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Precision Cardiovascular Medicine with Big Data and AI

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Abstract

Cardiovascular disease remains the leading cause of death and disability worldwide. The convergence of big data and artificial intelligence (AI) is reshaping precision cardiovascular medicine through multimodal integration of electronic health records (EHRs), imaging, omics, and wearable data across the care continuum, enabling predictive, diagnostic, therapeutic, and system-level optimization. However, translation into durable clinical benefit remains constrained by evidentiary gaps, implementation complexity, and fragmented governance architectures.

Keywords Artificial intelligence; Big data; Cardiovascular Disease; Multimodal data integration; Precision medicine

1. Introduction

Cardiovascular disease (CVD) remains one of the leading causes of death worldwide, posing a serious threat to human health and quality of life. The global burden continues to escalate, particularly in the context of population aging [1, 2]. Between 1990 and 2019, the number of CVD cases increased from approximately 31.3 million to 55.5 million, and CVD-related deaths rose from 12.1 million to 18.6 million [3]. The burden is projected to increase further, with CVD-related deaths expected to reach 35.6 million by 2050 [4]. CVD is characterized by substantial heterogeneity across genetic background, genotype, and clinical phenotype, which complicates mechanistic understanding and challenges uniform diagnostic and therapeutic strategies [5].

Despite this growing global burden, conventional research methodologies and clinical paradigms remain inadequate to fully address the complexity of CVD [6]. Traditional clinical studies, particularly randomized controlled trials (RCTs), are often constrained by long study durations, high costs, and homogeneous study populations [7], thereby neglecting the intrinsic heterogeneity among patients [8]. Moreover, current diagnostic and classification systems largely rely on single clinical indicators, which not only hinder precision diagnosis and risk stratification but also limit the effectiveness of individualized interventions [9].

In response to these challenges, emerging technologies, particularly artificial intelligence (AI), have rapidly gained traction in medicine, offering novel frameworks and analytical tools for cardiovascular research [10]. Machine learning (ML) and deep learning (DL) have been increasingly applied across the biomedical spectrum, reshaping the landscape of disease investigation [11]. Unlike conventional clinician-driven assessments that depend heavily on experience and subjective judgment, AI demonstrates superior capacity for complex pattern recognition in imaging and clinical data [12].

In summary, the convergence of big data and AI holds immense promise for transforming complex biomedical information into next-generation diagnostic and prognostic models, while advancing both clinical and biological discovery. However, performance gains do not equate to outcome

improvement, real-world value is often constrained by implementation rather than algorithm [13, 14]. This review aims to synthesize recent progress in the application of big data and AI technologies to cardiovascular research and to outline future directions for personalized risk prediction, precision intervention, and whole-cycle disease management.

2. Conceptual Framework of AI Use in Cardiovascular Medicine

Digital technologies have long supported cardiovascular care. However, AI-driven cardiovascular medicine is not equivalent to digitally assisted care. Unlike static technologies, AI is adaptive and interactive, enabling data-intensive models to be embedded into clinical workflows and, in selected settings, to support closed-loop decision support within defined care pathways [15]. These intrinsic characteristics make AI an important enabler of precision cardiovascular medicine, as it enables the integration of heterogeneous data sources to better capture disease heterogeneity and support diagnostic classification, risk stratification, and individualized interventions [16]. Methodologically, AI comprises algorithms that iteratively learn patterns from data to perform recognition, inference, or decision tasks without explicit rule-based programming. ML, the core foundation of medical AI, is commonly categorized into supervised learning (SL), unsupervised learning (UL), and reinforcement learning (RL) [17]. SL learns mappings between inputs and labeled outcomes for classification, regression, and event prediction, whereas UL discovers latent structure in unlabeled data and is widely used in large-scale electronic health records (EHRs) and cohort analyses to identify subgroups [18, 19]. DL, a major branch of ML, uses multi-layer neural networks to learn high-level representations directly from high-dimensional, unstructured data [20]. RL addresses sequential decision-making by learning state-action strategies to optimize long-term objectives, with potential applicability to treatment strategy optimization and dynamic intervention timing [21]. For clinicians, functional positioning along the care pathway is often more practical than algorithm-based taxonomy. This review categorizes the applications of AI in the cardiovascular field into the following four key dimensions. Predictive precision, encompassing early warning of disease risk and trajectory prediction. Diagnostic precision, supporting refined disease identification, staging, and subtyping. Therapeutic precision, involving the individualized timing and benefit-risk

tradeoffs. System-level precision, including remote monitoring, intelligent alerts, and personalized interaction, embedding precision medicine into chronic disease management and prevention.

3. Types and Applications of Big Data in Cardiovascular Disease

CVD is a complex and heterogeneous chronic disorder characterized by considerable variability in pathophysiology and clinical presentation. With the rapid advancement of medical informatics and analytical technologies, big data has substantially expanded the scope and depth of both clinical and translational research, offering unprecedented opportunities for precision cardiovascular medicine [22]. (Figure 1)

3.1 Data Sources and Types

Structured data form the cornerstone of cardiovascular big-data research and typically include EHRs, longitudinal clinical cohorts, laboratory test results, and biomarker profiles [23, 24]. EHRs capture structured information such as demographic characteristics, diagnostic codes, prescriptions, and laboratory values [25]. These datasets comprehensively document patients' clinical trajectories and medical histories, are amenable to standardization, and facilitate model development and risk prediction [26]. Beyond traditional risk factors, EHRs often incorporate biomarkers and medication data—variables that were frequently overlooked in earlier predictive models [27]. Long-term observational cohorts such as the Framingham Heart Study [28] and the UK Biobank [29] provide extensive longitudinal data that underpin analyses of disease natural history and the long-term effects of cardiovascular risk factors.

Unstructured data encompass medical imaging, free-text clinical notes, and data streams from wearable devices. Imaging modalities such as coronary computed tomography (CT), cardiac magnetic resonance imaging (MRI), and echocardiography have become indispensable tools for diagnosis and prognostication. DL algorithms now enable automated detection of coronary lesions and assessment of cardiac function [30, 31]. Natural language processing (NLP) transforms unstructured clinical narratives into structured representations suitable for downstream analysis [32]. The Multi-rater Prism (MrPrism) framework integrates convergent (ConP) and divergent (DivP) prisms through iterative calibration, enabling segmentation self-correction and confidence

modeling under multi-annotator settings [33]. Furthermore, hybrid architectures combining Bidirectional Encoder Representations from Transformers (BERT) with character-level embeddings (CHARACTER-BERT) have enhanced cardiovascular risk factor extraction and improved clinical decision-support systems [34]. Wearable devices continuously record physiological signals, including electrocardiogram (ECG), activity levels, and sleep metrics, providing a foundation for real-time event monitoring [35].

Emerging data sources offer deeper insights into the molecular mechanisms and interindividual variability underlying CVD. Single-cell sequencing, spatial omics, metabolomics, and microbiome profiling provide multidimensional perspectives on disease initiation and progression [36, 37]. Single-cell RNA sequencing and spatial transcriptomics have been employed to construct cellular atlases of the post–myocardial infarction microenvironment, elucidating the functional heterogeneity of distinct cell subpopulations [38-40]. Microbiome research has further revealed the intricate host–microbe interactions that influence cardiovascular health [41]. Metabolomic studies have identified circulating metabolites such as trimethylamine N-oxide (TMAO) as potential biomarkers linked to atherosclerotic risk, with implications for prognosis and therapeutic intervention [42]. In addition, social, behavioral, and environmental exposure data are increasingly integrated into cardiovascular risk models to capture the holistic impact of external determinants on cardiovascular health [43].

3.2 Multimodal Data Integration Technologies

The inherent complexity of CVD and its marked heterogeneity make any single data source insufficient to capture the full spectrum of pathophysiology. Multimodal data integration has therefore emerged as a cornerstone of precision cardiovascular medicine. However, effective integration remains challenging due to cross-modal heterogeneity, variable data quality, and legal and regulatory constraints.

3.2.1 Data Standardization and Interoperability

Data standardization represents the foundation of multimodal data integration, encompassing terminological harmonization, unified data formats, and semantic interoperability [44]. International frameworks such as Fast Healthcare Interoperability Resources (FHIR) and the Common Data

Model (CDM) have been instrumental in enabling cross-platform and cross-institutional data sharing. FHIR provides standardized resources for healthcare data and facilitates efficient exchange via modern web technologies, while CDM provides unified syntactic and semantic structures that enable consistent storage and analysis of heterogeneous datasets [45, 46]. The adoption of the Observational Medical Outcomes Partnership (OMOP)–CDM has further enabled integration of multi-institutional EHR data, supporting standardized and scalable cardiovascular research across centers [47].

3.2.2 Cross-Modal Fusion Approaches

Multimodal fusion integrates imaging, omics, clinical, and behavioral data within unified analytical frameworks, to leverage the complementary strengths of diverse data sources [48]. EHRs provide longitudinal clinical trajectories, imaging captures structural and functional signatures, wearable devices record continuous physiological metrics, genomics reveals inherited susceptibilities, and environmental or lifestyle data contextualize external exposures [49]. Joint multimodal modeling not only identifies latent patterns inaccessible to single modalities but also elucidates genotype–phenotype–function couplings [50]. Recent advances in multi-view learning and attention mechanisms, offering dynamic weighting and contextual representation, have become central to integrative analyses across imaging, genomics, and clinical domains [51].

