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Ethical, Legal, and Social Implications of Polygenic Risk Scores in Primary Care: Consent, Governance, and Trust

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ABSTRACT

Polygenic risk scores (PRS) are increasingly promoted as tools for improving disease risk stratification and preventive care in primary healthcare settings. By aggregating the effects of thousands of common genetic variants, PRS offer probabilistic insights into an individual's susceptibility to complex diseases beyond conventional clinical risk factors. Despite growing evidence of potential clinical utility, the integration of PRS into primary care raises significant ethical, legal, and social implications (ELSI) that remain insufficiently addressed. This paper critically examines these implications with particular focus on consent models, governance frameworks, data protection, equity, and trust in patient–clinician relationships. Drawing on international policy developments and emerging clinical experiences, the analysis explores challenges related to informed, broad, and dynamic consent; regulatory oversight and accountability; data privacy and re-identification risks; disparities arising from ancestry bias and unequal access; and the communication of probabilistic risk in time-constrained primary care settings. The paper argues that without robust governance structures, transparent consent processes, and sustained trust-building measures, the deployment of PRS risks exacerbating health inequities, undermining autonomy, and eroding public confidence in genomic medicine. It concludes by offering practical recommendations for responsible implementation, emphasizing the need for proportionate regulation, clinician education, equity-oriented validation, and patient-centred communication to ensure that PRS adoption in primary care aligns with ethical principles and public health goals.

Keywords: Polygenic Risk Scores, Primary Care, Genomic Ethics, Consent and Governance, Trust and Equity.

INTRODUCTION

Risk assessment is pivotal to the practice of medicine, and emerging polygenic risk scores (PRS) hold promise for improving risk stratification [1]. A PRS aggregates the combined effect of thousands of common genetic variants of small effect on an individual's risk for a given disease. PRSs are constructed separately for each of hundreds of diseases and traits. They can be interpreted as an individual's position relative to the population distribution of genetic liability [2]. The further an individual's score deviates from the norm, the greater their genetic advantage or disadvantage. There is evidence that a PRS adds independent predictive value over conventional clinical risk factors from lifestyle-related behaviours to family history [3]. Key to the utility of PRSs is the existence of a genetic instrument, large-scale genome-wide association studies (GWAS), that identify the variants with a verified association[3]. Following multiple rounds of training and validation on prospective cohorts, the Damer score, for instance, has emerged as the first open-access population-specific PRS optimized for the diagnosis of dementia.

Even with growing evidence of potential clinical utility, important ethical, legal, and social implications arise in the consideration of deploying PRSs in primary care [2]. The provision of genomic information has the potential to contribute to inequities, expose individuals to stigma or discrimination, and affect the clinician–patient relationship issues that have been widely explored and documented at the national and international levels. Addressing these implications has unparalleled urgency, especially with plans underway to deploy a polygenic score for dementia in Alberta, and potential forthcoming plans for other traits and even national implementation [3]. Polygenic risk scores may open avenues for new and critical health data that further individual care,

preventive measures, and population health programs; yet they also pose considerable and poorly governed bioethical dilemmas [5].

Conceptual Foundations of Polygenic Risk Scores

Polygenic risk scores (PRS) summarize an individual's genetic predisposition to complex traits based on the additive effects of common single-nucleotide polymorphisms (SNPs) identified by genome-wide association studies (GWAS) [8]. The predictive value of PRS is enhanced by the availability of genome-wide genotyping and whole-genome sequencing technologies, coupled with extensive public datasets that characterize the genetic and environmental risk for diverse traits across multiple populations [9]. PRS can be used to generate risk estimates at different life stages: from the fetal stage onward, through biofluids, and at higher resolution through tissue samples [6]. This information is particularly valuable in the identification of children at risk of developing conditions like mood disorders or psychosis, allowing the institution of preventive interventions even before symptoms appear [2]. Nonetheless, for successful use and communication of PRS, practitioners and patients must have a clear understanding of their construction, interpretation, limitations, and potential clinical utility [6]. Current estimates suggest that as much as 25% of individual differences in disease and behaviour are associated with non-mendelian traits [3]. Drop-out behaviours are not limited to behavioural disorders, brain disorders, and psychiatric disorders; genetic analyses of children predicted the ability to develop intellectual capacity and measure the permissiveness of parental attitudes [4]. Population studies across 224 traits make it possible to identify traits susceptible to drug or substance abuse in individuals defined as genetically predisposed. Combined with the existence of traits with failed prediction, "Sweet-Spot" conditions become a candidate for favouring conditions that favour recurrence with recurrence across generations [2]. Detecting alternative splicing in the study of addiction behaviour represents a challenge, requiring the identification of condition experiments, dry-lab residue, database search of such activities, a detector-free approach, and the creation of study programs that indicate a lack of behaviour across conditional states [3]. For traits concentrated in brain areas, the discovery of interacting trait space using a free-standing kernel offers new approaches; simultaneously capturing bulk-RNA measurements and spliced-junction introduces alternative-time-scale resulted by high variation of attention; finally, much of the trait space found across scRNA data tracks is unfolded pseudotime [2].

