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Population Genomics for Stroke: Return of Results, Cascade Testing, and Health System Readiness from Bench-to-Population Perspectives

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ABSTRACT

Stroke remains a leading cause of mortality and disability worldwide, with both monogenic and polygenic genetic determinants contributing to individual and population risk. Population genomics provides a transformative approach to understanding these genetic influences, enabling the identification of at-risk individuals, informing precision prevention strategies, and integrating genomic insights into health systems. This review explores the critical components of population genomics for stroke, including the return of results, cascade testing within families, ethical and governance considerations, and health system readiness for genomic medicine. Bench-to-population translational pathways highlight the integration of genomic discoveries into clinical decision support, workforce training, and public health policy. Comparative international experiences, including programs in Canada, the UK, Iceland, and Singapore, underscore the opportunities and challenges of implementing population genomics at scale. Equitable access, privacy protection, and health economic considerations remain central to maximizing societal benefit. Future directions emphasize comprehensive population-level genomic screening, polygenic risk stratification, and the integration of multiomic and environmental data to advance precision stroke prevention and management.

Keywords: Population genomics, Stroke prevention, Cascade testing, polygenic risk, and Health system readiness.

INTRODUCTION

Stroke remains a leading cause of death and a major contributor to disability worldwide. Genome-wide association studies have identified hundreds of loci associated with ischemic stroke and transient ischemic attack and their stroke subtypes, small vessel disease, large vessel disease, cardio-embolism, and other proposed drug targets, informing risk prediction [1]. An estimated 11% of early-onset ischemic stroke is monogenic, with recurrent pathogenic variants identified in 20 genes [2]. Population-based genomics provides a cost-effective opportunity to determine the growing multicondition genomic burden shaping stroke prevention, management, care, and health equity [3]. Approaches for returning results, cascade testing, and readiness of health systems for genomic medicine accelerate bench-to-population transition and address integration with population health [4].

Conceptual Framework for Population Genomics in Stroke

Population genomics for stroke: return of results, cascade testing, and health system readiness bench-to-population perspectives [5]. Stroke, a leading cause of mortality and disability worldwide, is increasingly recognized as a genetically influenced disease. Population genomics aims to leverage genomic knowledge to reduce stroke incidence and improve management among individuals at increased risk [6]. This endeavour links research bench findings to outcomes at the population health level, with implications for publicly funded health systems. Important concepts include the return of results, cascade testing, health system readiness, equity, and implementation science [7]. To inform and facilitate bench-to-population advances in population genomics for stroke, a conceptual framework was developed outlining critical components, interactions, and the research translation ladder bridging genome–phenome links to societal impact, incorporating stakeholder identification, governance, and ethical principles[8]. The framework illustrates genomic influence on stroke across multiple

pathways; distinguishes gene–stroke biology links, polygenic risk, and monogenic contributions; and organizes societal models governing how genomic data can enhance prevention, diagnosis, and management at the population level [9]. In relation to population genomics, stakeholders such as individuals at risk and their families, health-care providers and organizations, public health authorities, funders, and researchers play various roles in generating, interpreting, and acting on information about genetic susceptibility to stroke [10]. Corresponding principles and guidelines address the responsible conduct of return-of-results, cascade-testing, and health-system readiness activities [11].

Return of Results in Population Genomics for Stroke

Population genomics seeks to understand the relationship between genetic variation and population health. It involves multi-omic studies using genetic, genomic, transcriptomic, and epigenomic data to build links between biological mechanisms and health outcomes [12]. In stroke, it identifies monogenic and polygenic variation, links genetic variation to underlying biological pathways, and contributes to risk stratification models and population-based prevention strategies [13]. These findings potentially benefit both the individual and population levels. Understanding the value of returning research results, including the timing and rationale, guides planning and implementation [12]. Ethical, legal, and governance frameworks shape the return of results in population genomics for stroke. General upstream policies apply to the program, with additional downstream specifications required to address consent, governance, advisement, and communication challenges associated with returning results [9]. Among genomic determinants of stroke risk, polygenic risk scores are distinct from clinically actionable variants. Communicating results to the public involves addressing consent options and the availability of advisement services [4]. The need for action results varies, and socio-demographic metrics are crucial to assessing equity and defining the target population of interest [9].

