ISSN: 2996-3885

Cardiology & Cardiovascular Research

Review Article

The Evolution of Cardiovascular Risk Assessment: From Framingham to Multi-omics

Emmanuel Auchi Edafe[1]*, Val-Ugboma Demi Somtoolisa[2], Nweke Chidera Colette[2] and Christian Kenneth Nweke[2]

[1]*Department of Medicine, University of Port Harcourt, and University Teaching Hospital, Nigeria.*
[2]*Medical personal, waiting for housemanship, Nigeria.*

Abstract

Cardiovascular disease (CVD) remains the leading cause of global morbidity and mortality, making early and accurate risk assessment a critical public health priority. This narrative review explores the profound evolution of cardiovascular risk stratification through three major developmental leaps.

The first leap encompasses the establishment of traditional, population-based risk algorithms, such as the Framingham Risk Score, Pooled Cohort Equations, and QRISK, which utilize standard clinical parameters to estimate short-to-long-term incidence of cardiovascular events. While foundational, these static models often miscalculate risk in diverse, contemporary, or global populations. The second leap highlights the integration of novel biomarkers and non-invasive cardiovascular imaging, notably coronary artery calcium (CAC) scoring, which allows clinicians to detect subclinical atherosclerosis and refine individualized residual risk. The third and current leap is driven by the advent of artificial intelligence (AI), continuous wearable monitoring, and multi-omics—including genomics, epigenomics, transcriptomics, proteomics, and metabolomics. Together, these technologies are shifting risk prediction from episodic evaluations to dynamic, highly personalized profiling.

Furthermore, this paper addresses the specific challenges of cardiovascular risk screening in low-resource environments, such as Nigeria, emphasizing the necessity for non-laboratory-based charts and mobile health technologies to bridge the screening gap. Ultimately, the future of cardiovascular prevention lies in the convergence of multimodal data fusion, federated learning, and digital cardiovascular twins, which will enable truly proactive and precise cardiovascular care.

Keywords

Evolution, Cardiovascular, Risk Assessment, Framingham, Multi-omics.

Corresponding Author Information

Emmanuel Auchi Edafe
Department of Medicine, University of Port Harcourt, and University Teaching Hospital, Nigeria.

Received: April 29, 2026; **Accepted:** May 31, 2026; **Published:** June 09, 2026

Citation: Emmanuel Auchi Edafe, Val-Ugboma Demi Somtoolisa, Nweke Chidera Colette, Christian Kenneth Nweke. The Evolution of Cardiovascular Risk Assessment: From Framingham to Multi-omics. Cardiol Cardiovasc Res. 2026; 4(2):1-10.

Introduction

Cardiovascular disease is a term that encompasses all disorders affecting the heart and blood vessels [1]. They include coronary artery diseases, cardiomyopathies, rheumatic heart diseases, heart failure, thromboembolic diseases, cardiac valvulopathies, cerebrovascular diseases, peripheral artery diseases, and congenital heart diseases [1].

Cardiovascular diseases are responsible for approximately one-third of deaths globally and are recognized as the leading causes

of mortality worldwide, with low-and-middle-income countries bearing the largest burden of CVDs [2]. This burden extends beyond mortality, contributing significantly to reduced quality of life, loss of productivity, and escalating healthcare expenditures [2-4] Thus, placing extra demands on the already strained economies of these countries.

The persistent and expanding global burden of CVDs necessitates the prevention and timely diagnosis of these diseases. Preventive strategies such as lifestyle modification, pharmacological therapies, and risk-factor control have proven efficient in reducing morbidity and mortality when implemented before the onset of irreversible cardiovascular damage [5,6]. As a result, modern cardiology prioritizes the early identification of asymptomatic individuals who may be at increased risk of future cardiovascular events.

Cardiovascular risk assessment tools are used to stratify individuals' risk of developing cardiovascular disease. Traditional cardiovascular risk assessment has been the bedrock of preventive cardiology for decades [7]. One of the earliest of them is the Framingham Risk Score, which paved the way for other tools such as the Atherosclerotic Cardiovascular Disease (ASCVD) Risk Estimator, Systematic Coronary Risk Evaluation (SCORE2), and the United Kingdom score (QRISK) [5,7,8]. These models have been used to standardize cardiovascular risk evaluation and inform therapeutic strategies. However, despite the triumphs of the traditional risk assessment tools in reducing cardiovascular morbidity and mortality, they have limited precision and are unable to personalize prognosis [8]. This is attributable to the fact that they are more concerned with clinical findings than they are with genetic and biological variables.

Rapid developments in digital health technologies, biomarker discovery, advanced imaging, and artificial intelligence have made it possible to move toward more precise and dynamic approaches [5,8]. This is the basis for the second and third evolutionary leaps in cardiovascular risk assessment. The second evolutionary leap includes the use of biomarkers, inflammatory mediators, and imaging modalities to identify subclinical cardiovascular diseases. Taking us several steps further, the third evolutionary leap is driven by artificial intelligence, wearable devices, and genomics. Altogether, these developments have made it possible to analyze complex clinical, demographic, and biochemical data to predict the risk of cardiovascular diseases with a higher degree of precision [8].

While significant progress has been made in the development of new approaches to cardiovascular risk assessment, the existing body of knowledge remains fragmented. This fragmentation creates a knowledge gap in understanding the interrelationship and practical implications of the novel and traditional risk assessment leaps. Hence, there is a need for a comprehensive narrative review that examines these advances with a cohesive framework, highlighting their strengths and limitations.

This narrative review explores three major evolutionary transitions in cardiovascular risk assessment, paying attention to their scientific basis, merits, drawbacks, and clinical relevance for more precise cardiovascular risk stratification.

Methodology

This study was conducted as a narrative review aimed at highlighting major advances in cardiovascular risk assessment beyond traditional prediction models. A literature search was conducted using PubMed, Cochrane Library (Database / Evidence Base) and Google Scholar to identify relevant peer-reviewed articles published between January 2010 and May 2026, although earlier studies were included where historically relevant. This search was done in English.

Search terms included a combination of MeSH terms and keywords using Boolean operators. For example, ("cardiovascular disease" OR "cardiology") AND ("risk") AND ("assessment" OR "stratification"). Articles were selected based on relevance to the objectives of the review, with emphasis placed on studies evaluating emerging approaches to cardiovascular risk prediction. The identified literature was narratively synthesized into three thematic domains representing the evolutionary shifts in cardiovascular risk assessment.

