Precision Medication 3 (2026) 100078

Contents lists available at ScienceDirect

Precision Medication

journal homepage: www.keaipublishing.com/en/journals/precision-medication/

Integrating precision medicine and artificial intelligence to prevent cardiotoxicity in cardiovascular drug therapy

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ARTICLE INFO

Keywords:
Cardiovascular disease
Precision medicine
Pharmacogenomics
Artificial intelligence
Multi-omics
Personalized therapy

ABSTRACT

Precision medicine refers to tailoring therapeutic interventions to an individual's genetic, molecular and phenotypic characteristics, while multi-omics integrates genomics, proteomics and metabolomics data to provide a systems-level view of disease. Together with artificial intelligence (AI) driven predictive modeling, these approaches enable early identification of cardiotoxic risk and optimization of drug therapy in cardiovascular diseases. The present review explores the possibility of precision medicine to overcome cardiotoxicity associated with conventional cardiovascular disease (CVD) treatments. It highlights the integration of biomarker-driven therapies, pharmacogenomics, and multi-omics technologies to improve therapeutic efficacy and minimize the risk of adverse drug reactions. Additionally, the review assesses the emerging contributions of artificial intelligence (AI) and network medicine in improving cardiovascular diagnostics and developing personalized treatment regimens. The discovery of genomics, proteomics, metabolomics into cardiovascular research has significantly increased our understanding in disease etiology and variability in response of drug. Furthermore, AI-driven predictive models and machine learning algorithms play key role in minimizing clinical risk and support precision-guided decision, ultimately enhance patient outcomes. The advancement in omics technology, AI and customized therapy is expected to revolutionize cardiovascular care, despite current challenges in clinical implementation. The integration of cutting-edge approaches into standard clinical practice would maximize treatment effectiveness and guarantee patient safety.

Introduction

The cardiovascular diseases (CVDs) are one of the leading causes of morbidity and death globally and responsible for significant global health burden, highlighting the urgent need for innovative approaches for risk assessment and treatment. Population-based models are used in traditional clinics to predict disease progression, evaluate cardiovascular risk, and advise on treatment options. However, the intrinsic variability present in cardiovascular pathophysiology is affected by intricate interaction of environmental, genetic, molecular and lifestyle factors.[1] The precision medicine is very helpful in driving transformative changes by customizing therapy based on person's genetic, phenotypic and molecular, characteristics. The advancement in omics technologies such as genomics, proteomics and metabolomics have empowered clinicians and researchers to improve diagnostic and therapeutic approaches away from population based towards personalized care.[2,3] However, the integration of artificial intelligence (AI) and machine learning in cardiovascular therapy has facilitated the discovery of novel diseases subtypes, improved drug efficacy and optimized individualized treatment strategies.[4,5]

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https://doi.org/10.1016/j.prmedi.2026.100078
Received 7 July 2025; Received in revised form 6 December 2025; Accepted 11 December 2025
Available online 25 March 2026

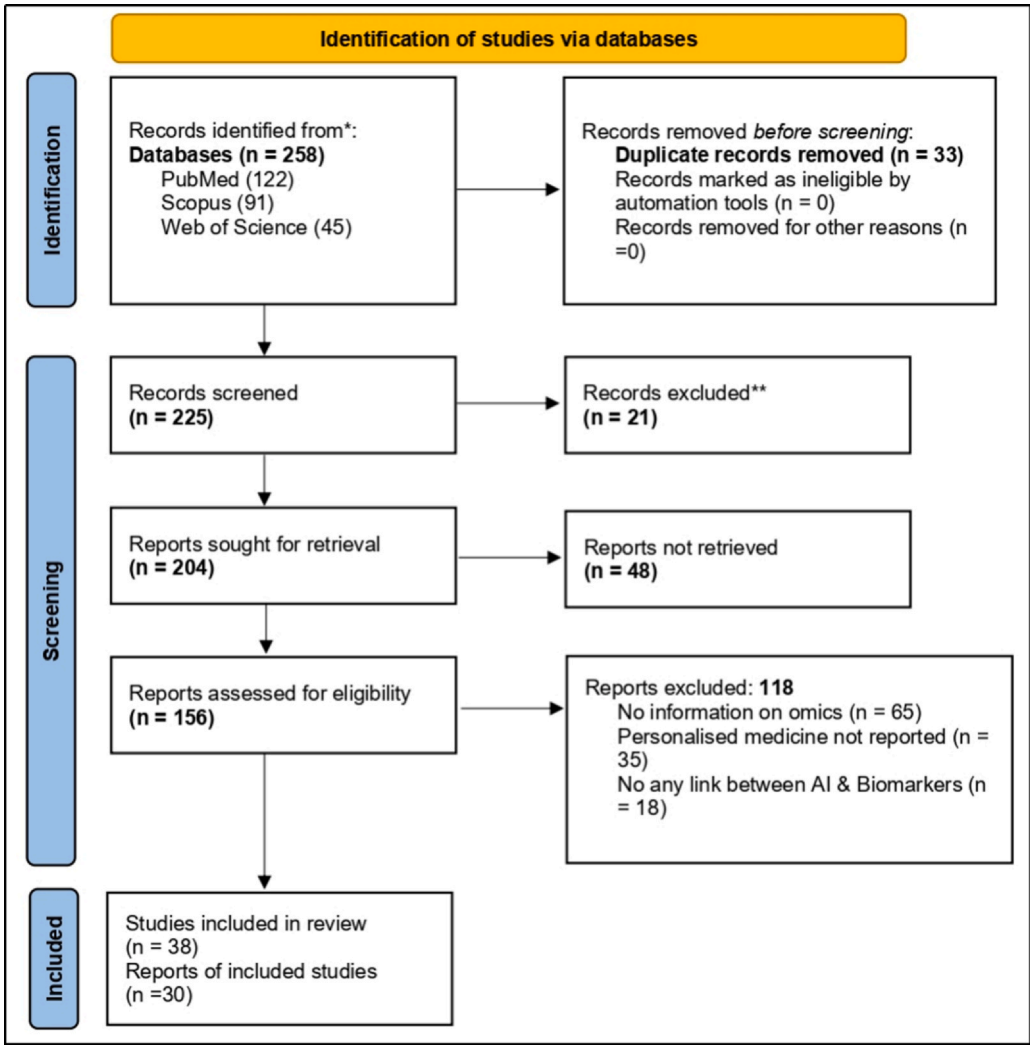

Fig. 1. A PRISMA flowchart illustrate the screening and selection process, including the number of studies identified, screened, excluded and included. (Source: Page MJ, et al# BMJ 2021;372:n71.[17]).