Depending on the level of integration, three primary fusion strategies are employed in machine learning: early (feature-level), intermediate, and late (decision-level) fusion [52]. Early fusion combines multimodal inputs into a unified feature vector prior to model training, suitable for low-dimensional and well-defined features. Intermediate fusion, also known as joint or middle fusion, merges latent representations across modalities within neural network hidden layers, often leveraging autoencoders or attention modules, to model high-dimensional heterogeneous data effectively [53, 54]. Late fusion aggregates predictions from separate unimodal models at the output stage, which is particularly advantageous for highly diverse biomedical datasets [53]. Selecting an appropriate fusion paradigm according to data structure and research objectives has become a critical step in the design of precision cardiovascular studies. (Figure 2)

3.2.3 Privacy Protection and Secure Data Sharing

Cross-institutional cardiovascular big-data research must balance data utility with individual privacy, typically operating under a three-tier framework of regulation, technology, and governance.

At the regulatory level, the European Union's General Data Protection Regulation (GDPR) mandates compliance with principles such as lawfulness, fairness, and transparency, and data minimization in processing health and genetic data [55, 56]. The U.S. HIPAA Privacy Rule enforces a minimum-necessary standard for disclosure [57]. ISO 25237 outlines pseudonymization protocols to guide de-identification procedures [58].

At the technical level, pseudonymization and anonymization form the foundation for mitigating re-identification risk [59]. Combining removal of direct identifiers with k-anonymity and ℓ-diversity can reduce residual risk through generalization and suppression [60, 61]. Differential privacy adds calibrated noise to preserve statistical validity while ensuring individual confidentiality [62]. Federated learning (FL) has emerged as a practical framework for cross-institutional model training, enabling decentralized learning through parameter sharing without data exchange [63]. Homomorphic encryption and secure multiparty computation further allow encrypted inference on MRI or CT data, including convolutional neural network (CNN) or long short-term memory (LSTM) operations, supporting end-to-end security [64-66].

At the governance level, data sharing typically follows principles of minimal access and tiered authorization, releasing only essential fields to verified entities after rigorous de-identification and semantic obfuscation [67]. Blockchain-based audit trails are increasingly used for tamper-proof traceability, enhancing accountability and regulatory compliance [68].

4. Advances in the Application of AI in Cardiovascular Disease

AI is transitioning from proof-of-concept to selected real-world clinical implementation. In cardiovascular medicine, AI is increasingly used to support risk assessment, imaging interpretation, and therapeutic decision-making along the care continuum. (Figure 3)

4.1 Coronary Artery Disease (CAD)

CAD is a prototypical data-rich disease in which AI is increasingly used to improve phenotyping, risk stratification, and treatment decision support across the diagnostic to therapeutic continuum.

4.1.1 Diagnostic and Phenotypic Precision

Imaging remains the most active field for AI applications in CAD. Early ML models enabled quantitative coronary analysis, with noninvasive fractional flow reserve derived from CT (FFR-CT) representing a major milestone. Subsequent multicenter studies confirmed its ability to refine treatment decisions, reduce unnecessary invasive angiography, and predict short-term cardiovascular events [69]. U.S. Food and Drug Administration (FDA)-approved HeartFlow software further established FFR-CT as a clinically deployable, noninvasive approach [70]. In parallel, new cardiac magnetic resonance (CMR) pulse sequences (e.g., LIBRE) enable free-breathing, high-resolution vascular imaging [71]. The 2021 American College of Cardiology/American Heart Association (ACC/AHA) guideline upgraded coronary computed tomography angiography (CCTA) to a Class I, Level A recommendation for suspected CAD evaluation [72].

DL has markedly enhanced the efficiency and precision of coronary image interpretation. AI algorithms can automatically perform coronary artery calcium (CAC) scoring and 3-D reconstruction of the coronary tree [73, 74]. Super-resolution DL reconstruction (SR-DLR) maintains CCTA image quality with 60% lower radiation dose [75]. Plaque characterization has gained increasing attention, with the SCOT-HEART trial identified low-attenuation plaque volume >4% as a fivefold predictor of myocardial infarction [76]. The Vision Transformer–based DL model PlaqueViT enables automated detection and delineation of coronary plaques and luminal structures without any manual preprocessing or postprocessing steps [77].

For intravascular imaging, DL-based segmentation and classification enable reproducible quantification of vulnerable plaque features. Vergallo et al. developed a fully automated method for fibrous-cap quantification on intravascular optical coherence tomography (IVOCT) images, using DL-based semantic segmentation to precisely localize lipid-rich plaques and dynamic programming to delineate the cap boundary and compute minimal thickness [78]. A DenseNet-121 deep-learning model demonstrated superior accuracy in distinguishing normal, stable, and

vulnerable plaques, exceeding expert-level performance [79]. By integrating the optical flow ratio (OFR) and lipid-cap ratio (LCR), AI systems achieved comprehensive risk stratification of non-culprit lesions and successfully identified patient subgroups with markedly elevated recurrence risk [80]. A Vision Transformer-based model trained on CCTA enabled fully automated diagnosis of plaque erosion [81]. AI-enhanced CT characterization of plaque morphology may reduce the need for invasive imaging in selected patients. In optical coherence tomography (OCT) and intravascular ultrasound (IVUS), classification performance has improved from early semi-automated approaches (70–80% accuracy) [82, 83] to modern ResNet/DenseNet pipelines with accuracies up to 91.7% [84]. A multicenter convolutional-neural-network model further improved automated identification of fibrous plaques on OCT, achieving 97.6% accuracy [85]. Following percutaneous coronary intervention (PCI), neointimal morphology within the stent is a critical determinant of long-term patency and restenosis. The DeepNeo model automatically segments the lumen, neointima, and stent struts on OCT, accurately quantifying neointimal thickness and tissue characteristics [86].

While these tools provide a novel basis for objectively identifying high-risk lesions, realizing their clinical added value faces critical barriers. Many current studies remain centered on technical performance rather than patient-centered clinical outcomes.

4.1.2 Personalized Risk Prediction

AI is extending CAD risk assessment beyond traditional scores by integrating large-scale clinical variables with genetics and multi-omics data. Polygenic risk scores (PRS) predict CAD risk independently of conventional factors [87]. Approximately 8% of individuals have at least a threefold higher CAD risk, and 0.5% have a fivefold increase [88]. The meta-genetic risk score (metaGRS), encompassing 1.7 million variants, showed that individuals in the highest 20% of genetic risk develop CAD at an earlier age [89]. A PRS model derived from Chinese cohorts demonstrated a threefold higher risk in the highest versus lowest quintile [90]. The next-generation multi-ancestry PRS improved predictive performance across diverse populations [91].

Integration of multimodal data further enhances prediction accuracy [92]. An AI model based on

plasma proteomics quantified organ-specific biological aging, revealing that accelerated cardiac aging conferred a 250% higher risk of heart failure [93]. AI-based quantitative analysis of CCTA plaque progression combined with PRS identified genetically high-risk individuals with faster plaque progression and higher major adverse cardiovascular events (MACE) risk [94]. The FAI-AI model reported in *The Lancet* integrates perivascular fat inflammation with the AI-Risk algorithm to predict 10-year cardiac death or MACE [95]. For patients with high inflammatory risk but without significant anatomical stenosis, intensified statin or anti-inflammatory therapy guided by AI risk estimation may fill the gap left by current guidelines. Multimodal models combining CCTA, MRI, ECG, and EHRs variables generally outperform conventional approaches for MACE prediction [96, 97]. In addition, the AWCOP model developed by Chinese researchers integrates tongue, facial, and pulse-wave features with clinical variables through a Transformer architecture, achieving high-precision prediction of coronary stenosis severity [98].

However, a profound translational gap exists between improved predictive accuracy and enhanced clinical outcomes. Risk prediction does not equate to prevention. Improved discrimination does not guarantee prevention benefit.

4.1.3 Toward Therapeutic Precision

AI not only synthesizes multidimensional clinical and biological information but also provides individualized therapeutic recommendations [99]. In revascularization decision-making, AI-driven strategies have shown substantial promise. Quantitative flow ratio (QFR) enables noninvasive identification of flow-limiting lesions and effectively guides the management of multivessel ST-segment elevation myocardial infarction (STEMI) [100]. An ML study suggested that for complex triple-vessel disease, younger individuals with left ventricular enlargement may derive greater benefit from PCI than from coronary artery bypass grafting (CABG) [101]. In 2025, a study applying offline reinforcement learning (RL) to data from over 40,000 patients demonstrated that AI-optimized revascularization strategies could improve outcomes by approximately 32% compared with clinician-driven decisions [102]. Large language models (LLMs), such as ChatGPT, have also been used for decision simulation, achieving moderate concordance with real-world Heart Team

recommendations in multivessel CAD management [103].

In pharmacologic management, AI is emerging as a powerful tool for precision therapy optimization. The optimal duration of dual antiplatelet therapy (DAPT) remains a persistent challenge. The AI-DAPT model dynamically predicts ischemic and bleeding risks over 36 months post-PCI, continuously updating estimates as new clinical data become available to support personalized antiplatelet therapy [104]. Genotype-guided DAPT de-escalation strategies in acute coronary syndrome (ACS) patients reduced bleeding events and improved cost-effectiveness, adding 57.7 quality-adjusted life years (QALYs) while saving approximately €810,000 in a simulated 1,000-patient cohort [105].

In complex real-world clinical contexts, decision-support systems should be deployed as auditable aids within Heart Team workflows, explicit inputs, uncertainty reporting, and traceable recommendations, rather than automated decision makers.

4.2 Heart Failure (HF)

HF affects approximately 64 million individuals worldwide. It is characterized by recurrent clinical instability, marked heterogeneity, and variable response to therapy. Consequently, delayed recognition of decompensation, coarse disease classification, and complex treatment decisions remain persistent challenges in routine practice [106-108].

