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Pharmacogenomics and Polygenic Risk Scores in National Health Insurance Systems: Clinical Workflows, Outcomes, Cost-Effectiveness, and Equity

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ABSTRACT

Pharmacogenomics and polygenic risk scores (PRS) offer transformative potential for precision medicine by tailoring prevention, diagnostics, and treatment strategies to individual genetic profiles. National Health Insurance (NHI) systems provide an optimal framework for large-scale implementation, promoting equitable access, population-wide health impact, and cost-effectiveness. This review synthesizes evidence from pilot programs, clinical workflows, and biobank-based genomic analyses to examine pharmacogenomics and PRS integration into healthcare systems. We highlight strategies for patient selection, consent, workforce training, and electronic health record integration, alongside economic evaluations, equity considerations, and ethical challenges. Findings indicate improved therapeutic efficacy, reduced adverse drug events, and enhanced population health outcomes when genomic data inform clinical decision-making. Implementing these approaches at scale requires coordinated policy frameworks, infrastructure investment, and continuous evaluation to ensure equitable benefit across diverse populations. The analysis provides actionable recommendations for policymakers, healthcare providers, and researchers to guide sustainable adoption of genomics-informed care within national health insurance systems.

Keywords: Pharmacogenomics, Polygenic Risk Scores (PRS), National Health Insurance, Precision Medicine, and Health Equity.

INTRODUCTION

Pharmacogenomics and whole-genome polygenic risk scores (PRS) promise to transform prevention, diagnostics, and treatment in common diseases [1]. Real-world experience is accumulating in national health systems with diverse characteristics, ranging from publicly funded systems providing universal access to medicines to mixed public-private systems with regulated reimbursement for selected indications [2]. Countries implementing pharmacogenomics and PRS at the national scale propose pilot schemes for multiyear evaluations of safety, efficacy, equity, and cost-effectiveness [3]. Such evaluations inform broader engagements between health, science, and finance ministries, regulatory authorities, and other stakeholders [4]. Countries conducting these evaluations generally feature publicly funded health systems providing universal access to medicines, including Finland, Iceland, and Sweden [5]. Observations from these pilot schemes and parallel initiatives in mixed funding systems, Belgium, France, Singapore, and Switzerland provide pertinent lessons for broader global capability development [1]. Pragmatic, observable, and actionable policy-ready recommendations emerge from the analysis framed by evidence gathered over several years by a transdisciplinary group of scholars and practitioners from diverse fields[3]. The collective exercises, conducted during a series of seminars exploring emerging genomic technologies and their societal implications, have produced influential agendas addressing the European Union, OECD, and World Health Organization [6]. The current analysis positions pharmacogenomics and PRS within these broader concepts and provides a complementary, national health-system-focused perspective. Although other components appear relevant, pharmacogenomics and PRS currently benefit from considerable attention, systematised analyses, and operational piloting [5].

Conceptual Foundations: Pharmacogenomics and Polygenic Risk Scores

Pharmacogenomics studies the relationship between a person's genome and their response to a drug. A genetic variant at a specific location in the genome may affect the metabolic pathway of a medicine, thereby impacting therapeutic efficacy and safety [7]. Capitalizing on pharmacogenomics in clinical practice potentially leads to the administration of the right drug at the right dosage to the right patient, as well as optimized combination therapy. Nevertheless, the implementation of pharmacogenomics in clinical settings remains limited worldwide [8]. Polygenic risk scores (PRSs) quantify the cumulative impact of multiple small-effect variants in the genome on an individual's disease risk. Such variants are typically implicated by single-nucleotide polymorphisms (SNPs) [10]. Computational methods estimate a PRS based on the weighted sum of risk alleles carried by a subject according to a large reference genome-wide association study (GWAS) meta-analysis. Population-specific PRS instruction sets have been constructed to support high-quality PRS building [9]. PRS may also complement the information provided by pharmacogenomics and emerge as a promising option to stratify patients in the first step of pharmacogenomic deployment [11]. The consideration of pharmacogenomics and PRS for national health insurance systems serves to identify scalable, economical, and clinically impactful strategies for improving therapeutic efficacy and safety at the population level, challenges that are particularly pressing for low- and middle-income countries, given that promoting universal access to drugs constitutes a prominent health equity objective [12].

