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Review Article

Atherosclerotic Cardiovascular Disease (ASCVD) Risk Scoring: Present Landscape and Future Directions for Precision Prevention

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Abstract

Atherosclerotic cardiovascular disease (ASCVD) has emerged as the major cause of global mortality and morbidity. Risk of ASCVD can be assessed by using various conventional risk assessment tools like SCORE2, and Pooled Cohort Equations (PCE) which are associated with various drawbacks. This article demonstrates the conventional models limitations and explores a precision-based and multidimensional approach for prediction of risk. We review the integration of coronary artery calcium (CAC) scoring, novel biomarkers (e.g., hsCRP, Lp(a), ApoB) and polygenic risk scores (PRS) alongside the emerging role played by environmental exposures and social determinants of health (SDOH). Recent advancements in artificial intelligence (AI)-including federated learning, deep learning and natural language processing- are providing real-time and dynamic estimation of risk by assessing multi-model data from omics, imaging and electronic health records platform. Ethical consideration and implementation challenges linked with application of these integrative model in clinical practice are also discussed in this. ASCVD prevention future lies in adopting adaptive and personalized options guided by AI enabled stratification of risk, with great focus on clinical utility, interpretability and equity. This evolving paradigm hold huge clinical advantage for more accurate assessment, earlier therapeutic intervention and improved clinical outcomes in patients across diverse populations.

Key Words: atherosclerosis; preventive programs; risk scores

Introduction

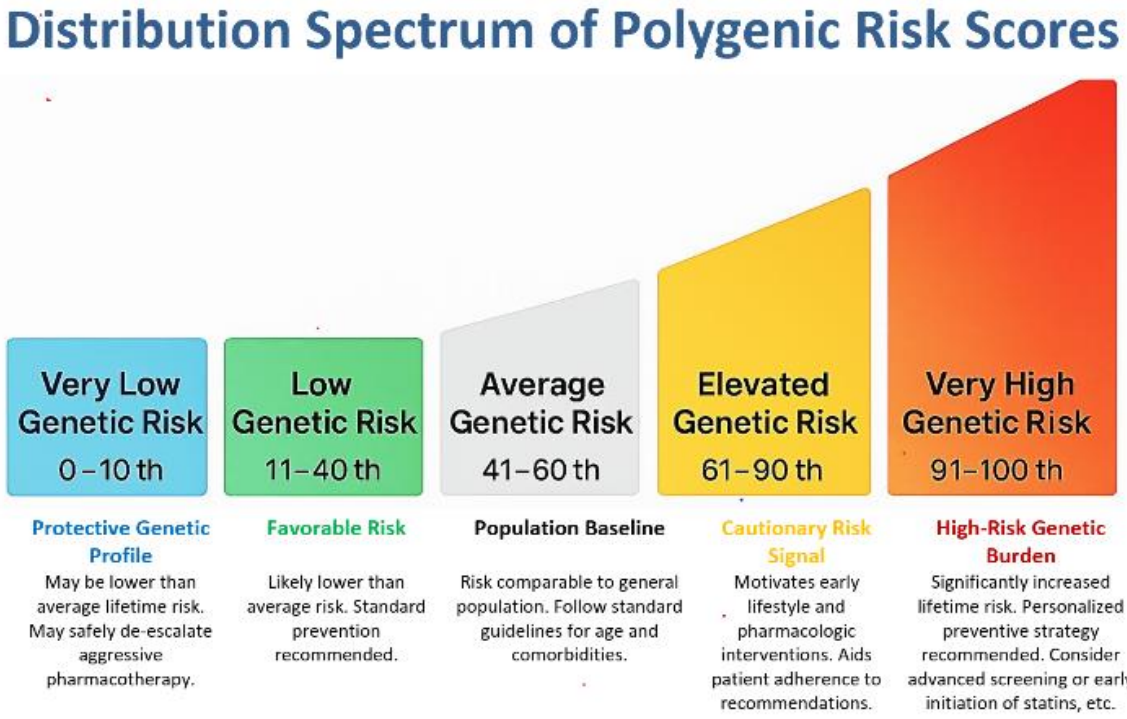
Atherosclerotic cardiovascular disease (ASCVD) remains the leading cause of morbidity and mortality worldwide, accounting for nearly one-third of all global deaths [1]. Accurate risk assessment is the cornerstone of preventive cardiology, guiding the allocation of pharmacologic and lifestyle interventions to those most likely to benefit. Over the past two decades, risk prediction models such as the Pooled Cohort Equations (PCE) and SCORE2 have become integral to clinical guidelines, enabling clinicians to estimate 10-year and lifetime ASCVD risk based on traditional risk factors including age, sex, blood pressure, cholesterol levels, smoking status, and diabetes [2,3].

Instead of widespread clinical utilizations, these models are associated with various drawbacks. Under-performance of these model has been noticed in certain ethnic groups, specifically in patients preset with severe inflammatory conditions and those present with atypical risk profiles [4]. Furthermore, emerging risk enhancers like high sensitivity C-reactive protein, lipoprotein(a) and apolipoprotein B or the severity and duration of diabetes are considered in conventional scoring methods. [5]. Sex-specific factors (e.g., premature menopause, preeclampsia) and family history are also insufficiently integrated, leading to risk misclassification, particularly in women and younger adults [6].

Recent advances in biomarker research and genomics have catalyzed the development of next-generation risk stratification tools. Coronary artery calcium (CAC) scoring, for example, provides direct quantification of subclinical atherosclerosis and significantly refines risk estimates in intermediate-risk individuals [7]. Inflammatory biomarkers, particularly hsCRP, have demonstrated independent predictive value and therapeutic relevance, as evidenced by trials targeting inflammation to reduce ASCVD events [8].

