Research Output Journal of Education 6(1):1-5, 2026

ROJE Publications PRINT ISSN: 1115-6139

https://rojournals.org/roj-education/ ONLINE ISSN: 1115-9324

https://doi.org/10.59298/ROJE/2026/611500

Ethical, Legal, and Social Implications of Polygenic Risk Scores in Indigenous Communities: Consent, Governance, and Trust

Kakembo Aisha Annet

Faculty of Education, Kampala International University, Uganda

ABSTRACT

Polygenic risk scores (PRS) are emerging tools in genomic medicine that estimate an individual's genetic susceptibility to complex diseases by aggregating the effects of multiple genetic variants. While PRS hold promise for advancing precision medicine, their application in Indigenous communities raises significant ethical, legal, and social concerns. This paper examines the implications of PRS within Indigenous contexts, focusing on informed consent, governance frameworks, trust-building, and data sovereignty. It highlights the limitations of PRS derived predominantly from European ancestry datasets, which undermine their predictive validity and exacerbate existing health inequities for Indigenous populations. The study further explores the importance of culturally appropriate consent processes that prioritize collective decision-making and respect Indigenous worldviews. It evaluates emerging Indigenous-led governance models and accountability mechanisms designed to safeguard community interests and ensure equitable participation in research. Additionally, the paper discusses legal considerations surrounding Indigenous data sovereignty, ownership, and cross-border data governance. Despite increasing global attention, significant gaps remain in empirical evidence and methodological approaches tailored to Indigenous populations. The paper concludes by advocating for inclusive, community-driven research practices, strengthened governance structures, and policy reforms that align genomic innovation with Indigenous rights, values, and self-determination.

Keywords: Polygenic Risk Scores (PRS), Indigenous Communities, Informed Consent, Data Sovereignty, and Genomic Ethics.

INTRODUCTION

The paradigm of health research has shifted to incorporate diverse perspectives on data governance, research design, and downstream benefits of research [1]. Polygenic risk scores (PRS) quantitative summary measures that account for the additive effects of many genetic variants through statistical modeling are instrumental for disease prediction and are increasingly translated to clinical practice. Internationally, Indigenous peoples are engaging with research and academic institutions to develop equitable, community-centred approaches to biological and environmental data governance and to ensure that research, data collection, and sampling adhere to Indigenous nations' principles, practices, and policies[2]. Ongoing geospatial and retrospective analyses indicate that PRS tools reflect population genetic structures that marginally differentiate some Indigenous populations from predominant European populations. Consequently, the applicability to Indigenous populations of PRS generated from predominantly European cohorts remains unresolved [1]. Nevertheless, local datasets are lacking, and the potential misalignment between the population structure of PRS training datasets and target cohorts is a widely acknowledged challenge for population applicability [2].

Conceptual Foundations of Polygenic Risk Scores

Polygenic risk scores (PRS) enable the quantification of an individual's genetic risk for certain conditions based on their genetic profile, thus informing both prevention and treatment choices [2]. Construction of PRS relies on results from genome-wide association studies, which identify variants statistically associated with traits in a reference sample [3]. The total number of risk-associated variants across the genome represents a trait's polygenicity, whereas the magnitude of their effects measures AVE. In theory, PRS can predict any genetic condition, but practical concerns limit their utility [4]. The frameworks for devising PRS focus on two aspects of genetic architecture, and only conditions fitting these hypotheses are amenable to PRS construction. Much of the existing evidence on PRS accuracy derives from populations of European ancestry [5]. Models integrating genome-wide genotype data with summary-level PRS data predict trait-by-trait estimate in Admixed individuals, but databases on PRS applicability in Indigenous communities are lacking. The literature considers health disparities within these groups but investigates PRS strictly in non-Indigenous cohorts [5].

Ethical Considerations and Informed Consent in Indigenous Contexts

Before undertaking biomedical research, obtaining informed consent from individual participants is essential [4]. However, the ethical and legal nuances of informed consent may change when considering Indigenous populations. To navigate these complexities, researchers must acknowledge that various communities approach consent differently, often based on diverse cultural and historical perspectives [4]. In many Indigenous groups, consent is rooted in a collective worldview, emphasizing the necessity of obtaining agreement from the entire community 5. Prior to engaging in any research involving genome-wide association study data from Indigenous populations, investigators need to clarify whether the appropriate unit to seek consent from is the individual or the community.

