Artificial Intelligence Review (2026) 59:173
https://doi.org/10.1007/s10462-026-11577-8

AI-enabled clinically aligned fewer-lead ECG approaches for detecting cardiovascular diseases

Tasriva Sikandar[1] · Md. Tariq Hasan[2] · AKM Azad[3] · Asaduzzaman Khan[1] · Mohammad Ali Moni[2,4]

Received: 7 August 2025 / Accepted: 23 April 2026 / Published online: 8 May 2026
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Abstract
The 12-lead electrocardiogram (ECG) is the clinical gold standard for cardiovascular disease (CVD) detection, though its use in self-care and resource-limited settings is constrained by complex configurations and reliance on specialised diagnostic infrastructure. Commercially available portable/wearable artificial intelligence-enabled ECGs (AI-ECGs) using fewer leads offer greater accessibility yet face clinical integration challenges due to misalignment with gold standard lead configurations, and restricted detection capabilities and clinical interpretability. Consequently, recent research emphasises development of clinically aligned fewer-lead AI-ECG approaches, where the leads are aligned with the 12-lead ECG and used individually or in combinations. However, these approaches remain largely pre-commercial, and comprehensive evaluation is needed to determine their potential and limitations for clinical and self-care acceptability. This review critically assesses 316 studies in terms of detected CVD types, selected leads and rationale for lead selection, and diagnostic performance of AI methods. Key findings reveal limitations in detectable CVD types, diagnostic consistency, incorporation of cardiac electrophysiology and lead interdependency insights, along with the limited adoption of advanced multi-task learning, adaptive methods and explainable AI models. This review also outlines future directions to develop compact and clinically aligned fewer-lead AI-ECGs, bridging the gap between innovation and practical application in clinical and self-care settings.

Keywords Electrocardiogram · Cardiac electrophysiology · 12-lead · Lead combination · Lead selection · Reduced lead · Artificial intelligence · Deep learning · Machine learning · Adaptive model · Multi-task model · Explainable model · Systematic review

1 Introduction

Cardiovascular disease (CVD) significantly contributes to global morbidity and mortality, posing a critical public health concern. Epidemiological studies across continents highlight its widespread impact on urban and rural populations (AIHW 2024; Heart Foundation 2024; Australian Bureau of Statistics 2023). Also, diagnostic delays as brief as ten minutes mark-

Extended author information available on the last page of the article

edly increase mortality rates, emphasising the urgency of prompt and accurate detection of CVDs (Scholz et al. 2018; Fan et al. 2021). Among the CVD diagnostic methods—blood tests, troponin test, echocardiograms, cardiac computed tomography (CT) scans, and magnetic resonance imaging (MRI)—traditional 12-lead electrocardiogram (ECG) remains indispensable and the clinical gold standard (Bonow et al. 2011; Nahar et al. 2013). Traditional 12-lead ECG records heart's electrical activity simultaneously through limb leads (Lead I, II, III), augmented limb leads (Lead aVR, aVL, aVF), and precordial leads (Lead V1–V6), collectively providing a comprehensive cardiac function estimation at any given moment (Garcia 2014). These leads are identified as clinically aligned leads, as they are widely established in clinical settings (Bonow et al. 2011; Nahar et al. 2013; Garcia 2014; Mohan et al. 2019; Zhang et al. 2023). Despite being the clinical gold standard, traditional 12-lead ECG requires meticulously placed wired leads at specific body locations, along with trained professionals and equipped laboratories or care rooms for accurate execution (Zhu et al. 2018; Wang et al. 2019; Mason et al. 2024). These requirements limit the application of traditional 12-lead ECG in rural or underserved areas lacking healthcare infrastructure and trained personnel, and in home settings where patient self-care is a consideration (Zhu et al. 2018; Wang et al. 2019; Mason et al. 2024; Zeidan and Farah 2024; Sørensen et al. 2011). Given the urgency of CVD diagnosis and the limitations of traditional 12-lead ECG, research has focused on developing simpler, user-friendly and accessible ECG approaches. This need has motivated the development of artificial intelligence-enabled ECG (AI-ECG) approaches integrated into portable/wearable devices (Zhu et al. 2018; Wang et al. 2019; Mason et al. 2024). Consequently, several AI-ECG approaches, including FDA-approved devices such as the AliveCor Kardia, Apple Watch, and Zio Patch, have emerged for detecting CVDs (Svennberg et al. 2022; Kamga et al. 2022).

AI-ECG approaches in most devices operate on data captured with fewer leads to detect CVDs (Svennberg et al. 2022; Kamga et al. 2022). However, the fewer leads in these devices do not align with the traditional 12-lead ECG, where leads may be used individually or in combinations depending on diagnostic needs (Elgendi 2012; Dörr et al. 2019). This deviation challenges healthcare professionals in interpreting results due to the lack of heart's electrical activity recording similar to that of traditional system. As a result, the interpretation of the disease becomes ambiguous, leading to confusion among users, including patients, doctors, and caregivers. Additionally, this deviation limits these devices to detect various CVDs that a traditional 12-lead ECG can identify (Elgendi 2012; Dörr et al. 2019; Foster and Torous 2019; Scquizzato et al. 2021). To illustrate these practical challenges, consider examples such as the Apple watch and AliveCor Kardia. The Apple watch, worn on one wrist and touched with the opposite hand's fingertip, utilises photoplethysmography (PPG) to measure blood volume changes and generate a pulse waveform. AI algorithms analyse this waveform and trigger an arrhythmia alert if five out of six consecutive tachograms are irregular within 48 h (Elgendi 2012; Dörr et al. 2019). However, the Apple watch can produce false-positives by recording frequent tachograms during physical activities, leading to unnecessary clinical visits (Foster and Torous 2019; Scquizzato et al. 2021). Similarly, the Kardia attaches leads sequentially to the fingertips, knee, and ankle. Sequential recording at different time and positions result in a fragmented estimation of the heart's electrical activity, as it changes rapidly (Svennberg et al. 2022; Kamga et al. 2022). Additionally, a clinical trial involving 445 cardiology and geriatric patients revealed that Kardia were unable to capture accurate data in 7% of cardiology and 21.4% of geriatric patients (Desteghe et al.