Moreover, polygenic risk scores (PRS) aggregate the effects of numerous genetic variants, identifying individuals at high lifetime risk even in the

absence of traditional risk factors [9]. However, the clinical utility of PRS is currently limited by a lack of validation in non-European populations and challenges in integrating genetic data into routine care [10]. Distribution spectrum of polygenic risk scores (PRS) in individuals with different risk scores is demonstrated in figure 1.



Integrating Polygenic Risk Scores into Provider Decision-Making

Use Case	Clinical decision making when personalized information is limited	Motivating patients to follow existing medical advice	Detecting high-risk patients overlooked by conventional methods
Decreased Risk	Useful for identifying patients who may not require aggressive intervention	May lead patients to dismiss the urgency of recommendations	May not apply strongly in low-risk individuals
High Risk	Useful to guide intensified preventive or therapeutic strategies	Often encourages adherence to physician advice due to elevated perceived risk	Valuable for identifying hidden high-risk patients not flagged by standard assessments

Table 1: Incremental Value of Biomarkers and Imaging in ASCVD Risk Prediction [18].

Emerging strategies utilizes machine learning and artificial intelligence (AI) to produce multidimensional data from imaging, biomarkers, genomics and electronic health records, offering the huge promise of more individualized and accurate risk assessment [11]. Furthermore, incorporating social determinants of health (SDOH)-like education, neighbourhood environment and socioeconomic status has been demonstrated to address health disparities and model performance [12].

As the field shifts towards prevention in a precise manner, the integration of social, biological, clinical and genetic data is poised to transform assessment of risk of ASCVD. This evolving paradigm major objective is to deliver more effective, personalized, equitable therapeutic options for prevention of cardiovascular disease, ultimately reduced the ASCVD global burden.

2.Contemporary Challenges in ASCVD Risk Estimation

2.1. Calibration and Discrimination in Diverse Populations

A quite significant role is played by conventional ASCVD risk scores, such as SCORE2 and PCE in guiding preventive strategies. However, significant variations have been observed in their discrimination and calibration across various socioeconomic, geographic and ethnic groups. For instance, studies reveal that the PCE tends to overestimate risk in contemporary U.S. cohorts, particularly among White populations, while underestimating risk in South Asian, Indigenous, and certain Black populations [13]. SCORE2, although recalibrated for European subpopulations, still demonstrates limited accuracy in Central and Eastern European countries, where ASCVD incidence remains high [3].

These discrepancies majorly originate from the original deviation cohorts, which often associated with lack of representation from minority or high-risk groups, and from secular changes in epidemiology of ASCVD due to improved management of risk factor and therapeutic strategies. In addition to this, 0.65 and 0.75 discrimination ability of these models has been measured by C-statistic, indicating only moderate assessment power. In individuals present with atypical risk profiles, such as those with HIV or premature menopause or chronic inflammatory diseases, this moderate performance is quite problematic whose risk assessment is systematically underestimated by traditional models.

2.2. Omission of Non-Traditional and Emerging Risk Factors

Current risk calculators majorly focus on blood pressure, smoking status, diabetes, sex and age, omitting non-traditional risk factors that have been robustly associated to ASCVD. Notably, the duration and control of diabetes, chronic kidney disease, autoimmune conditions, and markers of chronic inflammation are not routinely incorporated. This omission is consequential, as individuals with chronic inflammatory diseases (e.g.,

rheumatoid arthritis, systemic lupus erythematosus) have a 1.5- to 2-fold increased risk of ASCVD, independent of traditional risk factors [14].

Individuals with inherited risk, such as those present with familial hypercholesterolemia, can't be identified by using standard calculators due to absence of genetic predisposition and family history, who may present with normal profile of lipid but with significant lifetime risk. [15]. Clinical utility of these models in real-world, heterogeneous populations is further limited due to lack of integration of SDOH-including access to health care facilities, education, income and neighbourhood deprivation.

2.3. Temporal and Dynamic Risk Assessment Deficiencies

A critical limitation of current ASCVD risk scores is their static nature. Most models provide a one-time risk estimate, typically over a 10-year horizon, without accounting for changes in risk factor control, medication adherence, or the emergence of new risk modifiers over time. This approach fails to capture the dynamic trajectory of risk, particularly in younger individuals or those with evolving comorbidities. Emerging evidence supports the use of repeated risk assessment and incorporation of time-updated variables to better reflect the true risk continuum [16]. 10-years prediction risk of ASCVD in patients by pooled cohort equations is demonstrated in figure 2A. Predicted risk of ASCVD risk over 10 years is demonstrated in figure 2B.

