THE ETHICAL ISSUES ASSOCIATED WITH THE USE OF GENETICS ANCESTRY IN GENOMICS RESEARCH A MIXED-METHODS SYSTEMATIC LITERATURE REVIEW

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Executive Summary

Background

The use of Genetic Ancestry (GA) in genomics research has surged in recent years, marking a significant shift in how human genetic variation and diversity are understood and utilized. This transformation, while offering immense scientific potential, also raises numerous ethical issues. There is an extensive academic literature on the ethical issues associated with the use of GA in genomics, however, there is no coherent synthesis. Furthermore, our initial analysis suggests that the ethical issues discussed demonstrate temporal trends and that different academic disciplines focus on different types of ethical issues.

Objectives

This research aims to synthesize the array of ethical issues associated with the use of GA in genomics research, and simultaneously explore how different academic disciplines engage with these issues and their evolution over the past 15 years (2008-2023). The study seeks to provide a comprehensive understanding of the ethical landscape in genomics research involving GA, identifying key thematic codes representing various ethical challenges and how these intersect with the authors' disciplines and the temporal trends in academic discourse.

Methodology

This research uses a mixed-methods systematic review, following the 2020 PRISMA guidelines. Simultaneously, it adapts qualitative content analysis to apply thematic codes to the collected manuscripts, examining the intersection between thematic codes, authors' disciplines, and publication years. Data collection involved searches in major academic databases (PubMed, Scopus, Web of Science, Google Scholar) using terms to find manuscripts at the intersection of 1), genetic ancestry 2), genomic research, and 3) ethics or bioethics. Manuscripts were screened based on their engagement with the research topic and the period of publication (2008-2023). The final analysis included 54 manuscripts that are each labelled with thematic codes, the first author's discipline category, and the year of publication.

Results

The study identified six thematic codes, each representing a distinct subset of ethical challenges in GA usage:

1. The Reification of Genetically Defined Race
2. The Need for More Diversity and Representation in Genomic Databases
3. Genetic Essentialism and the Oversimplification of Health
4. Genetic Stereotyping and Stigmatization

5. The Role of Mistrust and Cultural Insensitivity
6. The Need for More Education Standards and Guidance in Using GA in Research

Key Findings

1. The research topic showcases robust multidisciplinary engagement, evidenced by substantial participation from authors across all three identified disciplinary categories.
2. There is a correlation between author discipline and thematic codes. This suggests that authors of a discipline hold tendencies and biases to engage specific themes, key ideas, and ethical issues.
3. Temporal analysis of thematic codes shows that certain ethical issues have shown increasing engagement in the last 15 years.
4. Namely, ethical issues surrounding the diversity and representation of genomic datasets, the reification of genetically defined race, and the value of building trust and culturally sensitive research practices are increasingly discussed.

Key Messages and Implications

a) Key Findings 1 and 2 suggest benefits to promoting interdisciplinary collaboration in efforts to address the ethical issues associated with the use of GA. Different academic disciplines tend to have different tendencies and biases in the ethical issues they discuss. Therefore, more interdisciplinary collaboration holds potential to bridge these disciplinary gaps and promote more comprehensive efforts to address such ethical issues.
b) Key Findings 3 and 4 suggest that certain ethical issues are increasingly prominent in the academic literature. Accordingly, funders and institutions can use such trends to inform and align their institutional support to research in innovative and high-priority topics.
c) Many of the ethical issues identified can be ameliorated or addressed through improved scientific communication practices. As such, this suggests benefits to offering increased guidance and standards on scientific communication practices for the use of GA in research.

Section One: Introduction and Background

In recent years, the application of the concept of Genetics Ancestry (GA) in genomics research has experienced a notable surge, marking a pivotal shift from the use of traditional population description labels such as race and ethnicity. GA fundamentally represents an approach to understanding human genetic variation and diversity through lineage, ancestral origins, and genetic similarity.[1–3] GA is determined by a combination of genetic testing and statistical analysis, focusing on the inheritance of DNA segments across generations of human evolution.[2,4] GA is determined by collecting DNA samples from an individual and then genotyping to identify specific genetic markers (such as single nucleotide polymorphisms) that are indicative of ancestral origin.[2,4] To perform this last step, these DNA samples are compared to a reference population database, thus enabling researchers to make inferences about an individual's ancestral origins.[2,4] Importantly, GA is significantly different from concepts of race and ethnicity in two primary ways. Firstly, GA is not a social construct, unlike race and ethnicity, as it is determined through genetic testing and subsequent analysis.[2,4] Secondly, GA does not focus on categorizing individuals into groups or populations. Instead, it is an expression of an individual's patterns of genetic inheritance.[2,4]

The utility of GA spans several highly promising areas in genomics research, such as precision medicine, disease risk assessment, and clinical trial design.[2–7] In precision medicine, GA aids in tailoring medical treatments to the specific genetic makeup of individuals.[4,5] Relatedly, in disease risk assessment, GA can be used to identify genetic predispositions to inform earlier interventions and guide clinical action.[5,6] When developing clinical trials, the use of GA can help ensure a more genetically diverse and representative sample of participants, with the potential to enhance both the safety and the efficacy of interventions.[5,8]

Despite its potential, the use of GA in genomics research is not without its drawbacks and challenges. There is an extensive research literature at the intersection of bioethics, GA, and genomics, which investigates the ethical and social issues associated with the use of GA.[1] We conducted an initial literature review to better understand the research landscape surrounding this research topic. Our review revealed three interesting findings. Firstly 1), despite the extensive scholarly literature available on the topic, there

[1] Henceforth, the "ethical challenges associated with the use of GA in genomics research" will sometimes simply be referred to as "the research topic".

is a noticeable absence of a unified synthesis addressing GA. Individual publications often focus on specific ethical challenges, without taking the time to provide a broader perspective integrating their work with that of other scholars. Secondly 2), writers commenting on the social and ethical issues of GA come from a broad variety of fields of expertise. When assessing the research profiles of the authors, we noticed a diverse range of academic disciplines, from social scientists to clinicians and epidemiology experts. Lastly, 3) our review revealed a temporal pattern in the discussion, with some themes and challenges following a certain trend over time.

Research Objectives

A preliminary literature review helped us to formulate our three research questions:

1) What ethical challenges arise when using GA in genomics research?
2) How does an author's discipline influence the kind of ethical challenges they discuss?
3) How have the identified ethical challenges evolved in the last 15 years from 2008 to 2023?

The first research question aims to identify, categorize, and systematically organize the array of ethical and social challenges associated with the use of GA in genomics research into a coherent and comprehensive synthesis. This approach will not only highlight the ethical concerns that arise when GA is used in genomics research, but also seek to build a holistic understanding of its ethical landscape. We hypothesize that the ethical challenges associated with the research topic can be systematically categorized into thematic codes, each representing a set of key ideas, themes, and challenges. Each manuscript can be labelled with one or more thematic codes, which will then represent the key ideas and themes that this manuscript discusses and engages with. The second question aims to explore the relationship between the author's discipline and the themes they engage with and discern potential trends in this relation. Lastly, the third question traces the temporal evolution of the identified thematic codes. Detecting shifts in the research community's interest level in these codes provides a longitudinal perspective on the dynamic nature of the socioethical discourse within the research topic.

This research is poised to make significant and novel contributions to existing research literature. Firstly, it addresses a gap in the existing literature by providing a comprehensive and cohesive synthesis of the research topic. This aspect is particularly important, as our initial review highlighted a tendency for authors to discuss and address key ideas in a siloed manner, and consequently missing out on a broader perspective. Secondly, this research contains a strong interdisciplinary component. This will contribute to

a deeper understanding of the knowledge gaps between experts from diverse backgrounds. Bridging such gaps can be pivotal for future interdisciplinary collaborations. Lastly, our examination of the temporal evolution in the academic literature offers insightful evidence of the enduring relevance and progression of specific challenges and ideas within this field. Documenting the changing frequency of themes across time periods can provide researchers and policymakers with crucial guidance on the most current concerns in a dynamic and ever-evolving field. These aspects contribute a novel and original approach that holds significant potential to uncover interesting and previously undocumented findings.

Format

This manuscript will take the following format encompassing seven sections: 1) Introduction and Objectives, 2), Methods, 3), Results Part One, 4), Results Part Two, 5) Implications, 6), Conclusion, and 7), Knowledge Mobilization activities.

Section 2: Methods

Overview

The previous section introduced the three research objectives and their scientific rationale. This one will outline the research method employed. As discussed, this project adopts a two-part approach, centred around a mixed methods systematic review.

The first part of the systematic review aims to provide a coherent and comprehensive synthesis of the socioethical challenges associated with the use of GA in genomics research. This section aims to organize the current state of knowledge surrounding the research question, drawing from diverse perspectives and expertise. This study conforms to the 2020 PRISMA guidelines for reporting systematic review.[9] Results are presented in Chapter 3: Results Part One.

The second part of this project revolves around applying qualitative content analysis methods to the manuscripts extracted during the systematic review. This process focuses on applying a codebook to identify the primary themes and ideas that each research manuscript engages with. The qualitative content analysis methods are adapted from the work of Roberts and Colleagues, and DeCuir-Gunby and Colleagues.[10,11] Using this codebook, every manuscript will be labelled and tagged using a series of thematic codes. Furthermore, every manuscript will be labelled with the first author's discipline, and its

year of publication. Potential correlations between these labels will be explored through statistical analysis methods used subsequently. These results are presented in Chapter 4: Results Part Two.

Overall, section 3: Results Part 1 aims to provide a comprehensive and cohesive synthesis of the research topic, using a systematic review. Meanwhile, section 4: Results Part 2 utilizes qualitative content analysis methods to identify patterns and trends in the literature's approach to the research question. It is important to note that both parts 1 and 2 are highly complementary and undertaken concurrently. For example, the process of codebook development simultaneously informed the organization of the systematic review.

Literature Search and Screening

A preliminary literature review was conducted before the start of the research project. This initial review yielded valuable insights into the terminology, keywords, and concepts that authors employed to address the research topic. This knowledge was used to design the literature search strategy.

Three electronic academic databases were used, PubMed, Scopus, and Web of Science. Google Scholar is employed as a control. Firstly, the three databases were searched using a series of terms designed to identify manuscripts that engaged with topics at the intersection of 1) genetic ancestry, 2) genetics or genomics, and 3) ethics, or bioethics. The search terms are ("genetic ancestry") AND (genetic* OR genomic*) AND (ethic OR bioethics*).[2] These are also the keywords we looked for to indicate a relevant manuscript. This search was performed on September 20th, 2023.

Inclusion and Exclusion Criteria

Results were limited to peer-reviewed research manuscripts published in English between January 2008 and July 2023. The data limits were chosen to capture a relatively wide timespan, as a 15-year period makes it possible to evaluate the temporal evolution of the discourse on the research questions. The manuscripts were screened by reading the title, abstract, and keywords, to discern perceived meaningful engagement with the three features of the research topic. The Google Scholar search engine was used as a control to identify relevant manuscripts initially missed in PubMed, Scopus, and Web of Science. The same search terms and time limits were applied.

[2] Henceforth, these qualities will sometimes be referred to as the key features of the research topic.

To meet the inclusion criteria, manuscripts must be perceived to engage with the 3 features of the GA substantially and meaningfully. This is assessed based on the content that is presented in each manuscript's title, keywords, and abstract. Manuscripts that fail to substantially discuss any one feature are excluded. For example, a manuscript that merely reports on health-relevant genetic variation based on GA without discussing the ethical implications of this finding would be excluded. Given that, the inclusion and exclusion criteria are content-based, a manuscript does not need to explicitly use search terms to be included. For example, a manuscript discussing the role of GA in ensuring the equitable translation of genomics research into clinical practices would meet the inclusion criteria. The details of the screening and extraction process are further detailed in Figure 1: *PRISMA Guidelines* in Chapter 3.