2017). Furthermore, unlike the traditional 12-lead ECG, both Apple watch and Kardia can detect only a few arrhythmias (Elgendi 2012; Dörr et al. 2019; Desteghe et al. 2017). These illustrations highlight the clinical integration difficulties of these approaches due to lead configuration misalignment with traditional 12-lead ECG (Atoui et al. 2010).

AI-ECG approaches in most devices operate on data captured with fewer leads to detect CVDs (Svennberg et al. 2022; Kamga et al. 2022). However, the fewer leads in these devices do not align with the traditional 12-lead ECG, where leads may be used individually or in combinations depending on diagnostic needs (Elgendi 2012; Dörr et al. 2019). This deviation challenges healthcare professionals in interpreting results due to the lack of heart's electrical activity recording similar to that of traditional system. As a result, the interpretation of the disease becomes ambiguous, leading to confusion among users, including patients, doctors, and caregivers. Additionally, this deviation limits these devices to detect various CVDs that a traditional 12-lead ECG can identify (Elgendi 2012; Dörr et al. 2019; Foster and Torous 2019; Scquizzato et al. 2021). To illustrate these practical challenges, consider examples such as the Apple watch and AliveCor Kardia. The Apple Watch incorporates two distinct cardiac monitoring modalities based on different physiological signals. The irregular rhythm notification feature uses the optical heart sensor to intermittently assess pulse irregularity suggestive of atrial fibrillation (AFib) via photoplethysmography (PPG), requiring multiple abnormal readings to trigger an alert. In contrast, the ECG app, accessed through the paired iPhone and initiated on the watch, records an on-demand single-lead electrocardiogram via electrodes embedded in the back crystal and Digital Crown, capturing electrical activity over approximately 30 s comparable to Lead I and generating a waveform that can be stored and shared for clinical review (Elgendi 2012; Dörr et al. 2019; https://www.apple.com/au/newsroom/2021/05/ecg-app-and-irregular-rhythm-notification-now-available-on-apple-watch/; https://support.apple.com/en-au/120278). Although useful for AFib and sinus rhythm screening, these modalities provide limited electrical information and a restricted scope of disease detection compared with a standard 12-lead ECG and may produce false-positive alerts, particularly during physical activity, leading to unnecessary clinical consultations (Foster and Torous 2019; Scquizzato et al. 2021). Similarly, the AliveCor Kardia platform comprises handheld devices for ambulatory rhythm monitoring. KardiaMobile records a single-lead ECG through simultaneous fingertip contact with two electrodes, whereas KardiaMobile 6L incorporates a third electrode to enable six-limb-lead recordings (I, II, III, aVR, aVL, and aVF) via finger contact and placement of the lower electrode on the left leg (e.g., above the knee or near the ankle) (Svennberg et al. 2022; Kamga et al. 2022; AliveCor 2025; HealthTech Guidance 2023). Despite these advancements, both devices lack precordial leads and therefore do not provide comprehensive spatial coverage of cardiac electrical activity relative to a standard 12-lead ECG. Clinical evidence further indicates practical limitations, with inaccurate or unsuccessful recordings reported in 7% of cardiology patients and 21.4% of geriatric patients, and although KardiaMobile reduces time to AF detection, there is limited evidence of improved downstream clinical outcomes following AF diagnosis (Svennberg et al. 2022; Kamga et al. 2022; Desteghe et al. 2017; Atoui et al. 2010; AliveCor 2025; NICE 2023).

Owing to the above challenges, current research focuses on developing clinically aligned fewer-lead AI-ECG approaches to detect various CVDs (Han et al. 2022; Perlman et al. 2016; Prabhakararao and Dandapat 2020; Abdar et al. 2019; Ribeiro et al. 2020; Jiang et al. 2022; Bachtiger et al. 2022). Here, clinically aligned fewer-lead refer to those from the

traditional 12-lead ECG, utilised individually or in combinations. The rationale for using clinically aligned leads is grounded in established cardiac electrophysiological principles, which define the relationship between the spatial origin of cardiac pathology and the ECG leads that best capture the corresponding electrical activity. For instance, septal abnormalities are predominantly reflected in leads V1 and V2, inferior wall involvement in leads II, III, and aVF, lateral wall pathology in leads I, aVL, V5, and V6, and anterior wall activity in leads V3 and V4. The conventional 12-lead ECG provides comprehensive spatial coverage by representing electrical activity from all major myocardial regions, forming the clinical basis for accurate detection of diverse CVDs (Garcia 2014; Bradfield et al. 2025; Meek and Morris 2002). Accordingly, when reducing the number of leads, retaining leads that are electrophysiologically aligned with these anatomical regions (i.e., clinically aligned leads) is considered important for preserving meaningful cardiac information, potentially supporting interpretability and diagnostic performance in AI-ECG systems (Han et al. 2022; Perlman et al. 2016; Prabhakararao and Dandapat 2020; Abdar et al. 2019; Ribeiro et al. 2020; Jiang et al. 2022; Bachtiger et al. 2022). Recent deep learning studies have further shown that eliminating redundant information through optimal selection of clinically aligned lead subsets can enhance model generalisability while achieving diagnostic performance comparable to that obtained using full 12-lead ECG configurations (Lai et al. 2021). By aligning AI-ECG methods with clinical standards, such as lead configuration, output results, and disease detection, current research aim to eliminate ambiguity and ensure clarity for users, including patients, doctors, and caregivers. Figure 1 summarises the limitations of traditional 12-lead ECG and portable/wearable AI-ECG approaches, and the concept of clinically aligned fewer-lead AI-ECG approach. Clinically aligned fewer-lead AI-ECG has seen