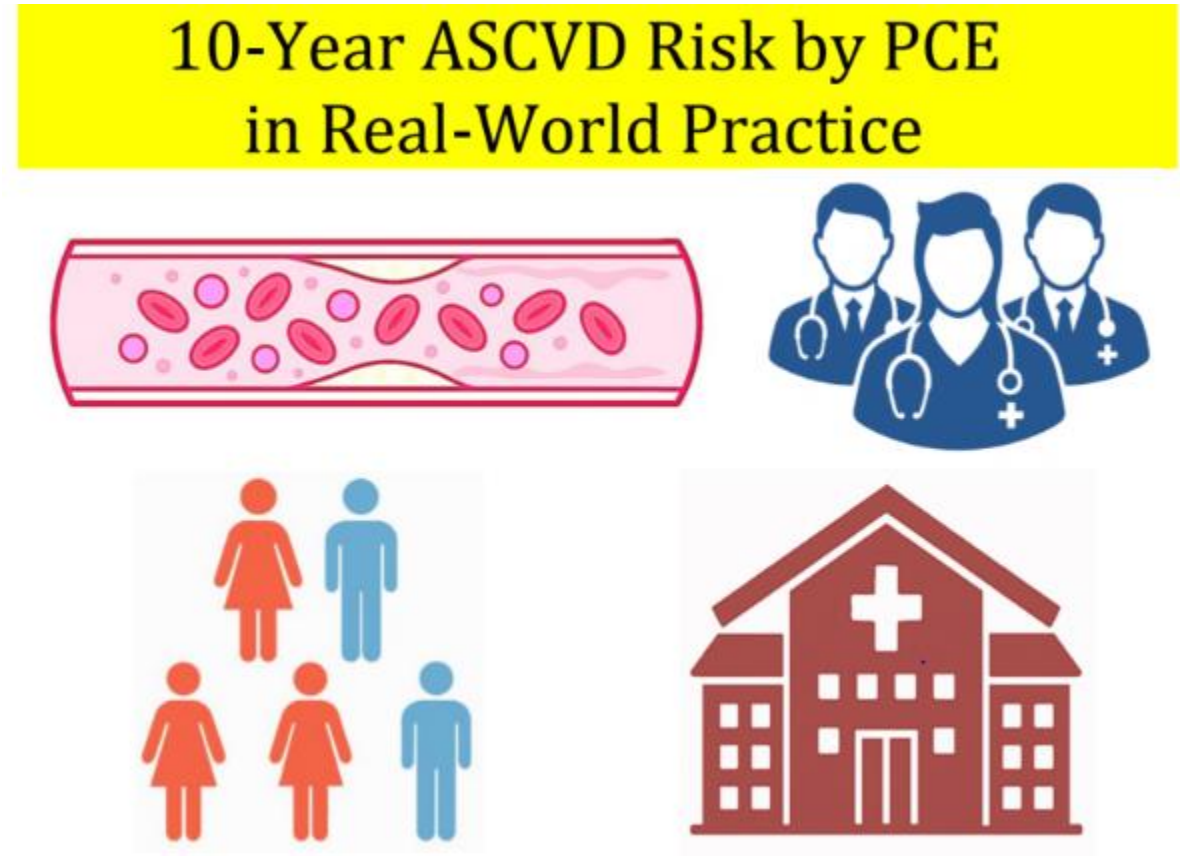


Figure 2A: 10-years prediction risk of ASCVD in patients by pooled cohort equations.

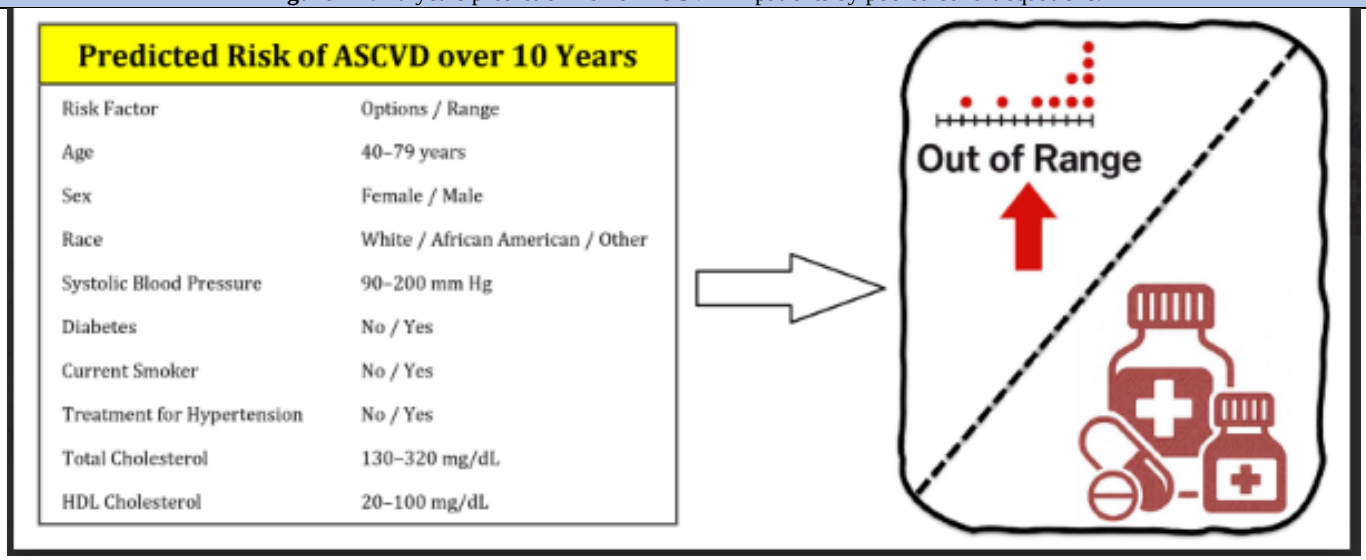


Figure 2B: Predicted risk of ASCVD risk over 10 years.