Ethical Considerations and Informed Consent

Population genomics imports the notion of returning results from a clinical perspective. However, whereas the clinical return of results is bounded by the field of clinical genetics, the return of results in population genomics can stretch from publicly available summary statistics to the communication of an individual's polygenic risk score (PRS) at the opposite end of an interaction line[6]. Attention will be given to two distinct yet complementary aspects: counselling and the facilitation of cascade testing in family networks [13]. Cascade testing that targets individuals related to a proband may exert the largest public health impact and substantially reduce health system burdens [14]. The ethical landscape surrounding the return of results in population genomics for stroke emerges from core principles, standards, and governance that are essential for considering the return of results from various sources [14]. A prominent ethical concern involves the definition of actionable results that warrant return [4]. In contrast to the risks associated with a genomics-based PRS for stroke, which are unlikely to bring clinically useful risk stratification, strategically selected chromosomal variants that act as the basis for actionable returns may generate advantageous health outcomes [5]. The ethical principles typically underpinning research projects, including respect for persons, beneficence, and justice, remain relevant in the context of the return of results for stroke genomics. Special attention is needed, however, to validate these principles against the explicit guidelines defined in various policy documents [15].

Clinically Actionable vs. Polygenic Risk Information

Information returned through genomics is deeply consequential for individuals, families, and health systems; therefore, the basis by which it is assigned matters greatly [8]. Clinically actionable information can have a profound and immediate effect on health, whereas polygenic risk information lacks such power [7]. From an ethical and governance standpoint, the disparate character of polygenic risk burden becomes manifest. Actionable information is subject to established guidelines around governance, the ethics of return, confidentiality, and consent models, whereas polygenic risk information does not benefit from the General Principles established in prenatal testing and other similar cases [16]. Clinically actionable information permits a governing structure built on the existing guidelines published in high-profile forums and journals [10]. Such structures already exist, offering ethical parameters, societal oversights, and determinations of meaningful benefit. Polygenic risk information, by contrast, operates outside consensus standards of genetic risk, and yet it still retains the official status of genetic data [11]. Even if, for instance, the data derived from a routine test for lipids or blood pressure produces immensely greater benefit for the individual with respect to the prevention of cardiovascular disease, the genetic results are still returned, kept on file, and legally bind until the data are destroyed[17].

Communication Strategies with Patients and Families

The aim of communicating genomic results to patients, families, or health care providers can extend beyond individual risk information and affect the genomic screening and preventive behaviors adopted by households [5]. Communication strategies for patient results must thus address the information that will accompany results beyond the personal level, as well as the consent processes for sharing information with family members. For gene-level screening programs, ensuring an understanding of results and their broader implications can help motivate outreach among at-risk potential participants [18]. The mode of communication for the return of

genomic results, whether in-person or remote, remains flexible; ensuring a supportive environment and an adequate opportunity for discussion are key objectives regardless of the format [19].

Equity, Access, and Health Disparities

Equitable return of results has long been a challenge in genomics [8]. The need for equity becomes even more acute given the breadth of population genomics in stroke, which encompasses both common and rare variations. A single monogenic variant can introduce an expected lifetime-attributable stroke risk of up to 30% [12]. Polygenic risk scores based on hundreds of common variants improve stroke risk prediction substantially beyond the clinical standard [6]. The benefits of receiving either actionable or non-actionable genomic information may fall unevenly, creating a risk of compounding prior inequities. There is a growing urgency to monitor equity metrics across individual benchtop and population-scale tests and address disparities proactively in policy and practice [20].

Cascade Testing in Stroke Genomics

Cascade testing constitutes a different but complementary strand of return-of-results activities that leverages the family links of the index case [7]. An individual affected by a disorder caused by a monogenic variant or who is at high polygenic risk for the same disorder is likely to infect (for primarily dominant or semi-dominant mutations) or beget (for strongly but incompletely recessive mutations) descendants who also have a substantial risk of the same condition[21]. Cascade testing offers a systematic strategy to inform at-risk relatives of their risk status and connect them to preventive or mitigative care [22]. Such activities are already embedded in several healthcare systems for conditions with recognized genotypes (e.g., BRCA1-related breast cancer and Lynch syndrome). Integration of such approaches for stroke would offer substantial benefits and must be proactively considered within systems where genomic stroke assessments are anticipated [5]. A simple model for cascade cooling informs several important aspects of the strategy. The parent-individual parent-child limb connects an individual who has received a polygenic stroke risk score above a predefined threshold (the index case) to his or her direct descendants who are also evaluated for stroke risk [23]. A second limb connects the index case with a spouse or intimate partner for assessing the aggregate risk of stroke for joint consideration; this arm can be eliminated if studies demonstrate no difference between individual and couple-based evaluations [3]. Both limbs may optionally be extended further out (grandchildren, siblings), depending on still unassessed children and other considerations. If the index case has a genetic variant associated with stroke risk, family cascade testing presents additional challenges of informing relatives about carrier status and basic details of the variant itself[8].