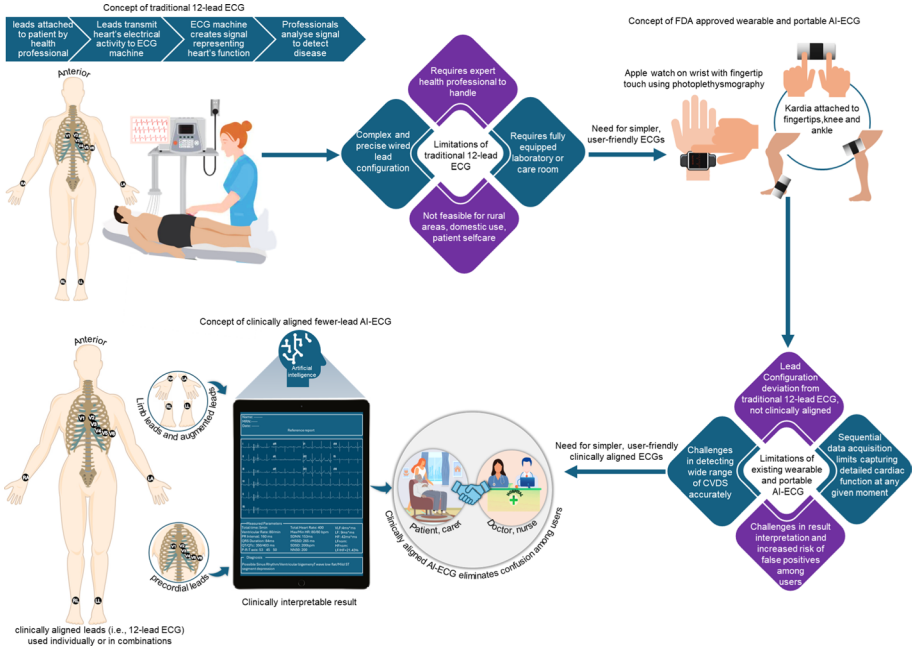


Fig. 1 Diagram showing the limitations of traditional 12-lead ECG and portable/wearable AI-ECG approaches, and the concept of clinically aligned fewer-lead AI-ECG approach

the most recent advancement with the stethoscope-based AI-ECG (Bachtiger et al. 2022), which is anticipated to receive FDA clearance. This approach detects Left ventricular ejection fraction by capturing data sequentially from 4 to 5 clinically aligned positions using two leads: a precordial lead and a limb lead. This approach achieved sensitivity, specificity and F-1 score of 71.7%, 86.4% and 43.9%, respectively (Bachtiger et al. 2022). However, the stethoscope's sequential data acquisition limits cardiac function estimation at a simultaneous instance for this approach. Additionally, this approach is still undergoing refinement to detect diverse CVDs with high detection performance. Consequently, the area of developing clinically aligned fewer-lead AI-ECG for detecting diverse CVDs with high diagnostic performance requires further exploration. In this context, it is imperative to comprehensively evaluate the detectable CVDs, selected ECG leads and lead selection rationale, and the diagnostic performance of AI methods reported in studies employing fewer clinically aligned leads to identify research gaps, enabling advancements and optimisation in these systems. Therefore, with a specific focus on these aspects, this study conducts a systematic review of currently available studies on clinically aligned fewer-lead AI-ECG approaches capable for detecting diverse CVDs with high performance.

2 Methods

This systematic review critically evaluates studies proposing clinically aligned fewer-lead AI-ECG approaches for CVD detection. To achieve this objective, relevant studies employing AI techniques with data derived from the standard 12-lead ECG —where the leads were used individually or in combination—were identified and systematically analysed. This systematic review follows PRISMA guidelines (Page et al. 2020) and is registered on PROSPERO (CRD42024519376). The review adopted a qualitative evidence synthesis approach. No quantitative pooling or meta-analysis of diagnostic performance metrics was conducted due to substantial heterogeneity across datasets, model architectures, lead configurations, and validation strategies.

2.1 Study search strategy and eligibility criteria

Search sources (i.e. electronic research databases), search terms and strategy (Supplementary Document 1 Table S1-S6) were developed in collaboration with an experienced research librarian, Marcos Riba, from The University of Queensland. Peer-reviewed literatures were searched on five databases namely PubMed, Embase, CINAHL, Scopus and Web of Science. Search was conducted on textual contents such as title, abstract and keyword of articles on December 19, 2023 with no publication date limits. To search across the databases, fundamental keywords and expanded search terms such as mesh terms, synonyms, related words, all fields and wild card symbols were selected and arranged using logical relations (i.e., AND, OR, NOT etc.). Peer-reviewed original journal articles (published and in press) that applied AI methods to data from gold standard 12-lead ECG—where the leads were used individually or in combination—for detecting CVDs were included. Only studies published in English were considered for inclusion. Detail inclusion and exclusions criteria are described in Supplementary Document 1 Table S7.

2.2 Study screening and selection

Studies retrieved from five databases included duplicates, which were removed through EndNote version 20, Covidence and manual marking. The remaining studies were screened through Covidence. Full description of screening and selection process with authors contribution is given in Supplementary Document 2 Section S1. Result from study screening and selection has been described and illustrated through a PRISMA diagram in Result Section (Fig. 2). Additionally, the trend in the number of published studies each year to highlight significant increases or decreases in research activity is provided in Result Section (Fig. 3).

