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Strategic Insights into Preventive Genomic Medicine for Neonatologists

Johannes Edy Siswanto[1], Lydia Pratanu[2], Jeremiah Hilkiah Wijaya[3]

Abstract

Genetic risk assessment is a cornerstone, evaluating an individual's genetic makeup through factors such as genetic variants, family history, and environmental influences to discern predispositions to specific diseases. However, there are several challenges and areas for improvement that need consideration. For instance, future research in preventive genomics will need to address how to best implement effective interventions at scale, consider cost implications, and determine the factors that characterize successful interventions. Additionally, there is a need to address the anticipated workforce shortage in certain medical specialties, such as rheumatology, by expanding training, increasing the utilization of telemedicine, and reducing burnout among practicing professionals. Moreover, the successful and sustainable implementation of preventive interventions, particularly in older adults, requires further insight into their attitudes towards prevention and reasons for participating in prevention trials. This insight can inform the design and recruitment of future interventions and public health policy. Methods encompass genetic testing, family history analysis, and lifestyle factor assessment. Implementing preventive genomic medicine in a LMIC presents a complex interplay of challenges and opportunities shaped by resource limitations and contextual nuances. The challenges include constrained financial and infrastructure resources, creating hurdles for genomic technology investment. The sustainability of current strategic frameworks relies on the capacity of public health programs, requiring leadership support and sufficient time to attain genomic workforce competency. Weaknesses in current preventive strategies, such as incomplete facilities and insufficient promotion, need addressing for sustainability.

Keywords: *Preventive genomic medicine,* precision*, strategy, LMICs*

Introduction

Preventive genomic medicine in neonatology has significantly impacted the field, offering the potential for personalized medical interventions and treatments.(Jen et al., 2024) Genomic sequencing has emerged as a promising diagnostic tool, enabling timely, specific interventions and treatments, including pharmacologic interventions tailored to individual patients.(Jen et al., 2024; Newson, 2022) The implementation of genomic medicine in neonatology has raised concerns about exacerbating health inequities, necessitating strategies to ensure equitable access to genomics in neonatal care. The rise of genetic testing and plans to embed whole genome sequencing in healthcare systems indicate the increasing importance of genomics in neonatology, paving the way for personalized interventions and treatments.(Jen et al., 2024;

[1] Department of Pediatric, Universitas Pelita Harapan, Tangerang, Banten, Indonesia
[2] Faculty of Medicine, Krida Wacana Christian University, Jakarta, Jakarta, Indonesia
[3]

Khoury & Holt, 2021; Newson, 2022) Furthermore, the use of genomic methods in psychiatric research and clinical practice to identify rare genomic variants in patients with neurodevelopmental disorders underscores the wide-ranging applications of genomics in medicine, including neonatology.

The translation of genomic discoveries into the practice of preventive medicine is crucial for addressing the evolving landscape of cancer genetics and genomics. Currently, approaches, benefits, and barriers to the translation of genomic information into the practice of preventive medicine are actively reviewed and described, emphasizing the potential integration of genomic information into preventive medicine.(Jen et al., 2024; Khoury & Holt, 2021; Pascale et al., 2022) Moreover, the strategic model employed by the National Institutes of Health Working Group on the Integration of Effective Behavioral Treatments into Clinical Care can enhance the integration of health promotion within preventive medicine through its technology-push, market-pull, and capacity-strengthening components.(Bellg et al., 2004; Jen et al., 2024) The concept of personalized health care, applying systems biology principles to medicine, is gaining traction, characterized by being predictive, personalized, preventive, and participatory (P4 medicine).(Carrasco-Ramiro et al., 2017; Galli, 2016; Hood, 2013) This aligns with the strategic approach to personalized medicine, incorporating family history, clinical data, behavioral factors, and genomics when applicable.