Pharmacogenomics in Clinical Practice

Pharmacogenomics, the study of how genes affect an individual's response to drugs, enters clinical practice in many health systems. Genetic variants can have strong effects on drug response and serve as an important basis for optimizing prescriptions in large populations' diverse therapeutic classes [13]. The clinical use of pharmacogenomic information is widely encouraged, accelerated by the availability of actionable prescribing recommendations, simplified interpretation tools, and embedded decision-support features in medication-ordering software [1]. National health systems adopt the formal context of pharmacogenomics in clinical practice. Policymakers endorse implementation based on population-level therapeutic needs, academic interest, health equity, offering the same healthcare opportunity, and budget-neutrality [2]. Patient selection criteria and implementation pathways are correspondingly tailored. Several distinct, complementary features drive the increasing uptake of pharmacogenomics in large health systems [14]. The rationale for pharmacogenomics is well-defined. Genetic factors contribute substantially to the inter-individual variability of prescription drug responses, and variants that exert clinically relevant effects are known for numerous frequently used, high-impact medicines, spanning many therapeutic areas [15]. A major appeal resides in the capability to address prescription indications and therapeutic responses of primary concern to healthcare systems, matching their central mandate to improve population health. Importantly, assistive software to deliver per-drug or per-gene recommendations is commonplace; practically every health system supports considerable regulating demand and workforce training received in universities [16].

Polygenic Risk Scores: Methodology and Applications

Polygenic risk scores (PRS) enable genetic risk stratification for complex diseases by aggregating many common genetic variants [3]. Building on the population-specific risk prediction framework developed for single-nucleotide polymorphisms (SNPs) [17], PRS estimation requires three steps: [1] building a model using genome-wide association study (GWAS) summary statistics from the relevant trait in individuals of similar ancestry; [2] generating a score for individuals using the selected model; and [18] estimating per-individual risk or the proportion of variance explained among the population. Application of PRS to malignancies has attracted particular attention because many countries already have well-established screening programmes for specific early-stage tumours. Estimates indicate that implementing a PRS-driven screening programme along with the existing standard-of-care physiognomies could lead to a substantial population health benefit. PRS-consistent pharmacogenomic signals enhance empirical medication-selection algorithms tailored to individual patients and local drug formularies [19]. Integration in clinical workflows permits straightforward test-selection guidance amidst the rapidly growing array of pharmacogenomic panel offerings, even when knowledge of the intended drug remains uncertain [20].

Relevance to National Health Insurance Systems

The ubiquity of genomics technologies is revealing the potential for precision medicine to transform national health such that variability in the uptake and the nature of pharmacogenomic and polygenic-risk-score initiatives cannot be understood without explicit consideration of national insurance frameworks [21]. Events in 2023 the passing of the UK's new Economic Crime and Corporate Transparency Act, significant reforms of the Italian and Spanish NHS, and major state-by-state changes to the US public-health system in the wake of COVID further underline the need to devise a clear NHS-consortium-wide approach to these matters and capture the leadership and initiative opportunities they provide to the NHS vis-à-vis other major jurisdictions [6]. It is already being widely acknowledged in UK academia that many health systems are now moving from COVID-19 emergency

provisioning back to regular programming, and so it is timely to refocus on the pressure points within the NHS that digital genomics has the potential to address [22]. NHS funding already has explicit tenure and universal access of relevance to both systems: pharmacogenomics and PGS clearly further points of convergence stand surprisingly apart outside the health sector at present, with the UK at one end of the spectrum (neither standard, respiratory very low weight) and Canada at the other (neither standard, respiratory moderate weight) [23].

Clinical Workflows for Implementation

Pharmacogenomics enables personalized medicine through tailored drug treatments based on genomic information [1]. This technology has been widely studied in cardiovascular and psychiatric disorders and is the leading genetic-testing application in health systems [24]. National Health Insurance (NHI) systems could provide coverage for pharmacogenomics as a benefit of significant public health value. Genomic technologies are already applied in monitoring and predicting the risks of several diseases in some NHI-supported health systems, including diabetes and polygenic coronary heart disease [25]. Polygenic risk scores (PRS) offer an opportunity to further develop and implement affordable national genomic medicine initiatives in NHI systems worldwide. PRS provides risk variations for common diseases by linking some of their reliable genetic risk variants into scores, creating the opportunity to monitor, evaluate, and mitigate the emergence of various diseases, including type 2 diabetes, coronary heart disease, breast cancer, and major depression, and thus allowing for a wider application of personalized medicine [26]. The need for national genomic medicine initiatives is already urgent and increasingly recognized in many NHI systems with an advanced public-health focus, as indicated by multiple countries adopting national genomic medicine strategies. Coverage for PRS-based national genomic medicine is being assessed for its health impact, cost-effectiveness, and equitable access across diverse NHI systems [9]. To plan and support such initiatives, many NHI systems are developing a comprehensive framework for capacity development and implementation and assessing the implications of PRS on clinical practice [27] Within national health systems, national HMO + PHI systems could adopt the Health-Monitoring Strategy (HMS), starting from monitoring and evaluating financially essential diseases with an advanced health-information-technology strategy and the availability of affordable tests [28]. The intensive study of PMS and PRS technologies within the national HMO + PHI systems provides encouraging findings and recommendations to shape extensive consideration of national public health decision-making and financing in several NHI systems[29].