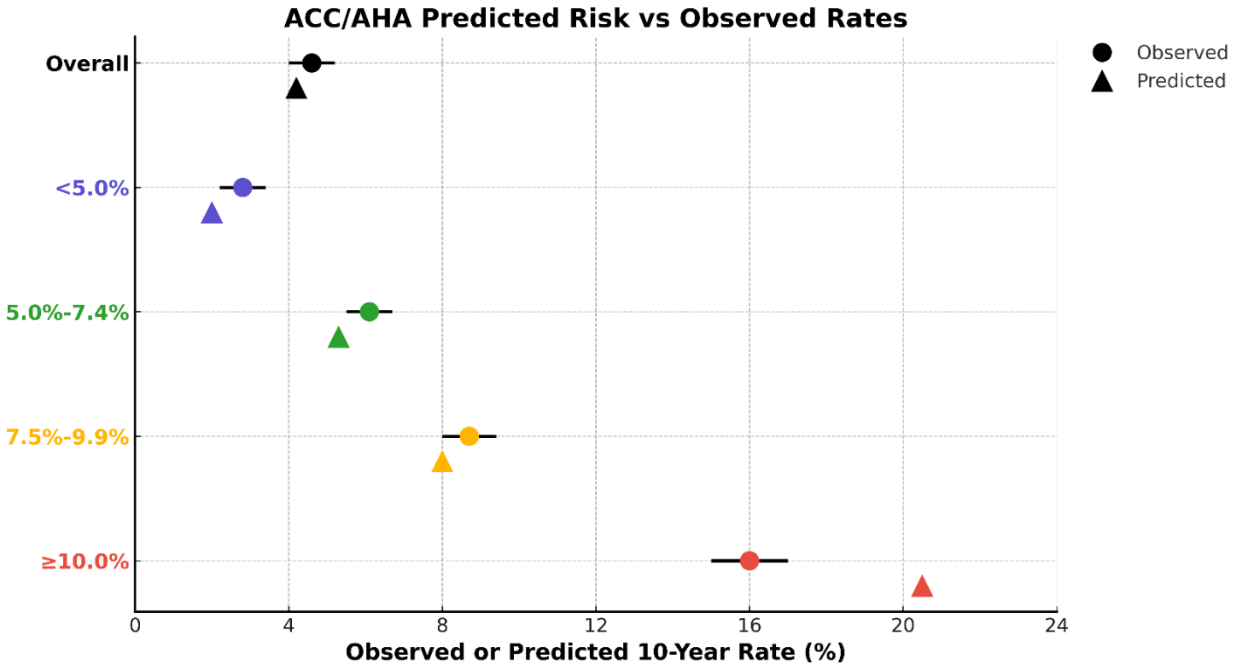


Figure 2C: Comparison of ACC/AHA predicted risk and observed rates over 10 years.

Moreover, traditional calculators do not account for the cumulative burden of risk factors, such as the duration of hypertension or hyperlipidemia, which has been shown to confer higher risk than point-in-time measurements. This limitation is specifically relevant in younger adults, where instead of low short-term risk estimates lifetime risk may be huge. Figure 2C demonstrate comparison of ACC/AHA predicted risk and observed rates over 10 years.

3.Integration of Advanced Biomarkers and Imaging

3.1. Role of Novel Biomarkers in Risk Refinement

The circulating biomarkers addition has been suggested to potentiate risk of ASCVD prediction, specifically in individuals at intermediate risk. hsCRP is the most extensively validated inflammatory marker, with elevated levels independently predicting ASCVD events even in the setting of low high-sensitivity C-reactive protein [17]. Other emerging biomarkers include lipoprotein(a) [Lp(a)], apolipoprotein B (ApoB), and high-sensitivity troponin, each associated with residual risk not captured by traditional metrics.

Despite their promise, the incremental value of these biomarkers in risk reclassification remains modest. For example, the addition of hsCRP to the PCE improves the C-statistic by only 0.01–0.03. The clinical utility of routine biomarker measurement is therefore debated, with guidelines recommending their use primarily in cases of clinical uncertainty or intermediate risk.

3.2. CAC Scoring as a Risk Modifier

Non-invasive imaging, particularly CAC scoring, has emerged as a powerful tool for individualized risk assessment. CAC quantifies subclinical atherosclerosis and provides incremental prognostic information beyond traditional risk factors. In the Multi-Ethnic Study of Atherosclerosis, individuals with a CAC score of zero had a 10-year ASCVD event rate of <2%, regardless of risk factor burden, while those with CAC >100 had substantially higher event rates [18].

CAC scoring is specifically useful in reclassifying individuals present with intermediate or borderline risk, guiding the intensification or initiation of statin therapy. However, its clinical utility is limited by cost, access and concerns regarding exposure to radiation and it remain underestimated in younger adults and women, where non-calcified plaques may be preferred. Incremental value of biomarkers and imaging in ASCVD risk prediction are shown in table 1 [18].

Tool/Marker	Incremental C-static	Clinical Utility	Limitations
hsCRP	+0.01-0.03	Intermediate risk reclassification	Modest improvement, cost
Lp(a)	+0.01	Identifies genetically mediated risk	Limited assay standardization
ApoB	+0.01	Residual risk in statin-treated	Not universally available
CAC Score	+0.05-0.10	Strongest for risk reclassification	Access, radiation, cost

Table 1: Incremental Value of Biomarkers and Imaging in ASCVD Risk Prediction

†hsCRP: high-density C-Reactive Protein; Lp(a): Lipoprotein(a); ApoB: Apolipoprotein B; CAC: Coronary Artery Calcium

4.Social and Environmental Determinants in Risk Prediction

4.1. Socioeconomic and Psychosocial Factors

A growing body of evidence underscores the impact of SDOH on ASCVD risk. Factors such as income, education, neighborhood deprivation, food insecurity, and access to healthcare significantly influence both the incidence and outcomes of cardiovascular disease [19]. Psychosocial stressors, including depression and social isolation, have also been linked to increased ASCVD events, independent of traditional risk factors.

Instead of their significance, SDOH are rarely utilized in risk prediction models. Latest advancements, such as the progression of the neighborhood-level and Social Deprivation Index, have suggested discrimination and improved calibration when integrated with clinical models. SDOH incorporation into risk assessment of ASCVD is quite

important for advancing health equity and targeted therapeutic interventions to undeserved and high-risk populations.

4.2. Environmental Exposures

Environmental exposures, including climate-related factors, noise and air pollution, are characterized as major contributors to risk of ASCVD. Huge exposure to fine particulate matter (PM2.5) is linked with 10-20% rise in risk of cardiovascular events per 10 μg/m³ increment [20]. However, in standard risk calculators, these exposures are not captured currently, representing a missed chance for risk stratification in a comprehensive manner.

5.AI and Machine Learning in ASCVD Risk Stratification

5.1. Electronic health record (EHR)-Driven and Multi-Modal Risk Prediction

Recent advancements in machine learning (ML) and AI potentiate the risk prediction models development that leverage multi-omic biomarkers, imaging data and large-scale EHRs. In comparison to conventional risk scoring methods in early-phase studies, these models have suggested superior discrimination and calibration. For example, incorporation of 400 variables in ML-based models has achieved a C-statistic of 0.80–0.85 for prediction of ASCVD, outperforming the SCORE2 and PCE.