2.3 Information and data extraction

Key insights were extracted from the fully reviewed studies, focusing on: (i) the types of CVDs detected, (ii) ECG lead(s) used for detection and the rationale for their selection and (iii) the comparative diagnostic performance (i.e., accuracy, sensitivity and specificity) of various AI approaches across varying lead configurations. Here, as many included studies utilised the same publicly available ECG datasets (e.g., PTB, PTB-XL, PhysioNet), dataset provenance was explicitly recorded during data extraction. When multiple studies were based on the same dataset, they were not treated as independent evidence, but rather

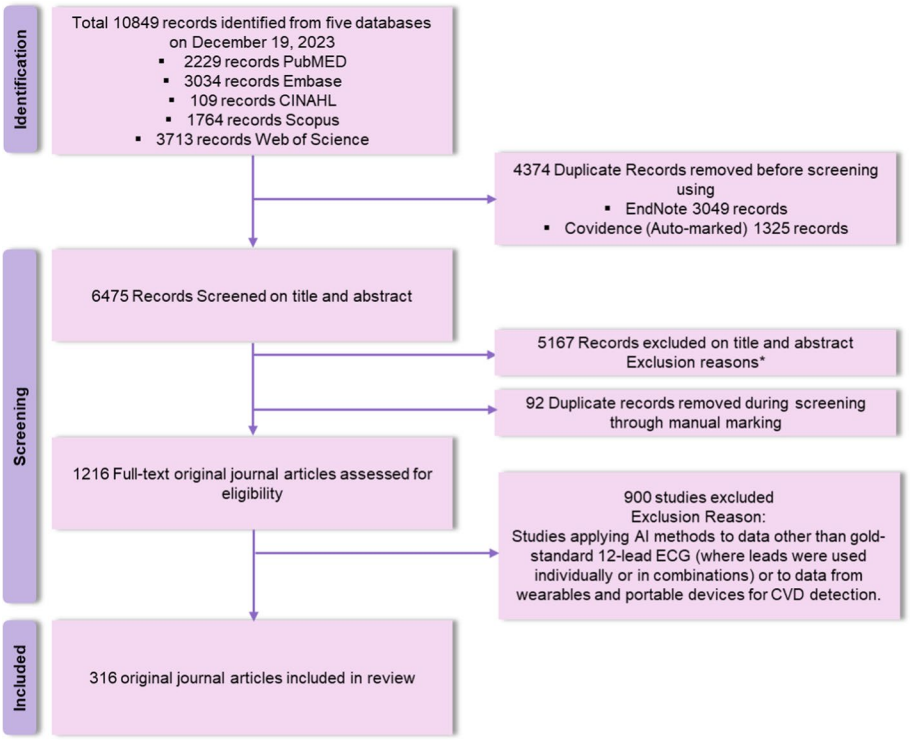


Fig. 2 PRISMA diagram presenting study selection process. * Exclusion reasons are stated in Supplementary Document 1 Table S7. List of all articles excluded after full text review are provided in Supplementary Document 3 as CSV file downloaded using Covidence

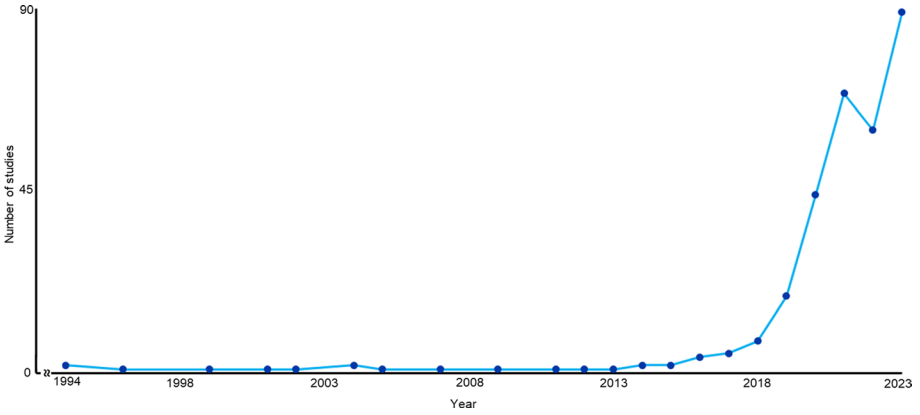


Fig. 3 Trend in the number of published studies over the years based on the 316 studies included in the full-text review

as distinct methodological evaluations applied to a shared data source. These studies were synthesised qualitatively, with attention to differences in model design, lead configuration, validation strategy, and experimental protocol, rather than being aggregated as independent statistical observations. Full description of information and data extraction process with authors contribution is given in Supplementary Document 2 Section S2.

Based on the type of CVDs detected, the identified studies were categorised into ten traditional CVD types (Bonow et al. 2011)—(i) Coronary artery disease (ii) Cardiomyopathies (iii) Arrhythmias (iv) Acute coronary syndromes (v) Heart failure (vi) Cardiac flatline, arrest (vii) Hypertrophy (viii) Heart valve diseases (ix) Heart muscle defect and (x) Conduction disorders. Result (Fig. 4) has been described and illustrated through a combined figure of scatter and bar plots showing comparison of the number of studies detecting different CVDs. Also, detail about number of studies and study references have been provided in Supplementary Document 1 Table S8.

The identified studies were grouped based on the number of lead(s) utilised for detecting various CVDs. During the extraction of this information, it is observed that most studies utilised publicly available datasets (e.g., PTB, PTB-XL, PhysioNet). In such cases, an additional verification step was performed on the publicly available dataset source to extract or verify the lead(s) information. Result (Fig. 5a) has been described and illustrated through bar plot showing comparison of the number of studies detecting various CVDs utilising different number of leads. Additionally, the rationales for using certain lead(s) were identified and presented through a diagram in Result Section (Fig. 5b). Also, detail of leads description and rationale for using them with study references is provided in Supplementary Document 1 Table S9–S10.