4.2.1 AI-Driven Early Warning and Risk Prediction

Early studies using EHRs have shown that DL can effectively capture temporal dependencies in longitudinal clinical trajectories, markedly improving early detection of HF events [109]. In a cohort of 37,229 hospitalized patients, a ML model that integrated unstructured clinical text improved identification of acute decompensated HF (ADHF), highlighting the value of fusing heterogeneous clinical data [110]. With expanding datasets, Transformer-based architectures have further advanced risk modeling. A UK study using >100,000 longitudinal EHRs integrating diagnoses and medications achieved superior HF risk prediction compared with conventional DL models [111]. The hierarchical Transformer framework Hi-BEHRT further enabled efficient modeling of ultra-long histories and improved 5-year HF onset prediction [112].

Integration of multimodal and wearable data is shifting HF risk prediction from static assessment to near–real-time surveillance. In LINK-HF, a multisensor chest patch generated alerts a median of 6.5 days before readmission [113]. The ECGX-Net model utilized cross-modal feature learning to fuse wearable ECG with transthoracic bioimpedance signals, achieving 94% accuracy in predicting ADHF [114]. Similarly, data from adaptive servo-ventilation (ASV) devices revealed that increases in apnea–hypopnea index (AHI) and inspiratory positive airway pressure (IPAP) occurred approximately 10 days before decompensation, suggesting their potential as early warning markers [115].

At Mayo Clinic, a CNN model using standard ECG alone accurately identified asymptomatic individuals with left ventricular ejection fraction (LVEF) ≤ 35%. AI-ECG–positive patients had a 4-fold higher risk of future ventricular dysfunction [31]. A noise-adaptive single-lead AI-ECG model outperformed the PCP-HF and PREVENT scores across YNHHS, UK Biobank, and ELSA-Brasil cohorts, enabling pre-clinical HF risk detection [116]. Given its low-cost, non-invasive, and scalable nature, AI-ECG represents a promising tool for early HF screening [117]. Metabolomic analyses from the UK Biobank further showed that incorporating metabolite profiles into risk models significantly improved prediction of incident HF and refined risk-stratified survival [118]. The AGES-RS study revealed that as few as 8–10 serum proteins could predict HF events independently of conventional clinical variables [119].

Despite these predictive milestones, the clinical translation of early warning remains uncertain. While platforms like LINK-HF achieve high accuracy, they frequently encounter the Telemonitoring Paradox, earlier alerts translate into clinical benefit only when healthcare systems can provide a reliable, standardized response.

4.2.2 Diagnostic and Phenotypic Precision

AI is transforming HF evaluation by enabling more precise diagnosis and phenotyping. The EchoNet-Dynamic algorithm, reported in *Nature*, automatically segments the left ventricle, estimates ejection fraction, and assesses cardiomyopathy from ultrasound videos, achieving expert-level performance [120]. Three-dimensional CNN architectures have also been applied to

heart failure with preserved ejection fraction (HFpEF) diagnosis, surpassing traditional clinical scores using only routine echocardiographic videos and identifying subgroups with higher mortality [121]. Most recently, the EchoGo Heart Failure v2 model outperformed both HFA-PEFF and H2FPEF scores for HFpEF diagnosis and risk re-stratification in multicenter validation [122]. The DROID model, trained on tens of thousands of echocardiograms, automatically quantified cardiac structure and function. Its derived indices independently predicted future HF, atrial fibrillation (AF), myocardial infarction (MI), and mortality [123].

Beyond imaging, omics-informed modeling supports molecular phenotyping of HF. Clustering analysis of >7,000 plasma proteins in 1,351 HF patients distinguished three molecular phenotypes with distinct survival, NT-proBNP levels, and renal function profiles [124]. K-means clustering of echocardiographic features in the STANISLAS and Malmö cohorts identified three asymptomatic phenotypes, with those exhibiting diastolic dysfunction and structural remodeling showing markedly elevated risks of cardiovascular death and HF hospitalization [125].

The application of unsupervised learning to large clinical cohorts has continuously refined our understanding of the disease phenotypic spectrum. Since the landmark 2015 study in Circulation that first defined three HFpEF phenotypes [126], methodologies have evolved. A 2023 UK study utilizing large-scale EHRs defined and validated five distinct HF subtypes [127]. In 2025, researchers used the Transformer model to identify seven clinically relevant subgroups in the longitudinal medical records of over 370,000 HF patients, including novel high-risk groups such as COPD type and thyroid dysfunction type [128]. In a Chinese cohort, a two-stage DeepCluster framework combined with a CNN identified three HFpEF phenotypes, metabolic/renal dysfunction-dominant, elderly female with AF and right-heart abnormalities, and younger male with dyslipidemia and hepatic dysfunction [129]. Moreover, CMR data from the UK Biobank revealed sex-specific HFpEF phenotypes. Latent class analysis (LCA) identified three clusters: male-multimorbidity type, obese female with abnormal waist circumference, and low-comorbidity hypertensive type, with distinct profiles in body habitus, lipid metabolism, medication use, and cardiac function [130].

Across diverse methodologies and populations, metabolic, atrial fibrillation/hemodynamic, and

cardio-renal subtypes have been consistently replicated, while emerging AI-driven frameworks continue to uncover novel high-risk clusters. Representative studies are summarized in Table 1. However, increasingly granular phenotypes are clinically useful only when they map to actionable decisions and are prospectively validated rather than serving solely as retrospective risk stratifiers.

4.2.3 Individualized Therapy Optimization

Unsupervised clustering enables identification of outcome-related phenotypes from clinical data, and suggests differential drug responses across HFpEF subtypes [131]. The PURSUIT-HFpEF registry revealed that mineralocorticoid receptor antagonists improved outcomes in diastolic-dysfunction dominant phenotypes, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (ACEIs/ARBs) and statins benefited metabolically burdened phenotypes, whereas β-blockers showed potentially adverse trends in multisystem-failure phenotypes [132]. Among heart failure with reduced ejection fraction (HFrEF) patients, a neural-network autoencoder combined with clustering demonstrated that those in sinus rhythm generally benefited from β-blockers, but efficacy was limited in elderly, mildly symptomatic, or low-heart-rate subgroups. Conversely, younger patients within AF phenotypes exhibited pronounced survival advantages [133]. In HFpEF subtypes with low comorbidity burden and younger age, spironolactone significantly reduced major composite outcomes, whereas benefits were attenuated in older, AF, or obese diabetic phenotypes [134]. Graph neural-network (GNN) approaches using large-scale EHR data captured dynamic clinical trajectories and comorbidity networks, enhancing prediction of ARB and statin efficacy across phenotypic clusters [135]. Emerging evidence also indicates that angiotensin receptor–neprilysin inhibitor (ARNI) benefits vary across the LVEF spectrum, with sex-specific signals [136]. Sodium-glucose cotransporter 2 inhibitors (SGLT2i) provided consistent benefits across phenotypes, particularly reducing readmission risk in metabolically and renally burdened HFpEF groups [137].

However, most evidence for differential drug responses derives from post-hoc analyses of retrospective data. The field necessitates prospective, randomized trials to demonstrate that phenotype-specific therapy allocation improves outcomes compared to standard guideline-directed

medical therapy.

4.3 Atrial Fibrillation (AF)

4.3.1 Enhanced Detection and Diagnostic Precision

Artificial intelligence has significantly enhanced the detection of atrial fibrillation, particularly in asymptomatic or paroxysmal cases. In 2018, a deep CNN achieved an area under the curve (AUC) of 0.997 from a single 17s photoplethysmography (PPG) waveform, outperforming conventional algorithms [138]. Large-scale real-world studies, such as the Huawei Heart Study, have confirmed the high positive predictive value of continuous PPG monitoring for population screening [139]. Wearable devices combining PPG with single-lead ECG not only improve detection rates but also enable long-term AF burden assessment [140]. More advanced applications include ultra-early warning, the WARN model can predict AF onset 30 minutes in advance using only R-R intervals [141]. At Mayo Clinic, AI-ECG identified subclinical AF from 10s sinus-rhythm ECGs [142]. More advanced models not only predict AF occurrence but also estimate the time to onset, and when combined with clinical risk scores, their predictive performance surpasses existing benchmarks [143]. By transforming Holter ECG into images and employing transfer learning, AI models achieve high-accuracy and interpretable AF classification [144]. The CNN-BiLSTM architecture integrated spatiotemporal QRS features with rhythm patterns, achieving beat-level AF detection with high precision in the MIT-BIH and MIMIC-III databases [145]. A knowledge-embedded Temporal-Spatial feature fusion Pseudo-Siamese Network (TSPS-Net), incorporating spatiotemporal feature fusion and noise-filtering modules (STCFM), enhances long-range contextual modeling and substantially improves the robustness of AF detection [146].

However, the proliferation of AI-driven screening raises critical concerns about overdiagnosis, as the detection of brief, subclinical AF episodes, which may not consistently correlate with stroke risk, can lead to unnecessary confirmatory testing and patient anxiety.

4.3.2 Risk Assessment and Anticoagulation Decision Support

Stroke prevention is central to AF management, yet anticoagulation inherently carries bleeding risk. The PRESTIGE-AF trial showed that in patients with AF and prior intracerebral hemorrhage,

direct oral anticoagulants (DOACs) reduced ischemic stroke but increased recurrent bleeding risk [147]. A large UK Biobank MRI study demonstrated that DL-derived left atrial structural and functional features were associated not only with incident AF but also with stroke and HF risk [148]. A CNN model using transthoracic echocardiography (TTE) videos could differentiate AF patients during sinus rhythm and predict 90-day AF onset [149]. The German MonDAFIS cohort predicted post-stroke AF risk within 7 days using only 1 hour continuous ECG monitoring data and age [150]. A hybrid MRI-DWI classifier combining radiomics and CNN features identified latent AF in stroke patients with class-activation-based interpretability [151]. The LAT-AI model integrating echocardiography and clinical variables predicted left atrial appendage thrombus, providing a non-invasive alternative to reduce procedural burden [152].