Cardiotoxicity is clinically observed during conventional treatment with cardiovascular medicines such as β-blockers, ACE inhibitors, ARBs, diuretics, statins, and antithrombotic or antiplatelet agents. These drugs cause cardiotoxicity through several mechanisms including the induction of arrhythmia, myocardial injury, imbalance in hemodynamics and electrolysis homeostasis as well as interaction between drugs.[6,7] Genetic polymorphisms that affect pathways such as β-adrenergic signaling, angiotensin converting enzyme (ACE) activity and the metabolism of statins elucidate the variability observed in patient responses.[8,9] This indicates that prescribing medicines informed by genomics data may augment both safety and therapeutic efficacy. The advancement in precision medicine plays crucial role in minimizing the cardiotoxic risk associated with the commonly prescribed cardiovascular medicines.[10–12] Development of novel pharmacogenomics-guided therapeutic strategies tailored to an individual's genetic profile has demonstrated potential in overcoming these challenges. By utilizing genetic information, clinicians can predict patients specific drug responses in better way, thereby reducing the dependence on trial-and-error prescriptions and maximizing therapeutic outcomes. The discovery of pharmacogenomics has been utilized in the clinical uses of anticoagulants like warfarin and antiplatelet agents like clopidogrel. This has demonstrated the capacity of personalized medicine in mitigating the risk of adverse cardiovascular events.[13,14]

Furthermore, researchers are able to identify minute genetic and molecular markers that are responsible for the development of CVDs by integrating multi-omics profile and real-world clinical data. These advancements provide breakthrough in insightful impact of precision medicine on remodelling cardiovascular care.[15,16] This review uniquely focuses on the integration of pharmacogenomics, multi-omics and AI-assisted analytics to design patient-specific cardiovascular therapies that minimize cardiotoxicity. Unlike previous reviews, it emphasizes mechanistic and translational insights that connect molecular profiling with clinical risk prediction. A systematic literature search was conducted in accordance with PRISMA 2020 guidelines. We searched PubMed, Scopus and Web of Science for articles published between January 1, 2010 and February 28, 2024; The following Boolean search strings were applied (adapted to database-specific syntax): PubMed ("cardiotoxicity"[Title/Abstract] OR "cardiac toxicity"[Title/Abstract]) AND ("precision medicine"[Title/Abstract] OR "personalized medicine"[Title/Abstract] OR "personalized therapy"[Title/Abstract]) AND ("artificial intelligence"[Title/Abstract] OR "machine learning"[Title/Abstract] OR "deep learning"[Title/Abstract]) AND ("pharmacogenomics"[Title/Abstract] OR "multi-omics"[Title/Abstract] OR "genomics"[Title/Abstract] OR "proteomics"[Title/Abstract] OR "metabolomics"[Title/Abstract]). Scopus (TITLE-ABS-KEY): TITLE-ABS-KEY ("cardiotoxicity" OR "cardiac toxicity") AND TITLE-ABS-KEY("precision medicine" OR "personalized medicine" OR "personalized therapy") AND TITLE-ABS-KEY("artificial intelligence" OR "machine learning" OR "deep learning") AND TITLE-ABS-KEY("pharmacogenomics" OR "multi-omics" OR "genomics" OR "proteomics" OR "metabolomics").

Web of Science (Topic): TS = ("cardiotoxicity" OR "cardiac toxicity") AND TS = ("precision medicine" OR "personalized medicine" OR "personalized therapy") AND TS = ("artificial intelligence" OR "machine learning" OR "deep learning") AND TS = ("pharmacogenomics" OR "multi-omics" OR "genomics" OR "proteomics" OR "metabolomics"). We selected PubMed for its comprehensive biomedical and clinical coverage and MeSH-based indexing, Scopus for its broad journal coverage and advanced citation analytics and Web of Science for curated multidisciplinary indexing and robust cross-disciplinary citation mapping; combined, these databases maximize retrieval of relevant peer-reviewed literature across basic, translational, and clinical domains. Searches were limited to English-language, peer-reviewed articles. Records were imported into Endnote, duplicates were removed, and titles/abstracts were screened independently by two authors; disagreements were resolved by consensus or by consulting a third author. Full-text screening was performed to determine final eligibility. The selection process (identification, screening, eligibility and inclusion) is presented in the PRISMA 2020 flowchart (Fig. 1).

Population Averages and the Shift Toward Precision Analytics in CVDs

Traditional cardiovascular research and clinical practice have long relied on population-based averages to define diagnostic thresholds, treatment guidelines, and risk assessments. While this approach has supported standardization, it also oversimplifies the biological and phenotypic heterogeneity among patients. Individuals within the same population may share similar cholesterol or blood pressure levels but differ profoundly in their genetic architecture, metabolic profile, or drug response, leading to highly variable therapeutic outcomes.[18,19] Precision medicine challenges this paradigm by moving beyond the “average patient” model and recognizing that cardiovascular disease exists along a continuum of phenotypic diversity. Instead of relying solely on group-based distributions, precision cardiology incorporates *multi-omics* data, imaging biomarkers, and lifestyle variables to define individualized risk profiles. Recent advances in machine learning and artificial intelligence (AI) further enhance this framework by identifying hidden patterns and clustering patients with similar molecular or clinical signatures.[20–22] For instance, AI-based unsupervised clustering has revealed distinct phenotypic subgroups among patients with chronic heart failure groups that traditional risk models failed to distinguish. These analytical approaches enable more precise prediction of disease progression and tailored interventions. Thus, by integrating AI-driven analytics with precision medicine, cardiology is evolving from population-level generalizations toward individualized, data-informed decision-making that reflects the full complexity of human variability.[23]