Evolution of cardiovascular risk assessment

Leap 1: Traditional Risk Scores

The original attempt at assessment and standardization and prediction of cardiovascular risk in patients moved the focus from simple but subjective clinical judgement by experienced health professionals to population-based risk scores. These risk scores emerged as a result of aggregated data from cardiovascular studies following individuals over time, identifying and analysing the data for variables common to participants with cardiovascular diseases.

Framingham Heart Study

The foremost of these cardiovascular studies is the Framingham study [9] (1948 - Present), based in Framingham, Massachusetts. This ongoing cardiovascular cohort study established the concept of "risk factors" itself [10].

Prior to its onset, the epidemiology of cardiovascular diseases was largely uncharted territory—inadequate research, few specialists, and diagnostic dilemma [11].

With the death of United States President, Franklin D. Roosevelt, linked to hypertensive heart disease and stroke in 1945, the succeeding President created the National Heart Act, allocating a $500,000 seed grant to cardiovascular epidemiological research and establishing the National Heart Institute, known today as the National Heart, Lung and Blood Institute, to conduct the study [12].

The epidemiological data derived from the Framingham study birthed breakthrough research in clinical manifestations and

diagnosis of cardiovascular diseases [12,13].

Particularly, the ideation of risk factors from the Framingham study resulted in the analysis of these identified factors to create risk scores. The first attempt by Truett et al. [13] used multivariate logistic models with 7 factors, and the first published risk profile by Kannel et al. [10] in 1976, adding 2 more factors.

The Framingham Risk Score

These laid a framework for the emergence of the Framingham Risk score for coronary heart disease [14], the most renowned among the cardiovascular risk scores. The variables used in this score included age, sex, total cholesterol, HDL cholesterol, systolic blood pressure, blood pressure treatment status, smoking status, and diabetes status.

Based on the results of these variables, the scoring system groups the 10-year risk into Low risk (<10%), Medium risk (10% - 19%), and High risk (>20%) categories.

It was a groundbreaking feat. The first recorded systematic approach to calibrate cardiovascular risk assessment was clinically applicable and backed by a validated epidemiologic inquiry.

However, limitations still permeate the use of the Framingham risk score. The data was predominantly Caucasian males, resulting in poor representation of other races. Since the originating Framingham study participants were individuals without a cardiovascular history, the crucial variable of family history is not considered in this risk score [6]. There is also a tendency to underestimate cardiovascular risk in the female population using the Framingham risk score [15].

In addition, the Framingham risk score only assesses risk for coronary artery disease, not total cardiovascular risk, thus exempting diseases like stroke, heart failure, and transient ischemic attacks. Finally, due to the predominance of Americans in the study, the risk score tended to overestimate or underestimate cardiovascular risk in other populations [5]

Regional Cardiovascular Risk Scores

Subsequently, various regions, noting this, designed risk scores for their population, based on their unique geographic and regional data, thus alleviating one of the Framingham risk score's key limitations.

In 2003, the European Society of Cardiology published the SCORE (Systematic Coronary Risk Evaluation) [16] based on data on fatal cardiovascular risk from 12 European cohort studies. This model was later updated in 2021 to SCORE2 [17], which increased sensitivity by including non-fatal cardiovascular risk data to better pinpoint high-risk persons, and calibrated different countries by risk. An age-specific model, SCORE2-OP [18] was also introduced for persons above 70 years.

The CUORE Project incorporated data from different Italian regions, resulting in the CUORE risk score and chart [19].

Q-RISK was established in the UK and found to be better calibrated to that region, surpassing Framingham and ASSIGN risk scores in that regard [20] stand out among this sect. The National Health Service supported the development of QRISK models in the United Kingdom. These algorithms incorporated socioeconomic status, ethnicity, family history, chronic kidney disease, rheumatoid arthritis, and atrial fibrillation, improving predictive performance in diverse populations. QRISK represented an important transition toward more inclusive and socially contextualized risk prediction.

Since 2007, it has been updated to QRISK2 with the addition of ethnic origins, type 2 diabetes, rheumatoid arthritis, atrial fibrillation, and chronic renal disease to the original parameters; QRISK3 includes additional variables like migraines, severe mental illness, erectile dysfunction, corticosteroids, atypical antipsychotics, chronic kidney disease, and standard deviation of systolic blood pressure. QRISK3 is currently recommended by NICE (National Institute for Health and Care Excellence) for formal cardiovascular risk assessment [21].

In Germany, the prospective cardiovascular Münster Study (PROCAM), which ran from 1986 to 1994, demonstrated that elevated triglycerides are an independent risk factor for an early myocardial infarction or cardiac death [22].

The China-PAR (Prediction for ASCVD Risk in China) equations addressed the tendency of Western models to overpredict risk in Chinese individuals. The project utilized 2 prospective cohorts comprising Chinese participants and was externally validated in 2 independent Chinese cohorts [23].

The first risk score to incorporate socioeconomic strata as a variable in assessing cardiovascular risk was ASSIGN (Assessing Cardiovascular Risk in Scottish Intercollegiate Guidelines Network) for Scotland and similar UK populations [6].

The World Health Organisation (WHO) derived a tool better suited for Low-and-Middle-Income countries (LMIC) called the WHO/ISH risk score, based on data from the Emerging Risk Factors Collaboration, including 21 global regions [24].

In 2013, the American College of Cardiologists and the American Heart Association (ACC/AHA) pooled the findings from different longitudinal cohort studies, including CARDIA (Coronary Artery Risk Development in Young Adults), ARIC (Atherosclerosis Risk In Communities), CHS (Cardiovascular Health Study), and Framingham, to create a sex and race-specific score called the Pooled Cohort Equations (PCE) [25]. This score was designed to estimate the 10-year risk of atherosclerotic cardiovascular disease (ASCVD) and aimed to improve generalizability by incorporating data from more diverse, multi-ethnic cohorts.

The addition of kidney function data and social determinants of health resulted in the PREVENT score by the American Heart Association [26].

These traditional risk scores played a cardinal role in introducing objectivity into the predominantly subjective and largely unexplored field of cardiovascular risk assessment. However, inefficiencies remain in the assessment of the 10-year risk of cardiovascular diseases when using these scores from their original derivation cohorts without proper recalibration for modern, diverse, or local populations.