ML frameworks have also predicted both thrombotic and bleeding events in catheter-ablation populations to optimize peri-procedural anticoagulation [153]. LLMs have analyzed EHRs to identify causes of suboptimal anticoagulation—including antiplatelet substitution, therapeutic inertia, and low AF burden [154]. AI-ECG alerts significantly increased oral anticoagulant prescriptions among non-cardiology clinicians [155]. Voice-based AI assistants automated follow-up, adherence checks, and medication support, improving treatment compliance and reducing physician workload [156]. These advances highlight AI's promise in remote and long-term management of AF anticoagulation.

Nevertheless, translating AF risk prediction into anticoagulation decisions remains non-trivial, as stroke and bleeding risks are dynamically balanced rather than independently optimized. Most existing models inform risk estimation but stop short of defining actionable thresholds for initiating, withholding, or intensifying anticoagulation in real-world clinical pathways.

4.3.3 AI-Guided Ablation Strategy and Recurrence Prediction

AI techniques are increasingly integrated into ablation planning and recurrence risk assessment. The TAILORED-AF randomized trial validated AI-guided ablation pathways using Volta AF-Xplorer software to identify spatiotemporal dispersion zones and perform targeted ablation beyond pulmonary vein isolation (PVI), yielding superior outcomes, particularly in patients with long-

standing AF or marked atrial remodeling [157]. CNN-LSTM networks modeled electrophysiological signals to precisely localize AF drivers and assist intra-procedural decision-making [158]. CARTONET leveraged cloud-based DL for anatomical mapping and reconnection risk prediction during ablation [159].

For recurrence risk stratification, ML and DL models consistently outperformed traditional scores. The CNNSurv model, based on clinical and echocardiographic parameters, identified elevated NT-proBNP, non-paroxysmal AF, and enlarged left atrial and appendage volumes as key predictors of recurrence [160]. A multimodal convolutional network combining electrogram (EGM), ECG, and clinical features outperformed CHA_2DS_2-VAScfor 1year post-ablation recurrence prediction [161]. A multimodal Transformer integration framework further incorporated ECG images, clinical, and intra-procedural data, achieving higher precision and demonstrating AI's potential for early recurrence identification in complex multimodal contexts [162].

Nevertheless, the generalizability of AI-guided ablation tools is constrained by center-specific mapping systems, operator technique, and variable signal acquisition or labeling, which may limit transferability across devices and workflows.

4.4 Hypertension

4.4.1 Identification and Screening

AI enhances hypertension identification and screening beyond office-based measurements. AI-enabled medical imaging supports noninvasive diagnosis and risk assessment. DL applied to retinal imaging has opened new avenues for noninvasive cardiovascular risk assessment [163]. Genetic studies based on retinal vascular fractal features have revealed associations between microvascular geometry, hypertension, and overall cardiovascular risk [164]. Multicenter studies have shown that AI can accurately identify hypertensive individuals from standard pharyngeal photographs [165]. Optical coherence tomography angiography (OCTA) combined with CNNs and Transformer frameworks achieved superior performance in distinguishing hypertensive from normotensive individuals [166], supporting early screening and complication prevention.

AI also shows value in identifying secondary hypertension. Multi-omics combined with ML can

distinguish primary from endocrine hypertension with 92% accuracy [167]. DL applied to EHR data, integrating over 12,000 laboratory and clinical note variables, enhanced the detection of secondary hypertension by merging structured and unstructured data [168].

Despite promising performance, most AI-enabled identification and screening approaches remain insufficiently validated in prospective studies.

4.4.2 Risk Prediction and Dynamic Monitoring

AI improves the prediction of hypertension onset and its complications. An XGBoost model trained on EHR data from 1.5 million individuals in Maine, US, prospectively predicted 1-year hypertension incidence and successfully stratified the population into five risk categories [169]. A longitudinal study using an LSTM network identified high-risk individuals up to two years before clinical onset [170]. PRS, when integrated with nonlinear ML algorithms, significantly improved systolic and diastolic blood pressure (BP) prediction [171]. Moreover, unsupervised clustering of >40,000 patients identified five hypertensive subphenotypes characterized by age, body mass index (BMI), comorbidities, and socioeconomic vulnerability, underscoring the role of social determinants in disease heterogeneity [172]. The 2025 AHA/ACC guideline recommends the PREVENT risk calculator to estimate 10 and 30 year CVD risk [173], marking the transition of big-data models from research to clinical guideline adoption.

Concurrently, AI-powered wearable technologies enable a shift from intermittent to continuous monitoring. Early studies demonstrated that BP could be estimated using pulse transit time (PTT) derived from combined ECG and PPG signals through regression algorithms [174]. Co-advancements in hardware and algorithms have improved monitoring stability. For example, dual-channel wrist devices integrating contact pressure and skin temperature sensors, combined with ML-based multimodal signal fusion, reduce inter-individual variability and the influence of device positioning [175]. Meanwhile, miniaturized flexible systems incorporating piezoelectric arrays, pressure-adaptive mechanisms, and deep learning maintain A-grade accuracy even in dynamic environments [176]. Similarly, flexible strain-sensor arrays integrated with DL models capture high-fidelity pulse waves from the wrist without precise positioning, enabling simultaneous prediction

of BP and cardiac functional parameters, demonstrating strong potential for personalized health management and remote telemonitoring [177].

Despite this potential, cuffless blood pressure estimation remains highly dependent on calibration and susceptible to motion artifacts and individual skin or vascular characteristics. Establishing clinically meaningful accuracy standards with robust multicenter external validation is therefore essential before routine diagnostic adoption.

4.4.3 Towards Personalized Management and Digital Care

AI supports personalized pharmacotherapy by predicting treatment response. The RIGIPREV study, integrating data from the EVA, LOD-DIABETES, and EVIDENT cohorts, applied a random forest model to predict improvements in pulse wave velocity (PWV) following ACEIs or ARBs therapy, generating personalized drug recommendations [178]. Another study used spectral analysis and ML to extract pharmacodynamic profiles of five commonly prescribed antihypertensive drugs, identifying response variability across 15 clinical parameters [179]. An Extreme Gradient Boosting model trained on >19,000 follow-up records effectively predicted patient-specific antihypertensive responses [180]. A Chinese study demonstrated that a data-driven clinical decision support system (CDSS) increased the proportion of appropriately treated visits from 62.2% to 77.8%, achieving an additional 1.6 mmHg reduction in systolic BP [181].

AI-enabled system platforms and digital interventions aim to extend management beyond hospitals, enabling continuous care for hypertension. In a 28 day follow-up study of 150 patients, wrist-worn PPG devices maintained stable performance [182]. Clinical trial evidence shows that remote monitoring significantly reduces systolic BP and improves BP control rates to nearly 70%, outperforming standard care [183]. Systematic reviews and meta-analyses have confirmed that mobile health applications can enhance adherence and patient self-efficacy [184], supporting the integration of behavioral and remote monitoring interventions. Moreover, electronic health literacy (e-HL) significantly influences engagement and persistence in remote blood pressure monitoring (RBPM), suggesting that digital follow-up should incorporate population stratification and personalized design [185].

Multimodal AI systems are increasingly applied in hypertension management. The Hyper-DREAM platform integrates clinical records, lifestyle data, and imaging features, leveraging LLMs for risk prediction and remote care, substantially reducing clinician workload [186]. The HyMNet framework combines fundus imaging and metabolic markers via the RETFound model to enhance hypertension detection accuracy [187]. Longitudinal multimodal predictive models have been used to estimate atherosclerotic cardiovascular disease (ASCVD) risk among newly diagnosed hypertensive individuals [188]. Furthermore, a WeChat-based multimodal intervention significantly improved BP control in patients with mild to moderate hypertension, demonstrating the real-world feasibility of AI-assisted digital management [189].

Nevertheless, most drug response evidence remains retrospective, and implementation is shaped by clinician judgment, patient preference, and medication access or reimbursement, which can attenuate the real-world uptake of algorithmic recommendations.

5. Construction of Intelligent Cardiovascular Health Management Platforms

5.1 Platform Architecture and Data Infrastructure

Significant progress has been made globally in constructing intelligent cardiovascular health management platforms. Modern systems are typically built on cloud architectures and mobile applications, integrating the Internet of Things (IoT) and wearable technologies to enable continuous physiological data acquisition and AI-driven analysis [190].

In China, EHR-based CDSS have significantly improved adherence to antihypertensive therapy and enhanced BP control [181]. The nationwide BASIC-OHCA registry achieved the first integration of emergency medical services (EMS), hospital, and follow-up data, providing a high-quality evidence base for out-of-hospital cardiac arrest management [191]. The Precision Medicine Platform jointly developed by the AHA and Amazon Web Services adheres to FAIR principles, allowing efficient cross-dataset search and secure cloud collaboration while promoting open cardiovascular science [192]. Similarly, the NHLBI BioData Catalyst platform provides secure cloud-based workspaces and multimodal analytic tools for cardiovascular precision medicine [193]. In Germany, the Medical Informatics Initiative (MII) established distributed integration centers (DICs) and

national core data sets (KDS) to enhance interoperability and data standardization across academic medical centers [194].

Sustainable platform development depends critically on improved interoperability and data security. The Internet of Medical Things (IoMT) is rapidly expanding in prehospital care, but data standardization and cross-domain interoperability remain key challenges. Cloud computing, RESTful APIs, and edge computing are now widely adopted, while emerging technologies such as blockchain and openEHR offer promising solutions for achieving higher levels of interoperability and privacy protection [195]. To enable meaningful cross-institutional computability, interoperability should be treated as a core architectural constraint from the outset rather than an afterthought. The optimal point for implementing standards is at the stages of data generation, study design, and initial collection, thereby avoiding reliance on the arduous cleaning and alignment of disparate local formats deployed after the fact [196]. Without unified standards and architecture-level integration, even technically advanced platforms can devolve into data silos, limiting scalability and constraining durable outcome improvement in chronic cardiovascular care.