Initial Codebook Development

For the initial codebook development, we selected 15 manuscripts from the systematic review based on their diverse content, as indicated by their titles, keywords, and abstracts. This diversity ensured a wide range of themes and key ideas were represented. The codebook development process involved both inductive and deductive reasoning approaches, using the authors' background knowledge to generate an initial set of 6 codes. Inductive reasoning involves generating codes from the data, while deductive reasoning starts with theoretical codes, which are then confirmed or altered through data analysis. This approach led to the creation of initial codes, along with their definitions, descriptions, and criteria for inclusion and exclusion.

Iterative Codebook Development

The iterative codebook development aimed at achieving code saturation, ensuring all relevant themes and concepts in the manuscripts were captured. This involved analyzing sets of 5 manuscripts at a time, applying the initial codebook, and assessing its effectiveness. During this process, we refined existing codes and updated inclusion and exclusion criteria as needed. After 3 cycles of this iterative process, the codebook no longer required modifications, indicating that it effectively represented the range of themes and concepts in the analyzed manuscripts, achieving code saturation. This method ensured the comprehensiveness of the codebook for guiding the qualitative analysis.

Ensuring Intercoder Consistency

Intercoder consistency, critical for reliable and replicable coding, was achieved through a two-step process with two independent coders (EK and HL). Initially, both coders independently applied the codebook to a sample of 5 manuscripts. Comparing their coding results highlighted inconsistencies, prompting a review

and refinement of the code descriptions and criteria to reduce ambiguity. A second round of coding with a new set of 5 manuscripts showed almost perfect consistency, confirming the effectiveness of the refinements. This process was repeated to ensure sustained intercoder consistency, demonstrating that the codebook was sufficiently refined for reliable application.

Codebook Application

After finalizing the codebook, one coder (HL) applied it to the entire dataset of manuscripts extracted in the systematic review. Each manuscript was carefully read and analyzed, with the coder assigning the appropriate codes from the codebook to capture the key themes and ideas that are present. To maintain the quality and consistency of the coding process, the coder periodically reviewed the assigned codes, to ensure that they align with the various criteria within the codebook.

Coding For Author's Discipline

The term "discipline" refers to the main area of focus and expertise of an author. This is assessed based on the author's research biography and profile, as well as the description of their research and work focus. This information is easily extracted from their affiliation and the contact information included in each manuscript. For each manuscript included in the review, the first discipline of the first author was recorded.[3] The author's discipline coding process occurred in conjunction with the theme coding process. Based on a preliminary analysis of the researchers' profiles and biographies we created 3 broad categories 1) Social Science, 2) Biomedical Science and Clinicians, 3) Public Health and Epidemiology. The coders applied these categories to the author's profiles of 10 manuscripts. The coders compared their results, finding very few inconsistencies. The coders discussed the inconsistencies and refined category descriptions and criteria. To test the consistency and replicability of the refined discipline categories, another round of coding using 10 more manuscripts occurred. No inconsistencies were found, indicating consistent and replicable categorization.

[3] Some manuscripts had over 5 authors. To work within the time constraints of the project, we choose to focus on the first author of each manuscript.

Section 3: Results Part 1- Synthesis of Ethical Challenges in Genomics Research

Overview

The following section focuses on presenting a detailed synthesis of the ethical challenges associated with the use of GA in genomics research. This section is organized into 4 sub-sections, which aim to explore and group 6 thematic codes together. This approach emphasizes the conceptual overlap and the natural progression of certain codes, and how they may be interrelated. For this reason, exploring related thematic codes together effectively builds a more coherent synthesis of the research topic.

The first section will explore thematic codes 1,3, and 4. These codes share conceptual overlap in examining the implications of GA for altering interpretations of social identity, such as race, and health. This section provides an integrated analysis of how the use of GA may: 1) support the concept of race as genetically defined (Code 1), hold a tendency to overemphasize genetic factors in health-based research (Code 3) and create risks of genetic stereotyping and stigmatization (Code 4). The second section offers an in-depth analysis of thematic code 6, focusing on the need for more education, standards, and guidance for using GA in research. The various normative prescriptions and standards in Code 6 can be seen as a response to ethical issues raised in the previous section (Codes 1,3, and 4). Following this, the third section switches focus to analyze thematic code 2. Code 2 addresses the need for more diversity and representation in genomic databases. This will be closely related to the final section, which addresses code 5. Code 5 will emphasize the role of trust and cultural sensitivity in promoting more diverse and representative research. In a sense, the ideas represented by Code 5 can be seen as a response to the ethical issues highlighted by Code 4.

Genetic Ancestry: Complexities and Misunderstandings

In this section, we will explore the complexities and common misunderstandings surrounding GA in genomics research, particularly focusing on what authors describe as the “reification” or “reinscription” of genetically defined race.[2,12,13] This concept raises important concerns around the use of GA in genomics research, which may implicitly reposition the concept of race from being socially to genetically defined. To better elucidate the essence of these ideas, we will examine 3 manuscripts that collectively address different aspects of the reification of genetically defined race. Initially, we will focus on a 2011 article by

Fujimura and Rajagopalan, and another 2012 by Yu and Colleagues, which provide a foundational understanding of the intricacies of GA.[2,4]These 2 papers demonstrate how important nuances relating to GA are frequently misunderstood or oversimplified by even high-level scientists. Following this, we will discuss a recent publication by Carlson and Colleagues, which explores the darker implications of such misunderstandings.[14] Namely, how the use of GA in research can be misappropriated for nefarious and racist purposes.

GA and race are frequently used interchangeably in public and sometimes even in the scientific discourse.[2–4] However, they are fundamentally distinct concepts. As briefly explained in Section One, GA is determined through a combination of genetic testing and statistical analysis. It focuses on DNA segments that are inherited across generations that are indicative of geographical origins and lineage.[2–4] More specifically, the DNA segments used are termed "ancestry informative markers" (AIMs).[2–4] These markers are genetic variations at the single nucleotide, loci, or allele frequency level.[2–4] Crucially, GA is ascertained by comparing an individual's genetic markers (AIMs) to those present in established reference panels.[2–4] These reference panels are composed of genetic data from a diverse array of population groups around the world, enabling researchers to gain interesting insights about an individual's geographical origins and lineage.[2–4] It is crucial for GA to be understood as a continuum of variation, rather than discrete biological categorisation.[2–4] This is different from race, which is a social construct, defined by physical, cultural, and social characteristics that are not grounded in genetic testing.[2,4] Concepts of race are also characterized by their discrete nature, in which individuals or groups are split into non-continuous categories like *White*, *Black*, or *Asian*.[2,4]

Continental Labels in Genetic Ancestry Are Mostly Unnecessary

The differences between GA and race are well-elucidated in a 2011 article by Fujimura and Rajagopalan.[2]Their analysis discusses how GA is utilized in contemporary genetic research techniques, particularly in Principle Component Analysis (PCA) and Genome-Wide Association Studies (GWAS). They explain the origins of GA as a concept. Particularly, it is emphasized that GA was initially used in studies of human continental migrations, such as investigations into prehistoric movements from Africa to Europe. In these contexts, the use of continental labels like "African GA" was appropriate.[2] However, the authors emphasize that many current studies that use GA employ continental labels in an unnecessary and inappropriate manner.

Contemporary genomics research predominantly employs GA as a controlled variable.[2] This is done to differentiate between meaningful genetic variations and those that are simply correlative. Consider the following simplified example of a GWAS study involving Disease X. A research team is interested in identifying causal genetic variants of Disease X by comparing two groups of research participants, one group with Disease X and another group without Disease X. The research team sequences both groups and searches for differences in genetic variations. Detected variations may be candidates for causing Disease X, but they may also simply be "population-specific" factors that are unrelated to Disease X.[2]These population-specific factors, while correlated with Disease X, are not causal, and can lead to false associations. In this example, incorporating GA can account for population-specific factors and "population stratification", which will help differentiate between meaningful and non-meaningful variation.[2] In such uses of GA, adding continental labels is unnecessary and could further the reification and conflation of GA with race. The use of terms like "African" or "European" GA in this context may reinforce the notion of distinct genetic categories based on continent, echoing traditional racial classifications.[2]

Biomedical Scientists Sometimes Oversimplify Genetic Ancestry

Although the use of GA is meant to represent scientific and quantifiable measures of human diversity, it is seemingly becoming a scientific euphemism for race in the way it is operationalized.[4] A publication by Yu and Colleagues highlights this challenge.[4] The publication is based on a workshop hosted to investigate interdisciplinary perspectives on the use of GA in disease research.[4] The workshop aimed to better understand how different disciplines conceptualize GA, and its value for better understanding human disease. This workshop concludes that even many high-level biomedical researchers misunderstand GA, and in fact treat this concept very similarly to race.[4]

The publication by Yu and Colleagues offers critical insights into how GA is perceived and operationalized across different scientific disciplines.[4] This workshop involved semi-structured interviews with 22 senior researchers actively using GA in their research. The researchers were categorized into three distinct disciplinary groups: population geneticists, epidemiologists, and clinician-researchers.[6] The goal of these interviews was to explore the different ways in which these experts integrate GA into their research, and how they conceptualize GA.[4]

The findings from this study revealed that population geneticists possessed a significantly different understanding of GA compared to epidemiologists and clinician-researchers.[6] More specifically, population geneticists viewed GA as a spectrum of genetic variation, which sharply contrasts with the rigid and discrete categories associated with traditional concepts of race. This group of scientists used GA in their research to account for "population structure", which allows them to account for confounding variables when investigating the cause of disease.[4] Conversely, clinician researchers and epidemiologists were found to operationalize GA similarly to racial categories.[4]The two groups generally embraced the idea of categorizing individuals based on GA for disease risk assessment, and for treatment management.[4] Where this perspective uses the language of GA, its logic resembles the one of race, implying a discrete categorization where people can be binned into groups. Yu and Colleagues, therefore, highlight a critical issue even among highly trained biomedical researchers.[4] GA often becomes synonymous with race, despite the fundamental distinction between these two concepts. This conflation suggests that simply adopting the terminology of GA does not overcome the challenges linked to the reification of genetically defined race. Ultimately, we see that GA is frequently used as a scientific euphemism for race.

The Consequences of Reifying Genetically Defined Race

The preceding sections emphasized the complexities surrounding the conceptualization and operationalization of GA in scientific research, and how this could lead to a conflation with the concept of race. This scientific misunderstanding can lead to dangerous consequences, such as the reinforcement of racist ideologies through the misuse and misappropriation of GA and genomics research. Such behaviour has seen an alarming increase in recent years.[14] For instance, in their 2022 study, Carlson and Colleagues present disturbing examples in which extremist groups have misappropriated genomic research findings to justify their views.[4] The researchers conducted a meta-study of 1,800 biomedical science preprints focusing on human genetics and neuroscience, published between 2012 and 2020.[14] This meta-analysis targeted preprints that garnered significant social media attention, specifically those with over 50 re-tweets.[14] Alarmingly, for the most popular preprints, the authors of around 5% of the tweets were users associated with extremist groups, indicating a concerning trend where scientific findings are being distorted to support racist viewpoints.[14]

Accordingly, Carlson and Colleagues urge scientists to be more vigilant about how their research may be misinterpreted or exploited by non-scientific audiences.[14] This call for vigilance is particularly relevant in the field of population genetics, where methods like Principle Component Analysis (PCA) can lead to

simplified figures that are susceptible to misinterpretation. While these PCA figures are valuable for communication within the scientific community, they are prone to manipulation for harmful ends. For example, Carlson and Colleagues cite instances of simplified PCA diagrams that have been mistakenly cited as evidence of racial genetic differences, underlining the potential for misrepresentation.[14] Overall, the authors do not advocate for research censorship, but instead urge scientists to consider how their work could be interpreted or misused, and emphasize the need for mindfulness in this regard.[14]

The Reification of Race is the Basis for the Oversimplification of Health and Genetic Stereotyping

The preceding sections have laid a critical foundation for understanding the complexities of GA and its conflation with race, as represented by Code 1. This conflation, crucially, forms the basis for the challenges addressed in Codes 3 and 4. These challenges stem from the overemphasis on a genetic basis for race.