Patient Selection and Consent

National health insurance systems are ideal for pharmacogenomics and polygenic risk scores because they generate public revenue for health care, promote equity of access, and cover large malfunctions [30]. National systems can cover tests for patients taking the 40% of drugs with high sensitivity to relevant genomic variants instead of requiring a priori patient selection, thereby targeting the majority of patients rather than only a small proportion at risk [31]. The systems address large population health concerns; preventive psychiatric pharmacotherapy cannot be salable because a 90% assurance of efficacy has not been achieved yet, and all epidemiological modeling has given ill-informed specifications; and cancer therapy routinely waits for recurrences to begin serious maintenance before recovery and trials both on clinical practice and AI models for predictive ability failed to inform specification [32]. Stakeholder capacity for biobanks establishing nation-wide pharmacogenomic studies is present and can build on established international biobanks and rapid-growth (4–5 years) bridges to the wider biomedical landscape [33]. Initially, selection and consent are given the highest priority. National coverage for a single-step test needs a broad safety margin because the efficacy is the lowest among the several cases being studied in parallel, precluding serious epidemic testing on-site [34]. The pharmacogenomic test is elaborated on first to encompass an extremely stable symptomatic antipsychotic that remains valid across medications and locations, and an informative polygenic-risk-score hairstyle. The first step addresses epidemiological scattering, specifying the highest incidence of casein–zero Grammy recipients, to avoid pure pharmacogenomics [9]. Missing factors indicate no sufficient incentive to disseminate intent. Since the polygenic risk score controls only a modest segment of practice, whereas prolonging animation or healthy scattering triggers vital change, the situation continues to lack an appropriate patient cohort [3]. The first uncomplicated precipitation briefly freezes. Industry ignores an interim observatory focused on large-scale checks, and the anti-social sentiment hesitates [35]. The institute becomes an interim organization to manufacture simple assays for national approval and discover a profile simple enough to remain executable at this platform [36]. External procurements separately glance at the polygenic chunk from specific readings at international urban centers, covering worldwide health drivers more widely. Collected carton-free genome batches, even despite their size, substantially diminish [18]. The probe must touch the location–drifting points, so the atlas compensates. Considering cash concerns, data entering the international stage attracts attention. Constraints restrict national observatories, hence industry cannot proceed [37].

Genomic Data Acquisition and Analysis

Safe and efficient acquisition of genomic data is crucial for the successful implementation of pharmacogenomics and polygenic risk scores into clinical workflows [15]. Several genotyping platforms are commercially available,

and next-generation sequencing is increasingly used in large-scale biobanks holding genomic and health data [6]. A clinical workflow for primary care pharmacogenomic testing has been implemented in the United States using the GeneSight Psychotropic test, especially where patients are on polypharmacy [38]. The GeneSight test provides a pharmacogenomic report indicating the expected efficacy and safety of several drug classes commonly used to treat depression, anxiety, and other psychological disorders [7]. The pharmacogenomic report assesses nine genes, and the selection of the assay depends on the medications a patient is taking [39]. When implementing pharmacogenomics into medication management for an extensive list of drugs and complex polypharmacy situations, very large data sets are required. Thus, a national biobank containing health records with linked genomic data is regarded as a central element of the strategy. The Danish National Biobank and the Icelandic deCode Biobank are two such biobanks [40]. Institutions also undertake genotyping at the point of care. Such intensive implementation of pharmacogenomics represents the US experience; regulatory and reimbursement frameworks differ from those in other countries [41]. Barriers to successful rollout include platform-specific variations in the pharmacogenetic information content delivered, the need for training and continuous education of health-care providers, and the speed and precision of genotype data generation and interpretation [42].

Decision Support and Treatment Algorithms

Pharmacogenomic datasets can exceed 600 million labeled variants; hence, computer-aided classification of pharmacogenomic variants from genome sequencing data is essential [11]. The One-Stop Pharmacogenomic Tool can annotate pharmacogenomic variants, identify prescribing medications, and suggest allele-specific treatment recommendations as a decision-support system to improve safe prescribing practices [15]. Clinicians can easily access One-Stop Pharmacogenomic Tool outputs through various formats: an Excel file with pharmacogenomic medications sorted by prescribing-category files with allele-specific treatment recommendations, output graphs showing six pharmacogenomic prevention categories (prescription only, prevention warnings, further investigation is needed, prevention not needed, opposite situation, and combination function), and a GRCh37 and GRCh38 human genome browser track file. Nevertheless, the integration of pharmacogenomic information into EHR systems is still limited [43]. Policies promoting widespread access to polygenic-risk-score testing in the general population are warranted because unimodal high-scoring individuals currently receive the majority of benefits [13]. Improving predictive accuracy for therapy-response prediction across the full distribution of polygenic-score values defines a more equitable target for further research; drug repositioning for such acutely underserved individuals should also be prioritized [44]. An automated clinical decision-support tool for polypharmacy and medication-associated problems identifies cases warranting pharmacogenomic determination 7.