5.2 Personalized Management and Remote Monitoring

Intelligent health platforms leverage rich data and analytical capabilities to deliver personalized care. The widespread adoption of these platforms has enabled more individualized management of chronic cardiovascular diseases [197]. The All of Us Research Program aims to recruit over one million participants from diverse populations, collecting health surveys, EHR data, wearable metrics, and biospecimens to facilitate population-specific risk prediction and precision treatment [198]. Its Digital Health Research Platform (DHRP) supports remote consent, multimodal data collection, and sustained participant engagement, enhancing the representation of minority and underserved groups [199]. AI-enabled systems allow continuous monitoring of symptoms and physiological parameters to support proactive management. A WeChat-based intelligent follow-up system in primary care improved patients' self-management ability and medication adherence [200]. The Patient-Centered Knowledge Graph (PCKG) integrates medical records, physiological, and behavioral data into a semantic health representation, enabling risk prediction and personalized

therapeutic recommendations [201].

However, converting technological potential into consistent clinical benefit is not automatic, and remote monitoring illustrates a clear efficacy-effectiveness gap. A systematic review and meta-analysis indicates that telehealth or telemonitoring may reduce short-term heart-failure related hospitalization and mortality [202]. Notably, the BEAT-HF trial, involving 1,437 heart failure patients, found that a combined intervention of health coaching and daily telemonitoring did not reduce 180-day all-cause readmission rates compared to usual care [203]. Digital monitoring is most likely to generate benefit when alerts are embedded within a defined, timely, and scalable response pathway aligned with local workforce capacity and care processes, rather than operating as a stand-alone data stream [204].

5.3 Human-AI Interaction and Patient Engagement

Within intelligent cardiovascular health management platforms, human-AI interaction constitutes the interface through which data infrastructure and algorithmic outputs are translated into communication, care coordination, and patient engagement. Medical chatbots have been deployed in chronic disease management for home-based self-support, where patients describe symptoms via mobile applications, and NLP dynamically identifies key information to provide preliminary advice [205]. Electronic patient-reported outcome (ePRO) systems have been shown in randomized controlled trials to enhance communication and treatment understanding, facilitating patient-centered cardiovascular care [206]. The NHS OpenSAFELY study demonstrated that online consultation platforms, covering over 50 million patients, experienced a marked increase in use during the COVID-19 pandemic, highlighting digital interaction as a key component of primary care [207]. On the clinician side, generative AI has been employed to draft patient messages, achieving comparable or superior scores in completeness and empathy compared with physician-generated responses, suggesting its potential to reduce clinical workload and improve communication [208].

However, platform-level interaction is neither inherently beneficial nor inherently equitable, as its effectiveness is strongly contingent on usability and digital accessibility. Evidence indicates that

online consultations require specific digital skills and access to appropriate devices, which may exclude a substantial proportion of older adults, estimates suggest that approximately 13 million older individuals in the US may face barriers to telemedicine use, implying that platform benefits can systematically diminish in disadvantaged populations [209]. Digital health literacy is independently associated with age, educational attainment, and access to technology, thereby shaping individuals' capacity to engage with and benefit from digital health services [210]. Consequently, rapid digitalization carries the risk of exacerbating existing health inequalities by disproportionately favoring populations with greater resources, knowledge, and technological familiarity [211].

In this context, clinicians play a critical mediating role. If patient-generated data streams and AI-driven alerts are not seamlessly integrated into existing clinical workflows and EHR systems, they may contribute to alert fatigue and increase cognitive and operational burden rather than improve care delivery [212]. Addressing these socio-ethical challenges therefore requires strategies that extend beyond technical deployment alone, emphasizing equitable design, inclusive implementation, and the cultivation of digital health literacy [213]. Practical approaches include co-designing platforms with diverse user groups, providing alternative access pathways such as simplified interfaces or telephone-based support, and implementing targeted digital literacy interventions for older adults and underserved communities [214, 215].

Only when enabling conditions, such as adequate digital skills, supportive clinician-patient relationships, and perceived usability are in place can intelligent management platforms meaningfully support patient engagement and self-management [216]. Ultimately, the objective of human-AI interaction in cardiovascular platforms is not the proliferation of digital tools, but the development of a digitally inclusive care ecosystem in which AI augments, rather than fragments, clinician-mediated care processes. (Figure 4)

6. Evidence, Implementation, and Governance Challenges

6.1 Evidence Quality and the Clinical Maturity of AI Applications

Conventional approaches to cardiovascular care still fail to address several critical clinical blind

spots. A substantial proportion of myocardial infarctions arise from nonobstructive coronary lesions that may appear insignificant on angiography, yet can harbor vulnerable plaque features missed by routine assessment [217, 218]. Similarly, real-world detection and control of AF and hypertension remain suboptimal, partly because their silent or paroxysmal presentations delay recognition and allow preventable stroke and target organ risk to accumulate over time [219, 220]. In heart failure, particularly HFpEF, the marked pathophysiologic heterogeneity and limited responsiveness to traditional therapies further underscore the need for phenotype-guided precision management [136, 221, 222]. Together, these unmet needs constitute the pragmatic drivers for the clinical adoption of AI.

However, a substantial translational gap remains between the technical promise of AI algorithms and the maturity of supporting clinical evidence. Current evidence is still dominated by proof-of-concept and retrospective studies. Models developed and validated on retrospective datasets are susceptible to optimism bias, potentially overstating generalizability across heterogeneous real-world clinical settings and patient populations [223, 224]. In parallel, most studies remain oriented toward surrogate endpoints, such as AUC, sensitivity, specificity, image-interpretation accuracy, detection yield, or other measures, rather than patient-centered clinical outcomes [225]. As a result, even tools with excellent diagnostic performance may fail to deliver measurable health benefits once embedded in complex care workflows. In a randomized clinical trial evaluating an AI-enabled smartphone behavioral intervention for hypertension self-management, the intervention improved patients' self-reported confidence in BP control, but did not produce a statistically significant reduction in systolic BP compared with a basic BP tracking app control [226].

Bridging the divide between technical validation and clinical implementation requires prioritizing prospective randomized controlled trials. Table S1 summarizes a growing body of such trials. While improvements in metrics have been reported, for example, increased AF detection through AI-supported screening [227] and reduced potentially unnecessary coronary angiography via FFR-CT−guided care [228], durable benefits on MACE or quality of life have often not been demonstrated with longer follow-up. Existing trials also remain frequently constrained by single-center designs

and limited sample sizes [229]. In summary, AI applications in cardiovascular medicine remain in an early phase of development and evolution. The current evidence landscape is characterized by relatively abundant technical validation but insufficient high level clinical effectiveness evidence. Future progress will depend on a fundamental shift in research paradigms, from unimodal, static performance evaluations toward dynamic, multimodal, and integrative clinical validation.

6.2 Implementation, Cost-effectiveness, and System Readiness

The most immediate barrier to implementation is the failure to integrate AI tools seamlessly into existing clinical workflows. In hypertension care, poor medication adherence and therapeutic inertia remain dominant constraints on long-term control rates [230, 231], underscoring that many chronic care bottlenecks arise not from insufficient risk identification but from limited downstream capacity, delayed treatment intensification, and constrained follow-up resources. If AI merely increases risk stratification or abnormality detection without a matched intervention mechanism, health systems may face a structural throughput problem, more detected needs without sufficient capacity to respond. This mismatch is particularly consequential in HF, where the window for early decompensation recognition is narrow and the burden of readmission is substantial [232-234]. When alerts do not reliably trigger standardized triage, follow-up assessment, and medication adjustment within a closed-loop pathway, predictive notifications can devolve into noise and amplify alert fatigue, potentially increasing the risk of missing clinically meaningful signals [212].

Beyond workflow coupling, interpretability and traceability directly shape adoption. The black-box character of complex models can erode clinician trust, as clinicians are generally reluctant to base decisions on recommendations they cannot explain [235]. Accordingly, incorporating explainable approaches, such as SHAP, Grad-CAM, and attention visualization, to improve transparency and auditability is an important enabler of adoption [236]. Importantly, highly granular risk estimates do not inherently confer clinical utility. If outputs cannot be mapped to explicit thresholds, authority, and operational pathways, technical precision may manifest as spurious precision. In CAD, risk is dynamic, and predictions become actionable only when tethered to evidence based pathways that specify preventive intensification, escalation to noninvasive imaging

evaluation, or optimization of revascularization strategy [237-240]. Similarly, in AF, increased detection through wearables does not automatically imply anticoagulation. It must be embedded in an operational decision framework that balances stroke and bleeding risks while accounting for patient preference and adherence realities [241, 242].

Successful deployment also depends on clear staffing models and accountability boundaries. Persistent ambiguity regarding who is responsible for acting on AI outputs can lead to delayed responses or inaction. Therefore, sustainable implementation requires explicit, accountable responsibility pathways and oversight mechanisms across developers, health care organizations, and clinicians [243]. Ambient AI tools documentation assistants may reduce administrative burden but introduce practical risks related to accuracy, narrative appropriateness, and potential erosion of clinician autonomy, warranting careful clinical oversight and evaluation [244].

From a system perspective, cost-effectiveness is a nonnegotiable constraint for scaling. Studies frequently report AI strategies as cost-effective or cost-saving [245]. However, these evaluations often underreport or omit key hidden and lifecycle costs. Systematic review evidence indicates persistent gaps in accounting for expenses related to system integration, workforce training, ongoing model maintenance or retraining, data infrastructure, and long-term technical support [246].