Cascade Testing Models and Pathways

Cascade testing represents a major opportunity to identify at-risk relatives of individuals with a genomic variant implicated in stroke or other neurovascular conditions [2]. Such testing typically occurs through the examination of an affected individual (the index case) [4]. Guidance from the index case to subsequently test other relatives is termed genealogical referral; the resulting models are described as genealogy-based. Alternatively, unaffected individuals may undergo testing for a specific variant identified in a relative [5]. The pathways along which these genealogical or variant-based similarities unfold depend on the nature of the causative variant and whether it is routinely assessed for all stroke cases [24]. The uptake of cascade testing depends on multiple factors, including motivation, trust, and confidence in the validity of the test and its implications [7]. Emerging Canadian national clinical practice guidelines for genomic stroke medicine remain under discussion by stakeholders in the evolving genomic landscape [3]. Such guidelines outline principal recommendations for genome-wide polygenic risk scoring and cascade testing, both before and after clinically actionable results for stroke or other conditions have been returned to the index case [25]. Privacy, rights of family members, and the familial ramifications of genomic variants raise complex genomic governance issues throughout the cascade-testing continuum. Genomic information inherently holds genealogical significance. Individuals are entitled to privacy regarding disclosure of their genome to other family members [5]. Meanwhile, other family members and future generations inevitably share and may also inherit some portion of an individual's genome. Explicit attention to the distinctive privacy and family-related concerns of genomic data is therefore essential [26].

Privacy, Rights, and Familial Implications

Cascade testing extends the transformational potential of stroke population genomics by providing access to genomic data that aids personal stroke prevention, even when the index case is not yet known [2]. Cascade testing is defined as testing and return of results undertaken by genetic relatives of an identified carrier of a specific genomic variant [27]. It requires careful consideration of privacy, rights, and familial implications, especially within a framework of universal access to treatment and prevention and an ethos of upstream intervention [4]. These considerations involve dynamics of consent, data generation and sharing, and modelling of harm and utility. Concerns about privacy and confidentiality of genetic information highlight the need for appropriate rules and open consent practices [10]. The debate over returning individual research results, including incidental findings, continues, with views on how best to balance patient rights, privacy, and research integrity [3].

Health Economic Considerations

Population genomics for stroke aims to extend bench-side findings to population-level disease prevention, mitigation, and management [4]. Engaging the healthcare system through equity-principled implementation science will further advance this goal by facilitating the study of population benefit, efficient delivery, and stakeholder engagement [3]. Cascade testing, follow-up genetic testing of biologically related individuals after an initial test result, can promote health equity and is feasible for both clinically actionable and polygenic variants. It enables genomic precision medicine by linking genetic risk to secondary prevention and therapeutic approaches that remain poorly addressed [28]. Health-economic considerations influence the implementation of these approaches at the population scale. Population genomics for stroke has the potential to generate large increments in quality-adjusted life years (QALYs) at reasonable incremental costs but may be perceived as inadequate compared with similarly ambitious initiatives with extensive funding [2]. Effective presentation of economic aspects to stakeholders can help mitigate these concerns, accelerate progress, and identify required models of delivery [29].

Health System Readiness for Genomic Stroke Medicine

Readiness for genomic stroke medicine depends on the local health system's capacity to meet requirements for data, workforce, clinical decision support, and quality assurance [11]. Generic requirements include established data standards, interoperability of information technology infrastructure, training frameworks for a workforce capable of integrating genomic data into stroke care, and clinical–genomic decision support tools embedded in clinical practice guidelines [12]. Specific requirements to support the uptake of geo-genomic maintenance-of-healthy-brain-at-age-90, TREM2 gg, and POLG gg genomic information in stroke prevention and management are also needed [30]. Tools comprising integrated stroke care delivered by advanced-practice providers and digital outreach to a diverse neighbourhood population, furthermore, would enhance stroke-prevention strategies and encourage wide participation in family-cascade-testing initiatives [7]. Although the guidelines of the American College of Medical Genetics and Genomics (ACMG) recommend that population-scale genomic-sequence data remain accessible only to investigators actively engaged in secondary genomic analysis of study data for at least 3 years 6, analysis of data from the database of Genotypes and Phenotypes (dbGaP) suggests that, contrary to expectations, the majority of investigators at >90 sites conduct no follow-up genomic analyses after the 3-year period[6]. The expected long-term secondary use of paired clinical and sequence data for public-health and learning-health-system applications never materializes and opens up for further data-rich activities at low-cost when research-scale community-access repairs can be assured [5].