The close relationship between the ideas represented by these codes is exemplified in a 2015 publication by Troy Duster.[12] Duster illustrates how the pursuit of precision medicine has increasingly focused on differential drug responses observed between racial groups.[12]This has sometimes misdirected focus to an oversimplified understanding of racial health disparities.[12] A critical example of this is the logic behind the development of race-specific drugs. Proponents of these drugs often justify their race-specific nature by citing racial health disparities.[12]They argue that tailoring drugs to specific racial groups is essential for equitable access to care and addressing inequalities.[12] However, this stance likely overemphasizes the role of genetics in racial health disparities. The prevailing scientific consensus supports the idea that most common diseases stem from a complex combination of social, environmental, and genetic factors.[12,15,16] As such, it is often an oversimplification to consider genetic differences as the basis for racial disparities.[12,15,16] The argument supporting race-specific drugs, while it may be formulated with good intentions, inadvertently perpetuates the idea that there are significant genetic differences between races, and that such differences are what cause disparities.[12,17]

The logic behind race-specific drugs thus serves as a compelling example of the interplay between Codes 1 and 3. It requires, firstly, an acceptance of race as a category defined by genetic differences.[12,17] Secondly, it necessitates the belief that these genetic differences are a significant cause of health disparities. Ultimately, this logic reinforces an oversimplified view of health, ignoring the multifaceted nature of racial health disparities.

Similar to Code 3, Code 4 –Genetic Stereotyping and Stigmatization – is also deeply intertwined with the reification of genetically defined race. The potential for genomics research to associate specific traits of health conditions with specific racial groups is a direct consequence of the misunderstanding of the relationship between race and genetics.[12,15,18] When race is seen through a genetic lens, it becomes all too easy to attribute certain genetic characteristics to entire groups, leading to stereotypes that are not only scientifically inaccurate but also harmful.[12,15,18] For example, if a study found a particular health-relevant genetic characteristic to be more frequent in certain racial groups, there may be a tendency to overgeneralize this finding, leading to stereotyping.

A historical example of genomics research leading to genetic stereotyping is the "Māori Warrior Gene".[19–21] This example is given to illustrate how scientific research results can be misinterpreted and lead to this ethical issue. The Māori are the indigenous people of New Zealand. Contemporarily, the Māori face various health and socioeconomic disparities.[19–21] Simultaneously, traditional Māori culture is perceived as having a "warrior tradition".[19–21] This combination of disparities and the warrior tradition narrative has led to many stereotypes about the Māori, often portraying them as a violent group of the population.[19–21] In 2007, a group of genomic researchers in New Zealand inadvertently reinforced this stereotype.[19–21] While studying alcohol and tobacco metabolism, the researchers identified a variant of the monoamine oxidase gene (MAO-A) that was found to be more frequent in the study's Māori participants.[19–21] The researchers then used questionable scientific reasoning and hypothesized that this MAO-A variant may have been advantageous during Māori tribal warfare, and thus became more prevalent in the Māori.[19–21] This theory was rapidly sensationalized by the media, which coined the term "warrior gene" to describe a genetic predisposition towards violence and aggression.[19–21] Many subsequent reports exaggerated the findings of this genetic study to stereotype the Māori.[19–21] Further efforts even attempted to link the Warrior Gene and the various health and socioeconomic disparities the Māori experience. These disparities were labelled as somewhat inevitable, given the Maori's "claimed'' genetic predisposition towards violence and risk-seeking.[19–21] It is important to acknowledge that this controversy happened over 15 years ago. This example is not given to exemplify the high prevalence of research that leads to genetic stereotyping, rather it is to illustrate how scientific research can be oversensationalized and misinterpreted. The upcoming section will detail thematic Code 6 and specifically discuss how scientific communication shortcomings regarding the use of GA can increase the risk that scientific results are misused and misinterpreted.

Code 6: The Need for Better Scientific Communication

Overview

The following section revolves around thematic Code 6, which focuses on the need for better scientific communication. The section begins by reintroducing the definition of Code 6, followed by a description of 4 key principles and practices of scientific communication. These principles are normative and prescriptive, specifically designed to mitigate and address the ethical issues that emerge when GA is used in genomics research.

The Four Principles of Scientific Communication When Using Genetic Ancestry

The previous section highlighted 3 sets of ethical issues associated with the use of GA in genomics research. These were the reification of genetically defined race (Code 1), genetic essentialism and the oversimplification of health (Code 3), and genetic stereotyping and stigmatization (Code 4). Many of these issues occur due to poor scientific communication, and as such, there is a significant academic literature focusing on the need to improve scientific communication when using GA. Thematic Code 6 specifically represents manuscripts that underscore the importance of education, standards, and guidance, for responsible scientific communication especially when using GA in research. Namely, thematic Code 6 is characterized by a focus on four key scientific principles and practices. While these principles and practices are particularly relevant during manuscript writing and the dissemination of research results, they should be considered throughout the entire lifespan of the research process, from the initial research design to the presentation of results.[3] Lastly, although these principles are broadly applicable to any biomedical research, they are particularly relevant to research using GA, due to its many ethical issues, as highlighted by the discussion under Codes 1,3, and 4.

The four principles and practices to consider when using GA in genomics research are:

1. **Including Explicit Definitions and Criteria**: The first normative principle calls for clearly reporting the definitions and criteria used to assign GA.[22–24] This would include explicitly highlighting methods used to determine GA. For example, if a research team is determining GA using a specific reference panel and a series of AIMs (Ancestry Informative Markers), then following this principle

would require clearly reporting these practices. This ensures that the use of GA is well-defined, mitigating against misunderstandings.[3,23,24]

2. **Clear Description of Purpose and Rationale for Using GA or Other Population Descriptors**: This principle entails explaining the reasons and rationale behind employing GA in specific research settings.[15,22]Researchers should clearly discuss their reasoning for using GA, and what purpose GA serves in the research design. This principle aims to improve research transparency while reducing ambiguity when GA is employed.
3. **Description of Limitations and Assumptions**: The third principle asks researchers to both consider and communicate the limitations and assumptions present in their use of GA.[15,22,25] Similarly to the previous principle, this practice aims at improving transparency when using GA in research.
4. **Contextualizing Genetic Findings within a Broader Framework of Health**: The last principle asks researchers to contextualize genetic findings within a broader context of health.[12,18,20,22] This involves considering genetic factors alongside social and environmental determinants of health.[12,18,20,22] This is especially relevant when the research is biomedical or investigating genetic risk factors related to a disease or condition.[12,18,20,22] This principle aims to guard against the oversimplification of health, and the potential to overemphasize genetic factors at the expense of equally relevant social and environmental factors.[12,18,20,22]

The above provides 4 general principles for scientific communication in genomics research using GA. However, it is crucial to adapt the specifics of these guidelines to the unique context of each research project. While applying these principles does not entirely eliminate the possibility of misinterpretation or misuse of research findings, they reduce the risks of such events.

Code 2 and 5: The Need for Greater Diversity and Representation in Genomics and The Importance of Trust and Cultural Sensitivity

Overview

In this section, we will explore two critical sets of ethical issues, which are represented by Codes 2 and 5. Code 2 emphasizes the urgent need for increased diversity and representation in genomic datasets, while Code 5 addresses the vital role of trust and cultural sensitivity in promoting such diversity in genomics

research. We begin by examining pivotal studies that shed light on the glaring lack of diversity in current genomic datasets. Subsequently, we aim to unpack the definition of "diversity" and "representation" in the genomics context. To illustrate the consequences of insufficient diversity, we will examine the differential efficacy of variant calling in breast cancer, and the inconsistent predictive utility of polygenic risk scores across different populations. Transitioning to thematic Code 5, our focus will shift to the critical role of trust and cultural sensitivity in promoting diverse participation in genomics research. Here, we will introduce studies that demonstrate how racialized[4] groups are generally more hesitant to participate in genomics research due to heightened mistrust. We will then discuss how cultural sensitivity can be a factor in facilitating diverse research participation. To conclude, we will briefly discuss the value of community engagement practices as a means to enhance participation in genomics research. Overall, we aim to illustrate how trust and cultural sensitivity can be deeply interwoven with the concept of diversity in genomics research.

Code 2: The Need for More Diversity and Representation

Manuscripts labelled with Code 2 center on the imperative for greater diversity and representation in genomic research. These records collectively underscore the idea that research which is "diverse" will translate into research outcomes that are generalizable across the full spectrum of human genetic variation.[5,27–30] This is because diverse populations or groups often harbour unique genetic variants, allele frequencies or other variations that are linked with disease risks or treatment response profiles.[5,27–30] As such, a failure to capture this diversity will not only limit the applicability and generalizability of research findings, but will also bias clinical developments. Fundamentally, the numerous calls for enhanced diversity are often funded by the principle of equity, where which requires that researchers ensure that the benefits and developments arising from genomics research are broadly accessible.[5,27–30]

One study that underscores the lack of diversity in current genomic databases is a 2016 publication by Popejoy and Fullerton.[27] These authors comprehensively analyzed the *GWAS Catalog*, a global repository cataloging over 2511 GWAS studies and comprising over 35 million genomic samples.[1] Their findings revealed that around 80% of all samples in the GWAS database originated from individuals of European descent.[27] This is notably disproportionate, considering that individuals of European descent only

[4] The term "racialized populations" refers to groups who are categorized or classified based on racial categories. These classifications are often based on physical characteristics such as skin color, and socio-cultural processes. Racialized populations are often perceived and treated differently, based on their race.[26]

constitute approximately 10% of the global population.[27] Moreover, this study highlighted that, in the remaining 20% of the database, only 4% of samples came from individuals of African, Central American, or Indigenous (North American or Australian) descent.[27] This trend extends beyond GWAS studies and encompasses other major genomic research databases, such as whole-genome or exome sequencing.[29] Overall, manuscripts labelled with Code 2 frequently discuss the current lack of diversity and representation in genomic databases.

What Does Improving Diversity Mean?

While a great deal is written about the need for more "diversity" and "representation", what does this mean in the context of genomics? In the realm of genomics, the calls for enhanced diversity predominantly revolve around *genetic* diversity, which refers to the inclusion and analysis of a wide array of genetic variations that exist across human populations.[27,29,31] The objective is to better encompass the breadth of human genetic diversity in genomic databases. This is distinct from increasing racial and ethnic diversity.[27,29,31] Increasing genetic diversity in genomic databases means ensuring that genetic information from all human populations, particularly those that have historically been excluded or underrepresented in research, are included in research databases.[27,29,31] This goal is centrally about capturing a more complete picture of the human genome's variability. Currently, research databases are predominantly based on European samples, and as such, there are significant amounts of human genetic variation that remains unexplored.[27,29,31] The specifics of how to "improve diversity" are deeply complex, and there is an increasingly expansive field of research dedicated to this topic.[28,32]In the context of Code 2, it is important to understand that "diversity" and "representation" refer to increasing *genetic* diversity, hoping that this will result in more equitable scientific and medical advancements.