Performance of various AI methods in detecting different CVDs using different numbers of ECG leads was assessed in terms of accuracy, sensitivity, specificity, precision, F1-score, AUC, and ROC. As accuracy, sensitivity, and specificity were the most consistently reported metrics across studies, these parameters were extracted for analysis. When studies reported performance across multiple datasets, within-study average values were calculated. Subsequently, unweighted mean ± standard deviation (SD) of accuracy, sensitivity, and specificity were computed as descriptive statistics only, with the aim of summarizing performance

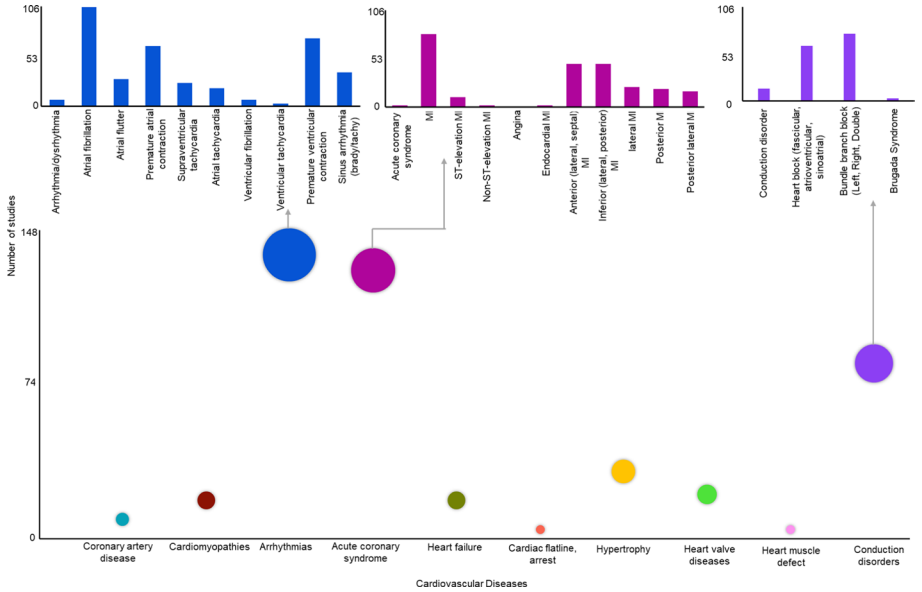


Fig. 4 Summary and comparison of the number of studies detecting different cardiovascular diseases. The X-axis and Y-axis in the scatter plot represent the ten types of cardiovascular disease and the number of studies, respectively, and the size of the circles in the scatter plot represents the volume of studies involved for different diseases. The X-axis in the bar plots represents subtypes corresponding to the cardiovascular diseases detected by different studies. The Y-axis in the bar plots represents the number of studies. MI refers to myocardial infarction

trends across heterogeneous studies rather than deriving pooled or inferential estimates. Due to substantial heterogeneity in datasets, sample sizes, disease definitions, lead configurations, and evaluation protocols, no weighting or meta-analytic modelling was performed. In addition, studies reporting the highest observed performance values for specific CVDs and lead configurations were identified to illustrate the upper range of reported results. These values were used for qualitative comparison and contextual interpretation and are presented alongside overall performance variability in the Results section (Figs. 6, 7 and 8 and Table 1).

2.4 Risk of bias and quality assessment

Given the qualitative evidence synthesis design of this review and the substantial heterogeneity across AI-enabled ECG studies—including differences in datasets, ECG lead configurations, model architectures, performance metrics, and validation strategies—a formal quantitative risk-of-bias tool such as QUADAS-2 or PROBAST was not directly applied. These tools were primarily developed for conventional diagnostic accuracy or clinical prediction model studies and, while widely used, may not fully capture methodological considerations specific to our AI-based research (Jayakumar et al. 2022; Hunik et al. 2025). In addition, QUADAS-2 is often incompletely applied in AI diagnostic reviews and may not adequately account for complexities such as heterogeneous datasets, diverse model architectures, and AI-specific validation strategies, prompting the development of AI-specific