Risk estimates can be dynamically update by AI-driven strategies due to availability of new data, facilitating time-updated, and personalized risk trajectories. Furthermore, AI techniques are being established to potentiate patient and clinician understanding of risk drivers and promoting shared decision-making [21].

5.2. Future Directions: Integrative and Equitable Risk Assessment

The future of prediction of ASCVD risk exist in the integration of social, genetic, biomarker and clinical data within AI-enabled platforms. Such multidimensional models have the capacity to deliver highly preventive, predictive and personalized care, while addressing disparities in assessment of risk. Ongoing risk includes ensuring equitable model performance, algorithm transparency and data privacy across wide populations [22].

6.Integration of Inflammation, Genetics, And Social Determinants In Risk Prediction

6.1. Interplay of Inflammatory Pathways and Genomic Risk in ASCVD

The convergence of genetic susceptibility and severe inflammation is highly characterized as a central driver of risk of ASCVD risk, beyond what is identified by conventional risk factors. While prior content has addressed the omission of non-traditional risk factors and the role of PRS, this section uniquely focuses on the biological and mechanistic interplay between inflammatory pathways and genomic risk, and their implications for risk prediction.

Chronic low-grade inflammation, as evidenced by elevated biomarkers such as hsCRP, interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α), is both a cause and consequence of atherogenesis [23]. Genome-wide association studies have identified variants in loci related to inflammatory signaling (e.g., IL6R, CRP, NLRP3) that modulate both systemic inflammation and ASCVD risk [24]. Notably, individuals with high polygenic risk for coronary artery disease (CAD) and concomitant elevated hsCRP exhibit a synergistically increased risk of major adverse cardiovascular events, suggesting that the co-occurrence of pro-inflammatory genotypes and phenotypes amplifies atherothrombotic risk [25].

Furthermore, findings of Mendelian randomization studies have suggested that genetically assessed rise in CRP and Il-6 causally rise in risk of ASCVD, suggesting a direct mechanistic association. This insight has increased the dual-risk models progression, integration of inflammatory biomarkers and PRS for accurate stratification of individuals present with huge risk for incident ASCVD, specifically those who may get clinical benefit from anti-inflammatory therapies [26]. Comparative risk of ASCVD by combined inflammatory and genetic status is demonstrated in table 2 [25,26].

Risk Group	10-Year ASCVD Event Rate (%)	Relative Risk vs. Reference
Low PRS + Low hsCRP	4.1	1.0
High PRS + Low hsCRP	7.8	1.9
Low PRS + High hsCRP	8.2	2.0
High PRS + High hsCRP	14.3	3.5

Table 2: Comparative Risk of ASCVD by Combined Inflammatory and Genetic Status

†ASCVD: Atherosclerosis Cardiovascular Disease; PRS: Polygenic Risk Score; hsCRP: high-density C-Reactive Protein.

6.2. Social Genomics: The Intersection of Social Determinants and Molecular Risk

Distinct from prior sections on socioeconomic and psychosocial factors, this section explores the emerging field of social genomics, which investigates how SDOH interact with genetic and epigenetic mechanisms to influence ASCVD risk. Social adversity—including chronic stress, discrimination, and neighborhood deprivation—has been shown to induce pro-inflammatory gene expression profiles (the "conserved transcriptional response to adversity"), characterized by upregulation of NF-κB–dependent inflammatory genes and downregulation of antiviral responses [27].

Epigenome-wide association studies reveal that adverse SDOH can modify DNA methylation patterns at loci implicated in vascular inflammation and lipid metabolism, thereby modulating the penetrance of genetic risk [28]. For instance, individuals present with huge polygenic risk for CAD who also faces huge social deprivation suggested accelerated incidence of ASCVD, independent of conventional risk factors [29].

These findings suggest a "double jeopardy" model, wherein the genetic predisposition and adverse social environments intersection is responsible for disproportionate elevation in risk of ASCVD. Incorporation of social genomics into various risk prediction models may potentiate calibration and facilitate targeted therapeutic interventions in huge-risk, socially disadvantaged populations [30].

6.3. Multi-Omics Integration for Precision Risk Prediction

While previous sections have demonstrated the individuals biomarkers and genetic scores additions, this section addresses the multi-omics data integration-encompassing proteomics, genomics, metabolomics and transcriptomics-into prediction of ASCVD RISK. Multi-omics approaches enable the identification of molecular signatures that reflect both inherited and acquired risk, providing a comprehensive view of the atherogenic process [31].

Recent prospective cohort studies have demonstrated that multi-omics risk scores, constructed from panels of plasma proteins (e.g., growth differentiation factor-15 [GDF-15], myeloperoxidase [MPO]), metabolites (e.g., trimethylamine N-oxide [TMAO]), and genetic

variants, outperform traditional clinical models in predicting incident ASCVD. For example, a C-statistic of 0.83 is achieved for 5-years ASCVD events on incorporation of a proteomics risk score > 50 proteins, in comparison to 0.72 for the PCEs [32].

Moreover, application of machine learning algorithms to mutli-omics datasets can uncover recent risk clusters, potentiate the novel endophenotypes assessment and personalized preventive options. The integration of multi-omics with EHR and SDOH data represents a critical frontier in the evolution of precision ASCVD prevention. Incremental predictive value of multi-omics models is shown in table 3 [32].

Model Type	C-Static (5-Year ASCVD)	Net Reclassification Improvement (%)
Pooled Cohort Equatins	0.72	-
Genomics + Proteomics	0.81	+18
Multi-Omics (All Layers)	0.83	+25

Table 3: Incremental Predictive Value of Multi-Omics Models

†ASCVD: Atherosclerosis Cardiovascular Disease.