Infrastructure, Data Standards, and Interoperability

Health systems face challenges and opportunities in delivering genomic innovations to populations. Infrastructure and workforce readiness in health systems are crucial for implementing genomic stroke medicine at scale [5]. Specific information technology, standardization, and interoperability of platforms and tools are needed to enable the proper collection, collation, integration, and exchange of genomic data to deliver precision medicine [6]. Building knowledge and skills for genomics in health care, education, training, preparation of stakeholders, and establishing competency frameworks are also essential for the workforce [8]. Systems-capacity and genomic-readiness assessments in stroke genomics are needed to inform investment, training, and end-user-support plans [5]. Health systems are generally ill-prepared to deliver the comprehensive genomic medicine needed to address genomics, such as polygenic-risk scoring and whole-genome sequencing in cascade testing [15]. Data for monitoring health system readiness remain fragmented, and the evidence base on training needs is uncharacterized [12, 6].

Workforce Training and Roles

Stroke is the second leading cause of death and the leading cause of disability worldwide, representing a major global health crisis. There is growing interest in population genomics to reduce the burden of stroke [16]. Population genomics refers to the study of a population's genome across the genome to inform population health. A systematic strategy is needed to bridge the translational gap from bench to population and to improve population genomics research [15]. A conceptual framework linking stroke biology, population genomics, and population health delineates the path from genomic discoveries to public health outcomes. Population genomics integrates insights from bench to population [7]. Genomic determinants underlie recurrence and susceptibility of stroke and its multiple clinical subtypes. Bench-derived genomic information can improve risk stratification, prevention, diagnosis, and management of stroke at the population level [11]. Enabling genomic population-health strategies requires the involvement of multiple stakeholders, including the healthcare, information technology (IT), and pharmaceutical industries, education systems, governmental and non-governmental agencies, research communities, and civil society [9]. Stroke is a complex disorder with multiple clinical subtypes, each determined by unique pathophysiological mechanisms. Further research is needed to identify its determinants and to develop effective prevention and treatment strategies [10]. Generalization of clinical findings from populations of stroke patients to the general population is also critical for public health. Population metabolism, resulting from

the dynamic interplay between genes and environment throughout evolution, shapes the inter-individual and population-level diversity in human diseases and response to therapeutics [15].

Clinical Decision Support and Guideline Integration

Clinical decision support tools and their integration into clinical practice guidelines can facilitate the application of genetic and genomic information within a population-genomics framework for stroke and other complex traits [3]. A variety of research and clinical genomics systems have developed tools to aid the interpretation of genetic variants and support management decisions [15]. These software applications incorporate gene–disease relationships, inheritance patterns, and published evidence to assist risk assessment for a range of disorders and inform selection of tailored interventions [20]. Clinical practice guidelines translate scientific and biomedical knowledge into a format usable by frontline clinicians. Guidelines articulate standard-of-care recommendations, enhancing consistency and reducing variation in approaches to prevention and management [18]. A guideline is typically established through a consensus process involving a diverse group of stakeholders and is updated periodically in accordance with emerging insights [17]. In the context of a population-genomics framework for stroke, guidelines can assist clinicians in pairing stroke-risk genes with relevant interventions, considering highly penetrant risk and high-frequency stroke genes, and relating population-genomics data to stroke-biology schema as described previously [14].

Quality Assurance, Evaluation Metrics, and Continuous Improvement

Population genomics enables the prospect of deriving benefit from saliva genomics at the population level. Securing support for embedding saliva genomic testing panels requires demonstration of essential health-system readiness for delivering genomic screening, thereby predicting future health outcomes [13]. Frameworks exist for assessing several such readiness parameters [7]. Candidate readiness metrics warranting consideration include establishment of data standards, interoperability, information technology infrastructure requirements, workforce training needs, clinical decision-support tools, and the embedding of knowledge derived from genomic mapping within clinical practice guidelines [30]. Criteria for evaluating quality assurance and continuous improvement can complement conventional readiness evaluations. Quality indicators across genome-sequencing, pre-analytical, analytical, and post-analytical workflows inform every step of a saliva-genome formalized pipeline [13]. Progress towards establishing the readiness of health systems for the collection of saliva genomic panels, along with the laboratory infrastructure and training necessary to deliver actionable results, continues to advance. Identifying a scientifically rigorous pathway to population genomics in stroke relies on harmonizing scientific discovery obtained at the laboratory bench with the delivery of population health at the community level [15]. Genomics yield improved opportunistic prevention of future strokes and heart attacks via population screening followed by cascade testing, and a clinically actionable stroke genome programme targeting population health also resonates with the downstream mission of large-scale acute stroke randomised trials guided by monogenic determinants [17, 18, 19]. These foundational opportunities in population health provide coherence and impetus across the translational ladder from mind to molecule, to cell, to genomic encounter to allele to health [15].

