, 4, 6
		Avoid stigmatization	1, 3, 4, 5, 6, 7, 8, 9
Legal	Protection of the Information	Actions to ensure the protection of biological samples, and all physical and electronic information	3, 4, 5, 6, 7, 9
	Testing	Circumstances of application	2, 3, 5, 6, 7, 8, 9
		Advantages, disadvantages and limitations	1, 3, 4, 5, 6, 9
	Health regulation	Qualified health personnel	2, 3, 5, 6, 7, 8
		Surveillance	7, 8
		Medical-patient-company responsibility	3, 5, 7, 9
		Countries responsibility	1, 4, 6, 7, 9
		Analytical validity	4, 6, 7, 8, 9
		Validity and clinical utility	6, 7, 8, 9
		Laboratory accreditation	7, 8
	Commercialization	Direct-to-consumer testing	5, 6, 9
		Medical tourism	7
		Advertising	6, 7, 9
		Cross-border business	4, 7, 9
Social	Counseling	Pre-clinical and post-results	1, 2, 3, 5, 6, 7, 8, 9
		In clinic	1, 2, 3, 4, 5, 6, 7, 8, 9
	Training	Education and dissemination	1, 3, 4, 6, 7
	Reporting of Results	Concept of health and disease	3, 9
		Communication of the risks	3, 4, 5, 7, 8, 9
		Unexpected findings	3, 4, 5, 7, 8, 9
	Accessibility	Access to services under the principle of justice	1, 2, 3, 4, 6, 8, 9

Universal Declaration on the Human Genome and Human Rights, UNESCO 1997
Oviedo Convention, Council of Europe 1997
Review of Ethical Issues in Medical Genetics, WHO 2003
International Declaration on Human Genetic Data, UNESCO 2003
Declaration of Reykjavik, WMA 2019
Medical genetic services in Developing Countries. The Ethical, Legal, and Social Implications of Genetic Testing and Screening, WHO 2006
Guidelines for Quality Assurance in Molecular Genetic Testing, OECD 2007
Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Genetic Testing for Health Purposes, Council of Europe 2008
Report of the International Bioethics Committee on Updating Its Reflection on the Human Genome and Human Rights, UNESCO 2015

Ethical field in ELSI documents

The ETHICAL domain serves as the foundational support across all analyzed documents, as each recognizes the protection of human rights and dignity as a primary ethical concern. These principles underpin both the legal and social aspects of ELSI. Key criteria within this domain include *Patient Rights* and *Non-discrimination*, reflecting the bioethical principles of beneficence, autonomy, and non-maleficence.

The *Patient Rights* criterion encompasses the patient's entitlements throughout the entire GGT process—from arrival at a healthcare institution (public or private) to the handling of results, whether these are securely stored indefinitely or destroyed, depending on the circumstances.

The *Non-discrimination* criterion ensures that patients are treated equally regardless of their genetic or genomic results, both within and outside healthcare settings, in accordance with the International Bioethics Committee's Report on Non-discrimination and Non-stigmatization [52]. This criterion is divided into three sub-criteria:

Avoidance of reductionism – preventing the overemphasis on genetic factors while underestimating behavioral, psychosocial, and environmental influences.

Genetic exceptionalism – recognizing the unique nature of genetic data, which can reveal information about the individual, their family, and potentially carry cultural significance, requiring special handling.

Avoidance of stigmatization – ensuring that no individual, family, group, or community is marginalized due to a genetic test result.

Non-discrimination is widely cited as a fundamental patient right and is the most referenced criterion among the analyzed documents. Both *Patient Rights* and *Non-discrimination* are cross-cutting criteria that must be upheld throughout the GGT process, with mechanisms implemented to ensure compliance.

A comparative analysis of the nine documents, showing the proportion of ethical, legal, and social sub-criteria covered, reveals a strong orientation toward the ethical domain **(Figure 3)**. The highest percentages of ethical coverage were observed in UDHG (100%), OC (75%), HGD (88%), DR (63%), APOC (88%), and MGS (63%). While REI and IBC emphasize social criteria, and GQA primarily addresses legal aspects related to quality and regulation, these findings highlight that no single document comprehensively covers all ELSI criteria. Therefore, combining multiple documents is necessary to create a more complete and robust guideline.