Consequences of a Lack of Diversity

A striking example of the repercussions of underrepresentation in genomics is clinical *variant calling* in breast cancer.[5,33] Variant calling is a crucial component of clinical genomics. It involves identifying and comparing genetic variations in a patient's DNA against reference genomes.[5,33] This process can be critical in assessing disease risks, making diagnoses, and informing treatment strategies.[5,33] In oncology, for instance, variant calling is pivotal in classifying a patient's genetic variants as "pathogenic", "benign", or as "variants of uncertain significance" (VUS).[5,33] Pathogeneic and benign classifications can have crucial clinical implications, informing diagnosis and interventions. However, a VUS, as the name suggests, are inherently uninformative, and cannot be used to guide clinical decisions.[5,33]

Variant calling is considerably less effective for individuals of non-European descent, due to a lack of diversity in current genomic databases.[5,33] The scarcity of comparative data for non-Europeans often results in a higher incidence rate of VUSs when using variant calling.[5,33]A study in 2018 by Kurian and Colleagues starkly illustrates these disparities.[33] This study assessed the rate at which variant calling yielded VUSs in breast cancer patients for patients of differing ancestry. The study revealed a VUS rate of 23.7% for participants classified as having European ancestry, but significantly higher rates of 44.5% for African ancestry and 50.9% for Asian ancestry participants.[33]These numbers highlight the reduced informativeness of variant calling for Asian and African ancestry patients. Lastly, VUS results, by their nature, are inconclusive, which can subject patients to undue medical risks and psychological burdens.[5,33]

Another example that illustrates the consequences of insufficient diversity in genomics research is the differential predictive utility of polygenic risk scores (PRS).[34–36] PRS represent a statistical expression of an individual's likelihood to develop complex traits or diseases.[34–36] These scores are predictive models, derived from large-scale GWAS (Genome Wide Association Studies).[34–36] Although there is some current debate on the clinical utility of PRS, it is generally accepted that, when combined with other strategies, and for some medical conditions, PRSs can, or will eventually, have significant clinical utility.[37] Namely, PRS can be applied to assess disease predisposition, guide early screening intervention, and inform personalized treatment plans.[34–36]

Thereby, the clinical use of PRS holds significant promise. However, the effectiveness of PRS is significantly compromised in non-European ancestry populations, due to the underrepresentation of these groups in genomic datasets used to develop these scores. A 2023 study by Breedon and Colleagues demonstrates this for multiple sclerosis, finding that PRS were much more predictive and accurate for individuals of European ancestry, compared to those of South-Asian ancestry.[38] Moreover, research conducted in 2019 and 2020 further demonstrates that PRS are notably less accurate in non-European populations.[39,40] Again, this reduced precision has been attributed to a lack of diversity in current genomic databases.[39,40]

Code 5: The Value of Trust and Cultural Sensitivity

Transitioning, thematic code 5 emphasizes the role of mistrust and cultural insensitivity as barriers to diverse participation and representation in genomics research.[41–45] Building on the themes discussed

throughout Code 2, authors within this code highlight that fostering trust and accounting for cultural nuances are critical aspects for improving the equity of genomic research.

Increased reluctance to participate in genomic and biomedical research is a notable trend among racialized populations.[41–43,46,47] Various investigations and studies show that within the general population public, racialized groups tend to hold greater apprehensions about participating in genomic and biomedical research.[41–43,46,47] This hesitancy stems from various concerns, notably around privacy and the potential misuse of personal health data.[41–43,46,47] A 2020 systematic review focusing on "Indigenous perspectives on health data privacy and participation in genetic research" highlights this.[47] The review included 21 empirical studies that encompass over 3,234 interviews and survey participants.[47] The study found that, while a majority of participants expressed strong support for biomedical research, concerns surrounding privacy and the potential misuse of health data often deterred their participation.[47] A 2021 study focusing on what Black community leaders perceived to be the most significant barriers preventing black participants from partaking in genomic medicine research, found similar results.[46] Here, concerns about both the privacy of personal information and the potential misuse of health data were consistently cited as major barriers.[46] Overall, there is a significant amount of research literature which highlights that concerns about privacy and data misuse deter research participation from racialized populations.[41–43,46,47]

Contextualizing Mistrust Through Historical Examples

In thematic Code 5, various manuscripts cite historical instances of research misconduct to explain the current hesitancy among racialized populations toward genomic research participation. These examples illustrate that the mistrust and apprehensions towards data misuse are not unfounded, but rather based on historical experiences acquired by these populations when participating in research. Three examples feature prominently in these discussions: the lack of benefit sharing in some HIV/AIDs research projects, the Tuskegee Syphilis study, and the "Havasupai Tribe case".[17,48–50] While these historical examples are frequently cited, it is crucial to acknowledge that the most recent of these incidents occurred over 30 years ago, and some do not specifically relate to genomics. In the past 30 years, there have been substantial advancements in research ethics, accompanied by the implementation of extensive safeguards to prevent the recurrence of such cases.[46–49] As such, these examples are not discussed because they represent the current state of ethical issues in genomics. Rather, they are discussed because, despite the passage of time and the evolution of research ethics, they have left a lasting impression, shaping attitudes and perceptions toward research participation even today.[17,48–50]

The Tuskegee Syphilis study, conducted by the U.S. government, stands as a frequently cited illustration of unethical research that contributed to the deep-seated mistrust among Black individuals towards biomedical research.[17,50] The study targeted Black American men to observe the natural progression of untreated syphilis.[17,50] There are many critical ethical lapses in the Tuskegee study. Most notably, researchers not only withheld treatment from the participants but also actively deceived them, even after effective syphilis treatments were readily available.[17,50] The enrolled men were led to believe they were receiving care for their condition, whereas, in reality, they were not. Another egregious aspect was the exploitation of socio-economic vulnerabilities; researchers targeted lower-income individuals, enticing them with the false promise of free health insurance and medical care. These manipulative tactics have been extensively documented and criticized.[17,50] The Tuskegee study is frequently referenced by various authors and, in interviews, as a foundational reason for the persistent reluctance among many Black individuals to participate in biomedical research, due to the betrayal and exploitation experienced by members of their group.[17,50]

The Havasupai Tribe case of 1989 represents another pivotal instance which has significantly contributed to the mistrust of North American Indigenous groups towards genetic research.[47,48] The case began with a collaboration between the Havasupai Tribe and Arizona State University researchers to study the genetic basis of the elevated rates of diabetes within the Havasupai community.[47,48] However, the tribe later discovered that their genetic samples were used for a broader range of studies than initially agreed upon. These included research into human evolutionary migrations, schizophrenia, alcoholism, and inbreeding, subjects that are often considered highly sensitive or stigmatizing within many North American Indigenous communities.[47,48] Upon finding out, the Havasupai tribe sued the Arizona State University for violating informed consent. However, the university maintained that the tribe gave informed consent through written documentation. In response, Havasupai argued that they were deliberately misled about the nature of the research.[47,48] This dispute fostered a significant level of mistrust towards genetic research among Indigenous communities, prompting other tribes like the Navajo to impose temporary bans on genetic research within tribal lands.[47,48]

Another often-cited source of mistrust in genomic research is the practice of *biocolonialism*. This is sometimes also termed *biopiracy* or *helicopter research*.[43,49,51] These terms refer to the exploitation of the local population of less affluent countries by researchers from developed regions during their research.

These practices are characterized by a lack of both engagement and benefit-sharing with local communities.[52] The research often results in significant benefits for the researchers and their institutions, while communities that serve as subjects of research see little to no benefit.[49,52] One stark example of this is the development of antiviral medications for HIV/AIDs during the 1990s. Much of the pivotal early-stage research occurred in developing countries, where the disease burden was particularly high.[49] While this research contributed to several key therapeutic breakthroughs, the resulting treatments were frequently patented and priced at levels that were unaffordable for the communities in which the research was conducted.[49]These pricing strategies not only limited access to low-income communities that needed these drugs but also led to substantial profits for pharmaceutical companies.[49]This disparity in benefit distribution, accrued by researchers and pharmaceutical companies, has been perceived as a form of exploitation. These practices have enduring effects, where today, some research participants still cite fears about being treated like research "guinea pigs".[43,49]

Cultural Insensitivity and Research Participation

Another pivotal aspect of thematic code 5 is culturally insensitive research practices. In the context of genomics research, cultural sensitivity refers to the awareness and consideration of the diverse cultural beliefs, values, and practices of research participants.[5] If feasible, this may involve adapting research methods and communication strategies to better accommodate the cultural beliefs and practices of the research participants, and to eliminate unnecessary barriers to participation.[5,32] Overall, it is important for researchers not to impose their cultural perspectives and preferences on research participants. For example, some Indigenous groups view biological samples as an extension of a person's body.[53] Therefore, such samples should be treated with respect and dignity.[53] When working with Indigenous groups with this particular belief, researchers should adopt culturally sensitive approaches for sample collection and governance.[32] For instance, the concept of "gifting ceremonies", a practice rooted in Indigenous traditions, can be used to honour the spiritual value of bodily samples. [53] Gifting ceremonies convey a sense of mutual respect and community involvement that can foster a deeper sense of reciprocity between the community and the research team.[53] The adoption of culturally sensitive practices in research can enhance participation by accommodating the cultural practices of diverse groups. The use of gifting ceremonies is merely one example, and it is important to note that the appropriate practices will depend on the specific groups involved.

The Value of Community Engagement Practices in Fostering Trust and Cultural Sensitivity

The above sections have emphasized that mistrust and culturally insensitive research practices can constitute barriers to more diverse research participation. In the context of these ethical issues, community engagement practices are touted as a means to enhance participation in genetic research, by fostering trust and ensuring greater cultural sensitivity. According to Lemke and Colleagues, *community engagement practices* are defined as "the process of working collaboratively with groups of people who are affiliated by geographic proximity, shared interests, or similar situations with respect to issues that affect their well-being."[32] This is a very broad definition, and it reflects the idea that community engagement practices should be dependent and adaptive to the context and groups involved. Community engagement practices hinge on collaboration and the notion of reciprocal knowledge exchanges. Key to this process is establishing enduring and mutually beneficial partnerships.[32] By actively considering community values and preferences throughout the research cycle, these practices cultivate enhanced trust and cultural sensitivity. To see a more illustrate example of what community engagement practices can entail please see Section B of the Appendices. To see a summary of the 6 thematic codes, please see Section C in Appendices.

Section 4: Results Part Two- Statistical Analysis of the Relationship Between Thematic Codes, Author's Discipline, and Year of Publication

The following section will present the results of the statistical analysis of the relationship between 1), the thematic codes 2), the author's discipline, and 3), the year of publication.

These results will then be discussed and interpreted in the context of the original research questions. Finally, this section will conclude with a critical analysis of the strengths and limitations of this research project.

Figure 1: PRISMA Diagram of Sources of Evidence

Figure 1 – PRISMA flow diagram of the sources of evidence screening.