The integration of genomic sequencing into neonatal care has the potential to revolutionize the field by enabling personalized medical management and targeted prevention and treatment of diseases.(Galli, 2016) Additionally, the use of genetic testing in neonatology is likely to be more cost-effective than in other clinical settings, emphasizing the potential benefits of preventive genomic medicine in this field. Moreover, the increasing focus on evidence-based medicine has substantially contributed to improving the quality of medicine in neonatology, highlighting the importance of incorporating genomic data into clinical decision-making.(Galli, 2016; Hood, 2013) Here, we aimed to provide a comprehensive narrative review about the current state of preventive genomic medicine.

Integration of Preventive Genomic Medicine

The integration of genomic information into neonatal care has the potential to revolutionize the early detection and prevention of genetic diseases, thereby improving long-term health outcomes for infants.(Hood, 2013; Pascale et al., 2022) This approach involves the use of genomic sequencing and analysis to identify genetic variations that may predispose newborns to certain conditions, allowing for early intervention and personalized treatment strategies (**Figure 1**). One of the key reasons why preventive genomic medicine is important in neonatology is its ability to identify genetic disorders before symptoms manifest.(Cho, 2015) By conducting genomic screening in newborns, healthcare providers can detect genetic conditions at an early stage, enabling timely interventions to prevent or mitigate the impact of these disorders. This early detection can lead to improved clinical management, better outcomes, and reduced healthcare costs.(Cho, 2015; Tommel et al., 2023) Furthermore, preventive genomic medicine allows for personalized and precision medicine in neonatology. By understanding an infant's genetic makeup, healthcare providers can tailor treatment plans to address specific genetic risks and variations.(Tommel et al., 2023) This personalized approach can lead to more effective interventions, reduced adverse drug reactions, and improved long-term health outcomes for neonates.