In all these regional risk scores, African nations were left behind. There were no study from the sub-Saharan Africa included in these risk design and score. Hence, they are left to the mercies of using the WHO or European or American risk models.

Leap 2: Risk Scores with Biomarkers and Imaging

The second evolutionary leap in cardiovascular risk assessment was marked by a transition from the use of traditional risk assessment tools such as the Framingham Risk Score to the use of cardiac biomarkers and imaging tools. There was a shift from phenotype-based prediction toward a deeper dive into the biological mechanisms involved in cardiovascular disease.

Biomarkers

Biomarkers offer insight into the underlying mechanisms involved in cardiovascular diseases, such as inflammation, oxidative stress, myocardial injury, and metabolic dysregulation [27].

Inflammatory Biomarkers: While inflammation is implicated in the pathogenesis of cardiovascular diseases, a prospective study by Abouezzeddine demonstrated that C-reactive protein level was not predictive of cardiovascular outcomes following adjustment for clinical risk factors [28]. However, another prospective study by Mohebi, which took into account the predictive value of 24 inflammatory markers, including macrophage colony-stimulating factor-1 (MCSF-1), interleukin-8 (IL-8), and interleukin-1α (IL-1α), found that they had a significant predictive value for major adverse cardiac events [29]. Notably, neither study adequately accounted for potential confounding variables such as age and sex, factors that have been shown to significantly influence both inflammatory biomarker levels and adverse cardiovascular outcomes [6]. Collectively, these findings suggest inconsistency in the predictive utility of inflammatory biomarkers in cardiovascular disease, potentially due to methodological differences and inadequate adjustment for key confounders. This highlights the need for further investigation into more reliable and clinically applicable biomarkers for cardiovascular risk stratification.

Cardiac Biomarkers

Although inflammatory biomarkers provide insight into the atherogenic processes underlying cardiovascular disease, cardiac biomarkers reflect ongoing myocardial injury and cardiovascular stress. A study by Saeed et al showed that cardiac biomarkers such as N-terminal pro–B-type natriuretic peptide (NT-proBNP) and high-sensitivity cardiac troponin T(hs-cTnT) had a high predictive value for cardiovascular disease, particularly heart failure, over a 4-year follow-up period [30]. Their predictive value was reportedly improved when combined with a third biomarker, high-sensitivity C-reactive protein [30]. Similarly, Osei and Balha reported that NT-proBNP and hs-cTnI have superior predictive value for heart failure and major adverse cardiovascular events when compared with clinical factors or other biomarkers [31]. Furthermore, Jansen et al. observed that repeat troponin measurements obtained 12 months after an initial cardiovascular event improved cardiovascular risk prediction beyond that achieved with single baseline measurements. Despite these promising findings, variability in biomarker combinations, measurement strategies, and follow-up approaches limits consensus regarding the optimal use of cardiac biomarkers in cardiovascular risk prediction [32].

Metabolic Biomarkers

Conventional cardiovascular risk prediction has historically relied on lipid measures such as total cholesterol and low-density lipoprotein cholesterol (LDL-C) [33,34]. However, there is increasing evidence that residual risk persists even among individuals who achieve optimal lipid targets [33]. This limitation has prompted increasing interest in novel metabolic biomarkers, including apolipoprotein B (ApoB) and lipoprotein(a) [Lp(a)], which may more accurately reflect atherogenic burden. In a prospective study, Willeit et al. demonstrated that elevated Lp(a) independently predicted cardiovascular disease outcomes over a 15-year follow-up period and improved risk prediction beyond conventional measures [35]. This is in consonance with findings from a study by Hoogeveen et al., who reported that remnant lipoproteins and Lp(a) were causally associated with residual risk of atherosclerotic cardiovascular disease (ASCVD) among statin-treated individuals. These findings suggest that emerging metabolic biomarkers may improve cardiovascular risk stratification, particularly in individuals whose risk remains underestimated by conventional lipid parameters.

Imaging

Technological advances have made it possible to visualize cardiac markers. Non-invasive imaging tests such as echocardiography, coronary computed tomography angiography, and coronary artery calcium score are now being considered in discussions regarding cardiovascular risk assessment for primary prevention. With these imaging techniques, it is possible to detect asymptomatic cardiovascular diseases and monitor disease progression.

Echocardiography

Echocardiography, when integrated with clinical indices, serves as an important tool in cardiovascular risk stratification. Its utility extends beyond diagnosis to prognostication, particularly in patients with heart failure. Evidence suggests that echocardiographic parameters can classify patients with heart failure with preserved ejection fraction (HFpEF) into distinct strata with varying prognostic outcomes [36]. Furthermore, transthoracic echocardiography is

recommended within the first three months following an index acute cardiovascular event and may be repeated periodically in individuals with chronic coronary syndromes to monitor disease progression and guide management [37]. Despite its clinical utility, echocardiography has notable limitations. The accuracy and reproducibility of findings are highly operator-dependent, making the technique susceptible to both intra-observer and inter-observer variability [37]. In addition, factors such as suboptimal image quality and poor patient cooperation may impair image acquisition and limit its effectiveness in cardiovascular risk assessment.

Coronary Computed Tomography Angiography (CCTA): Coronary computed tomography angiography (CCTA) has emerged as an important non-invasive imaging modality for the early detection and risk stratification of coronary artery disease (CAD). Beyond its diagnostic role, CCTA provides valuable prognostic information by enabling visualization and characterization of coronary atherosclerotic plaques, thereby facilitating risk stratification based on plaque burden and phenotypic features [37].

The prognostic utility of CCTA has been demonstrated in several studies. Findings from the Scottish Computed Tomography of the Heart (SCOT-HEART) trial showed that, among patients presenting with stable chest pain, the addition of CCTA to standard care was associated with a reduction in coronary heart disease mortality over a five-year follow-up period compared with standard care alone [38]. Similarly, a retrospective study by Yoon et al. reported that CCTA was more useful than the Framingham Risk Score in cardiovascular risk assessment among patients with stroke and in predicting major adverse cardiovascular events in asymptomatic individuals [39]. These findings highlight the expanding role of CCTA beyond diagnosis toward prognostic assessment across diverse patient populations.