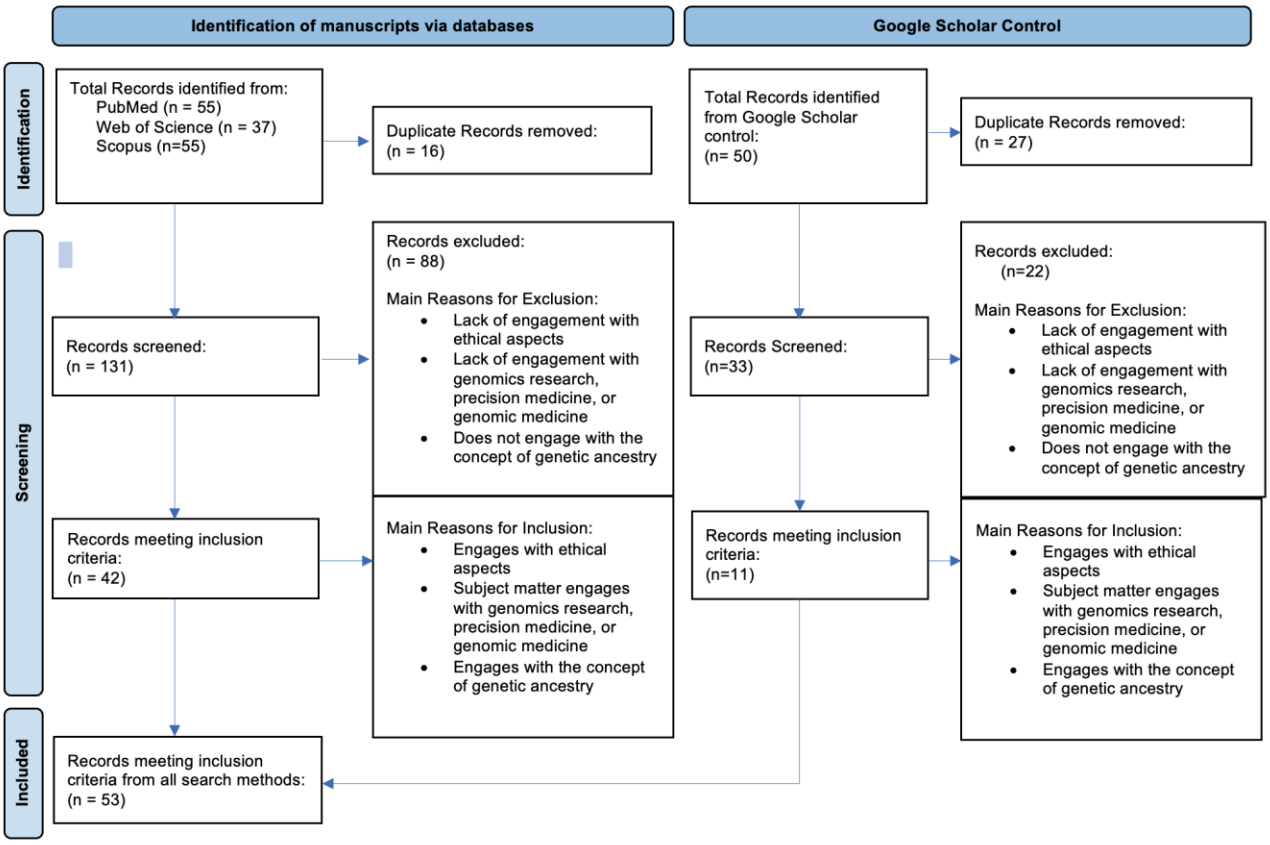

Figure 1 displays the sources of evidence based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[1] As described in Section 2: Methods, using the search terms and specifications, PubMed returned 55 records, Web of Science returned 37 records, and Scopus returned 1247 records. Due to the high number of records returned from Scopus, a strategic decision was made to focus on the most relevant and recent records. Consequently, the first 55 records from Scopus were screened. From this pool of records, 16 were duplicates and eliminated. This is consistent with research the principles of systematic literature reviews, which prioritize the relevance and quality of records over an exhaustive enumeration.[54] Overall, this led to 131 records being screened with 43 meeting the inclusion criteria. After this, Google Scholar was used as a control. The same search terms and settings were used. The first 50 records are retained. 27 of the records were duplicates and eliminated. The

remaining 33 were screened with 11 meeting the inclusion criteria. Overall, 53 records met the inclusion criteria.

Figure 2: Total Author's Discipline Composition

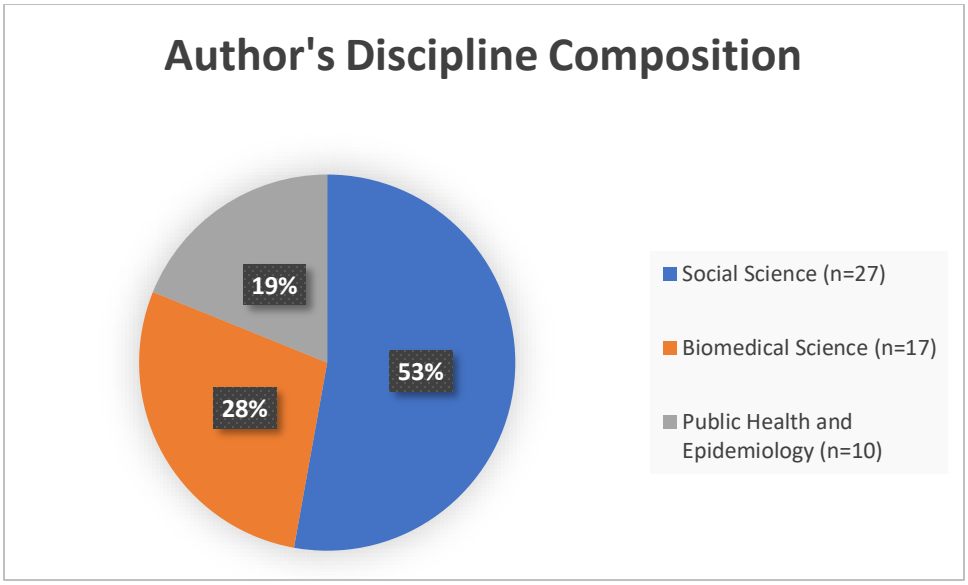

Figure 2 displays the total breakdown of the author's discipline by one of three categories: Social Sciences (n=28), Biomedical Science (n=15) and Public Health and Epidemiology (n=10).

Figure 2.1: Total Thematic Code Composition

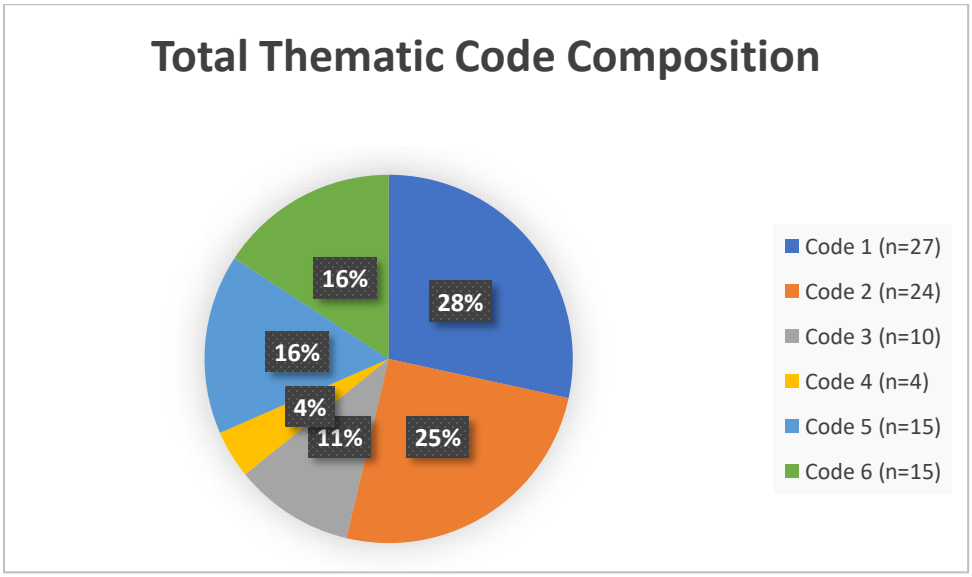

Figure 2.1 displays the total thematic code composition of the extracted manuscripts. As noted in Section 2: Methods, a manuscript can be labelled with more than one thematic code. As such, the sum of the thematic codes (n=95) is greater than the total number of manuscripts (n=53).

Figure 3: Number of Records Per Year

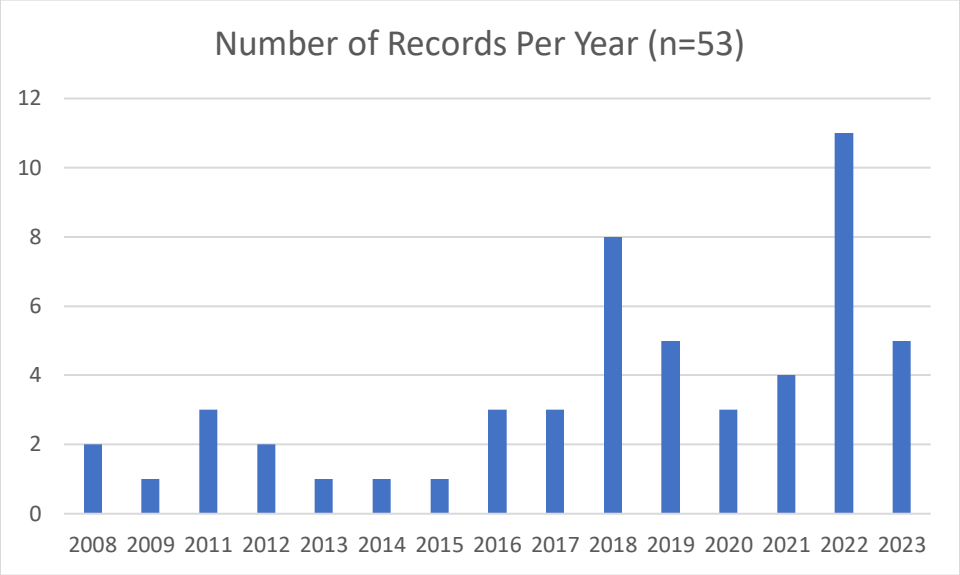

Figure 3 displays the number of records per publication year.

Table 1 The Pearson Correlation Coefficient of Each Code

Thematic Code	**Pearson's Correlation Coefficient**
Code 1: The Reification of Genetically Defined Race	0.503
Code 2: Insufficient Diversity and Representation in Genomic Datasets	0.736
Code 3: Genetic Essentialism and the Oversimplification of Health	0.327
Code 4: Genetic Stereotyping and Stigmatization	-0.249
Code 5: Challenges in Mistrust and Culturally Insensitive Research	0.807
Code 6: The Need for Improved Scientific Communication	0.356

Table 1 displays Pearson Correlation Coefficients (PC) for each code, which represents the relationship between thematic code's frequency and year of publication. The PC represents the strength of the correlation from a value of -1 to 1.

Figure 5: Discipline Composition of Each Code

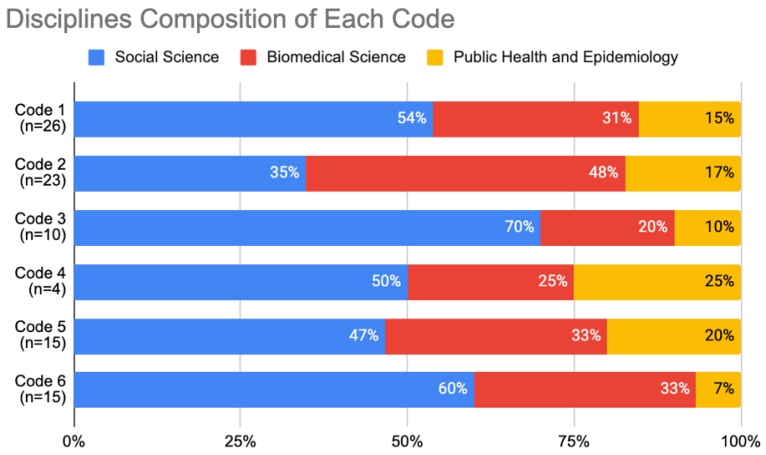

Figure 5 displays the authors' disciplinary composition for each thematic code.

Figure 6: Code Composition of Each Discipline

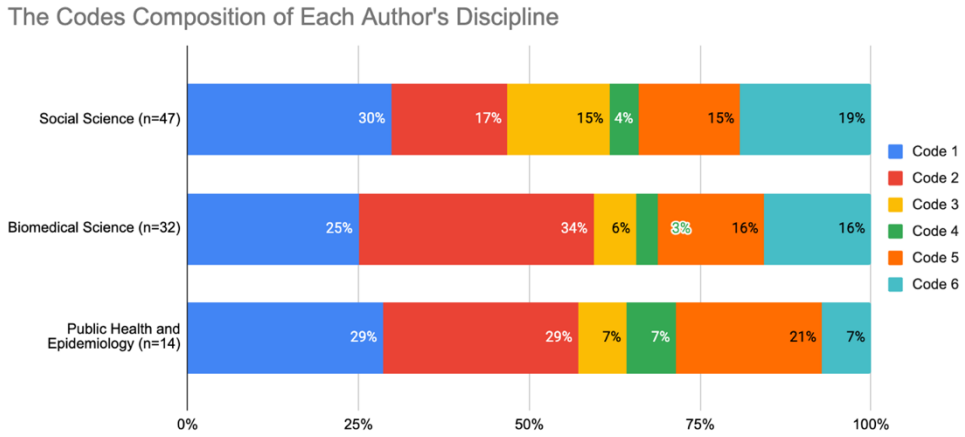

Figure 6 is the inverse permutation of Figure 5. This displays the thematic code composition of each author's discipline. Together, Figures 5 and 6 highlight the mutual relationship between the author's discipline and each thematic code.

Table 2: Overrepresentation of Disciplines by Thematic Code

Thematic Code	Overrepresented by Authors Specializing In
Code 1 (n=26)	Social Science (+4%)
Code 2 (n=23)	Biomedical Science (+17%)
Code 3 (n=10)	Social Science (+20%)
Code 4 (n=15)	Public Health and Epidemiology (+6%)
Code 5 (n=15)	Biomedical Science (2%) and Public Health and Epidemiology (+1%)
Code 6 (n=15)	Social Science (10%) and Biomedical Science (+2%)

Table 2 displays each thematic code and whether overrepresented by any discipline. The baseline comparison for this table is based on Figure 2.