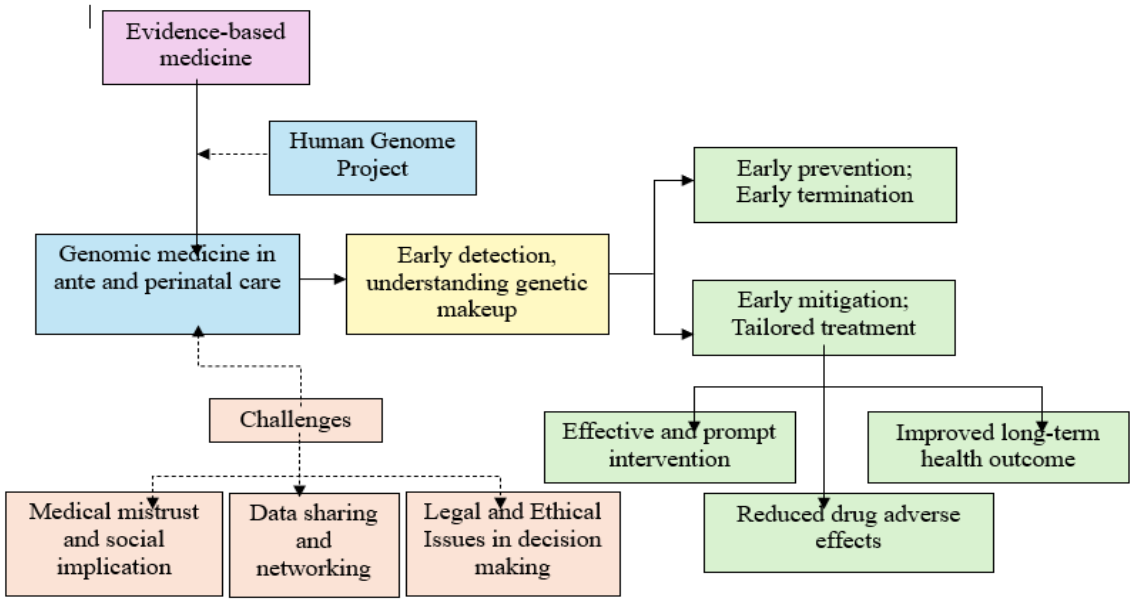

Figure 1. Preventive genomic conceptual framework

A newborn registry is a crucial component for the establishment of preventive genomic medicine, serving as a cornerstone for prioritizing healthcare interventions. Newborn screening (NBS) plays a pivotal role in preventive medicine, serving as a fundamental system from birth through lifelong care. The integration of genomic sequencing in newborns has the potential to transform healthcare by enabling early detection and personalized interventions based on individual genetic predispositions. This approach aligns with the broader strategy in newborn bloodspot screening, highlighting the significance of genomic medicine. Implementing newborn sequencing not only facilitates the early detection of genetic diseases but also enhances the understanding of disease natural history, leading to more effective medical care for infants. Additionally, newborn sequencing can streamline the diagnostic process, ultimately improving health outcomes for newborns. The utilization of genomic information in the newborn period is a significant area of research, with initiatives such as the Newborn Sequencing in Genomic Medicine and Public Health (NSIGHT) consortium exploring the implications and opportunities associated with this technology. Population screening of newborns is attracting global interest as a preventive healthcare measure, with the potential to lay the foundation for personalized medical care and preventive actions based on each child's genome throughout their lifetime. The insights gained from newborn screening are invaluable as we transition into the era of predictive and personalized genomic medicine. Newborn screening is acknowledged as a successful public health program that promotes health and prevents diseases.

Creating a network or referral system between hospitals is crucial for facilitating the rapid diagnosis of genetic abnormalities, particularly when utilizing whole genomic sequencing, which can be costly. This network enables the sharing of resources, expertise, and data, leading to more efficient and cost-effective genetic testing processes. One key importance of establishing such a network is the ability to pool resources and expertise from multiple hospitals, allowing each institution to contribute its unique skills, equipment, and knowledge. This collaboration provides access to a wider range of genetic testing technologies and

specialists, significantly enhancing the accuracy and speed of diagnosing genetic abnormalities. Moreover, a network or referral system helps overcome the financial barrier associated with the high cost of whole genomic sequencing by sharing the financial burden among participating hospitals, making it more feasible for institutions with limited resources to offer this service. Additionally, sharing data and best practices among hospitals in the network can lead to improved diagnostic accuracy and efficiency. Collectively analyzing genetic data and outcomes enables healthcare professionals to identify patterns and trends that may not have been apparent in individual settings, enhancing the quality of genetic testing and interpretation for more precise and timely diagnoses of genetic abnormalities.

Financial modeling for preventive genomic medicine is crucial for evaluating the economic feasibility and sustainability of integrating genomics into healthcare practices. Through financial models, healthcare systems can assess the costs and benefits associated with implementing preventive genomic medicine strategies. A critical aspect of financial modeling in preventive genomic medicine involves considering cost-effectiveness. It is essential to understand the costs of genomic testing, interpretation, and follow-up care, as well as the potential savings from early disease detection and prevention. Furthermore, financial modeling can assist in determining the return on investment (ROI) of preventive genomic medicine. By quantifying the potential savings from disease prevention or reducing the need for expensive treatments through early intervention, healthcare systems can make well-informed decisions regarding resource allocation. Moreover, financial modeling can support the development of reimbursement strategies and payment models for genomic services. Understanding the financial implications of genomic testing and counseling, along with the potential cost-savings in disease prevention, is crucial for designing sustainable payment structures.