Despite its clinical benefits, concerns remain regarding the widespread use of CCTA. Exposure to ionizing radiation raises concerns about cumulative cancer risk, particularly in younger patients and those requiring repeated imaging. In addition, image quality may influence diagnostic accuracy and interpretation, while the absence of universal standardization in data acquisition and reporting, alongside interobserver variability, may affect consistency in clinical application [40]. Consequently, although CCTA represents a promising tool for cardiovascular risk assessment, its limitations necessitate careful consideration in routine clinical practice.

Coronary Artery Calcium Score

Coronary artery calcium (CAC) scoring is a non-invasive imaging technique derived from coronary computed tomography angiography (CCTA) that quantifies the amount of calcified plaque within the coronary arteries. It has gained relevance as a tool for the primary prevention of atherosclerotic cardiovascular disease, particularly among asymptomatic individuals, due to its ability to improve cardiovascular risk prediction. By estimating the extent of coronary calcification, CAC scoring aids in identifying subclinical atherosclerosis and refining risk stratification, especially in individuals at borderline or intermediate cardiovascular risk [41].

The joint guidelines of the American College of Cardiology and American Heart Association, as well as those of the European Society of Cardiology, support its use in risk stratification [42,43]. However, the ESC primarily recommends CAC scoring in asymptomatic individuals with intermediate cardiovascular risk, whereas ACC/AHA guidelines suggest its use among intermediate-risk patients who remain uncertain about initiating statin therapy after clinician–patient discussion [37,42,43]. Despite these recommendations, both guidelines discourage routine CAC assessment in low-risk individuals, given the limited additional prognostic value and concerns regarding unnecessary radiation exposure and healthcare costs [42,43].

Despite the progress made by the 2nd evolutionary leap in cardiovascular assessment, they do not render the achievements of the 1st leap redundant. Rather, there is a melting point where cardiovascular risk assessment tools from both leaps meet to enhance cardiovascular outcomes [44]. This approach recognizes that cardiovascular disease is multifactorial, involving complex interactions between clinical risk factors, molecular pathways, and structural changes that may not be adequately captured by a single assessment too [42]. Emerging evidence suggests that multimodal strategies improve cardiovascular risk prediction beyond conventional approaches alone. For instance, the integration of CAC scoring with traditional risk models has been shown to enhance reclassification of intermediate-risk individuals, thereby guiding preventive interventions such as statin initiation more effectively [41]. Likewise, combining inflammatory biomarkers with imaging findings may identify individuals at heightened residual cardiovascular risk despite optimal control of conventional risk factors [31].

Leap 3: Artificial Intelligence, Genomics, Continuous Monitoring

The 3rd evolutionary leap in cardiovascular risk assessment saw a shift from static clinic-based risk scores to continuous, technological-enhanced prediction systems.

Unlike the traditional risk score and even the inclusion of biomarkers and imaging, this era reveals real-time, dynamic risk calibration and earlier identification of subclinical cardiovascular diseases.

The wave of wearable technologies, the integration of artificial intelligence (AI) in cardiovascular medicine, and the use of multi-omics in cardiovascular risk assessment are key components in this shift.

Wearable Technologies

The advent of wearable technologies such as smartwatches, fitness trackers, ECG/EKG devices, headbands, and sensory clips has improved individualized data collection.

The sensors used in these wearable technologies vary, and can be classified as biometric, environmental, and motion sensors.

The sensors range from an accelerometer which measures the acceleration in a single or multiple directions; ballistocardiography which measures the body's mechanical recoil from ventricular contraction to quantify cardiac outputs; electrocardiogram which measures electrical activity of cardiac impulse; impedance plethysmography that detect changes in blood electrical conductivity to measure pulse volume; magneto plesmythography which uses hall effect sensors to track cardiovascular activity via movement of magnets; phonocardiogram that detects subaudible vibrations created through the opening and closing of heart valves; photo plethysmography which uses an optical sensor to detect blood volume changes within the microvasculature; and remote dielectric sensing that quantifies the dielectric coefficient of tissues, which correlates with fluid concentration [45].

With a combination of these sensors, a variety of variables can be tracked—blood pressure, ECG monitoring, sleep tracking, physical activity, exercise monitoring, etc. Although the wearable technology brings ease and continuous monitoring into the equation, the issue of standardization and validation remains, especially in the case of blood pressure measurement in an ambulant patient [45].

Artificial Intelligence (AI)

Machine Learning programs are able to detect patterns from cardiovascular data faster and to more depth than humans. Coupled with the influx of individualized data, this means better analysis of richer, more detailed data.

Thus, data from wearable technologies can be enhanced by computer modelling to achieve truly personalized care as opposed to the one-size-fits-all approach typical of conversational risk scores [45].

If wearable technology continues feeding computational models over time, the concept of the 'digital twin' might be realised. This means a highly personalised virtual model of an individual's cardiovascular system, allowing for proactive simulation of health trajectories, flagging silent pathologies, and predicting adverse events before symptoms ever occur [46,47].

This occurs due to the hybrid integration of patient-specific data with the data-driven model and the mechanistic modelling of the individual anatomical, mechanical, and electrophysiological characteristics [46].

Studies have shown that AI models outperformed conventional risk models in discriminative performance [48]. The Concordance Index (C-index) is a score for evaluating the accuracy of prediction formulas by comparing agreement with the outcome; with 0.5 meaning no predictive ability (this occurring due to chance) and being the ideal prediction.

Based on the C-index, a gap still remains in the predictive ability of the traditional risk score, with Framingham, SCORE2, and PREVENT recording C-index values of 0.84 [49], 0.67-0.81 [26] and 0.69-0.73 [50], respectively. Thus, a need exists for optimizing prediction.

Multi-omics and Polygenic Risk Scores

Multiomics stands at the forefront of this shift. It is a holistic biological framework that analyzes data across multiple molecular layers, including genomics, epigenomics, transcriptomics, epitranscriptomics, proteomics, and metabolomics. By combining these massive biological datasets using advanced artificial intelligence and machine learning, clinicians can achieve a much deeper understanding of an individual's unique atherosclerotic cardiovascular disease (ASCVD) disease pathways [51].