Cardiovascular Pharmacology and Multi-Omics Approaches in Cardiotoxicity

Cardiovascular pharmacology is the branch of pharmacology that focuses on the study of drugs affecting the heart and vascular system. It includes the mechanisms of action, therapeutic uses and side effects of medications used to treat cardiovascular conditions such as hypertension, heart failure, arrhythmias, coronary artery disease and thrombosis. While the multi-omics refers to the integrated analysis of multiple layers of biological data including genomics (DNA), transcriptomics (RNA), proteomics (proteins), metabolomics (metabolites) and epigenomics (epigenetic modifications) to obtain a comprehensive understanding of biological systems, disease mechanisms, and treatment responses.[24] Clinical trials are essential for evaluating and forecasting medication results because they use highly representative data sets that change throughout the course of the investigations. However, variables from the environment, individual-specific variances, and genetic variants are still important enough to cause a considerable number of adverse events and treatment failures. Precision medicine is an evolving approach that promotes the customization of therapy, guided by local regulations and guidelines based on novel biomarkers and gene targets.[25,26] Several examples illustrate how drug reaction may be influenced by variation in genes and DNA.[27,28] For example, there is considerable individual variation in the effects of warfarin (an anticoagulants with limited therapeutic window). Research has documented variability in warfarin dosing requirements based on patient genotypes, particularly SNPs in the CYP2C9 and VKORC1 genes. Additionally, genetic variations that result in variations in the responsiveness to β-blockers (ADRB1, GRK4, ADRB2, GRK5), calcium channel blockers (CACNA1C, CACNB2), diuretics (ADD1, NEDD4L, NPPA), and angiotensin-converting enzyme inhibitors (AGTR1, ACE), have been found.[29,30] Clopidogrel (an antiplatelet drug), also exhibits considerable inter-individual variability, leading to a subset of non-responders. This variation is frequently ascribed to CYP2C19 dysfunctional alleles, which are connected to decreased drug responsiveness, whereas CYP2C19*17 hyperactive alleles have been attributed to an elevated threat of blood loss. Genome-guided dosage for warfarin, that includes assigning dosages determined by CYP2C9 and VKORC1 genotyping, has been supported by clinical trials like EU-PACT (European Pharmacogenetics and Anticoagulant Therapy-Warfarin) and COAG (Clarification of Optimal Anticoagulation through Genetics). With the introduction of future-oriented care that integrates improved profiling for more accurate illness categorisation and treatment, precision medicine.[31–33]

Cardiovascular research is becoming increasingly integrated into the digital, a data-driven world made possible by the vast amounts of ecological, physiological, and cellular information produced by several "omics" innovations. Instead of concentrating on the "average patient," medical studies and therapies are moving towards gaining a more thorough understanding of particular people and communities. This paper compares precision medicine's unique features to conventional methods while highlighting the main areas in which it may be used in heart disease, such as predictions, therapies, risk assessment, and diagnosis.[34,35] Physicians can manage cardiovascular illnesses according to each patient's unique proteomic, inherited, metabolic, or symptomatic makeup because of precision medicine. In order to use the emerging inherited, cellular, and metabolic techniques, clinical cardiology is undergoing a transformation change due to the adoption of emerging genetic, cellular, and metabolic techniques. Developing biomarkers such miRNAs, hs troponins, hsCRP and basic fibroblast growth factor (bFGF) have demonstrated significant promise in myocardial infarction by early and more accurate disease detection.[36–38] Recent advances indicate that metabolites like acylcarnitines,[39] fatty acids, and branched-chain amino acids[40] are powerful indicators of cardiac problems and may be used in conjunction with conventional markers such as cholesterol levels and troponin to forecast myocardial infarction or mortality in those with CVDs.[41,42] Similarly, heart failure biomarkers, including succinate, 2-oxoglutarate, alanine, 3-hydroxybutyrate, proline, pseudouridine, isoleucine, acetone, leucine, and creatinine, have demonstrated potential for outcome prediction.[43–45] Additionally, numerous genes were recently discovered that might soon make early risk identification easier. Although genomics presents implementation challenges, it has significantly advanced our understanding of disease variability, risk susceptibility, and treatment responses.[46,47] Future developments in genetic data generation and application tools will likely enable their integration into routine management of common diseases as mentioned in Fig. 2.

Using computerised biology technology, future sequencing and genome-wide association studies have the potential to improve the identification and management of CVD. By characterising mammalian cardiac peptides using mass spectrometry, proteomics may be able to further broaden its use in the treatment of CVD.[48] Transcriptomics provide information on how genes are expressed, and metabolomics is the result of multi-omics attempts to solve cardiovascular diseases at earlier stages. Collectively, “omics” technologies can play a pivotal role in individualizing therapy for cardiac conditions.[49]

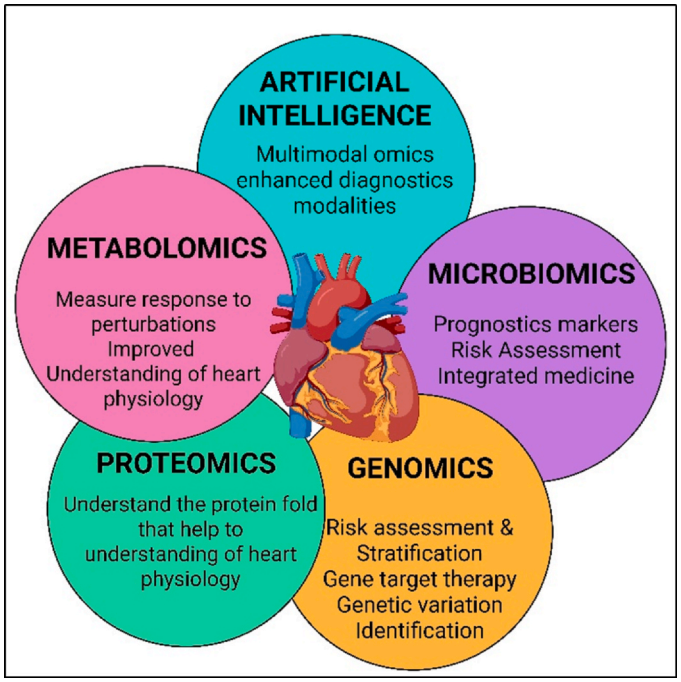

Fig. 2. Key areas of precision cardiology.