Foundations of Preventive Genomic Medicine

Preventive genomic medicine has evolved significantly over time, aiming to provide personalized and predictive healthcare. The concept of preventive genomic medicine is rooted in the Human Genome Project, triggering a medical revolution towards evidence-based, personalized, predictive, preventive, and participatory medicine.(Tommel et al., 2023) The emergence of systems medicine, also known as P4 medicine (predictive, preventive, personalized, and participatory), has been at the forefront of the post-genomic movement towards precision medicine.(Carrasco-Ramiro et al., 2017; Galli, 2016; Hood, 2013) Genomic medicine seeks to understand the contribution of an individual's genomic information, in the context of social and environmental factors, to their health. This approach has led to a shift from 'evidence-based medicine' to 'genomic medicine'. The historical context of preventive genomic medicine is closely linked to the advancements in molecular diagnostics and genomic analysis, increasing the understanding and interpretation of the human genome, allowing for a personalized approach to clinical care.(Carrasco-Ramiro et al., 2017) Furthermore, the affordability of next-generation genomic sequencing and the improvement of medical data management have contributed to the evolution of biological analysis from both a clinical and research perspective.(Abul-Husn et al., 2021; Lázaro-Muñoz et al., 2015) The implementation of genomic medicine has been highlighted as an opportune time for generalists to expand their leadership role in healthcare. As preventive genomic medicine continues to advance, it is essential to address challenges such as medical mistrust, ethical issues related to decision-making, and data sharing, which may widen inequities in genomic and precision medicine if not appropriately addressed.(Abul-Husn et al., 2021; Manolio et al., 2013) Additionally, the role of genomics in personalized medicine has been emphasized, particularly in the context of cardiovascular diseases, where precision medicine integrates clinical and pathological indices

with state-of-the-art panomic profiling.(Abul-Husn et al., 2021; Tommel et al., 2023)

Strategic Frameworks in Preventive Genomic Medicine

Implementing preventive genomic medicine in a high-income country necessitates a carefully orchestrated strategy for seamless integration into the healthcare system. Beginning with the foundational step of policy development and regulation, the establishment of a robust regulatory framework ensures adherence to guidelines for genomic medicine testing, data privacy, and ethical considerations.(Wolf et al., 2019) Collaborative efforts with regulatory bodies, medical associations, and ethical committees become imperative in addressing compliance issues. Public awareness and education form the second pillar, demanding the creation of comprehensive campaigns to enlighten the populace on the benefits, risks, and implications of preventive genomic medicine. Simultaneously, resources must be allocated to enhance healthcare professionals' understanding and communication skills regarding genomic information.(Avard & Knoppers, 2009; Carrasco-Ramiro et al., 2017; Khoury et al., 2022; Wolf et al., 2019) The third aspect involves substantial investments in genomic infrastructure, encompassing sequencing facilities, bioinformatics capabilities, and secure data storage systems. Collaborations with academic institutions and private sector partners play a pivotal role in advancing genomic research and technology. Subsequent steps include training healthcare professionals, integrating genomic data into electronic health records, and designing targeted screening programs for high-risk populations.(Khoury et al., 2022) Research and development efforts, coupled with funding allocations, contribute to identifying new genetic associations and supporting innovative genomic technologies and therapies. Genetic counseling services are expanded to provide informed decision-making support, ensuring accessibility for diverse populations.(Khoury et al., 2022) The establishment of an ethical and legal framework involves continuous updates to address emerging challenges, fostering transparency in genomic data use, and implementing stringent measures to protect patient privacy. Collaboration and international cooperation become crucial through engagements with organizations and research institutions, promoting knowledge sharing and participation in global initiatives.(Avard & Knoppers, 2009; Chen et al., 2023; Wolf et al., 2019) The final step emphasizes continuous evaluation, employing feedback from healthcare providers, patients, and stakeholders to refine strategies and enhance implementation effectiveness over time. Through a holistic approach to these strategic elements, a high-income country can establish a comprehensive framework for the successful implementation of preventive genomic medicine within its healthcare system.(Avard & Knoppers, 2009)

Implementing preventive genomic medicine in a LMIC presents a complex interplay of challenges and opportunities shaped by resource limitations and contextual nuances.(Rehman et al., 2016) The challenges encompass constrained financial and infrastructure resources, creating hurdles for genomic technology investment. However, these challenges provide an opportunity for LMICs to explore cost-effective solutions and prioritize essential genomic interventions aligned with health priorities.(Tekola-Ayele & Rotimi, 2015) Weak healthcare infrastructure poses another obstacle, impeding the seamless integration of genomic data, yet it offers an opening to gradually strengthen healthcare systems, beginning with essential components for genomic medicine integration. Limited awareness and understanding of genomics among healthcare professionals and the general population pose challenges, yet targeted education and awareness programs hold promise for building genomic literacy and fostering acceptance.(Rehman et al., 2016; Tekola-Ayele & Rotimi, 2015) Ethical considerations surrounding privacy, consent, and responsible genomic data use present