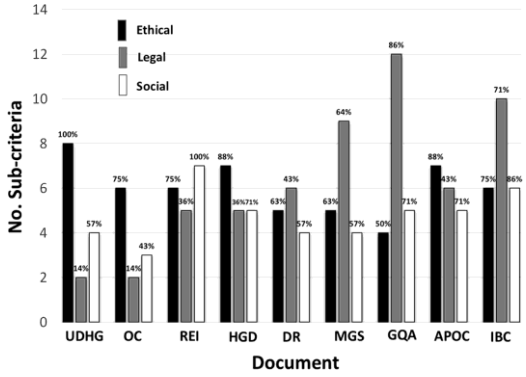

Figure 3. Number of sub-criteria covered by each international document divided into ETHICAL, LEGAL and SOCIAL fields. The percentages indicate how much of the total identified sub-criteria is covered by each field

Legal Field in ELSI documents

The LEGAL domain contains the largest number of criteria and sub-criteria related to GGT, totaling fourteen, though their representation differs across documents. Some documents, such as UDHG and OC, include only a few legal sub-criteria, like *Testing* and *Health Regulation*, and do not explore them in detail. The *Protection of Information* criterion emphasizes mechanisms—both temporal and procedural—to safeguard biological samples and any physical or electronic genetic data from unauthorized access, including their destruction when necessary. The *Testing* criterion specifies the circumstances under which GGT may be performed on a patient or their relatives, clarifying the scope and limitations of the test. The *Health Regulation* criterion is the most comprehensive, encompassing the role of national legal and regulatory frameworks to ensure the quality, reliability, and compliance of GGT practices. The *Commercialization* criterion extends this legal perspective to the provision and sale of GGT services and products, integrating technology commercialization with ELSI considerations as addressed in the GQA and IBC documents. This area is less frequently treated, reflecting both the research focus of most documents and the absence of a fully harmonized international regulatory framework for GGT, a gap that the present study aims to help address. Each country must adapt regulations according to its context while adhering to international standards and upholding the cross-cutting ethical principles.

Social field in ELSI documents

The SOCIAL domain focuses on distributive justice and equitable access to genetic information, encompassing four main criteria. *Genetic Counseling* defines the guidance provided by health professionals as non-directive, comprehensive, understandable, and respectful, covering all testing stages until the patient's questions are fully addressed. The *Training* criterion includes public policies, the development of qualified human resources, dissemination of genomic knowledge across society, and broad access to information via institutions, academia, and civil organizations. *Reporting of Results* involves communicating test outcomes, relevant contextual information, and unexpected findings

to patients and, when appropriate, their families, helping to prevent genetic determinism by emphasizing the role of environmental, biological, and psychosocial factors. The *Accessibility* criterion emphasizes the need for GGT services to be available to all who may require them, not solely to those who can afford them. Accessible GGT, accompanied by professional counseling, can serve as a routine public health tool for early disease detection, prevention, and the reduction of social inequities. Among these, *Genetic Counseling* is particularly prominent across all testing phases, although the other social criteria are also well represented in the analyzed documents. Nevertheless, clear implementation guidelines for countries are still limited.

Priority Criteria for Genetic/Genomic Testing

Not all criteria carry the same weight in international practice. Prioritization can be categorized into four groups: safeguarding dignity and human rights, ensuring quality services that protect patient health and best interests, promoting fair access to technology and healthcare, and strengthening the doctor-patient relationship. Analysis of the nine selected documents shows differences in the emphasis given to various criteria and sub-criteria, and **Figure 4** presents the coverage of the 29 sub-criteria ordered according to their frequency of citation in the analyzed texts.