Genomics is broadly defined as using genetic information to inform and optimize medical decision-making. Chan and Ginsburg proposed a "human genome toolbox" consisting of the human genome sequence (genomics), gene expression profiles (transcriptomics), proteins (proteomics), and metabolites (metabolomics). Genomics involves studying human genome sequences generated from whole-genome sequencing, single nucleotide polymorphisms (SNPs), and copy number variations (CNVs).[50,51] Transcriptomics focuses on the comprehensive study of RNA expression, encompassing approximately 25,000 transcripts. This includes both messenger RNAs and various types of non-coding RNAs, such as small interfering RNAs and microRNAs (miRNAs). Analysing miRNAs presents challenges due to their non-specific nature, but RNA sequencing plays a pivotal role in transcriptome analysis.[52] Metabolomics is the study of small molecule metabolites in which are non-protein entities are associated with a biological or physiological state. It is believed that there are around 5000 tiny-molecular intermediates in the human metabolic system. In the cardiovascular field, metabolite profiling has been applied to study conditions such as ischemia and coronary artery disease (CAD), providing insights into the metabolic changes that occur in these conditions.[53,54] However, pharmacogenomics investigates how genetic variations influence drug responses, encompassing changes in DNA sequences, chromosomal abnormalities, and epigenetic alterations of chromatin and DNA that do not alter the DNA sequence. Its primary aim is to identify genetic factors responsible for variability in drug responses to enhance drug efficacy and safety.[55] These fields are instrumental in the development of personalized or precision medicine strategies. Clinically, genomic markers are increasingly used for disease risk prediction and treatment selection as shown in Fig. 3. For example, long QT syndrome (LQTS), an autosomal dominant disorder, is connected to changes in twelve distinct susceptible alleles. Looking for these alterations genetically aids in directing therapeutic approaches. Patients with LQTS1 (KCNQ1 mutations) benefit from beta-blockers, while those with LQTS2 (KCNH2 mutations) or LQTS3 (SCN5A mutations) may not respond similarly. Metabolomic and proteomic approaches have also been utilized to differentiate between acute myocardial infarction and unstable angina in patients with acute coronary syndrome.[56,57] Furthermore, differences in platelet activation were found by proteomic evaluation of platelet samples from individuals who had and did not have non-ST-segment elevation. Notably, elevated quantities of the released acidic and cysteine-rich protein were found. The Corus™ CAD test is a genomic tool based on peripheral blood gene expression that has shown an association with the severity of coronary artery disease.[58] Advancements in these fields continue to transform personalized medicine by enabling earlier diagnosis, more targeted treatments, and better disease management. Warfarin therapy remains one of the most well-established examples of pharmacogenomics in clinical practice. It is a commonly prescribed oral anticoagulant with a narrow therapeutic index and considerable inter-individual variability in dose requirements. Genetic polymorphisms in *CYP2C9* and *VKORC1* are the major determinants of this variability, as they respectively regulate warfarin metabolism and vitamin-K epoxide reduction—both critical steps for maintaining therapeutic anticoagulation. Variants that reduce *CYP2C9* enzyme activity or alter *VKORC1* expression substantially influence the drug's effective concentration and safety profile.[59,60] The clinical importance of these findings is underscored by evidence from large genotype-guided trials such as EU-PACT and COAG, which confirmed that integrating *CYP2C9* and *VKORC1* genotyping into dosing algorithms improves the precision of initial dose prediction and reduces adverse outcomes.[61] Despite its success, genotype information explains only 10–20% of overall dose variability, indicating that additional genetic, environmental, and clinical factors contribute to warfarin response heterogeneity. Ongoing pharmacogenomic and multi-omics research aims to integrate these variables into comprehensive prediction models that will further improve anticoagulant safety and efficacy.[62,63]

Personalized Cardiovascular Therapy Using Nanobiotechnology

Artificial intelligence (AI) is playing a transformative role in the advancement of personalized medicine, particularly within the field of cardiovascular therapy. By leveraging machine learning algorithms, deep learning models and data-driven decision-making frameworks, AI enables the extraction of complex patterns from large-scale clinical, genomic, imaging and wearable sensor data. These capabilities facilitate the stratification of patients into distinct subgroups based on individual risk profiles, genetic predispositions, comorbidities and predicted drug responses.[64] For instance, AI can be used to identify phenotypic signatures from electrocardiograms (ECGs), echocardiograms, and cardiac MRI scans to predict adverse events such as arrhythmias or heart failure progression before clinical symptoms manifest. Similarly, machine learning models trained on multi-omics datasets can identify genetic variants or molecular biomarkers associated with variable responses to cardiovascular drugs allowing for the optimization of therapy selection and dosing. In the context of cardiotoxicity, AI-powered predictive tools can flag individuals at high risk of adverse drug reactions based on integrated clinical and molecular profiles, thereby supporting early intervention or alternative treatment choices.[65] Furthermore, AI-enabled clinical decision support systems can assist clinicians in designing tailored treatment plans that minimize adverse effects while maximizing therapeutic efficacy. As these technologies continue to evolve, the integration of AI into cardiovascular care promises to enhance precision, efficiency, and outcomes by delivering therapies that are not only evidence-based, but also individualized.[66] Nanobiotechnology is an interdisciplinary field that merges nanotechnology with biological and medical sciences to develop innovative diagnostic, therapeutic, and preventive solutions. For cardiovascular diseases (CVDs), nanobiotechnology offers unprecedented opportunities to revolutionize personalized therapy by providing precision-targeted interventions based on individual patient profiles.[67] Nanoparticles (NPs) are the foundation of nanobiotechnology and are essential in medication delivery due to their ability to precisely target sick tissues, gene therapy, and regenerative medicine. Nanoscale carriers such as liposomes, polymeric nanoparticles, dendrimers and inorganic nanostructures can be engineered to deliver therapeutics directly to damaged myocardial tissue, inflamed vascular sites or