challenges, but there is an opportunity to develop culturally sensitive ethical guidelines and involve local communities in decision-making processes. Genomic diversity in LMICs, marked by high genetic variations, presents challenges in defining reference genomes; nevertheless, there is an opportunity to conduct population-specific research for a deeper understanding of local genetic variations and diseases. Ensuring equitable access to genomic medicine across diverse populations is a challenge, but inclusive policies, community-based approaches, and public-private partnerships offer avenues for improved accessibility.(Radich et al., 2022) Insufficiently trained personnel in genomics challenge effective implementation, yet investing in capacity-building programs, local professional training, and incorporating genomics into existing healthcare training curricula can address this issue.(Radich et al., 2022; Rehman et al., 2016; Tekola-Ayele & Rotimi, 2015) Limited infrastructure for data management and storage is identified as a challenge, but scalable and cost-effective solutions, including cloud-based platforms and partnerships with international organizations, present opportunities for improvement (**Figure 2**).

Figure 2. Effective collaboration among stakeholders for the successful construction and implementation of preventive genomic medicine.

On the opportunities side, preventive genomic medicine holds the potential to significantly impact public health by identifying at-risk populations and enabling targeted interventions. Engaging in international collaborations allows LMICs to access resources, share knowledge, and participate in global research initiatives.(Tekola-Ayele & Rotimi, 2015) Innovative and adaptive technologies, such as mobile health applications and point-of-care testing, provide avenues to overcome resource limitations. Involving communities in the design and implementation of genomic programs ensures cultural sensitivity and community acceptance.(Radich et al., 2022; Rehman et al., 2016) Policy innovation becomes an opportunity to create flexible and innovative policies tailored to the unique needs of the LMIC context, promoting the responsible use of genomic information. Prioritizing genomic interventions for diseases with high prevalence and significant public health impact offers targeted opportunities.(Radich et al., 2022; Tekola-Ayele & Rotimi, 2015) Strengthening research capacities within LMICs contributes to global genomic knowledge and leverages local

expertise. Seeking international aid and donor support becomes an opportunity to fund genomics initiatives, research projects, and infrastructure development.(Radich et al., 2022; Sirisena & Dissanayake, 2019) By judiciously addressing these challenges and leveraging the opportunities, LMICs can strategically implement preventive genomic medicine, ultimately enhancing healthcare outcomes for their populations despite resource limitations (**Table 1**).

Table 1 Challenges and Opportunities of Genomic Medicine in LMICs and HICs

	Challenges		**Opportunities**
LMICs	Limited resources and infrastructure	a wide variety of diseases	Potential for early disease detection and prevention
	Variety of literacy levels	The multifactorial etiology sparks a passionate debate	Enhancing Health Outcomes by Comprehending Risks
	Inadequate healthcare facilities	Migration and diversity Interpreting complex genomic data	Guiding family planning decision
	Suboptimal referral systems Low adherence rates	Ensuring privacy and ethical considerations	Development of targeted interventions based on individual genomic profiles
HICs	Affordable access to reliable and high-quality essential medicines	Integrating personalized prevention into healthcare systems	Empowering professionals with a sustainable platform that enables effective knowledge-sharing
	Lifestyle changes	Race and genetic mapping	Economic financing and health insurance
		Changing demographic patterns	
		Reduces morbidity and increases survival	
		Optimal improvement in quality of life	

Note: LMICs: Low-middle-income countries

HICs : High Income Countries

Implementation Challenges and Ethical Considerations

Strategic frameworks are integral for identifying high-risk populations and implementing personalized prevention approaches.(Lázaro-Muñoz et al., 2015) This paper explores these frameworks, emphasizing the identification of high-risk populations and the application of personalized prevention measures.(Bull et al., 2000; Tommel et al., 2023) Genetic risk assessment is a cornerstone, evaluating an individual's genetic makeup through factors like genetic variants, family history, and environmental influences to discern predispositions to specific diseases. Methods encompass genetic testing, family history analysis, and lifestyle factor assessment.(Tommel et al., 2023) Additionally, population screening methods play a crucial role in identifying high-risk groups within larger communities, involving systematic collection of genetic and health-related data, such as large-scale genetic testing, epidemiological studies,

and predictive models.(Cho, 2015; Tommel et al., 2023)