Informed consent in Indigenous contexts requires attention to culture, time, and governance, all influenced by relationships within the community [5]. Consent must be appropriate to the cultural practices of the people concerned, considering the values, beliefs, and traditions that strongly influence their perceptions of consent. Consent must also reflect the time structure of those communities, which may differ from the time-locked present typical of colonial societies. Moreover, decision-making authority concerning whether, when, and how communities provide consent lies with the communities themselves [6].

Governance Frameworks and Accountability Mechanisms

Polygenic risk scores (PRS) have been proposed as aids for health prediction, screening, and personalized intervention [7]. The potential of PRS to exacerbate existing disparities in health predicts adverse outcomes for Indigenous peoples, for whom disproportionate care could have colonial consequences. Accordingly, guidance surrounding the inclusion of Indigenous peoples in PRS research continues to emerge. However, there is limited understanding of governance frameworks and accountability mechanisms that can safeguard the interests of communities involved in PRS research. Four-party within-community frameworks exist. The first prioritizes community governance and external researcher accountability [7]. The second emphasizes peer-community governance and external researcher-community accountability. The third emphasizes community and external researcher governance with internal and external accountability. The fourth maintains community governance while allocating researcher accountability within a multiparty system [8]. Indigenous-led governance frameworks do exist. The CIHR defines governance as decision-making authority and accountability exercised by communities over research involving their data, knowledge, or samples. CIHR regards governance as a research requirement and stipulates that Indigenous communities must make their own assessments of the appropriateness of PRS. Various documents provide detailed guidance regarding Indigenous governance around PRS research [9]. Governments of Canada frameworks specify protection from misuse or misrepresentation of cultural, social, and health data. These frameworks articulate the rights, ownership, and interests of Indigenous populations contributing to Western health-risk research, including those concerning knowledge and data circulation by external agents and other populations [9].

Trust, Community Engagement, and Relational Ethics

Polygenic risk scores (PRS) are measures derived from genome-wide association studies (GWAS) that estimate an individual's relative liability across a range of complex human traits and diseases based on genetic data[1]. Alongside phenotypic information, they have been used in prediction models that further estimate the likelihood of developing conditions such as breast and prostate cancer [4]. PRS generally have modest predictive performance, and even when available for a particular trait, their limited applicability across different ethnic groups is of particular concern for Indigenous populations [5]. Such limitations can contribute to health-care systems that further widen health disparity gaps, as demonstrated by PRS for traits including educational attainment and longevity in Māori [6]. To mitigate harm, a set of design principles has been proposed, based on collective experiences of engagement with Indigenous communities, particularly in New Zealand. These principles may help to ensure that research aligns with community interests and values and permit better consideration of governance, decision-making, and engagement [7]. As of 2018, eight bioethics opinions on initiatives involving Indigenous communities had been published, along with five frameworks and various empirical studies on engagement with Native American nations [10]. Another major report published in 2018 addressed biobanking principles articulated in prior frameworks, and similar efforts continue to be undertaken across other countries. Nevertheless, uncertainty remains regarding the extent to which these insights pertain to PRS research [11]. Moreover, even when directly applicable, profound inequities among Indigenous peoples in Canada mean that prior frameworks still lead to very different ethical positions[12]. In light of these information gaps, inquiries into the conceptual foundations and current state of knowledge on PRS in relation to Indigenous interests would provide ongoing benefit [13].

Legal Landscapes: Rights, Data Sovereignty, and Protection

Legal landscapes governing polygenic risk score (PRS) research intersect with the rights of Indigenous people and with the evolving discipline of Indigenous Data Sovereignty (IDS)[1]. Concerns around local laws, agreements, and Indigenous Data Sovereignty principles arise with cross-border data flows [1]. A lack of transparency regarding governance and support for local data stewardship and jurisdiction further compounds this misalignment [2]. Polygenic risk score research raises potential legal and ethical questions concerning Indigenous data. Laws governing the collection, use, sharing, and protection of personal and health information differ across States and Territories in Canada [2]. The ongoing development of Genomic Data Ownership Laws in New Zealand also provides context for polygenic risk score research and analysis. Compliance with Indigenous data sovereignty principles and legal requirements remains essential to establishing local governance arrangements that align with community interests[3].