6.4. Implementation Science: Bridging Precision Risk Models and Clinical Practice

Distinct from prior discussions of AI and machine learning, this section addresses the challenges and strategies for implementing integrative risk models—incorporating inflammation, genetics, and SDOH—into routine cardiovascular prevention. Despite the promise of multi-dimensional risk scores, real-world uptake remains limited by barriers including data interoperability, clinician education, and patient acceptability

Implementation science frameworks, such as the Consolidated Framework for Implementation Research, are being applied to optimize the integration of precision risk tools into clinical workflows [33].

Key strategies include:

- Embedding EHRs with risk calculators to facilitate point-of-care decision support.
- Provide training to clinicians in the interpretation of SDOH-informed and multi-omics risk scoring methods.
- Patient's engagement in shared decision-making, with culturally tailored communication of benefit and risk.
- Leveraging multidisciplinary teams and implementation champions to drive adoption.

Findings of pilot studies demonstrate that the integrative risk models utilization can improve control of risk factor, patient satisfaction and statin initiation rates, specifically in high-risk, underserved populations. However, intense randomized implementation trials are required to quantify the clinical outcomes of ASCVD and health equity.

6.5. Ethical, Legal, and Social Implications (ELSI) of Integrative Risk Prediction

While previous reports have not addressed this dimension, the rapid evolution of integrative risk prediction raises critical ELSI. The use of genetic, inflammatory, and SDOH data in risk stratification introduces new challenges related to privacy, consent, data ownership, and potential discrimination.

Key ELSI considerations include:

- Genetic Privacy and Discrimination: Certain protections are provided by the genetic information nondiscrimination act, but gap remain specifically for disability and life insurance [34].
- Algorithmic Bias: Non-representative datasets trained integrative models may potentiate disparities in clinical care and risk assessment [35].
- Informed Consent: SDOH-informed and multi-omics complexity risk scores challenges informed consent conventional models, necessitating novel therapeutic strategies to risk patient autonomy and risk communication [36].
- Data Security: The aggregation of social, biomarker and genomics data potentiate the data risk misuse and breaches, requiring security frameworks and
- The aggregation of genomic, biomarker, and social data increases the risk of data breaches and misuse, requiring robust governance and security frameworks and robust governance.

Addressing these ELSI issues is needed to ensure that integrative risk prediction advancement translate into socially, trustworthy and equitable cardiovascular risk prevention.

7.Future Directions: Ai, Precision Prevention, and Multidimensional Risk Models

7.1. AI-Driven Risk Prediction: Beyond Traditional Variables

While previous sections have demonstrated multi-model and EHR-driven risk assessment, this section will focus on AI algorithms next generations that leverage deep learning, natural language processing and federated learning in which unstructured data sources are utilized to extract nuanced risk signals. Recent advances in deep neural networks have enabled the integration of longitudinal EHR data, imaging, and even clinical notes to predict ASCVD events with improved discrimination and calibration, surpassing conventional regression-based models [37]. For example, convolutional neural networks applied to raw electrocardiogram (ECG) data have demonstrated the ability to predict future myocardial infarction risk independently of traditional risk factors [38].

Federated learning-a privacy-preserving AI approach- enables the robust risk model training across various institutions without sharing patient data sensitively, thus addressing concerns about representativeness and data privacy. Natural language processing further augment risk assessment by extracting relevant behavioral determinants and social determinants, which are often omitted from structural datasets. Comparison of AI-driven and traditional ASCVD risk models is demonstrated in table 4 [37,38]. AI applications in assessment of ASCVD risk are demonstrated in figure 3.

Model Type	Data Inputs	C-Statistic (Range)	Unique Features
Pooled Cohort Equations	Demographics, Lipids, BP, Diabetes, Smoking	0.66-0.77	Population-based, limited variables
Deep Learning (HER + Imaging	HER, imaging, labs, unstructured notes	0.78-0.87	Learns complex patterns, dynamic
Federated Learning	Multi-centre HER, imaging	0.80-0.86	Privacy-preserving, scalable
ECG-based AI	Raw ECG signals	0.80-0.88	Detects subclinical risk, real-time

Table 4: Comparison of AI-Driven and Traditional ASCVD Risk Models

†PCE: Pooled Cohort Equations; BP: Blood Pressure; ECG: Electrocardiogram; AI: Artificial Intelligence.

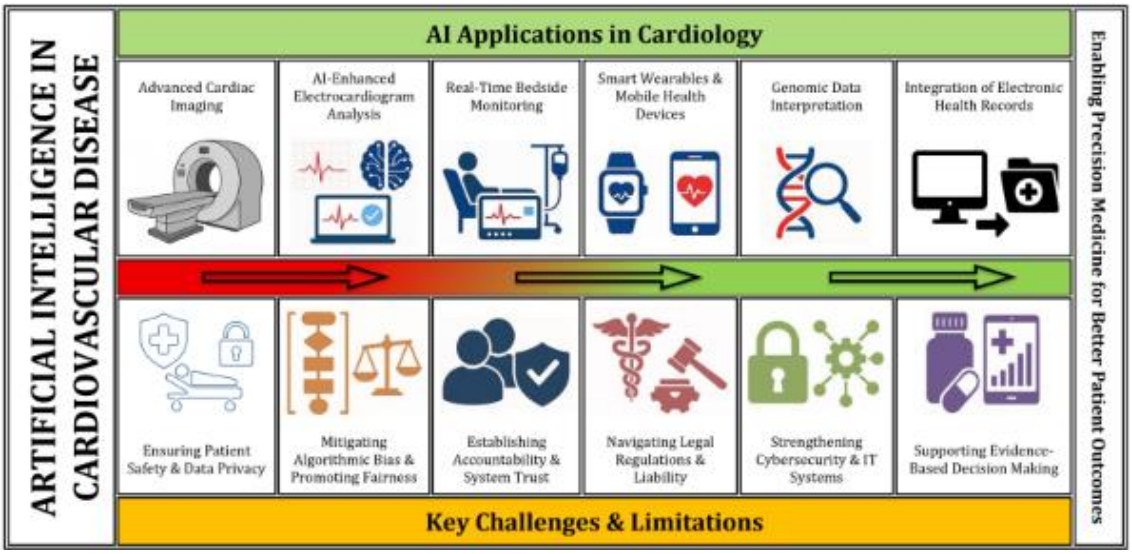


Figure 3: AI applications in assessment of ASCVD risk.