With the limitations of traditional risk factors, a more comprehensive option is necessary. This is possible by the integration of data from the different omic layers with the traditional risk score variables, and analysing with dedicated AI and ML models to build a solid predictive algorithm [51].

Numerous studies have shown the improvement in prediction following integration of multi-omic data [52,53]. In fact, a recent Framingham Heart Study investigating subclinical coronary disease and myocardial infarction with an integrative trans-omic approach (genome-wide association studies GWAS, DNA methylation, and gene expression) highlighted specific associated genes also linked to smoking, cardiac tissue homeostasis, and platelet function [54].

Bridging Genetics and Environment with Epigenomics

While the DNA sequence itself does not change, the way genes are expressed is highly adaptable. Epigenomics measures dynamic modifications to the DNA, like DNA methylation, that act as a biological archive of the environmental and lifestyle factors a person experiences throughout their life. Because epigenetic marks change over time, they can effectively link static genetic risk with external influences like diet, smoking, and aging, providing a mechanism to track physiological cardiac aging and uncover specific patient subgroups that may need closer medical surveillance [55,56].

RNA Profiling: Transcriptomics and Epitranscriptomics

At the RNA level, transcriptomics and epitranscriptomics explore how RNA molecules are created, modified, and regulated. Evaluating noncoding RNAs and microRNAs in the blood has proven valuable for determining the vulnerability of atherosclerotic plaques. For example, by profiling the RNA of carotid plaques, researchers have successfully categorized human atherosclerotic lesions into specialized molecular groups, making it easier to predict which plaque types are most likely to trigger severe cardiovascular events like strokes or heart attacks [57,58].

Real-Time Monitoring through Proteomics and Metabolomics

To understand the most immediate state of a patient's health,

proteomics and metabolomics evaluate the proteins and metabolites currently active in the body. Proteomics provides a real-time reflection of how a patient's genetic blueprint interacts with their current lifestyle, weight, and diet. Metabolomics captures a highly detailed, real-time snapshot of metabolic activity, identifying rapid biochemical shifts like inflammatory markers, amino acid imbalances, or subtle changes in lipid subclasses that tend to precede the onset of clinical symptoms. These tools are especially useful for identifying residual cardiovascular risk in patients who are already receiving standard preventative treatments [60,61].
Notwithstanding, multi-omics faces significant barriers to routine clinical use. These include high costs, the need for complex bioinformatics infrastructure, and a historical bias toward populations of European ancestry, which must be addressed to prevent widening global health disparities [51].

Cardiovascular Risk Assessment in Low-Resource Environments Like Nigeria

Low- and middle-income countries (LMICs) like Nigeria are currently experiencing an epidemiological transition, resulting in a surge of non-communicable diseases, particularly cardiovascular disease (CVD) [61,62]. The adoption of westernized diets, increased sedentary lifestyles, and rapid rural-to-urban migration are driving this escalating health crisis. Because sophisticated medical resources for treating acute cardiovascular events are scarce in these regions, prioritizing primary prevention through accurate and early risk assessment is mandatory.

Despite this necessity, routine cardiovascular risk screening in Nigeria remains severely suboptimal [62]. A survey of physicians in Southern Nigeria revealed that while the majority were aware of global risk calculators, only about 28% actually utilized them in clinical practice [61]. The primary barriers cited by healthcare providers were not simply time constraints, but a fundamental unfamiliarity with how to practically apply these risk estimation tools [61]. Furthermore, there is a glaring absence of validated risk assessment algorithms derived specifically from the indigenous Nigerian population, forcing clinicians to rely on foreign models that may miscalculate local risk profiles.

At the community level, especially in rural and agrarian areas, risk factors often go entirely undetected [63]. Studies demonstrate that a significant portion of these populations suffer from undiagnosed hypertension, hypercholesterolemia, and elevated fasting glucose, with nearly half of the individuals having never had their blood pressure measured. While non-pharmacological interventions like diet modifications are widely recommended, they are often exceptionally difficult to implement and sustain in typical rural environments. Also, essential cardiovascular medications are frequently unavailable at the primary healthcare level, further hindering effective intervention even when a high risk is successfully identified [64].

To overcome the financial and infrastructural limitations of LMICs, there is a strong push toward non-laboratory-based risk assessment models [12,65]. Tools that substitute expensive blood tests (like total cholesterol assays) with easily measurable physical metrics, such as body mass index (BMI) and blood pressure, can be administered quickly and affordably in a single clinic visit [65].

Although Nigeria has no region-specific risk chart, the World Health Organization (WHO) has also developed specialized risk charts tailored for various global regions to facilitate this kind of low-resource screening; the WHO/ISH risk score is based on data from 21 regions [65].

Furthermore, leveraging digital health technology shows promise; Nigerian physicians who use internet-enabled smartphones during consultations are significantly more likely to perform routine cardiovascular risk assessments [61].

Moving forward, it is important to conduct large-scale, population-based cohort studies within sub-Saharan Africa to develop and validate highly specific, localized risk prediction tools [61].

Combined with robust national initiatives—such as Nigeria's multi-sectoral action plan (NMSAP) for the prevention of non-communicable diseases—these adapted assessment strategies are essential for bridging the healthcare gap and reducing cardiovascular mortality in low-resource environments [64].

Future Trends in Cardiovascular Risk Assessment

The future of cardiovascular risk assessment points to a fundamental shift away from static, episodic, and population-based calculators toward dynamic, proactive, and hyper-personalized medicine. As digital health technologies mature, the methodologies used to predict and prevent atherosclerotic cardiovascular disease (ASCVD) will increasingly rely on continuous data integration and advanced computational models [47].

The Emergence of Cardiovascular Digital Twins

Perhaps the most transformative concept on the horizon is the development of the digital cardiovascular twin [46,47]. This involves creating a highly personalized, virtual computational replica of a patient's heart and vascular system [45]. Rather than assessing risk at a single clinical visit, a digital twin continuously ingests real-time, multimodal data from wearable sensors, electronic health records, and periodic cardiac imaging. By combining known physiological laws (mechanistic modeling) with artificial intelligence (data-driven modeling), these virtual avatars will allow clinicians to proactively simulate disease trajectories, predict the occurrence of adverse events, and virtually test the efficacy of pharmacological interventions or pacemaker settings before applying them to the actual patient [46,47].