Current Evidence on Polygenic Risk Scores in Indigenous Populations

Polygenic risk scores (PRS) quantify genetic predisposition for complex traits by aggregating effects of multiple genetic variants [11]. PRS based on common variants account for a substantial proportion of heritability for many adverse health outcomes [3, 4]. Despite recent advances in machine learning and tremounds of available data, the predictive power of PRS remains modest [5, 6]. Most existing PRS are optimized for northern European populations, raising questions about their generalizability and potential transferability to Indigenous groups. PRS modelling relies on genome-wide association studies (GWAS). PRS derived from population-specific (or closely related) GWAS generally outperform PRS based on unrelated populations [7]. This limitation results in correlations between polygenic score and PRS when scores are calculated on the basis of non-representative training data [8]. Moreover, PRS production and use may involve complex socio-technical systems, including flow of biological material, laboratory procedures, storage and transfer of data, funding and other governance arrangements, and even conceptual framing. An understanding specific barrier provided by uneven ancestry coverage, as well as identifying frameworks that remain unaffected by such constraints, represents a pragmatic avenue for research [9].

Gaps in Knowledge and Methodological Challenges

Polygenic risk scores represent a measurable attempt to understand how genetic and environmental variations may contribute to common human phenotypes and the associated consequences [7]. From a statistical perspective, polygenic risk scores facilitate the prediction of complex human traits as discrete variables, albeit with several constraints. The credibility of polygenic scores' prognostications diminishes as these traits take on extreme values; hence, substantial evidence is lacking regarding their clinical utility and broader societal ramifications [8]. Indigenous peoples are particularly relevant in these deliberations because of their ongoing struggles for sovereignty and jurisdiction over biogenetic resources within the necropolitical paradigm in colonial nation-states [9]. Further, genetic research requires bodily and biological materials endowed with distinct sociocultural interpretations among Indigenous groups [4]. Within colonial frameworks, consent is typically framed as an individual rather than a collective act; a much broader understanding of community engagement is warranted. Consent, therefore, requires anchoring within established systems of common property rights that account for all biological and bodily materials [5]. Collectively, regulated private and public databases support national and international monitoring of genomes, phenomes, environmental exposures, and health records associated with environmental rights [4]. Global data sharing enables systematic genotyping worldwide, sophisticated imputation of millions of untested variants, and opportunity to evaluate environmental dynamism on risk trajectories. Polymerase chain reaction-based surveillance characterizes circulating variants, AIDS920 enables trace-back to origin points, and GISAID provides lineage assessments for counterfactual scenario modeling [3].

Policy Implications and Practical Recommendations

Polygenic Risk Scores (PRSs) are the result of polygenic prediction algorithms informed by thousands or millions of common genetic variants captured in genotyping platforms [11]. They quantify, at the individual level, genetic susceptibility to complex diseases [10]. Most studies confirm that the predictive capacity of PRSs is still weak, barring some exception for special contexts (e.g., skin pigmentation)[11]. To date, there are no publications reporting on the use of PRSs in Indigenous populations, whether their associates' risk factors are culturally relevant, or how to satisfy a valid informed consent (IC) in a way that respects Indigenous governance and jurisdiction [12]. The use of PRSs generates deep ethical issues associated with IC, governance and trust. Specific features of these countries call for special efforts to improve long term impact of research [13, 14].

CONCLUSION

The integration of polygenic risk scores into health research and clinical practice presents both opportunities and challenges, particularly for Indigenous communities. While PRS offer potential benefits in disease prediction and prevention, their current limitations, especially the reliance on non-representative datasets, risk reinforcing existing health disparities. Ethical concerns surrounding informed consent underscore the need to move beyond individualistic frameworks toward collective, culturally grounded approaches that respect Indigenous governance systems and decision-making processes. Effective governance frameworks are central to ensuring accountability, transparency, and equitable benefit-sharing. Indigenous-led models of governance and data stewardship provide critical pathways for aligning research practices with community priorities and values. Moreover, legal frameworks grounded in Indigenous data sovereignty are essential for protecting the ownership, control, and appropriate use of genetic information, particularly in the context of global data sharing. Trust remains a foundational element in the relationship between researchers and Indigenous communities. Building and sustaining this trust requires meaningful engagement, long-term collaboration, and adherence to relational ethics that prioritize reciprocity and respect. Despite emerging frameworks and ethical guidelines, significant gaps persist in both the scientific evidence and the practical implementation of PRS in Indigenous contexts. Ultimately, advancing the responsible use of PRS demands a paradigm shift toward inclusive, community-centered research that integrates ethical, legal, and social considerations at every stage. Policymakers, researchers, and institutions must work collaboratively with Indigenous communities to co-develop frameworks that ensure genomic innovations contribute to health equity rather than deepen existing inequalities.