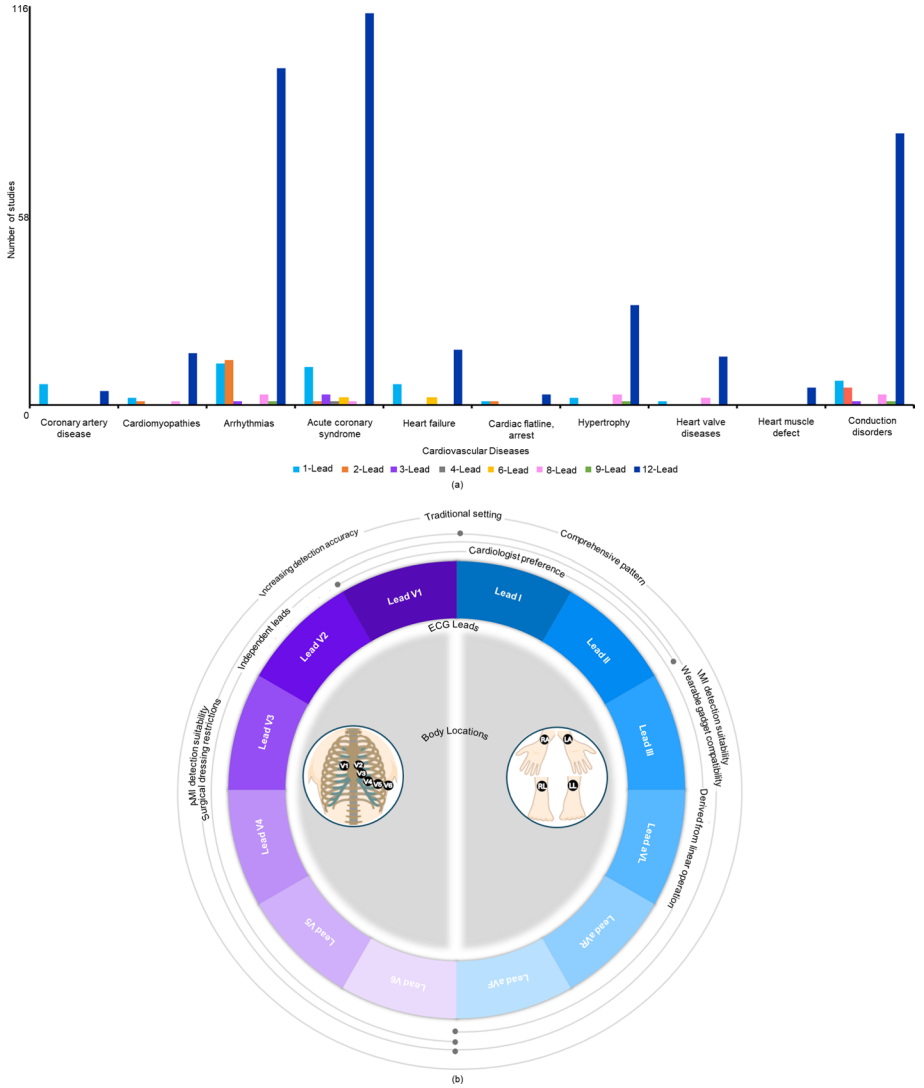


Fig. 5 **a** Summary and comparison of studies detecting different cardiovascular diseases using different number of leads. The X-axis and Y-axis represent the ten types of cardiovascular disease and the number of studies, respectively, and the different colour of the bars represents number of leads utilised to detect diseases **b** Rationales for using different numbers of ECG lead

extensions (e.g., QUADAS-AI) (Jayakumar et al. 2022). Similarly, PROBAST has limited specificity for AI or machine learning–based prediction models, motivating the development of PROBAST-AI (Hunik et al. 2025). Also, QUADAS-AI and PROBAST-AI tools remain in early stages of adoption and are primarily intended for quantitative diagnostic accuracy evaluations (Kolbinger et al. 2024; Guni et al. 2024); therefore, they were not directly applied in this qualitative synthesis. In this context, we conducted a structured qualitative appraisal to assess methodological quality and potential sources of bias across

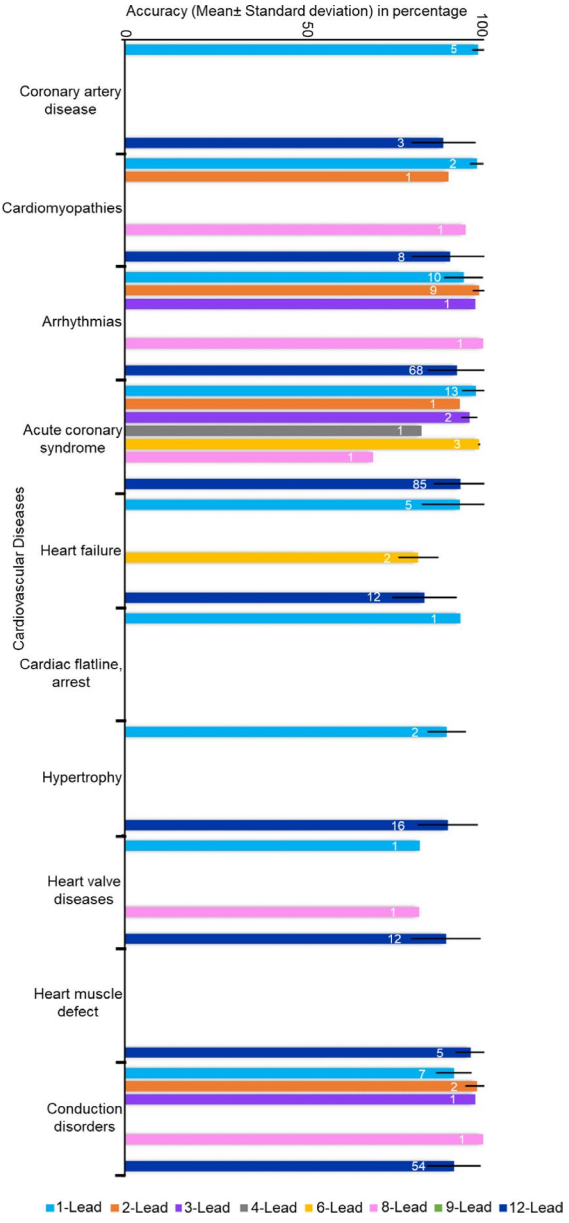


Fig. 6 Mean ± SD (standard deviation) accuracy (in percentage) achieved by different AI methods for detecting various CVDs using different numbers of leads. Bar colours indicate number of leads; numbers within bars denote study counts

included studies. The appraisal focused on domains particularly relevant to AI-enabled ECG research, including: (i) dataset provenance and representativeness, (ii) ECG lead selection and clinical alignment, (iii) model development and validation strategy (e.g., internal versus external validation), (iv) transparency and completeness of performance reporting, and (v) reproducibility considerations such as dataset availability and methodological detail. Each domain was assessed descriptively during full-text review to identify potential sources of bias and to contextualise reported performance, rather than to generate a numerical qual-