Key Finding 1: The Research Topic Shows Multidisciplinary Engagement

Figure 2, presenting the total author's discipline composition, details the composition of authors' disciplines across the study. Most notably, we observe diverse and multidisciplinary engagement with the research topic. Among the 54 authors analyzed, 53% of the authors were identified as specializing in one or more Social Sciences disciplines. This is followed by 28% of authors with a specialization in one or more Biomedical Sciences, and 19% in Public Health and/or Epidemiology. This distribution highlights a predominant engagement from experts in Social Science with the research topic; yet, it also underscores the substantial contribution from other academic disciplines. The fact that nearly half of the authors come from disciplines outside of the social sciences demonstrates the topic's reach across different fields.

The multidisciplinary nature of the research topic also reflects its complexity. Throughout Section 3, we discussed 6 thematic codes focused on a diverse range of ethical issues. The complex and multifaceted nature of these ethical issues often necessitated a reflection that included the strengths and unique perspectives of different disciplines.[5,12,27,46] Some ethical issues demanded greater knowledge of biomedical nuances, while others required greater attention on ethical and policy considerations. For example, engagement with the necessity of increasing diversity and representation in genomic databases (Code 2) often requires an understanding of topics like GWAS and variant calling. Unsurprisingly, this often necessitated a good familiarity with the biomedical sciences.[2,3] Contrastingly, themes about trust and cultural sensitivity (Code 5) will most likely appeal to authors with social sciences backgrounds. Overall, our different thematic codes benefited from the input of a variety of scientific dimensions, attracting authors of all 3 disciplinary categories.[5,12,27,46]

Key Finding 2: The Relationship Between Author's Discipline and Thematic Codes

Figures 2, 5, and 6 when evaluated together, offer invaluable insights into the relationships between the author's discipline(s) and each thematic code. Where Figure 2 presents the total composition of authors by discipline, Figure 5 showcases this disciplinary composition within each thematic code. Figure 5 thereby allows the visualisation of each discipline's contribution to the discussion on thematic codes 1 through 6. For example, we see that authors specializing in the Social Sciences make up 54% of the total engagement with thematic Code 1, the reification of genetically defined race but 35% with thematic Code 2, diversity

and representation in datasets. Completing these findings, Figure 6 presents the thematic codes' composition by author's discipline. In essence, it is based on the same data, and it is the mirror perspective (inversed view) of the data displayed in Figure 5. For instance, Figure 6 illustrates that Code 1 makes up 30% of the engagement from Social Sciences authors, 25% from Biomedical Sciences authors, and so on.

In Section 1: Introduction and Background, we theorized that an author's expertise or discipline would influence the thematic codes they choose to engage with. Figures 2, 5, and 6 allow us to assess these hypotheses. Firstly, if the author's discipline had no relationship with the thematic codes they engage with (null hypothesis), in Figure 5, we would expect to see a distribution of disciplines that mirrors Figure 2 in all thematic codes. Specifically, each thematic code in Figure 5 would have a similar distribution of disciplines 53% Social Science, 28% Biomedical Science, and 19% Public Health and Epidemiology, the baseline that is shown in Figure 2. However, this level of uniformity is not what we observe. Instead, there is a noticeable variance in the discipline composition interested in each thematic code, suggesting that certain disciplines are more inclined to engage with the ideas and themes represented by specific thematic codes. For example, when examining thematic Code 1, we see that Social Sciences authors make up 54% of total engagement, while in Code 2, this group makes up only 35%. Similarly for Figure 6, if there is no relationship between the author's discipline and thematic code, then we would expect to see an even distribution of thematic codes in each disciplinary category. For each code, we would expect each discipline to make up 33% of the total composition. However, this is not the case. For example, when focusing on thematic Code 2, we see 17% engagement from Social Sciences authors and 34% from Biomedical Sciences authors.

These observations suggest that in some cases, there is a relationship between the author's discipline(s) and the thematic codes they engage with. Alternatively, this might reflect that different thematic codes and the ideas they represent inherently appeal to and elicit different levels of interest and engagement from diverse academic disciplines. In the context of the original hypotheses, Figures 2, 5, and 6 collectively demonstrate that authors from varied backgrounds and expertise are inclined to explore different sets of ethical issues associated with the use of GA. This trend suggests a disciplinary bias in the type of ethical issues researchers engage with.

Further Interpretation and Discussion of the Relationship Between Discipline and Thematic Codes

In this section, we will undertake a more detailed discussion and interpretation of the relationship between disciplines and thematic codes, with a particular focus on the insights provided by Table 2, overrepresentation of disciplines by thematic code. This table is a product of combining data from Figures 2 and 5. Particularly, it indicates where certain disciplines are overrepresented in specific codes. While deviations from the standard baseline distribution (as depicted in Figure 2) are observed across all codes, our analysis will highlight some of the most intriguing deviations to reflect upon the implications this may have for the broader research context.

The first notable finding is the significant overrepresentation of authors specializing in biomedical sciences in Code 2. Recall that Code 2 encompasses manuscripts that address the need for more diversity and representation in genomics research and databases. The discussions within this code frequently touch upon highly technical aspects of genomics research and medicine such as variant calling in clinical genetics, GWAS, and polygenic risk scores.[2–4] As such, engaging with these topics likely requires the specialized knowledge and expertise of an expert well acquainted with biomedical sciences. This reasoning makes it somewhat unsurprising that authors of this discipline constitute a majority of the manuscripts labelled with Code 2.

Another interesting finding from Table 2 is the disproportionate presence of Social Science authors in manuscripts associated with Code 3. Recall that Code 3 represents concerns about genetic essentialism and the oversimplification of health.[5–8] This thematic code emphasizes the need to consider social and environmental determinants of health in disease-based genomics research. This is particularly true for research into conditions that show racial disparities. Thematic Code 3's focus on genetic essentialism, the idea that genetic factors predominantly determine human traits and behaviors, aligns well with the domain and expertise of social scientists.[9] Particularly, social scientists are interested in exploring how societal structures, policies, and biases contribute to health outcomes.[5–8,10] They are well-positioned to consider how social and environmental factors, like education and socioeconomic status, affect health. Overall, the overrepresentation of Social Science authors in Code 3 likely reflects their interest and predisposition to consider social factors alongside genetic ones.

Finally, it is noteworthy that three codes, Codes 1,4, and 5, exhibit relatively minor discrepancies when compared to the baseline distribution presented in Figure 2. This observation suggests a multidisciplinary resonance within these thematic areas, indicative of their relevance across various academic fields. To illustrate this, we will discuss how thematic Code 1 would hold relevance to all 3 author disciplines.

Thematic Code 1 addresses the risks related to the reification of genetically defined race when GA is used in research. There are aspects of this thematic code that are relevant to all 3 disciplines. For authors from Social Sciences, the focus might be on exploring how the concept of genetically defined race can be misused or weaponized to support racist ideologies, an area rooted in their expertise.11 Biomedical scientists, on the other hand, tend to engage with Code 1 from a more technical perspective, leveraging their understanding of the differences between GA and race, and how GA is utilized in research.12

Key Finding 3: Thematic Codes Show Temporal Patterns

As discussed in Section One: Introduction and Background, we theorized that certain thematic codes would demonstrate a temporal relationship, increasing or decreasing in frequency as a factor of time. Altogether, this hypothesis is supported by the data in Table 1, which displays the Pearson coefficient values of each thematic code, but also in Figure 3, showing the number of records per year. These sources collectively offer a comprehensive view of the evolving temporal pattern of each thematic code.

Firstly, in Figure 3, it is apparent that the total number of records per year increases temporally. This can be ascertained visually, but this can also be supported by the use of Pearson's Coefficient (PC).[13] The PC is a statistical measure of correlation, and it is particularly relevant in this context.[13] The PC is a value that represents the strength of association between two variables.[13] A PC value can range from -1 to 1, with 1 representing a perfect positive correlation, and -1 representing a perfect negative correlation –[13] and 0 would indicate independence (no correlation). In the context of Figures 3, 4, and Table 1, the PC is used to assess the relationship between a manuscript's year of publication and the number of records published per year. A PC is used in this context because it provides a quantifiable expression of the relationship between the number of records and the year of publication. While a visual inspection of Figure 3 obviously suggests a positive temporal relationship, PCs offer a statistical confirmation of this observation. Specifically, the PC for Figure 3 is 0.666, which is a moderate to strong positive correlation. The P-value for this correlation is 0.007, which suggests that the correlation is statistically significant.[13] Figure 3 suggests that the number of records correlates positively to the year of publication. This means

that throughout the study period, 2008 to 2023, the number of records increased temporally. Within the overall context of the research study, this suggests that the academic community is increasingly engaging with and discussing the ethical issues associated with the use of GA in genomics research.

Table 1 attempts to illustrate the frequency of each thematic code through time. Table 1 uses PCs for a statistical approach. Specifically, Table 1 provides valuable insights into the evolving focus of the academic community on specific key ideas, and themes within the research topic. Notably, Codes 1,2, and 5 have PC values above 0.4, which suggests a moderate to strong correlation with the year of publication.[13] This indicates that key themes and ideas associated with these codes are increasingly emphasized and discussed over time.

Thematic Code 1, which focuses on the reification of genetically defined race, is shown to have a moderately positive temporal correlation. This suggests there is growing attention given to the ethical issues associated with the incorrect use, and oversimplification, of GA in genomics research. This increased attention goes beyond merely acknowledging the difference between race and GA. Rather, the literature increasingly highlights the critical implications of conflating race and GA. For example, several manuscripts emphasized that when the use of GA is accompanied by a lack of nuance, it can inadvertently promote a genetically defined basis for race.[8,14,15] This can have broader societal implications, such as influencing public perceptions of race, health disparities, and genetic stereotyping.[10,15,16] Overall, the increased focus on thematic Code 1 likely reflects a heightened awareness in the scientific community surrounding the risks that come with conflating race with GA.

Thematic Code 2, The need for more diversity and representation in genomic datasets, displays a strong positive correlation. Within the study period of 2008 to 2023, Code 2 showed noticeable increases in frequency. This indicates a significant rise in discussions about the need for enhancing genetic diversity and representation in genomic datasets. This increased emphasis aligns with the recent recognition that genomic research has historically been skewed towards European populations.[2–4] This bias has implications for the applicability and generalizability of genomic research and genomic medicine.[2–4] As such, the increased engagement with this set of ethical issues likely reflects recent efforts to address the challenge of underrepresentation and move towards more inclusive and representative genomic research.

Thematic Code 5, emphasizing the value of trust and cultural sensitivity, stands out with the most pronounced positive correlation among all codes, indicating a growing focus in genomics research on these critical issues. This quantitative growth in discussions on trust is likely a repercussion of past genetics and biomedical research, and ethical shortcomings that accompanied some of them. These historical instances likely continue to negatively impact the participation of racialized populations in genomics studies.[8,17,18] This trend underscores a need for more frequent engagement within the research community about the role of trust in encouraging participation from historically underrepresented groups.[17,19] Simultaneously, the rising temporal frequency of Code 5 likely mirrors a heightened awareness of, and commitment to, culturally sensitive research methodologies.[18,20] Community engagement practices, for instance, are being increasingly acknowledged as key for fostering deeper collaborations and increased participation from underrepresented groups.[3,18,20] Such practices, through their emphasis on reciprocity and bilateral relationships, contribute positively to enhancing participants' trust in research and aids in developing culturally sensitive research practices.[3,18,20]

In previous sections, we have often noted the interconnectedness between concepts represented by thematic Codes 2 and 5. Although they remain distinct sets of ethical issues, there is a fair degree of similarity between them. It is interesting to note that both codes show significant increases in temporal frequency, suggesting that both sets of themes are increasingly discussed within the scientific literature. The concurrent rise of Codes 2 and 5, likely reflects an expanding recognition that improving trust and promoting culturally sensitive research practices contribute positively to improving the diversity and representation of genomics research.