REFERENCES

1. Russo Carroll S, Plevel R, Jennings LL, Garba I, Figueroa-Rodríguez OL, Begay RL, et al. Extending the CARE principles from tribal research policies to benefit sharing in genomic research. Front Genet. 2022;13:873337. doi:10.3389/fgene.2022.873337. (pubmed.ncbi.nlm.nih.gov)
2. Lewis CM, Vassos E. Polygenic risk scores: from research tools to clinical instruments. Genome Med. 2020;12(1):44. doi:10.1186/s13073-020-00742-5. (pubmed.ncbi.nlm.nih.gov)
3. Palk AC, Dalvie S, de Vries J, Martin AR, Stein DJ. Potential use of clinical polygenic risk scores in psychiatry—ethical implications and communicating high polygenic risk. Philos Ethics Humanit Med. 2019;14(1):4. doi:10.1186/s13010-019-0077-8. (pubmed.ncbi.nlm.nih.gov)
4. Ugwu CN, Eze VH. Qualitative research. IDOSR Journal of Computer and Applied Sciences. 2023 Jan;8(1):20-35.
5. Tindana P, Depuur C, de Vries J, Seeley J, Parker M, Bull S. Informed consent in genomic research and biobanking: taking feedback of findings seriously. BMC Med Ethics. 2020;21(1):18. doi:10.1186/s12910-020-0458-6. (pubmed.ncbi.nlm.nih.gov)
6. O'Neill CA, Harding A, Harper B, Stone D, Ducharme MB, Heitman E, et al. Conducting research with tribal communities: sovereignty, ethics, and data-sharing issues. Environ Health Perspect. 2012;120(1):6-10. doi:10.1289/ehp.1103904. (pubmed.ncbi.nlm.nih.gov)
7. Aramoana J, Koea J. An integrative review of the barriers to Indigenous peoples participation in biobanking and genomic research. JCO Glob Oncol. 2020;6:83-91. doi:10.1200/JGO.19.00156. (pubmed.ncbi.nlm.nih.gov)
8. Nneoma UC, Udoka EV, Nnenna UJ, Chukwudi OF, Paul-Chima UO. Ethical publication issues in the collection and analysis of research data. Newport International Journal of Scientific and Experimental Sciences (NIJSES). 2023;3(2):132-40.
9. Baker DB, Kaye J, Terry SF. Governance through privacy, fairness, and respect for individuals. eLS. 2016. doi:10.1002/9780470015902.a0026827. (onlinelibrary.wiley.com)
10. Sabatello M, Bakken S, Chung WK, Cohn E, Crew KD, Kiryluk K, et al. Return of polygenic risk scores in research: stakeholders' views on the eMERGE-IV study. HGG Adv. 2024;5(2):100281. doi:10.1016/j.xhgg.2024.100281. (pubmed.ncbi.nlm.nih.gov)
11. Atutornu J, Milne R, Costa A, Patch C, Middleton A. Towards equitable and trustworthy genomics research**.** EBioMedicine. 2022;76:103879. doi:10.1016/j.ebiom.2022.103879. (pubmed.ncbi.nlm.nih.gov)
12. Haring RC, Henry WA, Hudson M, Rodriguez EM, Taualii MM, Sinha D, et al. Views on clinical trial recruitment, biospecimen collection, and cancer research: population science from landscapes of the Haudenosaunee (People of the Longhouse). J Cancer Educ**.** 2018;33(1):44-51. doi:10.1007/s13187-016-1055-7. (pubmed.ncbi.nlm.nih.gov)
13. Corpas M, Fatumo S. Generalisation of genomic findings and applications of polygenic risk scores. Genome Med. 2023;15(1):57. doi:10.1186/s13073-023-01193-8. (pubmed.ncbi.nlm.nih.gov)
14. Hiratsuka VY, Hahn MJ, Woodbury RB, Hull SC, Wilson DR, Dillard DA. Alaska Native genomic research: perspectives from Alaska Native leaders, federal staff, and biomedical researchers. Genet Med. 2020;22(12):1935-1943. doi:10.1038/s41436-020-0895-7. (pubmed.ncbi.nlm.nih.gov)

CITE AS: Kakembo Aisha Annet (2026). Ethical, Legal, and Social Implications of Polygenic Risk Scores in Indigenous Communities: Consent, Governance, and Trust. Research Output Journal of Education 6(1):1-5. https://doi.org/10.59298/ROJE/2026/611500