7.2. Dynamic, Time-Updated Risk Estimation

Distinct from the static, baseline risk estimates provided by current calculators, emerging AI-enabled models are capable of generating dynamic, time-updated risk trajectories.

With the objective to recalibrate an individual risk of ASCVD in real time, these models assimilate new laboratory data, lifestyle data, medication changes and clinical events on routine basis. This strategy is specifically useful for patients with evolving risk profiles such as those with new-onset hypertension, incident diabetes or inflammatory biomarkers changes.

Moreover, dynamic risk estimation supports adaptive prevention strategies, allowing clinicians to intensify or de-escalate therapies based on the most current risk assessment. For example, a patient whose risk increases due to rising hsCRP or low=density lipoprotein-cholesterol (LDL-C) despite therapy may warrant earlier initiation of anti-inflammatory or lipid-lowering agents [8]. Static vs dynamic risk estimation in ASCVD prevention is demonstrated in table 5.

Feature	Static Models (PCE, SCORE2)	Dynamic AI Models
Risk Calculation Frequency	Once (baseline)	Repeated, real-time
Data Inputs	Baseline Clinical/lab data	Time-varying, multi-modal
Adaptation to New Events	No	Yes
Clinical Utility	Population-level	Personalized, adaptive

Table 5: Static vs. Dynamic Risk Estimation in ASCVD Prevention.

†PCE: Pooled Cohort Equations; AI: Artificial Intelligence.

7.3. Multidimensional Risk Models: Integrating Omics, Imaging, and SDOH

While previous sections have discussed multi-omics integration and social genomics, this section emphasizes the convergence of multi-layered data streams—genomics, proteomics, metabolomics, advanced imaging, and social determinants—within unified risk models. These multidimensional models are designed to capture the heterogeneity of ASCVD risk across diverse populations and to identify high-risk individuals who may be missed by traditional tools.

For instance, the integration of PRS with CAC scoring and SDOH metrics has demonstrated superior risk stratification compared to any single domain alone [25]. Proteomic risk panels, incorporating dozens of circulating proteins, further refine risk prediction, particularly in intermediate-risk individuals [32]. Data domains in multidimensional ASCVD risk models are shown in table 6 [25]

Domain	Example Variables	Incremental Value
Genomics	PRS, monogenic variants	Early-life risk, family history
Proteomics	hsCRP, GDF-15, MPO, Lp(a)	Inflammation, plaque instability
Imaging	CAC, carotid plaque, vascular age	Subconical atherosclerosis
SDOH	Income, education, neighborhood, stress	Healthy equity, access
Clinical	BP, lipids, diabetes, smoking	Baseline risk

Table 6: Data Domains in Multidimensional ASCVD Risk Models

†PRS: Polygenic Risk Score; hsCRP: high-sensitivity C-Reactive Protein; GDF: Grow/Differentiation Factor; MPO: Myeloperoxidase; Lp(a): Lipoprotein(a); SDOH: Social Determinants of Health; BP: Blood Pressure.

7.4. Precision Prevention: Targeted Interventions Based on Individualized Risk

The paradigm of precision prevention moves beyond risk prediction to actionable, individualized intervention. AI-augmented risk models enable the identification of distinct risk endotypes—such as inflammation-dominant, lipid-dominant, or genetically driven ASCVD—each of which may benefit from tailored preventive strategies [26]. For example, individuals with high PRS and elevated Lp(a) may be prioritized for early PCSK9 inhibitor therapy, while those with persistent inflammation despite statins may benefit from anti-inflammatory agents such as colchicine or canakinumab [8].

In addition, multidimensional risk models facilitate shared decision-making by providing patients with personalized risk trajectories and the projected benefit of specific interventions. Digital health platforms and mobile applications are increasingly being used to deliver individualized risk feedback, promote adherence, and monitor response to therapy in real time [22]. Precision prevention strategies by risk endotype are shown in table 7 [26].

Risk Endotype	Key Features	Targeted Intervention
Inflammation- dominant	High hsCRP, GDF-15, MPO	Anti-inflammatory therapy
Lipid- dominant	High LDL-C, Lp(a), ApoB	Statins, PCSK9i, Lp(a) inhibitors
Genetic	High PRS, monogenic variants	Early screening, aggressive Rx
SDOH-driven	Low SES, high stress, poor access	Community interventions, navigation
Mixed	Multiple domains elevated	Multimodal, team-based care

Table 7: Precision Prevention Strategies by Risk Endotype

†hsCRP: high-sensitivity C-Reactive Protein; GDF: Grow/Differentiation Factor; MPO: myeloperoxidase; LDL-C; Low-Density Lipoprotein-C; Lp(a) Lipoprotein(a); ApoB: Apolipoprotein; PRS: Polygenic Risk Score; SDOH; Social Determination of Health; SES: Socioeconomic.