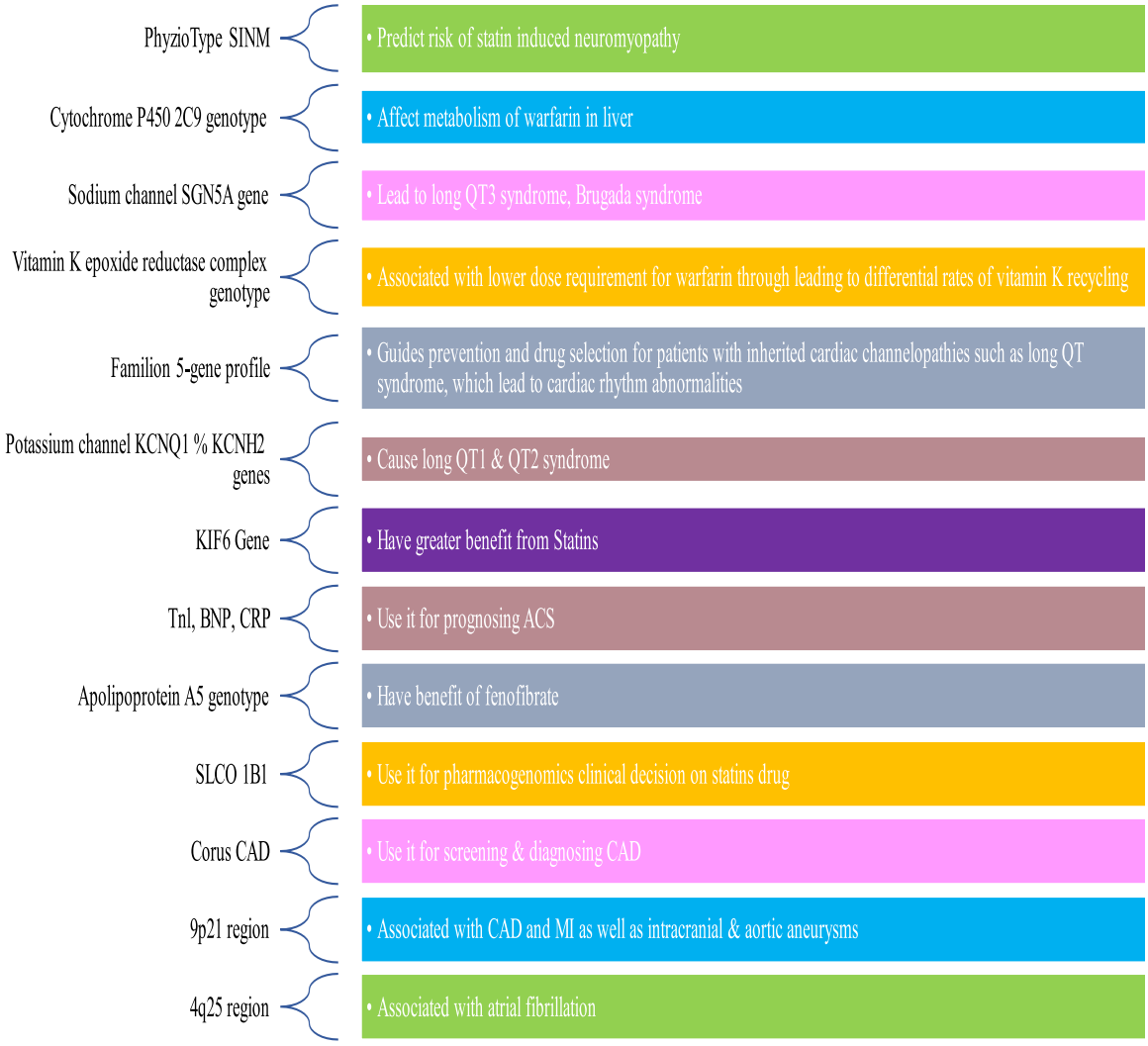

Fig. 3. Illustrations of genomic biomarkers used clinically in CVDs.

atherosclerotic plaques with high precision and minimal systemic toxicity. Moreover, AI can be used to optimize nanoparticle design by predicting interactions between nanocarriers and biological targets based on material properties, biodistribution profiles, and patient-specific variables. Integrated AI–nanotechnology platforms also enable the development of "smart" theragnostic systems—nanoparticles that combine diagnostics and therapy—allowing for real-time monitoring of treatment efficacy and adjustment of dosing strategies in a closed-loop fashion.[68] A wide variety of nanoparticles are employed in CVD therapy, each possessing distinct physicochemical characteristics. Among them, liposomes are spherical vesicles composed of phospholipid bilayers that are able to encapsulate both hydrophilic and lipophilic therapeutic agents. Solid lipid nanoparticles (SLNs) are another lipid-based approach, consisting of solid lipids that provide good biocompatibility and durability, making them especially efficient for delivering poorly soluble cardiovascular medicines. Nanobiotechnology also holds promise for repairing damaged cardiac tissue following myocardial infarction.[69] Combining stem cell-based therapies with nanomaterials can enhance myocardial regeneration. Nanofibers, such as electrospun nanofibers, provide a scaffold that mimics the extracellular matrix (ECM), promoting stem cell adhesion and differentiation. Nanohydrogels, which are injectable hydrogels loaded with growth factors or stem cells, localize and sustain therapeutic effects at the injury site. Magnetic nanoparticles can be guided by magnetic fields to the site of myocardial injury, improving localization and retention of therapeutic agents.[70] Tailoring nanomaterials based on a patient's immune profile and extent of myocardial damage enhances therapy precision.[71] However, integrating AI can help analyze biomarker profiles and predict the most effective nanobiotechnology-based therapies.[72] Nanobiotechnology-based personalized therapy has the potential to revolutionize the treatment of cardiovascular diseases. By enabling targeted, biomarker-driven interventions, nanobiotechnology can improve therapeutic outcomes while minimizing side effects.[73,74] As research progresses, this field is poised to play a pivotal role in the future of cardiovascular medicine.