Integration with Electronic Health Records

Integration of pharmacogenomic data into clinical workflows can be facilitated through health-record platforms that automatically retrieve drug-gene pairs identified in guidelines, along with other relevant clinical information [17]. Such systems can be configured to issue alerts and present guidance specific to the pharmacogenomic context. Various approaches can analyze this data to assess medication appropriateness, prioritizing the selection of pharmacogenomic testing among candidates who would benefit most from the intervention [45].

Workforce Training and Capacity Building

Further training of health professionals regarding pharmacogenomics is paramount, not just for the correct interpretation and communication of genomic information, but also more broadly for communication about population health topics [26]. Clear communication of genomic information is of utmost importance if patient safety is to be enhanced and the implementation of genomic analytics integrated into routine care delivery [8]. The appropriate interpretation of pharmacogenomic information encompasses an understanding of how the underlying biological mechanisms influence the hypothesized effect of the matched medication on health outcomes, but many health professionals lack training in basic human genetics [46]. Pharmacogenomics decision-support programs help to simplify the task of matching a genomic test result to the corresponding medication-descriptor pair and to collate current knowledge on pharmacogenomic associations, but parallel efforts to enhance the widespread training of such programs have not yet begun [12]. Both topics fall under the broader umbrella of training health professionals to engage security with a wider range of population health topics [47].

Clinical Outcomes and Evidence

Pharmacogenomics has yielded promising results in translating research into improved patient outcomes for cardiovascular and other complex diseases [48]. Evidence indicates that inherited genomic variants significantly influence individual response to specific antihypertensive drugs [10]. Numerous ongoing studies are assessing the clinical impact of polygenic risk scores on therapeutic efficiency, safety, and treatment selection in at least ten common conditions, ranging from cardiovascular and metabolic disorders to respiratory and psychiatric diseases [2]. Cardiovascular mortality associated with the misuse of several drugs derives significantly from adverse drug events and represents the second leading cause of death, further fuelling the assessment of pharmacogenomics and polygenic risk scores[12]. Encouraging results with cardiovascular drugs have contributed to interest in other areas [10]. The Joint National Committee defines hypertension as a major determinant of poor health.

Antihypertensive drugs constitute a principal therapeutic approach against hypertension, which is multifactorial and highly polygenic [49]. Efforts to implement pharmacogenomics at national or regional scales now focus on improving the efficiency of cardiovascular and antihypertensive treatment. Edited summaries would add value if needed [13].

Therapeutic Efficacy and Safety Signals

National Health Insurance (NHI) promotes equitable access to basic health services. All citizens should have health services according to their needs, irrespective of location, time, and economic situation, and patients should receive health services according to their preferences [16]. Equity-oriented health policies and insurance systems hinge on fair access to services, availability of appropriate curative and preventive measures, and equitable distribution of effective care and resources. Equity-oriented substance abuse interventions are categorized into medical and therapy-based measures [50]. Regular health education increases knowledge about the harms of substance use. Since population choice sets differ, public programs should match particular drugs with optimal remedies for primary and tertiary avoidance. Considering geographic, temporal, intercultural, and income-related substance use, and supplementary equity-oriented influences are vital for outreach interventions [17]. Economic evaluation investigates the benefits and costs of health interventions and finds appropriate resource allocation of interventions in resource-limited settings [17]. Pharmacogenomics and polygenic risk scores have immense promise for health equity and population health impact, particularly for large national systems such as the National Health Service, but evidence remains limited [23]. Clear benefits have been documented in health systems with varied characteristics [11]. Implementing interventions that yield population-wide benefit without an influx of new technology, at least initially, would ease clinical adoption while providing direct, immediate advantage. Early data now emerging additionally indicate that pharmacogenomics leads to improved therapeutic outcomes, reduced adverse events, enhanced patient safety, and increased therapeutic adherence [7]. Population-wide framework analysis of polygenic risk targeting highlights the potential efficiency of universal health system implementation [51]. The vast majority of pharmacological prescriptions are issued for patients who already carry risk factors for the targeted condition, enabling systematic population-scale genomic risk scoring to pre-empt severe health events long before the clinical onset of symptoms [10]. Further data are required to properly characterize the range of additional economic effects associated with such population-level implementation [52].

Population Health Impact

Polygenic risk stratification enhances the effectiveness and cost-effectiveness of screening programs [20]. However, risk-tailored screening is more complex than age-based programs, necessitating attention to organizational, ethical, legal, and social issues [13]. Public engagement, education, and collaboration with health professionals remain essential. Training for health professionals ensures comprehension of risk scores, effective communication, and appropriate patient support [53]. Developing these programs entails meticulous planning, understanding of underlying science, population sciences, ethical considerations, and policy formulation [14]. Research is now focused on evaluating therapeutic response rates across the polygenic score distribution rather than solely identifying high-risk groups. Sensitivity and specificity measures have limited clinical utility, as scores often exhibit sensitivities below 50% [13]. Although therapeutic response may correlate with disease risk, this cannot be assumed; further investigation into response to therapy is needed [54]. Targeted treatment of high-risk individuals can significantly reduce incident cases, with the potential to prevent 20% to 50% of cases by treating a small proportion of patients [11]. Negative prediction remains vital for identifying those unlikely to benefit, particularly when treatments incur high costs. The balance between the costs of treatment and the rights of patients is critically important, as expensive medications impose a persistent burden on healthcare systems while patient preferences must also be considered [14]. Genetic risk scores represent a step toward personalized medicine, requiring implementation aligned with the clinical and economic context of each disease [55].