Sustained integration depends on broader system readiness. Technical infrastructure, durable reimbursement and incentive structures, and a supportive organizational culture jointly determine whether AI can be embedded into routine care and maintained over time. AI tools may improve coordination and workflow but can also create additional work and are constrained by structural limitations such as connectivity, power supply, and device maintenance [247]. Evidence suggests that infrastructure and technical issues, psychological barriers, and workload concerns are major barriers to adoption, whereas training, perceived usefulness, and multi-stakeholder incentives are key enablers [14]. To ensure long-term sustainability and effectiveness of clinical AI tools, postdeployment monitoring and evaluation are essential to track performance stability, shifts in cost-effectiveness, and challenges such as data drift across diverse real-world settings [13].

6.3 Governance Challenges

The clinical translation of AI in cardiovascular medicine ultimately hinges on a mature governance ecosystem. This ecosystem must address three interdependent challenges: ensuring robust data governance in the era of multimodal integration, enforcing algorithmic fairness across diverse populations and real-world settings, and building an agile yet coordinated regulatory architecture amid a fragmented global landscape.

Pursuing precision through multimodal data fusion necessitates a fundamental reassessment of data governance. Conventional de-identification is increasingly insufficient. Evidence indicates that techniques such as refacing can elevate re-identification risks in ostensibly de-identified imaging data, underscoring the need for stronger technical and institutional safeguards when sharing large-scale multimodal clinical dataset [248]. Fragmented health management systems and low clinician satisfaction with EHRs contribute to inconsistent data capture, hindering the development and validation of robust AI using high-quality datasets [249].

Regulatory practice is evolving toward lifecycle oversight, yet the global landscape remains highly fragmented. Although the European Union, the FDA, and China have introduced specific AI oversight guidelines imposing strict clinical requirements [250, 251]. Unified standards regarding data privacy, accountability, and liability are still lacking [252]. In response to the iterative nature of software algorithms, regulators increasingly recognize the mutable characteristics of software as a medical device and have begun to institutionalize change control plans alongside post market surveillance as core governance instruments. The FDA has likewise emphasized building a more flexible regulatory ecosystem to enable innovation and adoption while safeguarding public safety and mitigating potential risks [253]. Against this backdrop, the FDA, the UK Medicines and Healthcare products Regulatory Agency, and Health Canada released a series of guiding principles on Predetermined Change Control Plans (PCCPs) for machine learning enabled medical devices. These principles aim to predefine and manage anticipated AI updates under assurances of safety and effectiveness, reducing regulatory inefficiency associated with full re-review at every iteration while strengthening obligations for risk control and ongoing monitoring [254]. The European Union's Artificial Intelligence Act (AI Act) represents a pioneering horizontal regulatory framework

designed to promote the ethical and safe integration of AI across sectors, including health care [255]. Across both clinical trials and real-world deployment, AI systems face risks including dataset shift, amplification of bias, and performance degradation risks that often span the entire lifecycle of a tool. Non-representative training and validation data can systematically disadvantage women, racial or ethnic minorities, or resource-constrained populations. After deployment, evolving data distributions may precipitate latent failure modes. Accordingly, bias assessment, continuous monitoring, re-evaluation and appropriate human oversight should be embedded as integral components of standardized governance [256, 257].

In summary, the future of AI in cardiovascular medicine depends on establishing a robust governance framework commensurate with the pace of technological iteration. (Figure 5)

7. Conclusions and Future Perspectives

AI is reshaping cardiovascular medicine with unprecedented breadth and depth. This transformation extends beyond incremental upgrades of individual diagnostic tools to the reconstruction of an end-to-end cardiovascular health continuum from risk detection to long-term management. Accumulating evidence suggests that, by integrating multimodal data, such as imaging, genomics, EHRs, and wearables, AI can enable earlier warning, finer phenotyping, and personalized risk stratification. Applications such as automated coronary plaque characterization, unsupervised clustering of high-risk heart failure phenotypes, and DL-based screening for silent AF increasingly translate the promise of precision medicine into actionable clinical workflows. Notably, the convergence of AI and wearable technologies is accelerating a shift from episodic, reactive care toward proactive and continuous management, supporting earlier intervention in chronic cardiovascular disease prevention [258, 259].

Despite this progress, a substantial translational gap remains between technical feasibility and durable clinical value. Most AI applications still emphasize performance gains, while real-world impact is constrained by the absence of closed-loop decision pathways, insufficient system integration, and immature governance ecosystems. Many high-accuracy early-warning models fail to scale without accompanying care pathways, and robust causal links between algorithmic

performance and improved hard outcomes have yet to be established. Persistent barriers, including data silos, algorithmic bias, unclear accountability, and regulatory lag, continue to limit large-scale deployment.

AI will evolve from a research instrument to a clinically reliable, individualized, and sustainable paradigm only through coordinated advances in multimodal integration, interpretability, closed-loop remote monitoring, and lifecycle governance. This transition requires controlled data sharing with privacy protection, fairness evaluation that is verifiable across populations, and institutionalized post-market surveillance and risk management, so that technical feasibility can translate into trustworthy long-term clinical value.

Ultimately, advancing AI-enabled cardiovascular care is a collective endeavor spanning disciplines, institutions, and governance levels. Close collaboration among clinicians, data scientists, engineers, ethicists, regulators, and patients, guided by shared accountability and clearly defined clinical goals, is essential for responsible, scalable, and clinically meaningful implementation.

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Author Contributions

Y.L. and YF.L. conceived this topic and arranged the outlines, revised the review. Q.X., M.Z. and YW.L. researched data for the article. Q.X., M.Z.,Y.L.,Y.C.,X.C., W.W., Y.L., J.J., Y.X. and Y.L. substantially contributed to the discussion of content. Q.X., M.Z. and YW.L. wrote the article. All authors reviewed/edited the manuscript before submission.

Competing Interests

The authors declare no competing interests.

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Figure legends

Figure 1. Data Sources and Types in Cardiovascular Disease Research. The main data types in cardiovascular research include structured data, unstructured data, and emerging data sources. Created with BioRender.com.

Figure 2. Strategies of multimodal fusion in cardiovascular research. Multimodal fusion in cardiovascular research mainly includes early, intermediate, and late fusion strategies. Created with BioRender.com.

Figure 3. Advances in the Application of AI in Cardiovascular Disease. This figure summarizes representative applications across coronary artery disease, heart failure, atrial fibrillation, and hypertension. Abbreviations: AI,artificial intelligence; ML,machine learning; DL,deep learning; CNN,convolutional neural network. Created with BioRender.com.

Figure 4. Intelligent Cardiovascular Health Management Platform. This figure illustrates three interrelated components of an intelligent cardiovascular health management platform: platform architecture and data infrastructure, personalized management and remote monitoring, and human–AI interaction and patient engagement. Together, these components outline a conceptual framework for proactive and data-informed cardiovascular care. Created with BioRender.com.

Figure 5. An integrated framework for evidence, implementation, and governance driven cardiovascular AI. This pyramid model illustrates the key elements required for the clinical translation of cardiovascular AI, progressing from bottom to top. A robust data ecosystem serves as the foundation. Building on this base, algorithmic fairness principles guide the development of unbiased and interpretable AI models. At the core, a coordinated regulatory framework supports lifecycle-wide governance, ultimately enabling the sustainable clinical translation and system-level integration of AI in cardiovascular medicine. Created with BioRender.com.