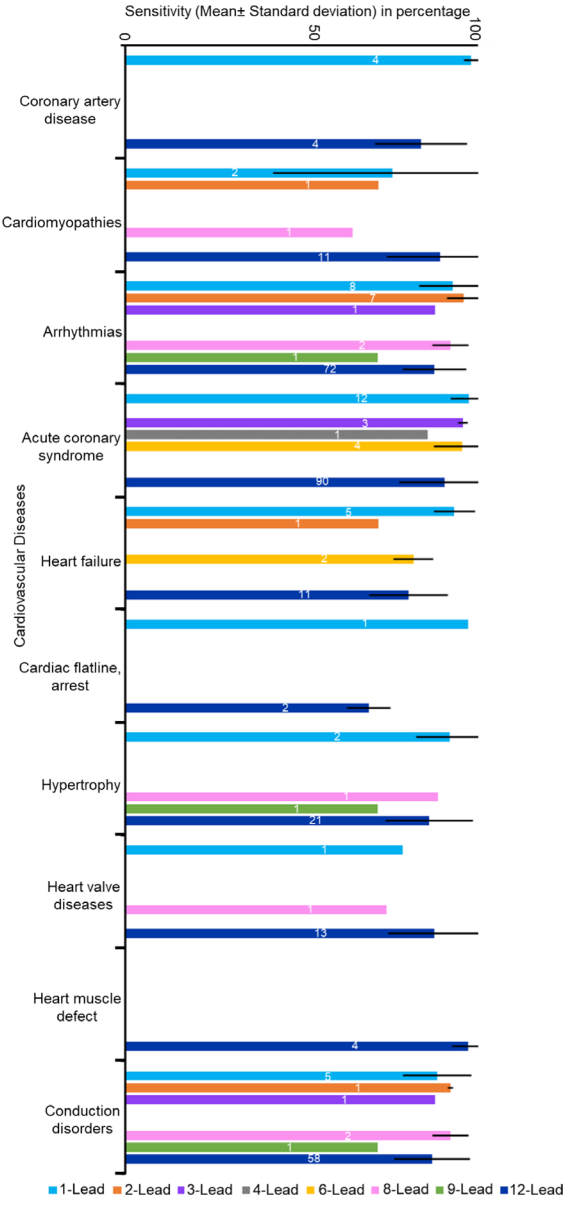


Fig. 7 Mean ± SD (standard deviation) sensitivity (in percentage) achieved by different AI methods for detecting various CVDs using different numbers of leads. Bar colours indicate number of leads; numbers within bars denote study counts

ity score or exclude studies. These domains were predefined prior to data extraction and were systematically examined for each included study during full-text review. No numerical scoring or study exclusion based on quality was performed; rather, the appraisal was used to contextualise reported performance, identify common methodological limitations, and inform the narrative synthesis and interpretation of findings.

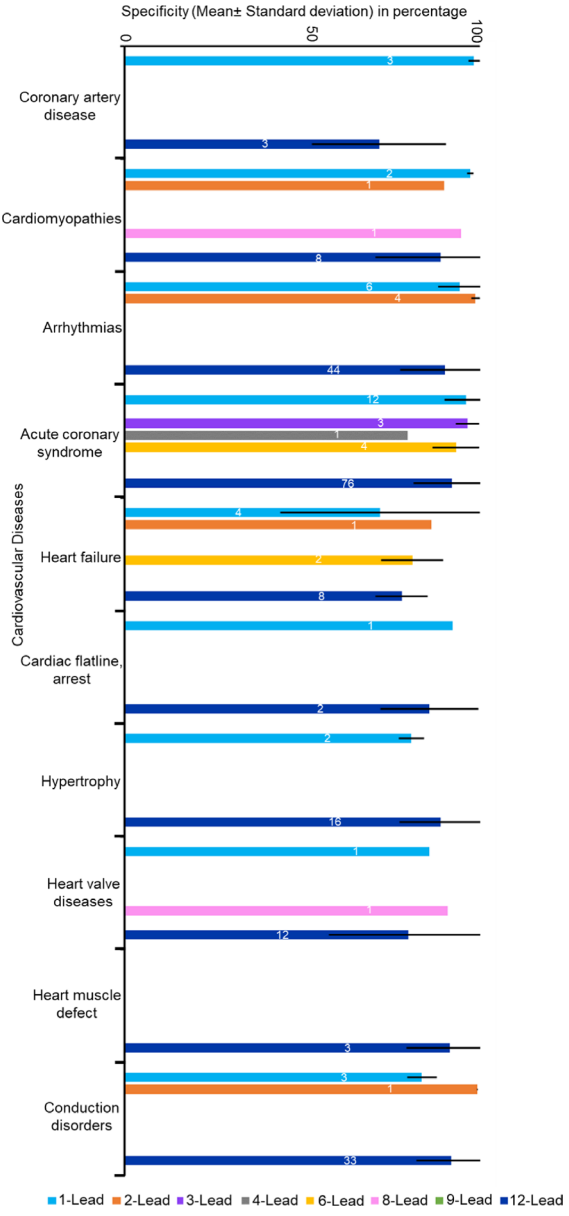


Fig. 8 Mean ± SD (standard deviation) specificity (in percentage) achieved by different AI methods for detecting various CVDs using different numbers of leads. Bar colours indicate number of leads; numbers within bars denote study counts

3 Results

Searching in the five databases (Fig. 2) retrieved 10,849 records which included duplicates. Duplicate removal resulted in 6475 records to be screened. After title and abstract screening, 5167 records were excluded. Also, 92 duplicate records were manually marked and removed. 1216 journal articles advanced to the full-text review and of these 900 studies excluded. These excluded studies applied AI methods to data other than 12-lead ECG

Table 1 Studies using advanced DL method for adaptability and explainability

Advanced DL method	Studies	Method name	Lead configuration	CVDs detected	Accuracy (%)	Sensitivity (%)	Specificity (%)
Adaptive and explainable AI(XAI)	Le et al. (2023)	CNN based lead wise attention module with XAI Grad-CAM (Gradient-weighted Class Activation Mapping) technique	3-lead	Arrhythmias, Conduction disorders	97.51	87.83	NP
Adaptive method	Ullah et al. (2021)	Attention-based CNN-LSTM	2-lead	Arrhythmias	99.3	99.29	NP
	Wang et al. (2021)	Non-local convolutional block attention module CNN	2-lead	Arrhythmias, Acute coronary syndrome, conduction disorders	93.14	NP	
	Khunte et al. (2023)	Gaussian noise adapted CNN	1-lead	Heart failure	NP	96.4	32.74
	Park et al. (2020)	Squeeze-and-excitation Residual Network (SE-ResNet)	1-lead	Arrhythmias, conduction Disorders	97.05	NP	NP
	Bachtiger et al. (2022)	Cloud collaboration based DL	2-lead	Heart failure (LVF)	NP	71.7	86.4
Multitask learning method	Ma et al. (2022)	Multi-scale CNN-LSTM hybrid	1-lead	Arrhythmias	99.89	99.86	98.02
	Zhang et al. (2021)	Global hybrid multiscale CNN	1-lead	Arrhythmias	99.84	99.65	99.98
	Li et al. (2020a)	Multi-scale CNN ResNet	1-lead	Heart failure	94.29	93.79	NP

(where the leads were used individually or in combinations) or to data from wearables/portables for detecting CVDs. Finally, 316 original journal articles (See References (AIHW 2024) to [316] in Supplementary Document 1) met the eligibility criteria and were included for review. The trend (Fig. 3) in the number of published studies over the years, based on the included 316 studies, depicts that initial research in this area began in 1994. The volume of studies remained relatively modest and fluctuating between 1 and 2 studies per year until 2014. Then, a notable increase occurred around 2015, specifically escalating from 19 in 2019 to 44 in 2020, and continuing to surge to 89 studies by 2023.