Consent in Primary Care: Informed, Broad, and Dynamic

In primary-care genomic testing, patients must provide informed consent, permitting the collection, analysis, and use of personal health data [7]. The conventional model, which emphasizes informed consent, prioritizes the ethical principle of autonomy and relies on conveying a large amount of detailed information prior to decision-making. Alternatives include broad consent, which expands the scope of data sharing and secondary use, and dynamic consent, which permits the patient to revise or elaborate upon preferences after the initial consent is given [9]. These approaches may be better suited for time-constrained settings, such as primary-care consultations, where perceived pressures undermine the autonomy of patients deciding whether to undergo testing [4]. Among the compliance responsibilities associated with these consent models, two remain pertinent to polygenic risk scores [9]. The first concerns understanding the range of information required prior to testing (e.g., genomic, phenotypic, familial), and the second concerns the availability of data to accommodate patients who are unable or unwilling to make their own choices. Clinicians routinely encounter patients who wish to designate others to consent on their behalf, whether because they are minors, cannot engage in decision-making processes, or prefer to have a healthcare professional assume responsibility [9]. Addressing these factors is crucial for the effective governance of polygenic risk scores and, more generally, for unlocking their potential to contribute to improved population health [8].

Governance Frameworks: Regulation, Oversight, and Accountability

The regulatory landscape for polygenic risk score (PRS) deployment in primary care is complex. PRS use intersects with diverse disciplines, such as bioethics, genomics, and data science, subjecting it to a broad spectrum of regulatory scrutiny, oversight, and standards [8]. Collection, storage, access, and sharing of health and genomic data invoke regulations around privacy, security, and confidentiality, as interlinked bioethics and data safeguards [5]. Governance frameworks delineate regulatory, oversight, and accountability structures. PRS deployment must adhere to standards defined through these frameworks and decided upon by policymakers addressing ethical, legal, and societal considerations [7]. Primary care clinicians deploying PRS lack responsibility for multifactorial regulatory and governance obligations originating outside their practice. Accordingly, multiple accountability pathways remain available: clinician to institution, institution to governing authorities, and institution to developer of the PRS calculator and supporting algorithm [6].

Trust and Patient-Clinician Relationships in Genomic Medicine

Trust remains fundamental to the patient-clinician relationship, particularly in genomic medicine involving polygenic risk scores (PRS) [3]. Trust flourishes when patients perceive transparency in how PRS are communicated, strong clinician competence regarding PRS interpretation, protection of patient confidentiality, and adoption of shared decision-making principles [4]. Such trust is critical not only for patients to accept PRS

but also for clinicians to avoid overestimating the predictive power of PRS and thereby inadvertently raising patient expectations and concerns [8]. Miscommunication is a significant risk because PRS convey probabilistic risk rather than certainties about future health, yet patients tend to interpret advice on lifestyle changes or monitoring as reflecting certainty about impending health issues. Generating unrealistic patient expectations increases the potential for subsequent disappointment and trust erosion [8]. Clinicians with good communication skills and training in probability mathematics are better positioned to deliver messages that align more closely with patient understanding [9]. Communication about PRS is further complicated by the uncertainties inherent in its predictive value and by the possibility that PRS may be invalid for particular patient populations. Some studies approach the calculation of PRS-specific calibration metrics, with population-specific calibration reported for a subset of common and complex conditions [5]. Gaps remain, however, between current knowledge and clinical use. Uncertainty also arises from modest effect sizes and low positive predictive values that accompany some PRS. In this context, the emergence of risk-reducing lifestyle interventions or treatments generates divergent scenarios with varying predictive utility and consideration of whether overconfidence in PRS remains plausible [8]. Policy approaches to PRS deployment across different jurisdictions reflect efforts to govern a technology with acknowledged limitations and uncertainties. Unequal reciprocal knowledge among patients and practitioners is one reason that the relationship remains vulnerable [3].