Equity in Access and Longitudinal Follow-Up

A major challenge for health-care systems is ensuring equitable access to pharmacogenomic and polygenic-risk information and safe, effective treatments guided by that information [12]. Longitudinal follow-up is critical, since many pharmacogenomic markers are relevant only for specific interventions that may not occur until years after testing, and the clinical utility of polygenic-risk scores typically diminishes after the period in which preventive measures could be taken [56].

Economic Evaluation and Cost-Effectiveness

Economic evaluations estimate the changes in costs and health benefits attributable to pharmacogenomics and polygenic risk scores compared to the absence of such actions [9]. Three health economic assessment approaches can be employed to inform national health insurance coverage decisions: [1] cost-of-illness studies quantify the economic burden of a specific disease within a defined population, [2] budget impact analyses assess the fiscal implications of introducing a new intervention into an existing health care system, [3] cost-utility analyses estimate additional costs associated with a new intervention divided by the extended quality-adjusted life years (QALYs) gained [57]. Direct and indirect costs arise from adverse drug reactions (ADRs); cost estimates often

stem from published studies. In countries with universal health insurance coverage, a cost-utility model featured a health government perspective that included direct medical costs reimbursed by the health authorities and indirect costs related to productivity losses in working-age individuals due to the occurrence of ADRs [17]. This model also considered pre-emptive testing, through which ordering a test before the patient starts treatment allows health care professionals to anticipate potential risk before treatment starts, including direct medical costs, such as wages lost from chronic diseases, and the cost of replacing absent workers[6]. Where end-user fees are minimal, such approaches could be standardized comparatively easily through advisory organizations and government agencies.

Additional Pharmacoeconomic studies†a have confirmed the potential cost-effectiveness for other pharmacogenes [58]. Conducting national registries, health authorities, and government agencies to assess direct medical costs associated with the medications, foremost among these are analytic steps [15]. A similar choice of costing perspective would tend to simplify this type of analysis in the frame of reference of national health systems. Further changes to this file would also allow a cost-utility analysis of the other scoring software calculated accordingly [59].

Direct and Indirect Costs

Investing in pharmacogenomics, even without immediate patient-specific benefit, can yield broader gains by enhancing the evidence base for wider national adoption, informing subsequent drug-development investments, and guiding genomic evaluation strategies to improve health equity [10]. In analyses of 88 global pharmacogenomics implementation studies, median total direct, indirect, societal, and system-specific costs were estimated at US$7.59, 0.66, 8.61, and 10.09 per patient, respectively [60]. Studies indicate a positive relationship between annual medication expenditures and pharmacogenomics-program cost-effectiveness, underscoring the benefits of phased national implementation to optimize health-system affordability and equity [13].

Budget Impact Analysis in National Systems

Budget impact analysis in national systems examines the implications of introducing pharmacogenomic testing and personalized medicine strategies [13]. Such initiatives necessitate the establishment of clinical knowledge resources, associated guidelines, and implementation frameworks [61]. Fundamental questions centre on cost-effectiveness, clinical utility, and their bearing on adverse drug reactions and treatment outcomes [5]. Given the influence of pharmacogenomic knowledge on medication selection, dosing adjustments, and treatment switches, the proposed interventions are projected to modulate overall healthcare expenditure [11]. Legal considerations, particularly the safeguarding of citizens against genetic discrimination, further shape the operational context [21]. The broader vision of pharmacogenomic knowledge deployment within healthcare systems aims to enhance patient welfare through tailored therapies and to optimise resource stewardship [62].

Value-Based Pricing and Reimbursement Scenarios

Substantial evidence already indicates the clinical utility, population health impact, and long-term equity of pharmacogenomics and polygenic risk score applications embedded in healthcare workflows [8]. However, national implementation at an insurance-systems level depends on economic considerations and assessments of cost-effectiveness relative to locally determined thresholds [63]. The economic evaluation component must incorporate both direct and indirect costs from the patient, provider, and societal perspectives. To date, there is considerably greater evidence and understanding than for other novel genomics-based approaches [7].

Scenarios that model these parameters using real-world unit-cost and probability data for Finland suggest potentially favourable cost-effectiveness across a range of patient subgroups for both interventions [2]. While encouraging, these findings remain preliminary, not least because robust economic analysis still lacks a coherent conceptual framework that formally articulates the relevant inputs, outputs, and time horizons of each modality. Nonetheless, promising evidence of economic value under various local conditions further underpins the continuance of ongoing implementation efforts [64].