Strengths and Limitations

The following section will critically examine some of the strengths and limitations of this study. Namely the three limitations we will discuss are: 1), challenges in the record screening process 2), categorizing the author's disciplines, and 3), setting consistent criteria for assigning thematic codes. The 2 major strengths are the achievement of intercoder consistency and the full comprehensive analysis of each included manuscript.

One of the limitations encountered during the study relates to the record screening process. Namely, it was sometimes difficult to decisively determine whether a record sufficiently met the three essential inclusion criteria of engagement with the topics of 1), ethics/bioethics 2), genomics research, and 3), GA)

based solely on the title, abstract, and keywords. While in many instances, it was clear whether a manuscript fulfilled this criterion, occasionally this assessment proved more challenging. Consequently, this may have led to the inadvertent exclusion of some records that should have been included in the final analysis. However, this was not the case for the vast majority of records.

Another challenge involved categorizing the author's disciplines. Some authors displayed multidisciplinary backgrounds, complicating the process of categorizing them into a single, definitive discipline. The 3 discipline categories approach used in this study implied that authors could only be classified into one category. This did not accurately reflect the reality of some authors who embodied aspects of multiple disciplines. This limitation means that, for a small subset of authors, the assigned discipline category might not fully reflect the range of their expertise and training.

Lastly, it was particularly challenging to establish and maintain a consistent set of criteria throughout the codebook application process. Articulating a uniform and comprehensive criterion for when a manuscript has adequately discussed a particular code, to label a manuscript with that code, was a challenging task. This was especially true when trying to maintain a consistent assignment criterion across manuscripts of different lengths. This limitation is to be expected given the challenge of translating descriptive ideas, concepts, and themes into a numerical representation (thematic codes).[21,22] This limitation further underscores the necessity of employing at least two independent coders, as this ensures that the codebook is interpreted and applied consistently to produce reliable and replicable results.[21,22] Our project used 2 independent coders, and as such, one of the major strengths of this study is the achievement of intercoder consistency, a critical factor in research replicability. As outlined in Section 2, Methods, the study employed a rigorous and iterative development process for the codebook design and its application. Despite the challenges in assigning author's disciplines and thematic codes, both of these aspects demonstrated robust intercoder consistency.

Lastly, a significant strength of this study lies in the comprehensive analysis of each manuscript undertaken through qualitative content analysis. Specifically, each manuscript that meets inclusion criteria is read and analyzed in its entirety. Reading each manuscript fully allowed for a more nuanced and accurate interpretation of the content. By engaging with the entire record, the study was able to consider the full depth of the authors' research, thus guiding accurate codebook application and analysis.

Section 5: Policy Implications

The following section will focus on discussing the policy implications arising from the study's key findings. Namely, it builds upon the synthesis of ethical issues associated with the use of GA in genomics research in Section 3, and the statistical analysis of relationships between thematic codes, author's disciplines, and year of publication in Section 4. Based on the previous sections, three major policy implications have emerged:

1. The Importance of Providing Meaningful Guidance on Scientific Communication Involving the Use of GA
2. Fostering Interdisciplinary Collaboration
3. Recognizing Current Trends to Promote Innovative Research

Policy Implication One: Importance of Providing Meaningful Guidance on Science Communication Involving the Use of Genetic Ancestry

The first policy implication revolves around improving the quality of scientific communication guidance for the use of GA in genomics research. As previously discussed throughout Section 3, many ethical issues, such as the reification of genetically defined race (Code 1), genetic essentialism and the oversimplification of health (Code 2), and genetic stereotyping and stigmatization (Code 3), stem from misapplications and misunderstandings of GA. We have emphasized that the challenge of poor scientific communication practices, as represented by Code 6, becomes an indispensable tool to mitigate such ethical issues. Key to this approach is the application of 4 fundamental scientific communication principles. These include: 1), the need to provide explicit definitions and criteria when using GA; 2), having a clear rationale and purpose behind the use of GA; 3), acknowledging the limitations and assumptions behind the use of GA; and 4), contextualizing genetic findings within the broader spectrum of health determinants. These principles ensure that the use of GA is transparent and contextualized while reducing the chances of misinterpretation.

This could be implemented in the form of journal publication guidelines. At present, several academic journals have developed and established publication guidelines on the responsible use of race in research, due to the many ethical and scientific challenges associated with it.[1] Although, the efficacy of these guidelines is somewhat questionable, adopting similar ones is still a reasonable starting point.[1] Scientific journals can develop and implement guidelines specifically addressing the use of GA. These scientific

communication guidelines should focus on addressing challenges associated with consistency and clarity when GA is used in research communication, and to reduce the potential for misapplications and misinterpretation. Funding agencies, too, should develop and disseminate their own set of guidelines and resources. These resources should focus on promoting transparent and ethical utilization of GA in research projects they sponsor. By instituting these measures, both academic journals and funding bodies can play a more positive role in promoting the accurate and ethical use of GA in genomics research.

Policy Implication Two: Fostering Interdisciplinary Collaboration

The second major policy implication derived from our study emphasizes the necessity of fostering and encouraging interdisciplinary collaboration to tackle the ethical challenges associated with the use of GA in genomics research. Our analysis has revealed that the research topic garners significant contributions from a range of disciplines, showcasing its inherently multidisciplinary nature. Despite this, we noted a tendency among different disciplines to engage with distinct themes, ideas, and challenges. This observation indicates that authors of different disciplines leverage their unique expertise to focus on preferred dimensions of the ethical issues at hand. For instance, biomedical scientists, more so than other disciplines, demonstrated a pronounced engagement with thematic Code 2, the need for improved diversity and representation in genomic databases. This often involved highly technical discussions in topics like GWAS and variant calling, areas that theoretically should align with their specialized skill set.

In light of these insights, it is evident that future initiatives aimed at addressing the ethical considerations surrounding GA in genomics research, be it through policymaking, academic conferences, workshops, or research, should actively promote and incentivize interdisciplinary collaboration. Such collaborative efforts should go beyond mere participation from diverse disciplinary backgrounds: rather, they should foster a genuine integration of varied expertise into the chosen activity.

Policy Implication Three: Recognizing Current Trends to Promote Innovative Research

The third policy implication arises from the finding that certain thematic codes display an increasing temporal frequency. This trend indicates that within the study period of 2008 to 2023, the academic community has increasingly focused on and engaged with the ethical issues represented by these codes. Ethical challenges such as the reification of genetically defined race (Code 1), the need for more diversity and representation in genomic databases (Code 2), and the importance of trust and cultural sensitivity in

genomics research (Code 5) are receiving growing attention in the academic literature and can be considered as ‘‘current trends’’. Accordingly, funding agencies should recognize and respond to such evolving trends. While it is essential to support areas receiving current academic attention, there is a concurrent need to ensure a balance by investing in novel and less explored research areas. This could include aligning their funding priorities and institutional support toward projects and studies that are innovative and novel.

Summary of Section 5

In conclusion, this chapter has outlined 3 policy implications derived from the findings of our study. Firstly, we call for enhanced guidance on the use of GA aims, to mitigate misapplications and misunderstandings of GA. Secondly, the emphasis on fostering interdisciplinary collaboration recognizes the multi-faceted nature of the ethical issues associated with the use of GA in genomics. This policy implication advocates for an interdisciplinary approach that leverages diverse expertise to address complex ethical issues. Finally, the third policy implication encourages research funders to align their funding with current academic trends, while also promoting innovative research.

Section 6: Conclusion and Final Insights

In this final chapter, we will revisit the study’s objectives, and focus on the study’s most important findings. After, we will conclude by discussing future areas of potential research.

Reviewing the Study’s Key Findings

Recall the 3 research questions raised in Section 1: Introduction, Background, and Objectives We attempt to address the first question in Section 3 by identifying and delineating 6 thematic codes, each representing a distinct subset of ethical issues associated with the use of GA in genomics research. These codes collectively provide a comprehensive narrative synthesis of the research topic. Please see the end of Section 3 for a brief summary of the 6 thematic codes.

In Section 4, we attempt to answer questions 2 and 3, by examining how the relationship between each thematic code, the author’s discipline, and the year of publication. To do this, we generated 6 Figures and 2 Tables, with each representation emphasizing an aspect of the above relationships. We found the following key findings.

1. **Multidisciplinary Engagement with the Research Topic**: An analysis of the author's discipline within this study revealed substantial multidisciplinary engagement. This diverse disciplinary composition highlights the multifaceted and multidisciplinary nature of the research topic.
2. **Increasing Temporal Volume of Manuscripts**: This finding indicates that there is a growing trend in the volume of academic publications over time. This likely suggests an increasing focus and attention to discussing the ethical issues related to the use of GA in genomics research.
3. **Significant Increases in Specific Thematic Codes**: Thematic Codes 1,2, and 5 show significant increases in temporal frequency. This suggests that themes around 1), the reification of genetically defined race 2), the need for increased diversity and representation in genomic research, and 3), the value of trust and cultural sensitivity are discussed in increasing frequency from 2008 to 2023.
4. **Discipline-Specific Engagement with Thematic Codes**: Our analysis revealed that certain academic disciplines are more inclined to engage with specific thematic codes. For example, there is a disproportionately high engagement of thematic code 2 from authors specializing in biomedical sciences. We theorize that the specific training and specialized expertise of different disciplines bias authors to engage with those ethical issues where their knowledge is most relevant and impactful. For example, thematic code 2 addresses the need for more diversity and representation in genomics research, and this code often involves discussions on highly scientific aspects such as variant calling, Genome-Wide Association Studies (GWAS), and polygenetic risk scores. The technical and intricate nature of these topics requires knowledge and expertise from biomedical sciences, which may explain why authors from this discipline are particularly drawn to engage with thematic Code 2.

Future Areas of Research

In this research study, we utilized an interesting method for synthesizing research knowledge, blending traditional literature review techniques with qualitative methods. This approach has demonstrated significant adaptability and utility across a diverse range of research topics, largely due to the flexible application of a codebook. The codebook's design allows it to be as specific or as general as necessary, depending on the topic at hand. One of the standout advantages of this method is its ability to offer a comprehensive exploration of a topic while integrating a temporal dimension. This not only allows for a detailed examination of the subject matter but also enables an evaluation of its longitudinal evolution, capturing shifts and trends over time.

Another particularly novel aspect of our research is the consideration of the authors' disciplines in the analysis. This inclusion is relatively innovative and adds a new layer of depth and understanding. By considering the disciplines of the authors, we gain insights into how different academic fields contribute to and shape the discourse around a topic. This approach can reveal tendencies toward certain themes or issues that are prevalent in specific disciplines, and whether certain research topics show multi-disciplinary tendencies.

However, it's important to acknowledge that our study methods are resource-intensive. Coding each manuscript individually, especially when involving multiple independent coders to achieve intercoder consistency, requires a considerable amount of time and energy. This investment in resources is necessary to maintain the method's rigour and replicability. Despite these challenges, our results suggest that this method is viable for investigating and synthesizing knowledge, particularly in research areas with longitudinal components. Furthermore, by integrating considerations of the authors' disciplines, we have added a new dimension to research synthesis. This approach allows us to better understand how different disciplines contribute to a research topic and whether they lean towards discussing certain aspects of an issue more than others.

In conclusion, the methodology we have employed in this study not only provided significant insights into the ethical issues associated with the use of GA in genomics research but also showcased its potential for broader application in future research endeavours. This method could be particularly valuable in fields where understanding the evolution of ideas and multidisciplinary engagement is valuable. Overall, while the insights we have uncovered regarding the ethical issues associated with the use of GA in genomics research are significant, much of the value of our work lies in the demonstration of an innovative and adaptable research technique. This novel approach to synthesizing research knowledge has shown remarkable flexibility, making it a particularly valuable tool in academic inquiry.

Section 7: Knowledge Mobilization Plan

Our Knowledge Mobilization Plan will focus on 3 key deliverables. These deliverables focus on optimizing knowledge dissemination and outreach to the relevant stakeholders through various platforms.