Equity, Access, and Beneficiary Outcomes

Polygenic risk scores (PRS) are hereditary risk estimation and stratification tools that help guide preventive measures in primary care [6]. Rapidly gaining traction since the first reliable estimates in 2014, PRS have clear public health relevance, particularly for prevalent, complex multifactorial traits such as coronary artery disease and many cancers [7]. However, PRS are not universally valid, and much published validation work is on European ancestry populations alone. Attention is also needed to the equity of access fundamental to beneficiary outcomes; PRS are especially costly and unguided in low-burden situations, so, without appropriate interim measures, disparities in access to other major offerings may be aggravated [8]. Consideration of fairness criteria in this context is unavoidable, yet formal frameworks and monitoring systems remain underexplored.

Data Privacy, Security, and Re-identification Risks

Genomic tests have the potential to improve health outcomes through early detection, preventive interventions, and optimized treatment. However, tests often do not realize this potential due to a gap between health knowledge and practice within the healthcare system [6]. Polygenic risk scores (PRS) constitute an opportunity to bridge this gap through a risk summary form based on research publications [4]. The design of PRS scenarios must consider the rapid generation of health-related information that raises complex ethical, legal, and social issues [3]. Proper handling of genomic data during storage, sharing, and secondary use fundamentally influences privacy risks, security responsibilities, and governance demands [8]. In practice, a typical data lifecycle commences with the collection of information related to genomic tests and personal status, following which records are generally stored within a centralized database. Security obstacles motivate limited safeguarding measures aimed at preventing unintended access to stored data that might permit inference of sensitive traits [3]. The need to share access for clinical, research, or regulatory purposes is addressed through the sharing of individual-level datasets or summary statistics pertaining to aggregated cohorts [3]. Disseminated datasets characterizing external cohorts, in conjunction with public data records corresponding to the entire genome or to closely linked single-nucleotide polymorphisms, suffice to enable re-identification attempts through inferences of genotype, ancestry, and status concerning the original cohort [6]. Finally, where individuals desire secondary use by third parties or intend to make personal-level datasets accessible, sharing options may be complemented by (constrained) direct-depositing into archives offering catalogued access to the underlying protocol while retaining control over the institution's night release on behalf of investigators[5]. Technical safeguards comprise pertinent tools and protocols for the protection of privacy and security in genomic datasets, while organizational safeguards include governance, audit, and risk-protection measures. Implementations may require the design of governance tools for the prospective PRS dataset, establishment of data-sharing policies to regulate and monitor dissemination to additional parties, and implementation of a system for supervision of ongoing research [6]. The broad array of re-identification scenarios is not exhaustively described in existing governance analytics, even though coverage remains theoretically possible 7. Consequently, formal self-protection still does not preclude elaborate alternatives to either test or infer fundamental participant attributes [5].

Clinical Utility, Validity, and Misuse of Polygenic Risk Scores

The clinical utility of polygenic risk scores (PRS) is defined by their capacity to support specific health-related decisions whose expected outcomes are widely recognized and valued [2]. The use of polygenic risk scores (PRS) raises ethical issues related to the potential to exacerbate health inequities, misinterpretation leading to stigma or discrimination, issues related to testing minors and prenatal testing, and challenges in communicating high risk[5]. Effective communication and interpretation of polygenic risk scores are central to preventing misunderstandings and ensuring appropriate treatment, given that psychiatric disorders are influenced by

interactions between thousands of variants of small effect that can be summarized in a polygenic risk score [3]. Such scores cannot be reliably generalized from one population to another; the same is true for other risk factors. Generalizing polygenic risk scores from Europeans to Hispanics/Latinos remains a challenge, with implications for access to other treatment resources [5]. Because current PRS are constructed mainly from European-descendant cohorts, the majority of research evidence for PRS and the majority of peer-reviewed publications concern this population, reinforcing disparities in European and non-European cohorts [7].

