Advances in Cancer Prevention
ISSN: 2472-0429
Ayesha, Adv Cancer Prev 2025, 9:2
Short Communication
Open Access

# Polygenic Risk Scores and Their Role in Cancer Risk Stratification

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**Keywords:** Polygenic risk scores; Cancer risk stratification; Genetic predisposition; Genome-wide association studies; Risk prediction models; Precision oncology

## Introduction

The emergence of polygenic risk scores (PRS) has revolutionized the landscape of cancer risk prediction, offering a more refined approach to identifying individuals at elevated genetic risk [1]. Unlike traditional risk models that focus primarily on high-penetrance mutations such as BRCA1/2, PRS aggregate the cumulative effect of numerous common genetic variants each contributing a small risk to provide a quantitative measure of an individual's inherited susceptibility to cancer [2]. Derived from large-scale genome-wide association studies (GWAS), PRS have demonstrated strong potential in stratifying populations based on genetic risk across various cancer types, including breast, prostate, colorectal, and melanoma. By integrating PRS into clinical and public health frameworks, researchers and clinicians can enhance early detection efforts, tailor surveillance strategies, and refine recommendations for lifestyle interventions or chemoprevention [3]. Importantly, the utility of PRS extends beyond individual-level risk assessment; they offer valuable insights into the polygenic architecture of cancer and help bridge the gap between genomics and precision oncology. However, their widespread adoption faces challenges related to ancestral diversity, clinical integration, and ethical considerations. This paper explores the construction, application, and limitations of polygenic risk scores in cancer risk stratification, highlighting their growing role in advancing personalized cancer prevention and management strategies [4].

## Discussion

Polygenic risk scores (PRS) have emerged as a powerful tool in cancer risk stratification, enabling a more nuanced understanding of genetic susceptibility. By aggregating the effects of thousands of low-penetrance single nucleotide polymorphisms (SNPs), PRS offer a complementary perspective to traditional monogenic risk assessments [5]. Their integration into clinical risk models holds promise for refining early detection strategies, individualizing screening protocols, and supporting targeted prevention efforts. In cancers such as breast, prostate, and colorectal, PRS have demonstrated the ability to identify individuals at significantly higher or lower risk than the general population even in the absence of high-risk mutations like BRCA1/2 [6]. For example, individuals in the highest PRS percentiles may exhibit a comparable or greater risk than those with known pathogenic variants, suggesting that PRS can be instrumental in flagging high-risk individuals who might otherwise be overlooked by conventional screening criteria [7].

Furthermore, PRS offer valuable insights into population-level risk distribution, which can inform public health strategies. When integrated with non-genetic factors such as lifestyle, family history, and environmental exposures PRS-based models become even more powerful and predictive [8]. This multifactorial approach aligns closely with the goals of precision medicine, enabling risk-tailored interventions that can potentially reduce cancer incidence and improve outcomes. However, several limitations must be addressed for PRS to reach their full potential in clinical practice. A major concern is the reduced predictive accuracy of PRS in non-European populations due to the underrepresentation of diverse ancestries in GWAS datasets. This disparity risks widening health inequities unless future studies prioritize the inclusion of globally representative cohorts [9].

Interpretability and communication of PRS results to patients also pose challenges. Unlike high-penetrance mutations with clearer clinical implications, PRS represent probabilistic risk, which may be harder for patients to understand and for providers to act upon. This necessitates the development of decision support tools, genetic counseling frameworks, and clear clinical guidelines for PRS interpretation. Moreover, ethical, legal, and social considerations such as data privacy, potential discrimination, and psychological impact must be carefully navigated. Policymakers and stakeholders should work collaboratively to ensure responsible implementation of PRS in healthcare settings. Despite these challenges, ongoing advancements in genomics, bioinformatics, and cross-ancestry GWAS are steadily improving the robustness and applicability of PRS. As we continue to validate and integrate PRS into diverse clinical settings, they are poised to become a cornerstone of personalized cancer risk prediction and preventive oncology [10].

## Conclusion

Polygenic risk scores represent a significant advancement in the field of cancer risk stratification, offering a data-driven approach to understanding genetic susceptibility beyond high-penetrance mutations. By leveraging the cumulative effect of numerous genetic variants, PRS enable more precise identification of individuals at varying levels of cancer risk, supporting early detection, targeted screening, and personalized prevention strategies. As genomic research expands and includes more diverse populations, the accuracy and applicability of PRS will continue to improve, enhancing their clinical utility. However, responsible integration into healthcare requires addressing challenges related to equity, interpretability, and ethical implementation. With continued interdisciplinary collaboration and rigorous validation, PRS have the potential to transform cancer prevention and precision oncology, ultimately improving outcomes and optimizing resource allocation in population health.

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**Received:** 01-Mar-2025, Manuscript No: acp-25-164380; **Editor assigned:** 03-Mar-2025, PreQC No: acp-25-164380 (PQ); **Reviewed:** 17-Mar-2025, QC No: acp-25-164380; **Revised:** 21-Mar-2025, Manuscript No: acp-25-164380 (R); **Published:** 28-Mar-2025; DOI: 10.4172/2472-0429.1000272

**Citation:** Ayesha R (2025) Polygenic Risk Scores and Their Role in Cancer Risk Stratification Adv Cancer Prev 9: 272.

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