Equity-Adjusted Economic Assessments

Pharmacogenomics and polygenic risk scores are increasingly recognized as promising strategies for personalizing healthcare. However, no health system can support all possible interventions [11]. Traditional cost-effectiveness analyses compare interventions to estimate the value placed upon healthcare. Economic assessments can be adjusted using equity weights to address health inequalities alongside efficiency and thus inform coverage decisions [5]. Health systems often prioritize efficiency in healthcare delivery above other considerations [65]. Equity-adjusted economic assessments measure the efficiency gains and distributions of health effects anticipated before implementing a new practice [17]. Together with available evidence on population health impacts, such assessments can guide the selection of interventions expected to maximize equitable health gains [2].

Implementation Challenges and Risk Mitigation

Guidelines for pharmacogenomics implementation indicate that patient data protection must remain paramount, with care taken to prevent the release of genomic data to unauthorized parties [5]. Supplementary consent

comprising an explicit indication of whether genomic and non-genomic data can be saved, shared, or reused facilitates compliance with legal obligations while optimally utilizing the data collected [15]. Data anonymization further reduces the ownership and privacy concerns associated with data sharing [9]. Socio-ethical issues such as stigmatization, discrimination, and clinical misuse of genomic and non-genomic data can also require mitigation procedures [6]. Even participatory platforms provide equal opportunities for requests and feedback, for instance, concerning genomic data ownership may not prevent abuses [66]. Existing legislation or ethical guidelines should therefore be reinforced using OKs to clarify the operational framework and avoid ambiguous interpretability in shared datasets [9]. Other anticipated challenges include securing the necessary technical infrastructure; ensuring that pharmacy professionals receive relevant technical training to adapt to embedded point-of-care completion requests; guaranteeing consistent access to the internet and software service providers; and covering equipment expenses for all practitioners to avoid dereliction of care and research obligations [7]. Stakeholder involvement throughout the entire planning and implementation phases promotes relevant contacted scientists [67].

Data Privacy and Security

Pharmacogenomic and polygenic risk score (PRS) technologies collect a significant amount of data from individuals. The large-scale datasets generated must be curated to ensure privacy and security 16 and compliance with national and international ethical standards [68]. Defined broadly, data privacy concerns the confidentiality of sensitive material; data security concerns the protection of data from theft, corruption, or unauthorized access. Both issues are interrelated and interdependent, but avoidable by adopting appropriate safeguards [11]. Privacy and security critically impact large genomic datasets, the proliferation of which raises the possibility of re-identifying individuals through unprotected personal health information [10]. Hacking incurs financial costs and diminishes public trust, and the publication of comprehensive genomic information creates opportunities for misuse [9]. In national health insurance systems, the ethical collection and use of genomic data are subjects of policy discussions. The implementation of pharmacogenomic therapies and PRSs entails safeguarding personal information throughout the clinical workflow [10]. Genomic data analysis must, therefore, adhere to ethical principles and organizational policies for responsible data sharing and secure data use [16]. The dissemination of guidance on best practices enables the pooling of secure datasets across jurisdictions to accelerate evidence generation for health promotion and the mitigation of treatment risks [69].

Ethical and Social Implications

Medical genetics raises ethical questions involving health equity/justice, access to services, and whether expanded opportunities benefit individuals/patients and wider communities [18]. The fairness of polygenic risk scoring (PRS) raises different considerations; relevant material for analysis of health equity, informed consent, social justice, and risk communication exists [2]. Use of polygenic risk scores in psychiatric contexts threatens to exacerbate existing inequalities. High educational attainment and social advantage consistently correlate with reduced incidence of serious psychiatric disorders [70]. A genetic-teratological framework describing the interaction of genetic variants and environmental influences converges with pathogenetic models. A focus on high polygenic scores, limited to large-scale models, leads to ethical challenges directly related to risk identification rather than to disease prevention or therapy [14]. As health-insurance companies attempt to adapt pharmacogenomic/polygenic-risk concepts for economic advantage, amplifying consideration of advantages/disadvantages for society assumes added importance [11].

Technical and Infrastructural Barriers

Delivery of genomic services faces technical and infrastructural barriers spanning multiple areas. Robust digital computing infrastructure, software, and applications are required for analysis, interpretation, and management of genomic data, while genomic testing also introduces new data processing, reporting, storage, and interoperability requirements [10]. Insufficient storage capacity, inadequate data management systems, reliance on standalone software, and inadequate data governance may impede implementation [12]. Improved accessibility and interoperability of electronic health records (EHRs) would facilitate integration of polygenic risk score (PRS) and pharmacogenomic data into existing clinical workflows [20]. National health insurance frameworks commonly contain a high proportion of disjointed, heterogeneous EHR systems, making aggregation of sensitive data and computation of PRS at the population level challenging. Advanced electronic health data analysis capabilities are needed to deliver these services effectively [71].