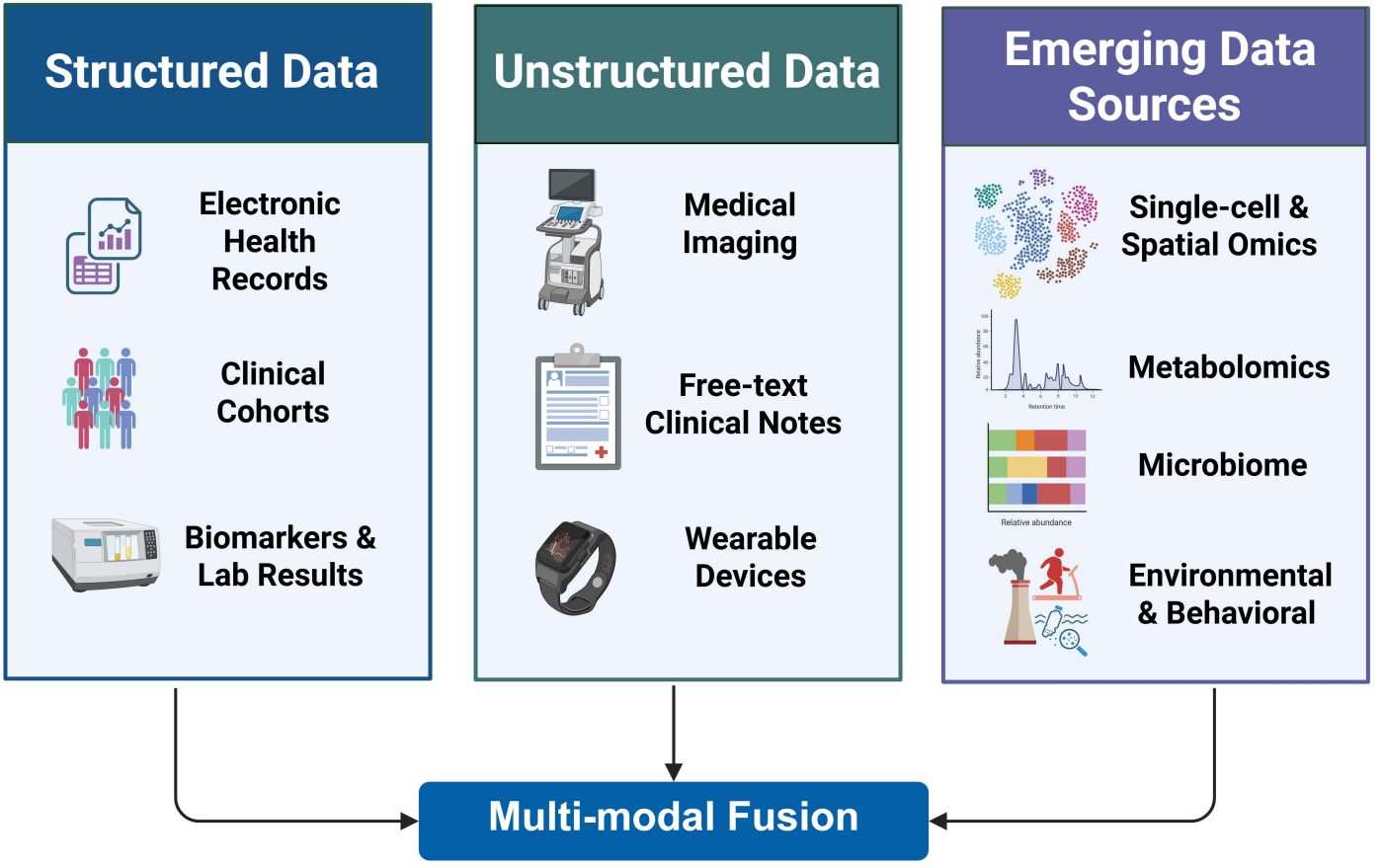
Tables

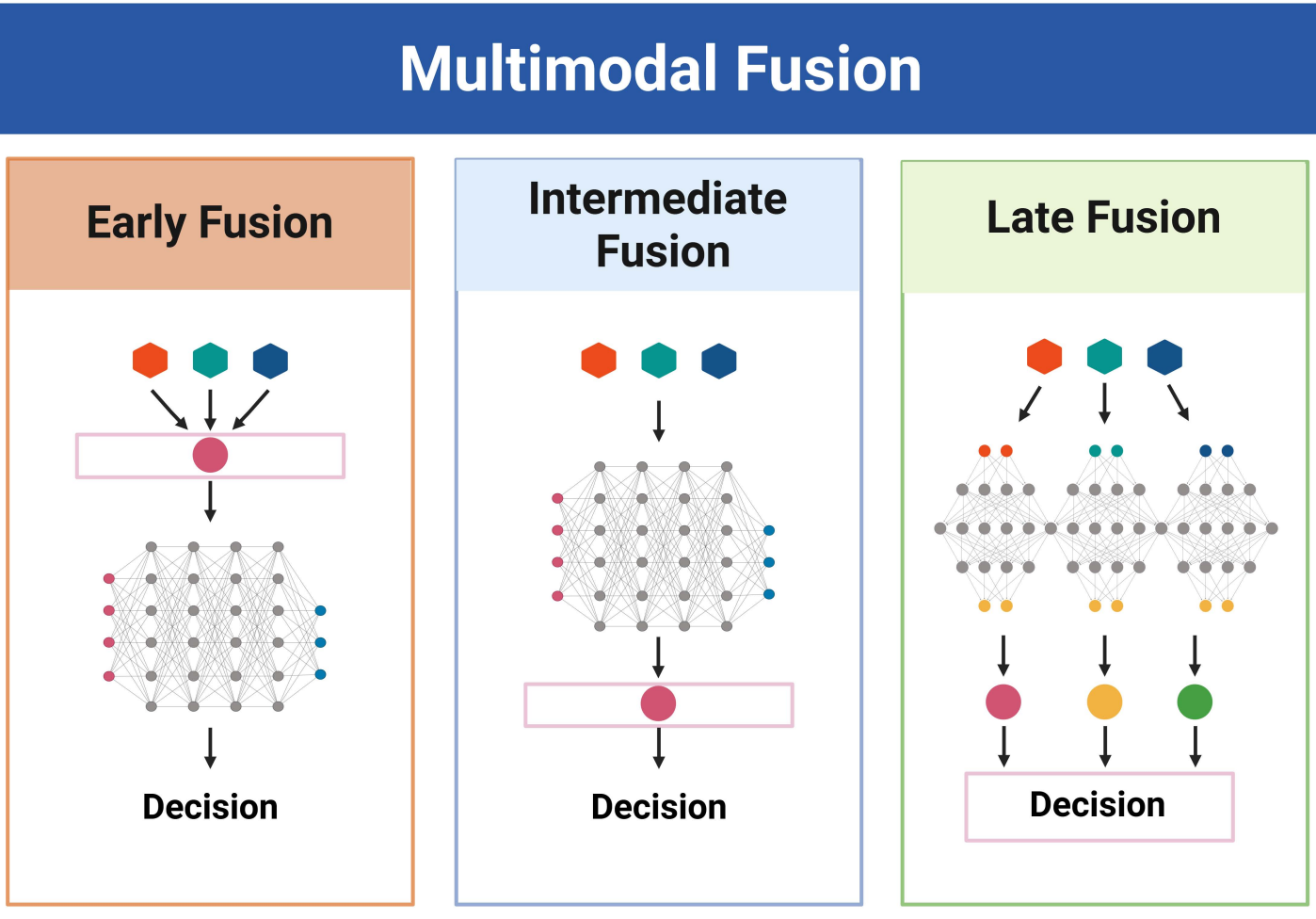
Table 1 Representative Studies on HF Phenotypic Subtyping

Study	Country/ Region	Data Source	Method	Phenotype Classification
Fan Z (2025)[128]	UK	CPRD	Transformer-based model	Cluster 1: early onset; Cluster 2: hypertension; Cluster 3: ischaemic heart disease; Cluster 4: metabolic dysfunction; Cluster 5: COPD; Cluster 6: thyroid dysfunction; Cluster 7: late-onset.
Rui Li (2025)[129]	China	Clinical Data	CNN-DeepCluster	Phenogroup 1: metabolic comorbidities, left ventricular hypertrophy, systolic and diastolic dysfunction; Phenogroup 2: AF, atria and right ventricle structural abnormalities, diastolic dysfunction;

				Phenogroup 3: unhealthy lifestyles, hyperlipidemia, liver dysfunction.
Bertrand A (2025)[130]	UK	UK Biobank	LCA	Group 1: most male and multimorbid; Group2: obesity, abnormal waist circumference, high females; Group 3: lower comorbidity, hypertension.
Matsuoka Y(2025)[260]	Japan	PURSUIT-HFpEF	LCA	Phenotype 1: Low comorbidity; Phenotype 2: Hypertension and CKD; Phenotype 3: AF and concomitant RHF; Phenotype 4: Systemic inflammation and concomitant RHF; Phenotype 5: Malnutrition and CKD.
Soltani F (2024) [261]	UK	NIHR	DBSCAN+GMM+K-means	Phenogroup 1: Younger, female, cardiometabolic and coronary disease; Phenogroup 2: More frail, lung disease and AF; Phenogroup 3: Systemic inflammation, diabetes, renal dysfunction.
Kyodo A (2023)[262]	Japan	NARA-HF、JASPER	Unsupervised ML+VBGMM+hierarchical clustering	Phenogroup 1: atherosclerosis and CKD Phenogroup 2: AF Phenogroup 3: younger and LVH
Choy M (2022) [134]	USA	TOPCAT participants	LCA	Phenotype 1: youngest,low co-morbidities; Phenotype 2: oldest, AF, pacemaker implantation, hypothyroidism; Phenotype 3: obese, diabetic, high co-morbidities.
Woolley RJ (2021)[263]	Scottish	BIOSTAT-CHF	Hierarchical clustering	cluster 1: diabetes mellitus, renal disease; cluster 2: oldest, age-related comorbidities; cluster 3: youngest, largest body size, least symptoms, lowest NT-proBNP; cluster 4: ischaemic aetiology, smoking and chronic lung disease, most symptoms, highest NT-proBNP and troponin.

Abbreviations: AF,atrial fibrillation; COPD,chronic obstructive pulmonary disease; CNN,convolutional neural network; LCA,latent class analysis; CKD, chronic kidney disease; RHF,right heart failure; ML,machine learning; DBSCAN,density-based spatial clustering of applications with noise; GMM, Gaussian mixture model; LVH,left ventricular hypertrophy; HFpEF,heart failure with preserved ejection fraction.

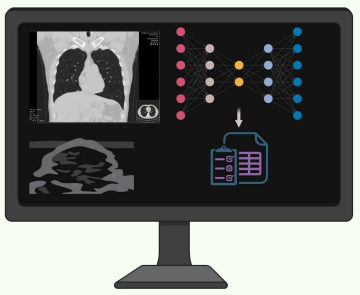

Structured Data
Electronic Health Records
Clinical Cohorts
Biomarkers & Lab Results
Unstructured Data
Medical Imaging
Free-text Clinical Notes
Wearable Devices
Emerging Data Sources
Single-cell & Spatial Omics
Metabolomics
Retention time
Relative abundance
Microbiome
Relative abundance
Environmental & Behavioral
Multi-modal Fusion


Multimodal Fusion
Early Fusion
Decision
Intermediate Fusion
Decision
Late Fusion
Decision

