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Tailoring Treatment Strategies Based on Polygenic Risk Scores: The Next Frontier in Precision Medicine

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Introduction

The last decade has witnessed a paradigm shift in how diseases are understood, diagnosed, and treated, catalyzed by advances in genomic technologies and the proliferation of large-scale biobanks. In this transformation, precision medicine has emerged as a guiding principle-an approach that seeks to tailor healthcare to individual variability in genes, environment, and lifestyle. Central to this movement is the concept of Polygenic Risk Scores (PRS), which aggregate the effects of numerous genetic variants across the genome to estimate an individual's predisposition to complex diseases. These scores hold promise not only for early detection and prevention but also for informing personalized therapeutic strategies. While the application of PRS in risk stratification is increasingly recognized, its role in guiding treatment decisions remains a nascent but highly promising frontier. As scientific understanding deepens and translational frameworks evolve, tailoring treatment strategies based on PRS is poised to become a cornerstone of next-generation precision medicine [1].

Description

Polygenic risk scores derive from Genome-Wide Association Studies (GWAS) that identify Single-Nucleotide Polymorphisms (SNPs) associated with disease phenotypes. Unlike monogenic disorders, complex diseases such as coronary artery disease, diabetes, schizophrenia, and most cancers arise from the cumulative effect of hundreds or thousands of genetic variants, each contributing modestly to overall risk. PRS encapsulate this aggregate risk into a single quantitative value, typically a weighted sum of risk alleles carried by an individual. This approach has proven particularly valuable in identifying individuals at the extreme ends of the risk distribution-those whose lifetime risk of disease significantly exceeds the population average. Traditionally, these scores have been used for risk prediction and early screening. However, emerging evidence suggests that PRS may also hold the key to differential treatment responses, drug efficacy, and adverse event profiles, thus offering a pathway toward truly individualized therapy [2].

One of the most compelling areas of PRS application is in cardiovascular disease. For instance, individuals with a high polygenic risk for Coronary Artery Disease (CAD) have been shown to derive greater absolute benefit from statin therapy than those with average or low genetic risk. In large prospective studies such as the JUPITER and FOURIER trials, genetically high-risk individuals experienced more significant reductions in cardiovascular events when treated with statins or PCSK9 inhibitors. This suggests that PRS can inform both the intensity and type of pharmacological intervention. Moreover, in the context of limited healthcare resources, prioritizing high-PRS individuals for preventive therapies could enhance cost-effectiveness and clinical impact. PRS can also guide clinical decisions beyond the binary "treat or not treat" question. For example, in patients with borderline cholesterol levels, a high PRS for CAD may tip the balance in favor of early statin initiation, while a low PRS might support watchful waiting and lifestyle modification [3].

In oncology, the utility of PRS in informing treatment decisions is beginning to surface. Breast cancer provides a pertinent example. PRS for breast cancer, constructed using data from millions of women, can stratify individuals not only by their risk of developing the disease but also by subtypes such as hormone receptor–positive or triple-negative breast cancer. This granularity opens new avenues for tailoring screening frequency, preventive interventions like prophylactic surgery, and even chemoprevention strategies. Furthermore, PRS could potentially inform therapeutic choices in diagnosed patients. For example, understanding a patient's genetic predisposition to aggressive tumor subtypes or chemotherapy resistance may support decisions around treatment intensification or alternative therapies. Although this area remains under investigation, preliminary findings suggest that PRS could one day function alongside tumor genomic profiling to guide a comprehensive, genomically-informed treatment plan [4].

Psychiatry, long hampered by the lack of objective diagnostic tools, stands to benefit enormously from polygenic insights. In disorders such as schizophrenia, bipolar disorder, and major depressive disorder, PRS are beginning to reveal genetic architectures that underlie heterogeneity in disease presentation and treatment response. Antidepressant response, for instance, appears to be partially heritable, with certain PRS profiles predicting better outcomes with specific classes of drugs. For patients with high polygenic risk for schizophrenia, early identification may enable preemptive therapeutic strategies or monitoring. Moreover, in cases where psychiatric symptoms are nonspecific or comorbid, PRS could support differential diagnosis and inform treatment selection. The translation of PRS into clinical psychiatry is still in its infancy, but its potential to refine therapeutic pathways and improve patient outcomes is substantial [5].

Conclusion

In conclusion, the application of polygenic risk scores in tailoring treatment strategies holds immense potential to revolutionize healthcare delivery. By capturing the complex genetic underpinnings of disease susceptibility and treatment response, PRS offer a powerful tool for guiding personalized therapy across a spectrum of conditions. While challenges remain in terms of predictive power, equity, ethical considerations, and clinical implementation, the field is advancing rapidly. As evidence accumulates and technologies mature, PRS-guided treatment strategies may soon become standard practice, ushering in a new era of precision medicine that is as individualized as the patients it seeks to serve.

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Conflict of Interest

None.

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