Continuous Telemonitoring and Wearable Sensors

Patient evaluation will increasingly transcend the hospital setting through the widespread adoption of the Internet of Medical Things (IoMT). The future of risk stratification will rely on continuous physiological tracking through consumer and medical-grade

wearables, such as smartwatches, biometric clothing, and ambient home sensors. By seamlessly recording continuous electrocardiograms (ECG), photoplethysmography (PPG), and physical activity levels in a patient's natural environment, machine learning algorithms will be able to detect hidden arrhythmias, hemodynamic deterioration, and subtle signs of impending heart failure days or weeks before overt symptoms necessitate hospital admission [8,45,47].

Multimodal Data Fusion

The most precise cardiovascular risk estimates of the future will be achieved through multimodal data fusion [8,51].

Artificial intelligence models will concurrently analyze diverse and highly complex datasets that human clinicians cannot synthesize manually. This includes merging advanced anatomical and functional imaging (such as cardiac MRI and CCTA) with clinical history, polygenic risk scores, and real-time omics data (proteomics, metabolomics, and epigenomics). This deep, multi-layered profiling will enable the identification of unique disease sub-phenotypes and residual risks, facilitating highly targeted therapies for individual patients [8,51].

Explainable AI, Federated Learning, and Medical LLMs

To successfully integrate these complex predictive models into routine clinical practice, several technical and ethical barriers must be addressed. Future development will heavily prioritize Explainable Artificial Intelligence (XAI) to overcome the "black box" nature of deep learning, ensuring that clinicians can interpret and trust the reasoning behind algorithmic risk predictions [8,46]. In addition, to safeguard sensitive patient data across global populations, federated learning architectures will be utilized. This allows predictive models to learn and adapt across diverse institutions globally without requiring the centralized transfer of private medical records [66,67]. Furthermore, domain-adapted Large Language Models (LLMs) and autonomous AI agents will be increasingly deployed as clinical co-pilots. These systems will translate complex, multi-dimensional risk data into guideline-concordant, human-readable documentation and provide actionable preventive recommendations directly to patients and physicians [47].

Adapting to an Aging Global Population

Finally, future risk assessment strategies must be calibrated to face the demographic reality of a rapidly aging global population. Epidemiological projections indicate that crude cardiovascular mortality will increase sharply by 2050, driven largely by an older demographic with complex comorbidities and atherosclerotic burdens. To prevent healthcare systems from becoming overwhelmed, future predictive models and digital screening tools must be exceptionally proficient at identifying subclinical disease early and guiding cost-effective, personalized primary prevention strategies tailored to the unique physiological profiles of adults [68].

Conclusion

Cardiovascular risk assessment is the cornerstone of prevention for cardiovascular disease. While traditional clinical risk scores provided the foundational first leap in standardizing patient evaluation, their limited precision necessitated further innovation. The second leap, integrating biomarkers and advanced non-invasive imaging, allowed clinicians to detect subclinical disease and better understand individual residual risk. Today, we are amidst a third evolutionary leap driven by artificial intelligence, multi-omics, and continuous wearable monitoring. By embracing these dynamic, hyper-personalized models and adapting them for diverse global populations, the medical community can move beyond static population-based predictions to truly proactive, and precise cardiovascular care.

References

1. Thiriet M. Cardiovascular Disease: An Introduction. Vasculopathies. 2019; 8: 1-90.
2. Stark BA, DeCleene NK, Desai EC, Hsu JM, Johnson CO, et al. Global, Regional, and National Burden of Cardiovascular Diseases and Risk Factors in 204 Countries and Territories, 1990-2023. JACC. 2025; 86: 2167-2243.
3. Mocumbi AO. Cardiovascular Health Care in Low- and Middle-Income Countries. Circulation. 2024; 149: 557-559.
4. Faiz Ullah, Atiq Ur Rehman, Khan RD, Orakzai H, Ahmadyar, et al. Cardiovascular Disease in Low and Middle Income Countries: Challenges and Solutions. Indus J Biosci Res. 2025; 3: 165-170.
5. Batsis JA, Lopez-Jimenez F. Cardiovascular risk assessment from individual risk prediction to estimation of global risk and change in risk in the population. BMC Med. 2010; 8: 29.
6. Jain D, Acharya S, Shukla S, Kaushik N. Cardiovascular Risk Assessment Scores: A Narrative Review. J Pract Cardiovasc Sci. 2024; 10: 57-63.
7. Hasabullah M, Kahtani F, Balkhoyor T, Al-Harbi L, Kinsara AJ. A Comparison of Four Cardiovascular Risk Assessment Instruments in Saudi Patients. Cureus. 2020.
8. Myśliwiec A, Bartusik-Aebisher D, Xavierselvan M, Paul A, Aebisher D. Deep Learning and Cardiovascular Diseases: An Updated Narrative Review. J Clin Med. 2026; 15: 3053.
9. McKee PA, Castelli WP, McNamara PM, Kannel WB. The Natural History of Congestive Heart Failure: The Framingham Study. N Engl J Med. 1971; 285: 1441-1446.
10. Kannel WB, Dawber TR, Kagan A, Revotskie N, Stokes J. Factors of Risk in the Development of Coronary Heart Disease—Six-Year Follow-up Experience: The Framingham Study. Ann Intern Med. 1961; 55: 33-50.
11. Benack RT. ETIOLOGY OF CONGESTIVE HEART FAILUREIN CLINICAL MEDICINE. Ann N Y Acad Sci. 1969; 156: 594-602.
12. Mahmood SS, Levy D, Vasan RS, Wang TJ. The Framingham Heart Study and the epidemiology of cardiovascular disease: a historical perspective. The Lancet. 2014; 383: 999-1008.