Advancements in Cardiovascular Medicine Using Big Data and Network Medicine

Network medicine, defined as an emerging discipline that applies network science—particularly protein–protein interaction and molecular interaction networks—to understand disease mechanisms, classify subtypes, and guide precision therapies. It is high level analytical framework that integrates genomics, proteomics, and clinical phenotypes into a comprehensive, systems-based perspective. This network approach utilizes interactome (an extensive network of physical protein-protein interaction - PPIs) to map disease specific subnetworks or modules. Each disease is associated with unique molecular subnetworks and for individual patients, personalized PPIs network (reticulotype), are constructed by mapping their genetic variants on disease specific

network. This personalized PPIs network mapping supports the development of targeted therapies by targeting abnormal reticulotype to restore normal network dynamics and enhance clinical outcome. This analytical approach is useful for revealing the molecular mechanism underlying functional subtypes of complex diseases.[75,76] Network medicine has been used to map fibrosis-related endophenotype network, known as fibrosome. This network integrates PPIs based on specific collagen functions and has been assessed in models of wound healing and pulmonary arterial hypertension (PAH), representing adaptive and pathological forms of fibrosis. The network has been further enhanced to emphasize the regulatory role of aldosterone, a pro-oxidant and pro-fibrotic hormone implicated in both adaptive and pathogenic fibrosis.[77] Menche *et al.* (2015) mapped disease modules within the human interactome and demonstrated how molecular overlap can distinguish mechanistic subgroups across complex disorders, including cardiovascular phenotypes.[78] More recently, Cheng *et al.* (2019) employed PPI networks to stratify patients with coronary artery disease into distinct molecular subtypes, which were associated with differential prognosis.[79] These findings provide empirical support for our assertion that PPI network analysis holds promise in identifying clinically relevant cardiovascular disease subtypes. Recent work directly applying network and PPI analysis to drug-induced cardiac injury supports the claim that interactome approaches can identify mechanistic modules relevant to cardiotoxicity. Proteomic and transcriptomic studies of anthracycline/doxorubicin cardiotoxicity have constructed PPI networks to identify hub proteins and subnetworks implicated in myocardial injury, thereby highlighting candidate molecular subtypes and therapeutic targets. For example, a translational proteomics study of anthracycline cardiotoxicity constructed a cardiotoxicity-associated PPI network to identify differentially expressed hub proteins and pathways altered by anthracycline exposure. Complementary transcriptomic analyses of doxorubicin-treated cardiac models have similarly used PPI and clustering methods to reveal gene modules associated with cardiomyocyte injury and immune-related responses. Moreover, integrative network analyses and weighted gene co-expression (WGCNA) studies have pinpointed hub genes and modules that correlate with anthracycline-induced cardiomyopathy phenotypes. Together, these empirical PPI and network studies demonstrate that interactome-based stratification can reveal biologically meaningful modules relevant to drug-induced cardiotoxicity; where direct clinical subtype classification is still emerging, we explicitly frame network-derived subtype discussion as a promising translational direction.[80–83] Expanding on these findings, recent studies have demonstrated how PPI-based systems pharmacology directly contributes to the prevention of cardiotoxicity. Zhao et al. (2023) utilized PPI mapping and network topology analysis to identify Nrf2, TNF, and IL6 as central hub nodes mediating doxorubicin-induced oxidative injury, suggesting that modulation of these pathways could attenuate cardiomyocyte damage.[84] Similarly, Sabry et al. (2025) emphasized that explainable AI (XAI) approaches integrated with genomic, transcriptomic, and metabolomic data can identify novel therapeutic targets and repurpose drugs for myocardial infarction and heart failure, underscoring the translational potential of network-driven strategies in precision cardiology.[85] In a recent multi-omics network reconstruction, Liu et al. (2025) integrated transcriptomic and metabolomic analyses with network proximity modelling to identify repurposable drugs for septic cardiomyopathy, a severe cardiac complication of sepsis. Their study revealed that acetaminophen and pyridoxal phosphate significantly improved cardiac function in vivo by modulating inflammatory and metabolic pathways, respectively.[86] Collectively, these examples demonstrate that network medicine is not purely descriptive but translational, providing a data-driven framework for identifying cardiotoxicity mechanisms, prioritizing therapeutic targets, and repurposing existing compounds for cardiac protection. By linking PPI-based molecular signatures with phenotypic outcomes, such approaches accelerate the movement from mechanistic insight to clinical intervention, aligning with the principles of precision cardiovascular therapy. The computational analysis employing betweenness centrality, a measure of node importance in a network, identified the Cas protein NEDD9 as crucial regulator in the transition of fibrosis phenotype. Notably, oxidative post-translational modification of NEDD9 at Cys18 was identified as a novel mechanism that promotes pathogenic collagen synthesis, a critical pathological feature in PAH. These findings highlight the potential of network medicine to shift from reductionist approaches to holistic methodologies in elucidating the genetic, epigenetic, and clinical phenotype (GECP) relationship. Such comprehensive strategies enable the identification of novel therapeutic targets and biomarkers for precision medicine.[87,88] The diversity in post-transcriptional mechanisms across endophenotypes in PAH further underscores the utility of network medicine. Initial investigations of microRNA networks identified miR-21 as a pivotal regulator of pathogenic signaling in PAH. Subsequent research has revealed that the miR-130/301 family modulates multiple PPI pathways associated with inflammation, vasomotor tone, apoptosis, and hypoxic responses.[89] Additionally, miR-34a-3p has been shown to regulate mitotic fission, linking epigenetic regulation to disrupted cellular metabolism in PAH. These microRNAs may drive vascular remodelling and morphological changes through their interactions with endothelin-1, vasoactive hormones, or hypoxic stimuli. Although significant progress has been made, more empirical data is needed to fully elucidate the interplay between microRNAs, post-transcriptional mechanisms, and genetic predisposition in complex vascular pathologies, including the development of plexogenic vascular lesions in PAH. Such insights could lead to the development of new therapeutic modalities that target microRNA-mediated signaling pathways.[90]