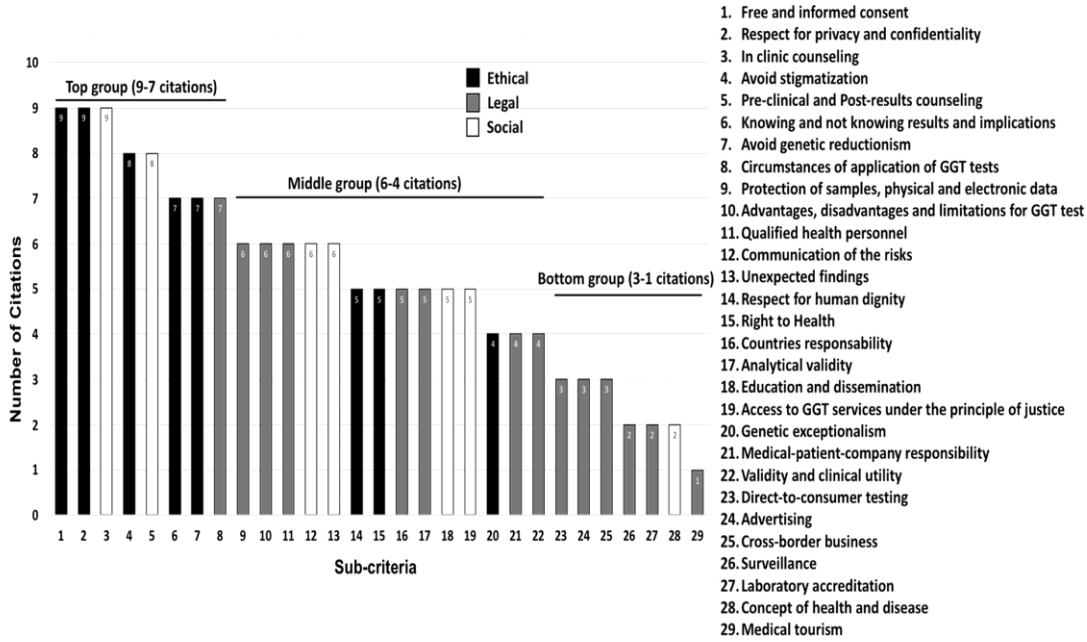

Figure 4. GGT Sub-criteria arranged according to the number of documents in which they appear

The frequency of citations for the sub-criteria can be organized into three groups, as shown in Figure 4. The top group includes sub-criteria cited seven to nine times, primarily encompassing the two ETHICAL criteria, *Patient Rights* and *Non-discrimination*. This prominence is expected, given that the protection of patient rights forms the foundation of all ELSI documents concerning the human genome. Within this group, only one sub-criterion belongs to the LEGAL field, which concerns the conditions under which a GGT test is validly applied. This sub-criterion is highly referenced because GGT is recommended exclusively for health purposes under medical supervision, discouraging its use for curiosity or non-medical purposes, such as direct-to-consumer (DTC) testing, which could lead to harmful health decisions. From the SOCIAL field, *Genetic Counseling* is included in this top group, reflecting the critical role of medical monitoring in the diagnosis and treatment of genetic conditions. Sub-criteria in this top group correspond mainly to the A and D prioritization approaches.

The middle group, cited four to six times, includes fourteen sub-criteria, with three from the LEGAL field—*Protection of Information*, *Testing*, and particularly *Health Regulation*—and three from the SOCIAL field—*Training*, *Reporting of Results*, and *Accessibility*. These sub-criteria align with prioritization approaches B, C, and D, highlighting both regulatory and social concerns.

The bottom group, cited only one to three times, contains eight sub-criteria, largely related to the LEGAL criterion of *Commercialization*. Few documents address commercialization of GGT within ELSI studies, although more recent publications, such as MGS, GQA, and IBC, have begun incorporating this aspect. Sub-criteria in this group correspond primarily to prioritization approach B. Additionally, Table 3 summarizes the criteria deemed relevant for an overall prioritization approach across the three ELSI fields, reflecting the urgency highlighted by the analyzed international documents.

Table 3. Priority criteria for genetic/genomic testing according to the analyzed documents

Ethical	Legal	Social
Patient rights	Protection of the information and biological samples	Counseling Accessibility
Non-discrimination	Health Regulation	Training

The seven priority criteria identified in this study are strongly represented across the analyzed documents, as illustrated in **Figure 4**. The ETHICAL priority criteria, *Patient Rights* and *Non-discrimination* (prioritization approach A), along with the SOCIAL criterion *Counseling* (prioritization approach D), are among the most frequently cited, while the remaining priority criteria appear in more than half of the documents. Notably, *Patient Rights*, *Non-discrimination*, and *Protection of Information* have been consistently highlighted from the earliest ethically oriented documents, maintaining their prioritization over time. The *Health Regulation* criterion (approach B) emerged as a priority roughly a decade later in response to the increasing use of GGT technology for both health and other purposes, emphasizing the importance of test safety and laboratory quality. Likewise, *Accessibility* (approach C) and *Training* (approach B) have gained recognition, reflecting the evolving social, cultural, and economic contexts of different countries.

These observations align with the WHO 2002 recommendations, which emphasized ETHICAL and LEGAL priorities and the importance of counseling, particularly informed consent and protection of privacy and confidentiality to prevent discrimination. Similarly, Granados-Moreno *et al.* (2018) highlighted *Counseling*, *Validity and Clinical Utility*, *Confidentiality*, and *Informed Consent* as especially relevant, consistent with our findings. They also recognized *Genetic Exceptionalism* and *Commercialization*, including intellectual property and direct-to-consumer testing, as pertinent to the bioeconomy of personalized medicine. The criterion of *Reporting of Results*, encompassing communication of risks and unexpected findings (approach D), was also identified as critical, appearing in over half of the analyzed documents. While approaches A, B, and C, and even counseling (approach D), can be codified through national laws and regulations, the reporting of results requires coordinated guidelines between health authorities, medical educators, physicians, and patients, as reflected in the recent Declaration of Cordoba and the IBC report on individual responsibility in health.