13. Truett J, Cornfield J, Kannel W. A multivariate analysis of the risk of coronary heart disease in Framingham. J Chronic Dis. 1967; 20: 511-524.
14. Wilson PWF, D'Agostino RB, Levy D, Belanger AM, Silbershatz H, et al. Prediction of Coronary Heart Disease Using Risk Factor Categories. Circulation. 1998; 97: 1837-1847.
15. Talha I, Elkhoudri N, Hilali A. Major Limitations of Cardiovascular Risk Scores. Cardiovasc Ther. 2024; 2024: 4133365.
16. Conroy R. Estimation of ten-year risk of fatal cardiovascular disease in Europe: the SCORE project. Eur Heart J. 2003; 24: 987-1003.
17. SCORE2 working group and ESC Cardiovascular risk collaboration. SCORE2 risk prediction algorithms: new models to estimate 10-year risk of cardiovascular disease in Europe. Eur Heart J. 2021; 42: 2439-2454.
18. SCORE2-OP working group and ESC Cardiovascular risk collaboration. SCORE2-OP risk prediction algorithms: estimating incident cardiovascular event risk in older persons in four geographical risk regions. Eur Heart J. 2021; 42: 2455-2467.
19. Giampaoli S, Palmieri L, Donfrancesco C, Panico S, Vanuzzo D, et al. Cardiovascular risk assessment in Italy: the CUORE Project risk score and risk chart. Ital J Public Health. 2007; 4.
20. Hippisley-Cox J, Coupland C, Vinogradova Y, Robson J, May M, et al. Derivation and validation of QRISK, a new cardiovascular disease risk score for the United Kingdom: prospective open cohort study. BMJ. 2007; 335: 136.
21. Recommendations | Cardiovascular disease: risk assessment and reduction, including lipid modification | Guidance | NICE [Internet]. NICE; 2023 [cited 2026 May 20].
22. Assmann G, Schulte H, Cullen P. New and classical risk factors--the Münster heart study (PROCAM). Eur J Med Res. 1997; 2: 237-242.
23. Yang X, Li J, Hu D, Chen J, Li Y, et al. Predicting the 10-Year Risks of Atherosclerotic Cardiovascular Disease in Chinese Population: The China-PAR Project (Prediction for ASCVD Risk in China). Circulation. 2016; 134: 1430-1440.
24. WHO CVD Risk Chart Working Group. World Health Organization cardiovascular disease risk charts: revised models to estimate risk in 21 global regions. Lancet Glob Health. 2019; 7: 1332-1345.
25. Goff DC, Lloyd-Jones DM, Bennett G, Coady S, D'Agostino RB, et al. 2013 ACC/AHA Guideline on the Assessment of Cardiovascular Risk. J Am Coll Cardiol. 2014; 63: 2935-2959.
26. Cho SMJ, Levin M, Chen R, Samarakoon R, Judy R, et al. AHA PREVENT Equations and Cardiovascular Disease Risk in Diverse Health Care Populations. JACC. 2025; 86: 181-192.
27. Racis M, Sobiczewski W, Stanisławska-Sachadyn A, Wirtwein M, Bluj E, et al. NADPH Oxidase Gene Polymorphism is Associated with Mortality and Cardiovascular Events in 7-Year Follow-Up. J Clin Med. 2020; 9: 1475.
28. AbouEzzeddine OF, McKie PM, Scott CG, Rodeheffer RJ, Chen HH, et al. Biomarker-Based Risk Prediction in the Community. Eur J Heart Fail. 2016; 18: 1342-1350.
29. Mohebi R, McCarthy CP, Gaggin HK, Van Kimmenade RRJ, Januzzi JL. Inflammatory biomarkers and risk of cardiovascular events in patients undergoing coronary angiography. Am Heart J. 2022; 252: 51-59.
30. Saeed A, Nambi V, Sun W, Virani SS, Taffet GE, et al. Short-Term Global Cardiovascular Disease Risk Prediction in Older Adults. J Am Coll Cardiol. 2018; 71: 2527-2536.
31. Osei AD, Blaha MJ. Combining Biomarkers and Imaging for Short-Term Assessment of Cardiovascular Disease Risk in Apparently Healthy Adults: A Paradigm-Shifting Approach. J Am Heart Assoc. 2020; 9: 017790.
32. Jansen H, Jaensch A, Schöttker B, Dallmeier D, Schmucker R, et al. Repeat Measurements of High Sensitivity Troponins for the Prediction of Recurrent Cardiovascular Events in Patients With Established Coronary Heart Disease: An Analysis From the KAROLA Study. J Am Heart Assoc. 2019; 8: 011882.
33. Hoogeveen RC, Ballantyne CM. Residual Cardiovascular Risk at Low LDL: Remnants, Lipoprotein (a), and Inflammation. Clin Chem. 2021; 67: 143-153.
34. Andersen CJ, Fernandez ML. Emerging Biomarkers and Determinants of Lipoprotein Profiles to Predict CVD Risk: Implications for Precision Nutrition. Nutrients. 2024; 17: 42.
35. Willeit P, Kiechl S, Kronenberg F, Witztum JL, Santer P, et al. Discrimination and Net Reclassification of Cardiovascular Risk With Lipoprotein(a). J Am Coll Cardiol. 2014; 64: 851-860.
36. Lewis GA, Pearce K, Williams SG, Schelbert EB, Macnab A, Miller CA. The utility of cardiovascular imaging in heart failure with preserved ejection fraction: diagnosis, biological classification and risk stratification. Heart Fail Rev. 2021; 26: 661-678.
37. Perone F, Bernardi M, Redheuil A, Mafrica D, Conte E, et al. Role of Cardiovascular Imaging in Risk Assessment: Recent Advances, Gaps in Evidence, and Future Directions. J Clin Med. 2023; 12: 5563.
38. The SCOT-HEART Investigators. Coronary CT Angiography and 5-Year Risk of Myocardial Infarction. N Engl J Med. 2018; 379: 924-933.
39. Yoon SH, Kim E, Jeon Y, Yi SY, Bae HJ, et al. Prognostic Value of Coronary CT Angiography for Predicting Poor Cardiac Outcome in Stroke Patients without Known Cardiac Disease or Chest Pain: The Assessment of Coronary Artery Disease in Stroke Patients Study. Korean J Radiol. 2020; 21: 1055.
40. Bienstock S, Lin F, Blankstein R, Leipsic J, Cardoso R, et al. Advances in Coronary Computed Tomographic Angiographic Imaging of Atherosclerosis for Risk Stratification and Preventive Care. JACC Cardiovasc Imaging. 2023; 16: 1099-1115.
41. Patel J, Pallazola VA, Dudum R, Greenland P, McEvoy JW, et al. Assessment of Coronary Artery Calcium Scoring to Guide Statin Therapy Allocation According to Risk-Enhancing

Factors: The Multi-Ethnic Study of Atherosclerosis. JAMA Cardiol. 2021; 6: 1161.