Regulatory and Policy Considerations

The growing awareness of the potential value proposition associated with pharmacogenomics and polygenic risk scores has resulted in increased policy interest and stakeholder attention [12]. Public health authorities, health ministries, and social insurance institutions worldwide are grappling with the question of how to optimally integrate these technologies into national health insurance systems [11]. Proposals have taken shape in clinical practice guidelines intended for physician use, in analyses targeting decision makers and managers, and in protocols directed at public agencies and social insurance organisations [2]. Nevertheless, a publication gap persists [21]. While the literature is rich in insights addressing the technical underpinnings of pharmacogenomics

and polygenic risk scores, and while substantial research has examined their long-term economic impact in national health insurance systems, publications exploring the practicalities of bringing these technologies into broad clinical use remain scarce [22].

Equity Considerations in Deployment

Signed genomic tests that assess multiple genes or variants simultaneously promise a more precise assessment of a patient's genetic susceptibility to disease than individual variants [5]. Targeting scarce healthcare system resources toward those individuals most likely to benefit from intervention could dramatically improve population health and the cost-effectiveness of public health interventions targeting genetic disease; nonetheless, increasing understanding of the pathogenic variants associated with a specific condition or disorder generates hundreds or even thousands of known variants in molecular databases [2]. Substantial differences across populations make such polygenic scores largely ineffective in practice [8]. Covariates essential to the construction of accurate polygenic scores are illustrative of this problem and extend well beyond traditional geographical, social, or economic aspects and include the burgeoning genomic landscape [11]. A limited understanding of the reach-and-use of genomic materials makes it utterly impossible to design efforts that address this issue [13]. Wider access to carrier screening, for example, introduces non-uniform choices, costs, and competing risks and also aggravates access disparities to the screening itself [12]. Policymakers considering the coverage of ever-expanding genomic-based technologies, analyses, or estimates must therefore ask themselves the following questions: are all segments of the population equally or similarly covered? If not, how can fair dispersion of benefit be achieved? [24] And, should a situation arise in which coverage unevenly extends across populations, how can unintentional negative side effects be uncovered and placed at the forefront of policy intervention? Dispositive of inquiry straddling the divide between science, technology, and society research is available to assist in uncovering unintended or unforeseen effects and is capable of directly informing coverage analyses [23].

Access Disparities and Social Determinants of Health

Health disparities represent preventable differences in the burden of disease, injury, violence, or opportunities to achieve optimal health experienced by socially disadvantaged populations, such as those affected by racial, ethnic, gender, or socioeconomic bias [24]. Pharmacogenomics (PGx) is one component of precision medicine that considers genetic variation among individuals. PGx can identify genetic differences that may affect drug efficacy or safety, thereby increasing adherence, preventing hospitalizations, and enhancing patient outcomes. However, implementation of PGx to date has not demonstrated a path toward health equity, particularly in the context of population-wide implementation [12]. Pharmacogenomic (PGx) data can facilitate more effective prescribing and help ameliorate the structural drivers of health disparities [11]. PGx information about drug clearance and dosage for particular medications becomes useful when patients' drug therapy is adjusted for other health conditions, the prescriber has limited access to the patient's full clinical history, or when the prescriber lacks familiarity with the medication. National implementation of PGx in large healthcare systems has been successful in stratifying risk assessment for several major drug classes [15].

Strategies to Promote Inclusive Benefit

Decisions about inclusion or exclusion of particular groups from new public health benefits often rely on fraught social criteria, such as ability to benefit; the inevitable consequence of such criteria is that new public health benefits offered through national health insurance systems are more widely adopted by some population groups than by others [2]. Traditionally, emphasis on professional judgment or narrow clinical criteria effectively concentrates in the upper strata of society, potentially transformative benefits such as pharmacogenomics and polygenic risk scores, while leaving those at the bottom to languish without access or recourse [25]. Widespread adoption of individual genomic and polygenic data aligns well with societal preferences during new technology development and deployment [26]. Addressing specification deficiencies in public benefit definitions for pharmacogenomics and polygenic risk scores can thus expand access and inclusiveness, align proposals more closely with contemporary expectations, and promote more equitable population outcomes by achieving earlier and wider uptake among underserved and disadvantaged[27].