Role of artificial intelligence (AI) and deep learning in CVDs

By using several layers of artificial neural networks to automatically produce recommendations from datasets used as training grounds, deep learning emulates how the human brain operates. It has gained significant attention in AI due to its rapid advancements and promising applications. This approach is highly effective in image recognition, such as facial recognition on social media platforms and image searches on search engines. Additionally, deep learning holds potential for cardiovascular (CV) imaging, including techniques like 2D and 3D speckle-tracking echocardiography (STE), angiography and cardiac magnetic resonance imaging. A key advantage of deep learning is its ability to perform unsupervised learning tasks, such as identifying novel drug-drug interactions, without requiring labelled data. Deep-learning algorithms enhance the capability of real-time CV imaging by improving spatial and temporal resolution, which may lead to better patient care and reduced healthcare costs.[91] Recently, deep learning has been applied in CV medicine, particularly in imaging. Neural network algorithms used in deep learning include convolutional neural networks (CNNs), recurrent neural networks (RNNs) and deep neural networks. CNN models have been successfully used to predict cardiac volumes in magnetic resonance imaging, while RNNs are widely employed in image captioning and language translation. Studies have demonstrated that RNNs can predict heart failure months before clinical diagnosis, outperforming traditional supervised machine-learning models.[92] For example, recent studies have provided concrete evidence of AI's capacity to predict drug-induced cardiotoxicity. Zhu et al. (2022) developed a convolutional neural network (CNN) that analyzed serial echocardiograms from patients receiving anthracycline therapy; the model detected subclinical left ventricular dysfunction with an AUC of 0.92, outperforming conventional clinical scoring.[93] Yagi et al. (2024) employed a machine-learning ensemble model integrating ECG-derived features with clinical parameters to identify early cardiac dysfunction in cancer patients treated with anthracyclines, enabling individualized cardioprotective interventions.[94] Similarly, Wang et al. (2024) developed a deep-learning model trained on cine and late-gadolinium–enhanced cardiac magnetic resonance (CMR) images to

automatically screen and diagnose multiple cardiovascular diseases, achieving AUC values above 0.98 across internal and external datasets. The model identified subtle myocardial abnormalities—often preceding measurable ejection-fraction decline—highlighting the potential of AI-enabled CMR for early detection and risk stratification of heart-failure progression.[95] Additionally, in the work by Agibetov *et al.* (2021), a CNN was trained on 502 CMR scans (amyloidosis cohort: n = 82). The model used 10-fold cross-validation. It achieved ROC AUC = 0.96, sensitivity = 94%, specificity = 90%. This level of detail (dataset size, split method, performance metrics) is included here to allow evaluation of generalizability and reliability.[96] In a more recent study, Paciorek et al. (2024) applied CNNs to T1-mapping and late gadolinium enhancement (PSIR) images from 200 subjects (137 with cardiac pathologies and 63 controls), reporting accuracies of 88% for PSIR and 70% for T1-mapping sequences.[97] Similarly, a CNN model termed Fibrosis Net demonstrated a classification accuracy of 96.05% in detecting myocardial fibrosis in ischemic cardiomyopathy, with an F1-score of 96.54%.[98] These examples highlight the versatility and diagnostic potential of CNN-based models in the cardiac MRI domain, providing a reproducible foundation for future AI-driven cardiotoxicity screening. Furthermore, deep learning has demonstrated superiority over conventional machine-learning approaches, such as support vector machines (SVMs), by leveraging multiple layers and complex transformations instead of being restricted to just two layers, as seen in SVM. In medical applications, deep neural networks have been utilized to classify electrocardiogram (ECG) signals, achieving an impressive accuracy of approximately 99% in distinguishing between normal, abnormal, and life-threatening conditions.[99] Deep learning has the capability to perform complex tasks without human intervention across various industries. Its applications range from self-driving technology and strategic game playing to generating mathematical textbooks, analyzing scientific literature to answer questions, and interpreting visual content in movies.[100] Additionally, machine vision software integrated into cameras, smartphones, and robots leverages deep learning for enhanced functionality. In the field of cardiovascular (CV) medicine, deep learning offers several promising applications.[101] Firstly, unsupervised deep learning can aid in uncovering novel risk factors for scoring systems or enhance existing models by incorporating hidden variables. Secondly, it can classify new genotypes and phenotypes associated with diverse cardiovascular diseases, such as heart failure with preserved ejection fraction, hypertension, pulmonary hypertension, and cardiomyopathy.[102] Thirdly, automatic deep learning algorithms are able to evaluate the possibility of attack and haemorrhage by optimizing the balance between scoring systems like CHA_2DS_2-VASc and HAS-BLED, which evaluate hypertension, renal and abnormalities in liver functioning, history of fatal strokes, risk of haemorrhage age, variable worldwide normalised ratios, medication use, and alcohol intake.[103,104] Furthermore, deep learning can assist in finding other stroke risk indicators, such anomalies in the left atrial appendage, left atrial strain identified by cardiac echocardiography, and immediate risk information via wearable technology.[105] These insights can be integrated into updated anticoagulant therapy models. Lastly, deep learning can be used to analyze enables electrocardiogram (ECG) patterns to prediction of left ventricular ejection fraction and can estimate coronary calcium scores using echocardiographic data.[106,107]

Overcoming implementation challenges for Precision Cardiology and AI-Driven Care

Despite the clear potential of pharmacogenomics, multi-omics and AI to reduce cardiotoxicity, multiple implementation barriers remain. These include the cost of sequencing and high-dimensional assays, limited access to testing in low-resource settings, data fragmentation and lack of interoperable clinical-omics infrastructures, regulatory uncertainty for AI/ML-based decision tools, clinician unfamiliarity with genomic interpretation and unclear reimbursement pathways. To move from promise to practice, pragmatic and coordinated solutions are required across technical, regulatory, economic and organizational domains.