42. Grandhi GR, Mirbolouk M, Dardari ZA, Al-Mallah MH, Rumberger JA, et al. Interplay of Coronary Artery Calcium and Risk Factors for Predicting CVD/CHD Mortality. JACC Cardiovasc Imaging. 2020; 13: 1175-1186.
43. Mach F, Baigent C, Catapano AL, Koskinas KC, Casula M, et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. Eur Heart J. 2020; 41: 111-188.
44. Moore R, Jensen M, Hatch J, Duranczyk I, Staats S, et al. Showing up: The Importance of Class Attendance for Academic Success in Introductory Science Courses. Am Biol Teach. 2003; 65: 325-329.
45. Williams GJ, Al-Baraikan A, Rademakers FE, Ciravegna F, Van De Vosse FN, et al. Wearable technology and the cardiovascular system: the future of patient assessment. Lancet Digit Health. 2023; 5: 467-476.
46. De Lepper AGW, Buck CMA, Huberts W, Van De Vosse FN, Dekker LRC, et al. From evidence-based medicine to digital twin technology for predicting ventricular tachycardia in ischaemic cardiomyopathy. J R Soc Interface. 2022; 19: 20220317.
47. Tasmurzayev N, Amangeldy B, Imanbek B, Baigarayeva Z, Imankulov T, et al. Digital Cardiovascular Twins, AI Agents, and Sensor Data: A Narrative Review from System Architecture to Proactive Heart Health. Sensors. 2025; 25: 5272.
48. Lee Y, Park K, Lee JH, Lee SH. AI prediction models with omics data utilization for atherosclerosis: A systematic scoping review and meta-analysis. Atherosclerosis. 2026; 416: 120747.
49. Carson AP, Lewis CE, Jacobs DR, Peralta CA, Steffen LM, et al. Evaluating the Framingham hypertension risk prediction model in young adults: the Coronary Artery Risk Development in Young Adults (CARDIA) study. Hypertens Dallas Tex. 2013; 62: 1015-1020.
50. SCORE2-Diabetes Working Group and the ESC Cardiovascular Risk Collaboration. SCORE2-Diabetes: 10-year cardiovascular risk estimation in type 2 diabetes in Europe. Eur Heart J. 2023; 44: 2544-2556.
51. Nordestgaard LT, Magni P, Sopić M, Chemaly M, Matic L, et al. Multiomics for Risk Stratification in Atherosclerotic Cardiovascular Disease. Circ Genomic Precis Med. 2026; 19.
52. Baragetti A, Mattavelli E, Grigore L, Pellegatta F, Magni P, et al. Targeted Plasma Proteomics to Predict the Development of Carotid Plaques. Stroke. 2022; 53.
53. Giral P. Targeted proteomics improves cardiovascular risk prediction in secondary prevention: the impact of statin treatment. Eur Heart J. 2022; 43: 3811-3811.
54. Møller AL, Vasan RS, Levy D, Andersson C, Lin H. Integrated omics analysis of coronary artery calcifications and myocardial infarction: the Framingham Heart Study. Sci Rep. 2023; 13: 21581.
55. Westerman K, Fernández-Sanlés A, Patil P, Sebastiani P, Jacques P, et al. Epigenomic Assessment of Cardiovascular Disease Risk and Interactions With Traditional Risk Metrics. J Am Heart Assoc. 2020; 9: 015299.
56. Yousefi PD, Suderman M, Langdon R, Whitehurst O, Davey Smith G, et al. DNA methylation-based predictors of health: applications and statistical considerations. Nat Rev Genet. 2022; 23: 369-383.
57. Vanhaverbeke M, Attard R, Bartekova M, Ben-Aicha S, Brandenburger T, et al. Peripheral blood RNA biomarkers for cardiovascular disease from bench to bedside: a position paper from the EU-CardioRNA COST action CA17129. Cardiovasc Res. 2022; 118: 3183-3197.
58. Northoff BH, Herbst A, Wenk C, Weindl L, Gäbel G, et al. Circular RNAs increase during vascular cell differentiation and are biomarkers for vascular disease. Cardiovasc Res. 2025; 121: 405-423.
59. Helgason H, Eiriksdottir T, Ulfarsson MO, Choudhary A, Lund SH, et al. Evaluation of Large-Scale Proteomics for Prediction of Cardiovascular Events. JAMA. 2023; 330: 725.
60. Neves LS, Saraiva F, Ferreira R, Leite-Moreira A, Barros AS, Diaz SO. Metabolomics and Cardiovascular Risk in Patients with Heart Failure: A Systematic Review and Meta-Analysis. Int J Mol Sci. 2024; 25: 5693.
61. Ofori S, Wachukwu C. Awareness and attitudes towards total cardiovascular disease risk assessment in clinical practice among physicians in Southern Nigeria. Niger Health J. 2026; 16.
62. Nduka SO, Emeneka OC, Nduka IJ, Onunkwo JC. Cardiovascular risk screening: a 10-year prediction cross-sectional study in a Nigerian agrarian community. Pan Afr Med J. 2024; 47.
63. Adje DU, Oparah AC, Megbolu T. Cardiovascular risk assessment in Community Pharmacies in Warri, Nigeria. J Pharm Bioresour. 2021; 17: 105-111.
64. Mbau L, Fourie JM, Scholtz W, Scarlatescu O, Nel G, et al. PASCAR and WHF Cardiovascular Diseases Scorecard project. Cardiovasc J Afr. 2021; 32: 161-207.
65. Bitton A, Gaziano TA. The Framingham Heart Study's impact on global risk assessment. Prog Cardiovasc Dis. 2010; 53: 68-78.
66. Chiu BK, Solez K, Sergi CM. Digital Pathology for E-Learning and Digital Education – A Review. J Inf Technol Appl Educ. 2014; 3: 164.
67. Parizad R, Hatwal J, Brar A, Desai R, Batta A, et al. Artificial Intelligence for Cardiovascular Risk Prediction: An Umbrella Review of Applications and Translational Challenges. Vasc Health Risk Manag. 2026; 22: 1-19.
68. Chong B, Jayabaskaran J, Jauhari SM, Chan SP, Goh R, et al. Global burden of cardiovascular diseases: projections from 2025 to 2050. Eur J Prev Cardiol. 2025; 32: 1001-1015.