Policy Implications and International Perspectives

Policy implications and international perspectives on PRS governance emerge as significant themes in countries adopting genomic medicine [9]. Widespread adoption raises inquiries on the comparative policy frameworks in place, the manner in which policy and practice diverge, and cooperative endeavors that may facilitate alignment. The policy landscape for PRS is elucidated with respect to two domains: the governing framework for safeguarding individual and population health when providing genomic tests and associated advice, and a broader procedure for the administration of significant data holdings [7]. Governance mechanisms, such as regulatory standards, oversight practices, and accountability frameworks for PRS, are varied across jurisdictions and are subject to heterogeneous adherence [2]. Alignments in optimal policy arrangements sustain genomic equity and risk-mitigation processes; disparities in policy and the institutional environment induce inequitable chromosomal vulnerability exposure [6]. Policy scrutiny delineates practice-oriented scrutiny priority for securing protection at the pre-participation stage and ensuring privacy and protection at the post-participation stage. Notions of data-sharing, communal ownership, and individual agency within medical policies are considered as an aspect of genomic medicine's changing development [5].

Practical Recommendations for Practice and Research

Polygenic risk scores (PRS) hold the potential to enhance population health by informing risk-reducing interventions, but their implementation in primary care is hindered by a broad set of ethical, legal, and social implications that coalesce around issues of consent, governance, and trust [2]. Accordingly, a package of practical recommendations is offered to support the responsible adoption of PRS in this context [9-15]. The specific ethical trade-offs associated with PRS concerning autonomy, beneficence, non-maleficence, and justice are uncommonly challenging, and guidance for primary-care practitioners that addresses the relevant considerations is rarely available [8]. Broad consent is likely to be the most appropriate approach, allowing the clinician to act in the patient's best interests while respecting the patient's ability to refuse access to their genomic data [3]. The governance frameworks that are put in place, regulatory regimes, oversight mechanisms, and a clear articulation of accountability must therefore be comprehensive, robust, and clearly communicated [6]. Centrally important for the approach taken to consent is the question of whether data are held solely within the clinical setting, or shared for secondary use, either within an institution or more widely [7]. When data-sharing arrangements exist, there is a strong justification for broad consent, allowing the patient to grant or refuse secondary use. When all data are securely held within the clinical environment, dynamic consent may be more appropriate [3]. In addition, the ethical analysis points to autonomy, beneficence, non-maleficence, and justice as the core principles that constitute PRS-related ethicality, thereby facilitating the identification of policy-relevant dimensions. Beyond consent and governance, the use of PRS in primary care also generates social implications relating to trust and the patient-clinician relationship [3]. Trust can be undermined if it is perceived that what is disclosed or withheld about the risk information is not in the best interests of the patient [3]. Specific forms of misconduct and malfeasance that risk damaging the trust relationship with patients and the public are also identified and govern the extent to which unethical uses of PRS are conceivable or probable[8]. Such consideration addresses the specific dynamic of PRS that renders clinician/patient power differentials and the extent to which misalignment of interests could occur [6].

CONCLUSION

Polygenic risk scores represent a significant development in genomic medicine, with the potential to reshape risk assessment, prevention, and early intervention in primary care. By translating complex genomic data into clinically interpretable risk estimates, PRS may support more personalized approaches to healthcare. However, this promise is accompanied by substantial ethical, legal, and social challenges that must be addressed before widespread implementation can be justified. This analysis demonstrates that consent remains a central concern, particularly in primary care environments characterized by limited time, variable genomic literacy, and power asymmetries between clinicians and patients. While traditional informed consent models may be insufficient in this context, broad and dynamic consent frameworks offer pragmatic alternatives provided they are supported by transparency, meaningful patient choice, and clear boundaries around data use and sharing. Governance structures must likewise evolve to clarify regulatory responsibilities, ensure accountability across institutional and technological actors, and protect patient interests throughout the data lifecycle. Trust emerges as a unifying theme across ethical, legal, and social dimensions of PRS deployment. Effective communication of probabilistic risk, appropriate management of uncertainty, and protection against misuse or over-interpretation are essential to

maintaining confidence in the patient–clinician relationship. These challenges are amplified by persistent inequities in PRS development and validation, particularly the overrepresentation of European ancestry populations, which threatens to entrench existing health disparities if unaddressed. From a policy perspective, the responsible integration of PRS into primary care requires coordinated international and national approaches that balance innovation with safeguards for autonomy, justice, and non-maleficence. Investment in diverse genomic datasets, clinician training, public engagement, and ongoing evaluation of clinical utility is critical. Ultimately, the ethical legitimacy and social acceptability of PRS in primary care will depend not only on technical performance but on governance frameworks that prioritize equity, transparency, and trust. Without these foundations, the clinical promise of polygenic risk scoring risks being outweighed by its societal costs.

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