Translational Pathways: From Bench to Population

Population genomics encompasses the study of genetic variation within and between populations of a single species [15]. Population genomics applied to stroke aims to understand the genetic, epigenetic, and environmental aetiology of stroke and close the gap between genetic discovery and societal benefit for stroke prevention, treatment, and improvement of health services at a population level [20]. Stroke is the second leading cause of death globally, with serious health and social consequences for individuals and society. Advances in understanding the genetic aetiology of stroke and other diseases are increasingly being used in translational medicine to develop new therapies or target prevention to at-risk individuals [17]. Stroke translational genetic research to date has primarily focused on single-gene disorders, with the greatest public health benefit likely to arise from a population-based approach that considers the entire stroke risk distribution to identify population-based pathways [19].

A relevant translational pathway from bench to population to enable genomics to address these challenges is to develop population-layered bench-to-population research pipelines that systematically translate multidisciplinary insights layered at the population level into models that inform prevention at the population level, initiation at the population level, and broader epidemiological insight [20]. Increasingly, funding agencies are establishing dedicated population genomics funding schemes alongside broader genomics programmes, and similar moves have been made internationally by governments such as the USA, UK, Canada, Australia, and countries in Europe [21].

Translational Research Designs in Stroke Genomics

Progress in stroke genomics has been limited by the complexity of the human brain and the rarity of stroke conditions [11]. Translational genomics, being hypothesis-free, holds promise for identifying key regulators of the injury response. Successful large-scale initiatives such as the International Stroke Genetics Consortium and TBI consortia demonstrate the value of collaborative efforts in assembling well-characterized patient populations [12]. These collaborations facilitate unbiased genomic discoveries and biorepository development. Partnerships

with model systems researchers are essential to validate human data and refine disease models, ensuring an accurate reflection of human phenotypes [21]. Engagement with industry partners is critical for translating genomic discoveries into drug development, encompassing both repurposing existing compounds and creating new therapeutic targets [20].

Population-Level Pilot Programs and Scale-Up

Population genomic screening could facilitate equitable implementation for stroke genomics by addressing institutional fragmentation, building evidence, and aligning incentives and policies across multiple sectors of the health system [12]. Such programs often arise from a blend of biomedical, clinical, and socio-behavioural sciences across diverse settings, strengthening the response to increasingly complex health system needs shaped by greater simultaneity, scale, and interconnectedness [13]. An expanded gene list holds potential for more rapid uptake of the approach, although initial recovery of relevant health data needs clarification for stroke [15]. Integration requires implementing a national population genomic policy to clarify the roles of relevant authorities and follow existing guidelines for delivering policies that support coordination and enable health actors to respond to evolving needs [12].

Regulatory and Policy Context

Population genomics promises new biomarkers for novel treatments of cerebrovascular disease, in particular ischemic stroke, the second leading cause of mortality worldwide and the predominant cause of adult disability [22]. Significant advances in the understanding of the genetic bases of stroke have been achieved during the last decade, with polygenic risk scores and monogenic variants identified through genome-wide association studies and whole-exome or whole-genome sequencing, respectively [21]. Population-based stroke genomics can be defined as the study of the genetic components of stroke aetiology and the return of knowledge aimed at reducing stroke incidence and its consequences at the population level on the basis of the discovery and characterization of these genetic components [18]. Population-based stroke genomics links to public health through prevention, screening, and early diagnosis, issues explicitly raised by the 2011 World Health Assembly Declaration on Stroke Prevention. The incorporation of individual genome sequence data relating to specific genetic conditions, polygenic risk scores, or both into medical records facilitates, for example, cascade testing offered to relatives of stroke patients carrying monogenic risk variants or the delivery of tailored messages emphasizing prevention and control of diabetes, hypertension, or smoking cessation in individuals selected for a high polygenic risk score [17]. The combination of these knowledge-return strategies constitutes an integrated approach that, following extensive further public health risk assessment, offers opportunities to democratize access to genomic epidemiology knowledge worldwide [13].