The availability and accessibility of essential medicines, crucial for preventive genomic medicine, significantly impact healthcare outcomes. In LMICs, limited resources and infrastructure pose challenges to the implementation of preventive genomic medicine, leading to suboptimal access to medicines for conditions like cancer and cardiovascular diseases.(Hood, 2013; Pascale et al., 2022; Sirisena & Dissanayake, 2019) Disparities persist, hindering effective management of non-communicable diseases, including neurological disorders and cancer. While HICs have seen success in reducing disease burdens through preventive genomic medicine, these achievements underscore the need to prioritize preventive strategies in LMICs.(Newson, 2022) However, challenges persist in ensuring affordable access to reliable and high-quality essential medicines, including those for cancer.(Bhinder et al., 2021; Kumar et al., 2023; Raz et al., 2022; Sethi et al., 2022) Beyond medication access, factors such as healthcare infrastructure, literacy, and disparities influence the implementation of preventive genomic medicine.(Halbert, 2022; Raz et al., 2022) Inadequate healthcare facilities, suboptimal referral systems, and low adherence rates in middle-and lower-income countries pose significant challenges, along with variations in healthcare infrastructure and literacy levels contributing to differing impacts across income countries.

Personalized prevention approaches, tailoring interventions based on individual genomic profiles is paramount.(Chen et al., 2023; Halbert, 2022; Khoury et al., 2022; Sethi et al., 2022) This method involves customizing interventions and preventive measures based on an individual's genetic predispositions, lifestyle factors, and environmental influences. This may include personalized lifestyle recommendations, targeted screening programs, and specific interventions tailored to an individual's genetic risk factors.(Döhner et al., 2021) Despite the great promise of personalized prevention approaches in preventive genomic medicine, challenges and opportunities exist. Challenges encompass interpreting complex genomic data, ensuring privacy and ethical considerations, and integrating personalized prevention into healthcare systems.(Döhner et al., 2021; Rasmussen et al., 2020) Opportunities include the potential for early disease detection and prevention, improved health outcomes, and the development of targeted interventions based on individual genomic profiles. In conclusion, strategic frameworks in preventive genomic medicine, encompassing the identification of high-risk populations and personalized prevention approaches, serve as a cornerstone for advancing genomic medicine, laying the groundwork for improved health outcomes and disease prevention.(MacEachern & Forkert, 2021; Rasmussen et al., 2020; Sisodiya, 2021)

Real World Example of Preventive Genomic Medicine

Preventive genomic medicine has demonstrated success in various case studies, particularly in resource-limited countries.(Dela Cruz & Alperstein, 2022) These achievements are observed in the implementation of genomic medicine, focusing on pharmacogenomics, genome informatics, and public health genomics. Successful examples of personalized prevention and treatments rely on rational clinical genomic analysis, playing a pivotal role in risk assessment, disease prevention, early diagnosis, prognosis, therapeutic selection, and monitoring.(Hodson, 2016; Khatri & Petrelli, 2020) The integration of genomics into medical practice has been driven by the success of large-scale genome studies and tailored cancer treatments customized for subsets of patients with specific genotypes. Furthermore, active patient involvement is crucial for the success of genomic medicine, necessitating community educational programs to convey a practical understanding of family history, genetics, and related ethical, legal, and social issues.(Wu et al., 2021)