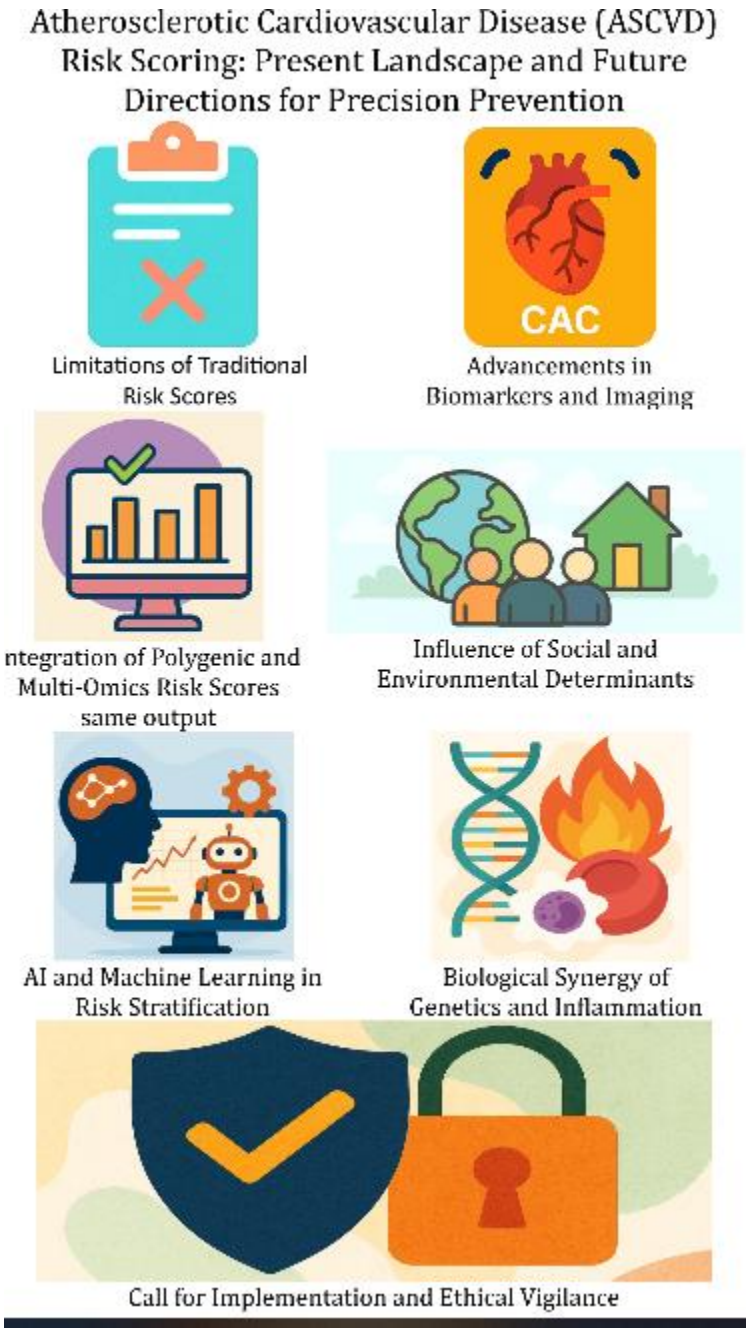
7.5. Real-World Implementation and Model Validation

While implementation science and ELSI have been discussed previously, this section focuses on the technical and operational challenges in deploying multidimensional AI risk models at scale. Rigorous external validation across diverse populations is essential to ensure generalizability and to mitigate algorithmic bias. Prospective studies, such as the PREVENTABLE and My Gene Rank trials, are evaluating the clinical utility, acceptability, and cost-effectiveness of AI-enabled and genomics-informed risk assessment in routine practice.

Major key operational consideration includes interoperability with patient engagement, explainable AI interfaces development, existing HER systems and clinician education to support shared-decision making. Furthermore, continuous post-departmental monitoring is needed to ensure equity, assess performance drift and adapt to evolving clinical guidelines. Solutions and challenges in implementing multidimensional risk models are demonstrated in table 8 [21]. Atherosclerotic cardiovascular disease risk scoring and present landscape & future directions for precision prevention are demonstrated in Central Illustration.

Challenge	Solution/Strategy
Data interoperability	Standardized data formats, APIs
Algorithmic bias	Diverse training datasets, fairness auditing
Clinician adoption	Education, decision support tools
Patient engagement	Digital risk communication, apps
Model drift	Continuous monitoring, recalibration

Table 8: Challenges and Solutions in Implementing Multidimensional Risk Models



Central Illustration: Atherosclerotic Cardiovascular Disease (ASCVD) Risk Scoring:

Present Landscape and Future Directions for Precision Prevention.

Conclusion

ASCVD risk prediction has evolved from traditional, population-based models—such as the PCE and SCORE2—to a new era of precision prevention that integrates genomics, inflammation, advanced biomarkers, imaging, and SDOH. A valuable foundation for population-level prevention has been provided by conventional risk scores, but their clinical utility is limited due to various drawback such as under performance in diverse populations, moderate predictive power and omission of significant risk modifiers like genetic susceptibility, socioeconomic factors and chronic inflammation.

Risk stratification in individuals has been improved with the addition of various biomarkers (e.g., hsCRP, Lp(a)), CAC scoring, and PRS), specifically in individuals with intermediate-risk and atypical risk profiles. In addition to this, need for multidimensional integrative models has been limited due to interconnection between inflammatory and genetic pathway, as well as adverse effect of social environment on molecular risk.

The future of prevention of ASCVD exist in the clinical utilization of dynamic, multidimensional and AI-enabled risk models that assimilate SDOH, imaging, clinical and omics date to deliver adaptive, equitable and personalized care. These recent advancements potentiate predictive accuracy and ability to assess distinct risk endotypes and guide targeted therapeutic interventions-such as early lipid-lowering drugs, anti-inflammatory therapies or community-based options-tailored to individual profiles risk. However, successful implementation into clinical field will need rigorous validation, attention to equity and ethical concerns and strict implementation science to ensure that across all population, precision prevention benefits are realized.

Author Contributions

The lead author of the review article is Dr Rohit Mody. Dr Debabrata Dash, Dr Bhavya Mody, Dr Umanshi Dash and Dr Rajeev Gupta had equal and substantial contributions in the formation of this review article. They were involved in conceptualization, data curation, formal analysis, resources, software, validation, visualization, writing - original draft, Writing, review & editing.

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Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

Ethical approval was not required since it is an accepted procedure

Consent for Publication

Written consent has been obtained to publish the review article from the guardian. The consent copy is available with the authors and ready to be submitted if required.

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