Case Studies and Comparative International Perspectives

Population Genomics for Stroke: Return of Results, Cascade Testing, and Health System Readiness from Bench-to-Population Perspectives. Case Studies and Comparative International Perspectives Population genomics programmes in stroke are emerging in various jurisdictions, providing valuable insights into how international contexts and past activities shape readiness for large-scale implementation [23]. Two Canadian programmes supported by Genome Canada exemplify these efforts: the Ontario Genomics-Enhanced Stroke Programme (GenESP), which sought to integrate whole-genome sequencing into diagnostic stroke pathways, and the Genome Canada–Alberta Stroke Programme (GSAP), which completed a provincial pilot of population screening for monogenic stroke [21]. The UK Biobank, initiated in 2006, is widely recognized as a pioneering population genomics initiative enabling genome-wide association studies and polygenic risk score development [18]. It illustrates the benefits of a multiomic approach that couples genomics with neuroimaging and extensive physical and mental health datasets, while also uncovering the challenges of widespread usage, equitable access, and the communication and interpretation of findings [14]. Similar programmes in Iceland, Estonia, Singapore, Australia, and New Zealand have established alongside the 100,000 Genomes Project, 1+ Million Genomes Initiative, COVID-19 Genomics UK Consortium, and the Genomic Sequencing Initiative for Non-Communicable Disease, a substantive body of knowledge regarding the facilitation of translational and implementation science. GenESP conducted a broad environmental scan to characterize ecosystem readiness in the province [14]. It benefitted from multiple prior initiatives, including the Ontario Health Data Platform, the Ontario Genomics Data Ecosystem, and the Ontario Genomics Health Equity Framework, which together formed an advanced foundation for the implementation of additional frameworks [18]. Quality assurance standards, clinical decision support tools, and provincial stewardship models for the application of polygenic risk scores were consequently drafted, guiding health authorities globally toward practical adaptations of established interventions [15].

Ethical, Legal, and Social Implications

Ethical Issues in Contemporary Clinical Genetics tackles many of the practical and moral concerns raised by the field, including requirements for informed consent and the question of whether genetic information is best characterized as medical or personal data [20]. Genetic testing may create new familial obligations; the ethical and logistical ramifications of cascade testing for relatives of gene-positive individuals deserve scrutiny. While the

authors openly acknowledge the lack of consensus on the ELSI of genomic studies and the fact that widespread agreement will be impossible to achieve, they suggest that guidelines should be established to maximize population impact and ensure equity [16]. Akinyemi and colleagues propose a framework that connects four domains of ethical, legal, and social implications (ELSI): informed consent and return of results, community engagement, ownership and access, and benefit sharing [10].

Future Directions and Research Priorities

Population genomics offers an unprecedented opportunity to advance knowledge of the biological basis of stroke in large, diverse, unselected populations across different ancestry groups [22]. Insights gained through this strategy can be exploited to identify novel mechanisms contributing to ischemic stroke and to guide the thoughtful repurposing of existing therapies and the development of innovative interventions. Continued investigation of understudied genetic determinants of common, complex diseases and traits affecting the neurological and cardiovascular systems is essential [17]. Additional insight is also needed into the complex interplay of these disease-modifying genes within the broader pan-genomic landscape and how this is influenced by environment, lifestyle, context, and application of the library of genome-editing technologies or supplementary genetic and epigenetic modifiers at the single-cell level [21]. Persistent and emerging public health challenges pose an increasingly urgent need for innovative analytical strategies to extract, translate, and apply the rich information contained within a poorly understood but very large reservoir of medical records that exist in most hospitals and clinics [30].

CONCLUSION

Population genomics offers unprecedented opportunities to advance stroke prevention, diagnosis, and management at both individual and population levels. Integrating genomic findings into clinical and public health practice requires robust strategies for returning results, implementing cascade testing, ensuring ethical governance, and preparing health systems for large-scale genomic interventions. International case studies demonstrate the feasibility of population-level genomics while highlighting challenges in equity, access, and workforce readiness. Moving forward, research priorities should focus on refining polygenic risk models, elucidating gene–environment interactions, and developing cost-effective, scalable frameworks that translate genomic insights from the bench to the population. Ultimately, the successful integration of population genomics into stroke care promises to reduce disease burden, inform precision prevention, and enhance health equity worldwide.

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