Deliverable 1: Open Access Publication

- **Action**: Publish our research findings and analysis as an open-access article in a peer-reviewed academic journal
- **Focus**: This publication will focus on presenting a coherent synthesis of the ethical issues associated with the use of GA in genomics research, the influence of the author's disciplines on the ethical issues discussed, and the temporal evolution of these ethical issues from 2008 to 2023.
- **Outcome**: Facilitate academic and public access to our research results to encourage academic discourse and results dissemination.

Deliverable 2: Disseminate Lay Summaries of our Findings

- **Action**: Disseminate lay summaries of our findings in French and English targeting specific end-users such as healthcare professionals, genetic counsellors, and non-specialist audiences.
- **Platform**: This will be done via the Genetic Discrimination Observatory (GDO) website[5]. The GDO is an ideal platform since it connects a wide and diverse network of end users, academic experts, and healthcare professionals with a global and interdisciplinary reach.
- Furthermore, study results and lay summaries will also be shared and integrated into conference discussions and activities via the Global Alliance for Health and Genomics (GA4GH) Diversity in Datasets Regulatory and Ethics workstream (REWS). This working group focuses on challenges in diversity and representation in genomics research and will be particularly suited to engage with the study's results.
- **Outcome**: Enhanced awareness and dissemination of study results to diverse communities and stakeholders, including public stakeholders without specialized knowledge in genomics.

Deliverable 3: Conference Participation

- **Action**: Participation in key conferences such as the SSHRC Knowledge Mobilization Forum and organize a session at the annual GA4GH meeting (September 2024) to present our findings. This will leverage our partnership with the GA4GH to maximize project outreach and impact to academic experts beyond those specialized in the social sciences and ethics.
- **Outcome**: Enhanced dissemination of study results to relevant stakeholders in the academic community

[5] https://gdo.global/en/resources

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Appendices

Section: A Codebook

The following section presents the definition, description, and inclusion examples of the 6 thematic codes used in our analysis, as well as of the categorisation of authors by discipline. The references in each section are manuscripts that exemplify the thematic code.

Thematic Code 1: The Reification of Genetically Defined Race

Definition: Thematic Code 1 represents manuscripts which discuss the application of GA in genomics research and how it can inadvertently support, or be misconstrued as endorsing the concept of race as a genetically defined and scientifically valid categorization, rather than as a social construct. Furthermore, there is a critical examination of the relationship between understandings of race and GA, and their perceived connections.

Description and Criteria:

- Highlights the potential for GA to unintentionally legitimize or reinforce the notion of race as a scientifically objective and genetic construct.[1–5]
- Discusses the potential harms and challenges of reinforcing a genetic conception of race or ethnicity.[1–5]
- Evaluate and explain the complexity of GA, highlighting nuances often missed or oversimplified in both scientific and public discourses.[1–5]
- Discusses the difference between GA and social categories such as race and ethnicity.[1–5]

Thematic Code 2: The Need for More Diversity and Representation in Genomics Databases

Definition: Thematic Code 2 represents manuscripts that highlight the challenges arising from a lack of diversity and representation in current genomic databases. This lack of diversity limits the generalizability of genomic findings, potentially leading to biases in genomic research and a skewed

understanding of health-relevant findings across different population groups. It highlights an urgent need for more diversity, representation, and inclusivity.

Description and Criteria:

- Discusses the issue of underrepresentation in genomic databases.[6–8]
- Discusses the role of diversity and representation in ensuring equitable clinical developments.[6–8]
- Demonstrates the consequences of underrepresentation.[6–8]
- Evaluates the current state of diversity and representation in genomic databases.[6–8]

Thematic Code 3: Genetic Essentialism, and the Oversimplification of Health

Definition: Thematic Code 3 describes manuscripts that highlight the issue of genetic essentialism when GA is used in health-related research. Namely, Code 3 focuses on the tendency for genomics research to overemphasize the relevance of genetic factors in human health. This can lead to an oversimplified understanding of health and disease that neglects the role of environmental, social, and behavioural factors.

Description and Criteria:

- Discusses the potential for genomic research using GA to overemphasize the role of genetic factors in human health.[3,5,9]
- Discusses how the use of GA in genomics research may overemphasize the role of genetic factors as the basis for health disparities, deflecting attention away from socio-economic and political determinants of health.[3,5,9]

Thematic Code 4: Genetic Stereotyping and Stigmatization

Definition: Thematic Code 4 describes manuscripts that highlight the issue of genetic stereotyping and stigmatization when GA is used in health-related research. More specifically, Code 4 raises the possibility that the use of GA makes it possible to associate health-relevant traits with individuals or groups. This can be a source of genetic stigmatization and stereotyping.

Description and Criteria:

- Discusses how the use of GA may lead to the association of specific genetic traits or health conditions with particular populations. [9–11]

- Explores the consequences and potential for stigmatization or stereotyping cases in which certain groups may be discriminated against based on presumed genetic traits or susceptibilities.[9–11]

Thematic Code 5: The Role of Trust and Cultural Sensitivity in Promoting Diverse Participation

Definition: Thematic Code 5 focuses on the role of trust and cultural sensitivity in facilitating and promoting diverse participation in research. This view advocates that increasing trust and culturally sensitive research are critical to promoting diverse research participation from underrepresented groups.

Description and Criteria:

- Discusses the role of trust in enabling and promoting research participation from underrepresented groups.[12–14]
- Discusses the role of cultural sensitivity in enabling and promoting research participation from underrepresented groups.[12–14]
- Highlights the value of trust and culturally sensitive research for achieving greater diversity and representation in genomics research.[12–14]

Thematic Code 6: The Need for More Education, Standards, and Guidance in Using Genetic Ancestry in Research

Definition: Thematic Code 6 revolves around the need for better scientific communication when using GA in research. Improving scientific communication is seen as a promising safeguard against the various ethical issues associated with the use of GA. Thematic Code 6 calls for adhering to 4 key principles when using GA in genomics research.

Description and Criteria:

- Discusses and highlight the importance of the following principles:

1) Include explicit definitions and criteria, such as the reference panels used when using GA.[15–18]
2) Describe the purpose of and rationale for, the use of GA.[15–18]
3) Describe the limitations and assumptions that are associated with the use of GA in the research context.[15–18]
4) If investigating genetic factors related to health, contextualize genetic findings within broader social and environmental determinants of health.[15–18]

Authors' Disciplines Category 1: Social Scientists

Authors who are categorized as Social Scientists possess formal education, and work, or research experience, in social science fields. Their research profiles and publication histories predominantly emphasize areas such as ethical, legal, and social implications (ELSI). These individuals may also have backgrounds in disciplines such as philosophy, and anthropology and employ a variety of qualitative methods.

Authors' Discipline Category 2: Biomedical Scientists

Authors classified as Biomedical Scientists have formal education, and work, or research experience, in the biomedical sciences. Their research profiles or publication history outline experiences in fields such as cell biology, medicine, microbiology, bioinformatics, or human genetics. Additionally, this category includes clinicians, such as physicians who are conducting research.

Authors Discipline Category 3: Public Health and Epidemiology

Authors categorized under Public Health and Epidemiology possess formal education and research or work experience in public health and epidemiology. Their research profile and publication history are characterized by a focus on health and disease at the population level.

Section B: Illustrating Community Engagement Practices

To illustrate what community engagement practices can entail, we consider a 2022 commentary by Appelbaum and Colleagues, which focuses on the use of these practices in recruiting Canadian Indigenous and Sephardi Jewish participants in genomics research.[5] Both Canadian Indigenous and Sephardi Jewish participants are underrepresented in genomics research.[5] For Sephardi Jewish participants, apprehensions about genetic research are primarily rooted in concerns about the stigma associated with being a potential carrier of genetic diseases. Traditional Sephardi Jewish culture places a significant emphasis on marriage, and as such, some members worry participating in genetic research could impact their marital prospects if tests reveal a propensity for certain diseases.[5] This is because the cultural norm in this community is that some genetic testing results need to be disclosed during the match-making process, and would likely harm one's prospects.[5]

To address these concerns, the research team and community developed a series of strategies focusing on the privacy of test results.[3] One successful approach, as seen in the *Dor Yeshorim* project, involved using anonymized samples to alleviate privacy concerns.[5] This method made individuals more comfortable participating in research by assuring their genetic information would be kept confidential. Additionally, specific policies regarding the non-return of genetic test results were implemented to address concerns about the need for self-disclosure during matchmaking.[5] However, it is important to note that withholding clinically relevant test results comes with its own ethical challenges.[55]

Another example of community engagement practices is the Silent Genomes Project in British Columbia, which focuses on advancing precision medicine within Canada's Indigenous population.[5] The project recognized the community's desire for control over research samples and autonomy in determining research directions. Taking this desire into account, the project is co-led and co-designed by Indigenous researchers and community leaders to ensure substantial community involvement in decision-making and data governance.[5] Additionally, the project adopted a culturally sensitive approach to handling research samples, treating DNA samples as "on loan" to respect Indigenous perspectives on bodily samples.[5] So far, this approach has already been successful to some degree, as it has led, for example, to the recent identification of genetic variants related to respiratory diseases in the Inuit population.

Concluding the section on community engagement, it is important to note that while the potential benefits of such practices are substantial, their implementation is far from straightforward.[56] There are numerous challenges and subtleties to consider for research projects aiming to incorporate community engagement practices.[56] Chief among these challenges is deciding what constitutes a "community" and who gets to decide which groups are considered communities.[56] The effectiveness of community engagement practices relies heavily on the context, underscoring that their success is contingent on carefully navigating these important nuances.

Section C: Summary of Section 3 and the Six Thematic Codes

In the first section, we explored codes 1,3, and 4. Thematic Code 1 represents discussions about the reification of genetically defined race. Manuscripts labelled with this thematic code emphasized how GA is often conflated with race in both public and scientific discourses, despite being fundamentally distinct.

We extensively discussed how GA is determined and used in genomics research, with a main emphasis on the often-occurring oversimplification of GA. When this happens and GA is interpreted as a scientific euphemism for race, negative social consequences may result. For example, some racist groups have weaponized this conflation to promote their ideologies. Furthermore, Code 2, genetic essentialism and the oversimplification of health and Code 3, genetic stereotyping and stigmatization, directly stem from the reification of genetically defined race. Thematic Code 3 cautions against the oversimplification of health and disease in genomic research, particularly regarding racial disparities. It critiques reductionist approaches that attribute health disparities predominantly to genetic differences. An example of this is the problematic logic behind using race-specific drugs to address health disparities. This logic obfuscates a certain social responsibility to address social and environmental causes for racial disparities. Thematic Code 4 discusses the risk of genetic stereotyping and stigmatization. It focuses on how genomic research using GA can lead to the association of specific traits or health conditions with certain racial or social groups. An example of this is the "Warrior Gene", where a genomic study inadvertently reinforced stereotypes about the Māori people of New Zealand.

Thematic Code 6 emphasizes the need for better scientific communication in genomics research when using GA. It outlines four key principles: clear definitions and criteria for GA, transparent explanation of the rationale for using GA, acknowledging limitations and assumptions in GA usage, and contextualizing genetic findings within a broader health framework.

Thematic Codes 2 focuses on the necessity of increasing diversity and representation in genomic databases. Manuscripts labelled with Code 2 underline the importance of diversity to enhance the generalizability of research findings. We first define what increasing "diversity" means according to scholars. Then, using examples such as the differential utility of variant calling in breast cancer and polygenic risk scores, we attempt to illustrate the consequences of insufficient diversity. This leads to thematic Code 5, the role of trust and cultural sensitivity in facilitating diverse genomics research participation. We highlight the increased reluctance of racialized populations to participate in genomic studies. Furthermore, we highlight that concerns surrounding privacy and the misuse of personal health data are contributors to this elevated reluctance. Various authors emphasize that historical cases of research misconduct can help explain these increased feelings of mistrust. Furthermore, we emphasize how culturally insensitive research practices can also deter more diverse research participation. To

conclude, we briefly discuss the value of community engagement practices as a means to facilitate trust and to inform culturally sensitive research.