The evolution of ELSI criteria has paralleled technological advances in GGT and the increasing need for national regulation. Although the UDHG is non-binding, many countries have used it as a foundation for national legislation. Initially focused on ethical issues in human genome research, it provides a starting point; however, broader aspects such as commercialization and regulation have become increasingly important. Widely accepted ELSI criteria, consistent with international bioethical standards as identified here, can serve as a robust basis for national regulations in personalized genomic medicine.

Given the differences in how documents address ELSI content, we propose updated specifications to complement one another. For the ETHICAL field, considerations for adults with full consent capacity should be expanded to include individuals with partial or no consent capacity, following the OC and APOC guidelines for authorization and REI recommendations on autonomy and informed consent. For the LEGAL field, HGD principles on collection, processing, use, and storage of genetic data and biological samples should be considered, including cross-border operations. Quality assurance in GGT services should combine GQA best practices with APOC recommendations on service quality and clinical utility, as well as IBC guidance for direct-to-consumer testing. Parameters for stakeholder responsibilities—including governments, scientists, regulators, media, and commercial actors—should also be integrated, along with mechanisms for addressing damages as outlined in UDHG. The recommended conditions for applying GGT tests, including benefits to patients, family members, and biological materials from

deceased persons, are detailed in APOC and supported by IBC guidance on understanding health and disease.

For the SOCIAL field, broad genetic counseling criteria from REI should be adopted for competent adults, children, adolescents, and individuals with diminished capacity, in combination with DR recommendations for physician and medical student counseling. Guidelines for addressing unexpected findings, ensuring distributive justice through the formation of civic organizations, and promoting bioethics education for patients and society are derived from MGS and REI, with GQA standards providing education and training requirements for laboratory personnel.

The ethical, legal, and social implications of research in the human genome have evolved into a dynamic, interconnected, and progressively sophisticated field. This development is reflected both in the evolution of international documents and the parallel emergence of national ELSI programs. Three core areas of focus emerge: clinical care and the doctor-patient relationship, protection of patients' and relatives' rights, and the benefits of an interdisciplinary approach. Together, these dimensions reinforce respect for human dignity, privacy, and rights, aiming to prevent discrimination based on genetic information. The most significant challenges remain within national health regulations and, particularly, in the governance of commercialization for GGT technologies.

To address these challenges, this work presents a first unified extract defining the parameters of each ELSI field, clarifying the meaning of ethical, legal, and social issues as outlined in major international documents over the past thirty years. This organized framework allows for the orderly inclusion of future elements as the field evolves. In its current form, it incorporates the three fundamental ELSI fields relevant to genomic medicine, tailored specifically to GGT: applicable bioethical principles, flexible legal frameworks to accommodate emerging technologies, and the socio-cultural context of science and technology. Within this framework, twenty-nine ELSI sub-criteria are grouped into ten main criteria, and seven top-priority criteria are identified, offering a practical foundation for reviewing, evaluating, or developing national regulations on GGT while supporting human rights and fostering the bioeconomy.

Although the minimum criteria identified are designed for GGT in medical contexts, they can be extended to other areas of genomic medicine, including biobanks, epigenetics, human genetic databases, and germline genetic modification. Expanding the study to include newborn testing, non-medical purposes such as ancestry exploration, or populations with limited consent capacity (e.g., prisoners or individuals with cognitive impairments) would also be valuable. Additionally, issues relevant to international research and governance, such as genomic sovereignty, data sharing, and global cooperation, should be considered in future ELSI analyses.

Given the interdisciplinary and evolving nature of ELSI, complementary fields are likely to emerge. For example, the OECD emphasizes that future health challenges can be addressed through the development and application of bioeconomic innovations—encompassing legal and commercial aspects such as intellectual property, functionality and safety verification, and authorization for distribution. The GE3LS program in Canada exemplifies this approach, integrating ethical, legal, social, environmental, and economic factors into genomic research. Incorporating a BIOECONOMY field into ELSI frameworks will be increasingly important, particularly as commercialization of GGT technology expands.

As ELSI studies transition from a primary focus on human rights to include commercial and technological applications, the need for harmonized regulations becomes urgent. Standardized ELSI criteria provide a foundation for creating, verifying, and enhancing national regulations, balancing bioeconomic development, social equity, and, above all, the protection of human dignity and rights. Despite this progress, the integration of ELSI considerations into GGT commercialization remains incomplete. Rapid technological advancement in GGT demands international harmonization of ELSI criteria, both in content and scope, to prevent confusion and ensure consistency. International and interdisciplinary panels of experts should prioritize accurate ELSI nomenclature and comprehensive criteria, and this work provides a structured contribution toward that goal.

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