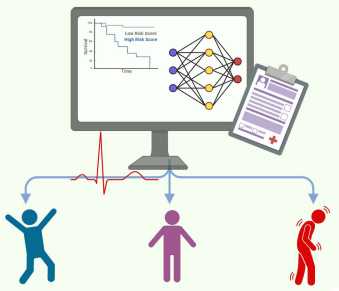
AI in Cardiovascular Disease

CORONARY ARTERY DISEASE

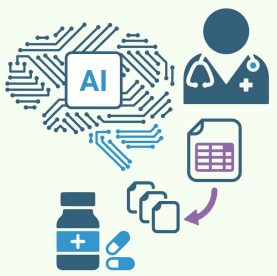
Diagnostic and Phenotypic Precision



Personalized Risk Prediction



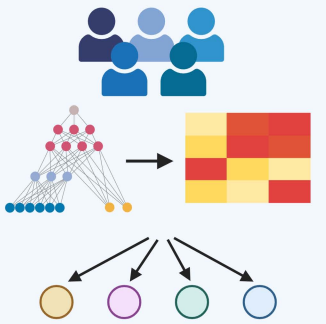
Toward Therapeutic Precision



HEART FAILURE

Early Warning and Risk Prediction

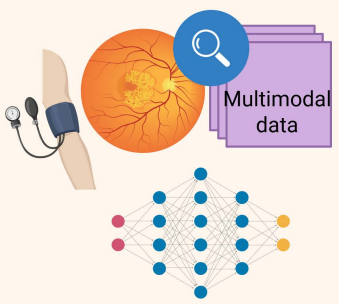
Diagnostic and Phenotypic Precision



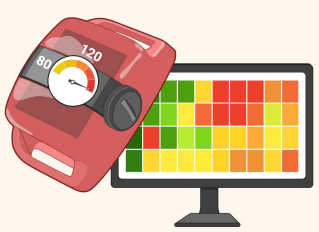
Individualized Therapy Optimization

HYPERTENSION

Identification and Screening



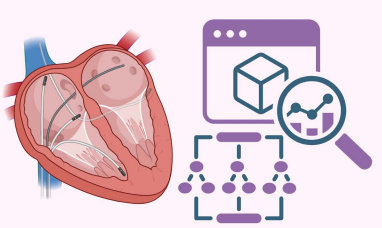
Risk Prediction and Dynamic Monitoring



Personalized Management and Digital Care

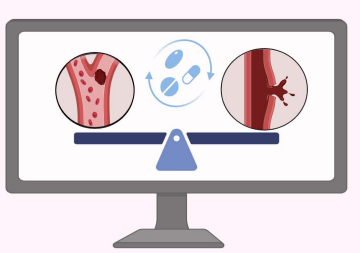
ATRIAL FIBRILLATION

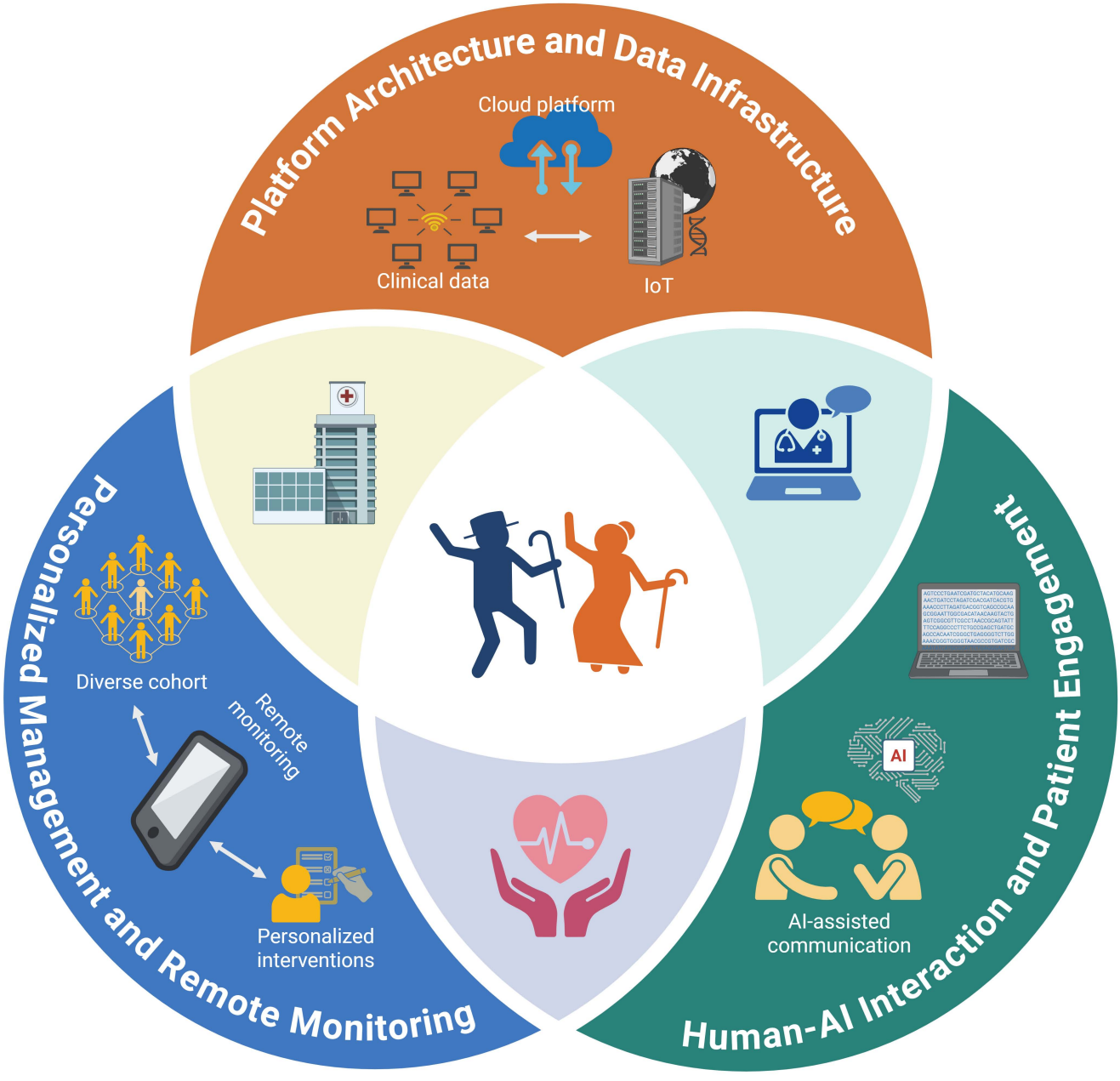
AI-Ablation & Recurrence Support

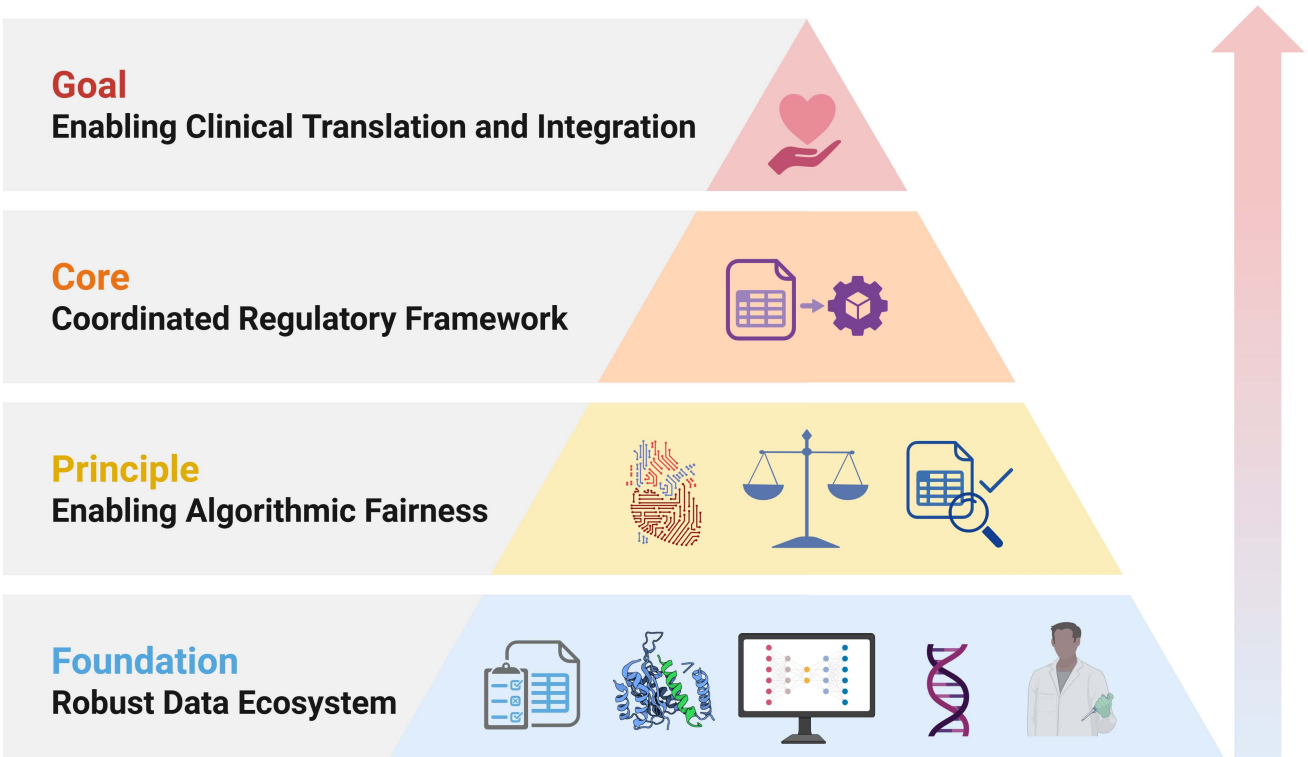


Detection and Diagnostic Precision

Risk Assessment and Decision Support




Platform Architecture and Data Infrastructure
Cloud platform
Clinical data
IoT
Personalized Management and Remote Monitoring
Diverse cohort
Remote monitoring
Personalized interventions
Human-AI Interaction and Patient Engagement
AI
AI-assisted communication


Goal
Enabling Clinical Translation and Integration
Core
Coordinated Regulatory Framework
Principle
Enabling Algorithmic Fairness
Foundation
Robust Data Ecosystem