Reducing cost and improving access

Centralization and scale are powerful levers for lowering per-sample costs: regional or national sequencing hubs and shared biobanking facilities can provide high-quality multi-omics assays at lower marginal cost than distributed small-volume labs. Public–private partnerships, philanthropic consortia, and pooled purchasing agreements for reagents and platforms can further reduce costs. Tiered testing strategies (targeted panels or genotyping as a first step, with reflex full-exome or metabolomics only when indicated) and use of point-of-care genotyping for high-impact variants are pragmatic ways to concentrate resources where they have the most clinical value. Cost-effectiveness analyses and pilot implementation studies (embedded in routine care) are essential to demonstrate clinical and economic benefit and to drive payer coverage decisions.

Regulatory pathways and clinical validation for AI/ML tools

Early and iterative engagement with regulatory agencies, together with prospective clinical validation, is critical. Developers should adopt best practices for model reporting (transparent performance metrics, clear description of training data and population characteristics) and implement post-deployment monitoring to detect performance drift. Hybrid evaluation strategies combining retrospective multi-centre validation with prospective, pragmatic clinical studies can provide strong evidence for safety and efficacy while accelerating adoption. Where possible, aligning model development with recognized frameworks (for example, standards for software as a medical device and the use of reporting checklists) will streamline regulatory review and improve clinician confidence.

Data interoperability, privacy and federated approaches

Integrating clinical and omics data is a technical and governance challenge. Adoption of FAIR (findable, accessible, interoperable, reusable) data standards, common data models, and standardized ontologies will facilitate multisite data aggregation. Where data sharing is limited by privacy or policy, federated learning and privacy-preserving analytics enable model training across distributed datasets without moving raw patient-level data, thereby preserving confidentiality while leveraging large, heterogeneous cohorts. Investment in secure cloud infrastructure and robust consent models is also necessary to support long-term data reuse.

Workforce, clinical workflows and reimbursement. Embedding precision medicine into clinical care requires trained personnel and clear decision workflows. Multidisciplinary teams (cardiologists, clinical geneticists, clinical pharmacologists, data scientists) and molecular case conferences help translate omics and AI outputs into actionable plans. Educational curricula and continuing-education modules for clinicians on genomic literacy and AI interpretability will reduce implementation friction. Finally, engagement with payers to design value-based reimbursement models for example, reimbursement linked to demonstrated reductions in adverse events or hospital readmission will be essential to achieve sustainable clinical adoption.

Collectively, these strategies — when pursued in parallel and supported by pilot demonstration projects, public data commons and harmonized regulatory guidance — can substantially lower barriers to clinical implementation and accelerate the translation of precision, AI-driven approaches into routine cardiotoxicity prevention and care.

Conclusion

The discovery of drugs for cardiovascular problems from a generalized approach to a precision-driven model holds significant implications for improving CVD management. Conventional pharmacological strategies have provided broad insights into disease mechanisms and therapy, but they frequently overlook the molecular and phenotypic diversity that defines individual responses. The emergence of synthetic drug therapy combined with precision medicine is modernizing clinical approaches to reduce cardiovascular risk. A major breakthrough in cardiovascular care is the capacity to classify patients according to their genetic makeup, metabolic profile, and biomarker signatures, allowing for more personalized and effective treatment with minimal adverse effects. Pharmacogenomics-based therapy has already demonstrated success in refining dosage for anticoagulants, lipid-lowering agents, and antihypertensive drugs. In addition, integration of AI-driven models and network medicine is unveiling novel patterns in cardiovascular disease mechanisms, enabling more precise and proactive clinical decision-making.

This review advances the field by synthesizing recent progress in pharmacogenomics, multi-omics integration, and AI-assisted analytics, illustrating how their convergence can mitigate cardiotoxicity and optimize therapeutic outcomes. By connecting molecular insights with predictive computational frameworks, the review emphasizes the translational bridge between bench discoveries and clinical implementation. Collectively, the synthesis highlights that effective cardiotoxicity prevention and cardiovascular care require both biological precision and system-level coordination among pharmacology, data science, and clinical medicine.

However, key research gaps remain. Large-scale prospective validation of AI and deep-learning models for cardiotoxicity prediction is limited; multi-omics datasets often lack standardization and interoperability; and cost and access inequities continue to constrain widespread adoption of precision testing. Further, ethical and regulatory frameworks governing AI-enabled decision tools are still evolving.

Future research should therefore focus on

(i) developing interoperable, privacy-preserving multi-omics and clinical databases; (ii) validating AI-based risk-prediction models across diverse patient cohorts; (iii) identifying novel omics-derived biomarkers of early subclinical cardiotoxicity; and (iv) designing adaptive clinical trials that integrate pharmacogenomic and AI-based decision-support systems.

Despite current limitations, ongoing research and innovation continue to accelerate the transition toward individualized cardiovascular medicine. By bridging these scientific, regulatory, and infrastructural gaps, the next generation of precision and AI-driven strategies can achieve the ultimate goal of cardiology—predictive, preventive, and personalized management of cardiovascular disease.

Declarations

Not applicable.

CRediT authorship contribution statement

Akrati Pathak: Writing – original draft, Visualization, Validation, Software, Resources. **Tarique Anwer:** Writing – original draft, Supervision, Resources, Project administration, Conceptualization. **Ankit Verma:** Writing – original draft, Visualization, Validation, Software, Resources. **Muhanad Alhujaily:** Writing – review & editing, Visualization, Validation. **Mushabbab Alahmari:** Writing – review & editing, Visualization, Software, Resources. **Saeed Alshahrani:** Writing – review & editing, Visualization, Software. **Nawazish Alam:** Writing – review & editing, Validation, Resources. **Yousra Nomier:** Writing – review & editing, Visualization, Validation. **Mohammad Firoz Alam:** Writing – original draft, Validation, Software, Resources.

Ethics approval and consent to participate

Not applicable.

Consent for publication

All authors have read and agreed to the published version of the manuscript and give their consent for publication in this journal.

Data availability

Not applicable.

Funding

Not applicable.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Declaration of Generative AI and AI-assisted technologies in the writing process

Authors have used AI tools such as ChatGPT, OpenAI, DeepSeek, to get assistance in the language editing and improvement of this manuscript.

Acknowledgements

Not applicable.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.prmedi.2026.100078.

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