The challenges of implementing genomic medicine have been acknowledged, with a proposed multidisciplinary translational research agenda for the successful integration of genomic medicine into policy and practice.(Bhinder et al., 2021; Wu et al., 2021) Additionally, the potential value of a genomic approach to medical care lies in its generalizability to public health, such as through better screening and prevention programs. The success of whole genome or exome sequencing has been demonstrated in early successes on recessive non-cancer hereditary diseases.(Bhinder et al., 2021; Di Sanzo et al., 2017; Mitchell et al., 2021) The growing availability of genomic tools and technologies enables more precise risk stratification and disease management, bringing personalized medicine to the community through public engagement. Moreover, the successful application of precision medicine in healthcare requires translational research, the integration of genomic and comprehensive data, development of bioinformatics platforms, and new paradigms of medical education.(Xu et al., 2022)

Future Directions and Emerging Technologies

The future of preventive genomics holds significant promise in terms of precision prevention and targeted interventions, but it also presents several anticipated challenges and areas for improvement.(Galli, 2016; Wong et al., 2023; Xu et al., 2022) The development and implementation of precision medicine in cardiology and other medical fields are expected to address the epidemic of noncommunicable causes of death and advance the understanding of human health and disease.(Khoury & Holt, 2021; Olivier et al., 2019) Furthermore, the next generation of precision-based, prevention-focused personalized interventions is anticipated to be optimized through a translational neuroscience framework, leading to significant implications for preventive intervention models.(Kessler, 2018) However, there are several challenges and areas for improvement that need to be considered. For instance, future research in preventive genomics will need to address how to best implement effective interventions at scale, consider cost implications, and determine the factors that characterize successful interventions.(Döhner et al., 2021; Johnson et al., 2021; Kessler, 2018; Khatri & Petrelli, 2020) Additionally, there is a need to address the anticipated workforce shortage in certain medical specialties, such as rheumatology, by expanding training, increasing the utilization of telemedicine, and reducing burnout among practicing professionals. Moreover, the successful and sustainable implementation of preventive interventions, particularly in older adults, requires further insight into their attitudes towards prevention and reasons for participating in prevention trials, which can inform the design and recruitment of future interventions and public health policy.(Alahdal et al., 2023; Rubin, 2015)

Critical Evaluation of Strategic Approaches

The current preventive genomic strategies have inherent strengths and weaknesses that necessitate addressing for their effectiveness and sustainability.(Carrillo-Perez et al., 2023) Genomic literacy and competency deficits contribute to missed opportunities to leverage the benefits of genomic information for improving health outcomes.(Bahcall, 2015) Anticipated to play a crucial role in promoting population health, genomics aims to target at-risk individuals and reduce the incidence of highly prevalent, costly, complex diseases, with applications across screening, prevention, and treatment decisions.(Bahcall, 2015; Carrillo-Perez et al., 2023) However, knowledge gaps persist, especially concerning the integration of genomic testing within healthcare systems.(Cordero & Ashley, 2012) The sustainability of current strategic frameworks relies on the capacity of public health programs, requiring leadership support and sufficient time to attain genomic workforce competency. Weaknesses in current preventive strategies, such as incomplete facilities and insufficient promotion, need addressing for

sustainability.(Cordero & Ashley, 2012; Lupski, 2016)

To ensure the effectiveness and sustainability of these frameworks, addressing weaknesses and knowledge gaps is crucial. This can be achieved through the development of a flexible and accessible tool to guide global nurse leaders, facilitating benchmarking of the current state of nursing genomic competency and integration, and measuring change over time.(Cyranoski, 2016; Morita & Komuro, 2016; Shendure et al., 2019) Additionally, integrating genomic medicine into personalized healthcare can provide a pathway for adoption, leveraging vastly improved predictive tools created as a consequence of genomic technologies.(Morita & Komuro, 2016) The development and prioritization of strategies to improve the implementation of healthcare guidelines are also essential for addressing weaknesses and enhancing the sustainability of healthcare systems.

Conclusion

In conclusion, preventive genomic medicine holds immense potential for transforming healthcare by enabling personalized, targeted, and proactive interventions. The integration of genomic information into preventive medicine, along with the active involvement of genetic counselors, will play a pivotal role in realizing the full potential of genome-guided preventive medicine.

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