Monitoring for Unintended Consequences

Considerable potential exists for polygenic risk scores to affect precision medicine approaches; monitoring and evaluation during the implementation phase of pharmacogenomics in clinical practice would therefore be prudent [11]. Precedents in monitoring pharmacogenomics in clinical practice exist within a community pharmacy pilot in British Columbia that evaluated testing for ~740 genetic variants affecting ~50 medications for chronic disease management [5]. Pharmacogenomic testing at the community pharmacy located the presence of actionable variants for 19.2% of tested patients, identified 29% more drug–gene interactions than documented in pharmacy systems or electronic medical records, and frequently uncovered duplicative and unnecessary prescribing, contraindications, and similar issues[7]. Most tested, 93%, considered polygenic testing helpful to their healthcare, and 91% would recommend it to others. Regular assessment documents whether additional pharmacogenomic results become available, any missed opportunities for drug optimizations, or less favourable

metric trends, guiding precise tailoring to local practice and informing subsequent assessments[8]. Polygenic risk scores are emerging as a potential solution to promote health equity in access to pharmacogenomic testing 2. Observed health disparities were already prescient; individuals receiving SSDI, Medicaid, or living in lower-SES neighbourhoods had significantly reduced access to pharmacogenomic tests and follow-up, and emerging inequities would deserve similar attention [13].

Policy Implications and Recommendations

At scale, pharmacogenomics is expected to improve the safety and purchasing value of prescription drugs, and polygenic risk scores to enhance prevention and detection of complex diseases [17]. National health insurance systems are considering whether and how to implement these approaches [12]. A collection of eleven frameworks from countries and jurisdictions representing nearly half of the global population suggests that pharmacogenomics and polygenic risk scores are, or are planned to be, under official consideration for national coverage in six[23]. Progress in systems where these processes are already implemented distinguishes lessons for scalable adoption of clinically relevant genotyping and data analysis within health care and health policy [22].

Guiding Principles for National Coverage

Coverage policies for pharmacogenomic tests have emerged at a national level. Guidelines for pharmacogenomic testing are available for specific drugs, genes, and gene-drug pairs, addressing drug metabolism, action, and risk of serious adverse drug reactions. The situation is less clear for polygenic risk scores [26]. Pharmacogenomic tests involved in the event prompt psychotropic medications for depression are already reimbursed by national health insurance systems or are undergoing payer consideration [7]. In contrast, polygenic risk scores for psychiatric disorders involved in the scenario are often not yet considered for reimbursement, even though guidelines recommend their use as decision support under specific patient conditions [7]. These scores support pre-emptive treatment for selected individuals exposed to certain social determinants of health throughout life 2. Coverage policies for polygenic risk scores in a similar event remain under discussion [4].

Scalable Implementation Pathways

The coordinated introduction of pharmacogenomics and polygenic risk scores in non-adoption countries should guide the implementation strategy, both to maximize the incremental population health gain and to identify engagement opportunities with low-coverage countries [23]. Integrated system preparedness for separate or combined workflows throughout preparatory discussions is vital, owing to interdependencies between scientific evidence, cost-effectiveness, equity, and work-delivery options in national health insurance systems [4, 27].

Research Agendas and Gaps

Interdisciplinary research is needed to evaluate polygenic risk scores (PRSs) for therapeutic targeting. Current guidelines advocate restricting PRS-based therapy to individuals with scores in the top decile or quintile [24]. However, therapeutic response rates should be examined across the entire PRS distribution, especially at lower scores, to identify nonresponders and to guide investment in other treatment options [24]. Sensitivity and specificity are inadequate measures for determining high-risk subpopulations because they operate over score intervals, and high scores often correspond to low sensitivity for response [25]. When targeting individuals with the highest predicted response, economic benefits accrue as the number needed to treat decreases and many additional cases are averted over population-wide treatment. Models supporting negative-prioritization approaches are informative. By flagging patients unlikely to respond, negative prediction remains crucial for controlling costs and prioritizing access to scarce therapies [28]. To achieve health equity through genomic medicine, research must shift from solely documenting disparities to addressing root causes [26]. Socioeconomic status shapes health research and service delivery, but tailored interventions are necessary rather than a one-size-fits-all model. Disparities in the injury burden from extreme heat and air pollution highlight the importance of environmental injustice, particularly for sexual minorities. Interracial and ethnic disparities stem from systemic discrimination; discrimination-mitigating policies must be diffused systemwide, and interventions are needed to counteract stereotype threat at schools. Ongoing efforts target waste reduction and unnecessary cost elimination [29]. The affordability of implementing genomic services in diverse learning health-care systems remains a challenge, yet progress continues alongside the integration of genomics into precision medicine [30-32].

CONCLUSION

Pharmacogenomics and polygenic risk scores have demonstrated significant potential to improve clinical outcomes, optimize therapeutic efficacy, and promote equitable access to healthcare when integrated within national health insurance systems. Successful implementation depends on the alignment of clinical workflows, robust genomic data infrastructure, economic evaluation, and targeted workforce training. Equity-focused approaches, ethical oversight, and longitudinal monitoring are essential to mitigate disparities in access and ensure that genomic innovations benefit all segments of the population. Future research should expand PRS evaluation across full-risk distributions, assess cost-effectiveness in diverse healthcare settings, and explore strategies to integrate genomic tools seamlessly into routine care. With coordinated policy, infrastructure, and research

support, national health systems can harness genomics to advance precision medicine, enhance patient safety, and optimize population health outcomes.

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