The result from the types of CVDs detected (Fig. 4) indicate that among the different categories of CVDs— arrhythmias (147 studies), acute coronary syndromes (139 studies), and conduction disorders (93 studies)—have been the primary focus of most studies (detail in Supplementary Document 1 Table S8). Specifically, atrial fibrillation (105 studies), premature atrial contraction (64 studies), premature ventricular contraction (72 studies), myocardial infarction (including anterior and inferior myocardial infarctions) (80 studies), heart block (62 studies), and bundle branch block (76 studies) have been the major concerns addressed by the majority of the research. Other conditions, such as coronary artery disease (CAD), cardiomyopathy, heart valve disease, heart muscle defects, and hypertrophy, have also been detected in various studies. However, the number of studies focused on these conditions is relatively limited.

Result from utilised leads for CVD detection (Fig. 5a) indicate that all types of CVDs are detectable with AI-ECG when using 12-lead configuration (detail with references in Supplementary Document 1 Table S9). Also, most diseases, except for heart muscle defects, can be detected using a single lead. Additionally, arrhythmias, acute coronary syndromes, and conduction disorders have been successfully detected using 2-lead and 3-lead configurations. For 1-lead based detection, leads such as I, II, V3, and V5 have been commonly used. In 2-lead based detection, combinations such as [Lead I, Lead II], [Lead I, Lead V1/V2/V3/V4/V5/V6], and [Lead II, Lead aVR] are frequently utilised, as reported in several studies. The rationale for using different ECG lead configurations (Fig. 5b) was driven by a combination of practical, clinical, and technical considerations (detail with references in Supplementary Document 1 Table S9-S10). Increasing detection accuracy often necessitates the use of all 12 traditional leads, as they provide a comprehensive spatial representation of cardiac electrical activity across cardiac planes (i.e. septal, lateral, inferior and anterior walls and arteries). Across the reviewed studies, cardiologist preference was most frequently associated with the use of leads I, II, and V1, primarily due to their ease of acquisition, suitability for rapid clinical assessment, and widespread familiarity in routine practice. Wearable device compatibility strongly favoured limb-lead configurations (leads I, II, III, aVL, aVR, and aVF), as these leads can be recorded using fewer electrodes positioned on the extremities and are commonly supported by wearable and ambulatory ECG devices. In scenarios involving surgical dressings, anatomical constraints, or ambulatory monitoring, chest leads V1-V6 were often selected, reflecting practical limitations on electrode placement rather than disease-specific electrophysiological targeting. Disease-driven lead selection was reported less frequently but was most evident for myocardial infarction (MI) detection. In particular, inferior myocardial infarction (IMI) detection commonly relied on limb leads (II, III, and aVF), reflecting their frequent use in studies targeting infarctions associated with the right coronary and circumflex arteries. Multi-lead subsets, including 3-lead, 6-lead, and 8-lead configurations, were also adopted based on considerations of lead independence and derivability, with several studies explicitly noting that leads III, aVL, aVR, and aVF can be mathematically derived from leads I and II, introducing redundancy within the standard 12-lead system.

Results from the diagnostic performance analysis (Figs. 6, 7 and 8) demonstrate substantial variability in reported accuracy, sensitivity, and specificity across AI methods, cardiovascular disease (CVD) types, and ECG lead configurations. It should also be noted that a substantial proportion of studies reporting high diagnostic performance relied on a limited number of widely used public datasets, and therefore the frequency of reported results does not necessarily correspond to independent empirical evidence. Importantly, the performance values summarised in Figs. 6, 7 and 8 originate from studies addressing different disease definitions, classification tasks, datasets, and evaluation protocols. As such, these results are not intended to represent direct or fair head-to-head comparisons between AI algorithms or ECG lead configurations. Rather, they illustrate the range of reported diagnostic performance achieved under heterogeneous, study-specific experimental conditions. While the mean ± SD values summarize the central tendency and dispersion of performance across heterogeneous studies, several individual investigations reported upper-bound performance values approaching 97–100% under specific experimental settings. It should be noted that these highest reported values typically originate from studies employing limited, curated, or single-source datasets and therefore may not reflect typical performance or generalisability

to real-world, heterogeneous clinical populations. The DL methods applied in the studies included different deep-layered architectures of convolutional neural network (CNN), Long short-term memory (LSTM) network, CNN-LSTM hybrid, decision tree and graph models, etc. In individual studies focusing on coronary artery disease detection, the highest reported accuracy, sensitivity, and specificity were achieved by a support vector machine (SVM) model, reaching 100% across all three metrics using a single ECG lead under specific experimental conditions (Kumar et al. 2022). For cardiomyopathy detection, a CNN achieved the highest reported accuracy of 99.74% using a 12-lead ECG (Dai et al. 2021) followed by a k-nearest neighbor (KNN) model with an accuracy of 99.27% (Adam et al. 2018) using single-lead, while decision tree and k-nearest neighbor (KNN) models attained peak sensitivity and specificity values, respectively, using 12-lead and single-lead ECG configurations (Adam et al. 2018; Shimojo et al. 2023). In arrhythmia detection, a Graph-CNN model reported upper-bound accuracy and sensitivity values of 100% using 12-lead ECGs (Duong et al. 2023), while Dense-CNN models achieved the highest reported specificity under similar lead configurations (Caires Silveira 2021). Also, among fewer-lead configurations, a Multiscale CNN–LSTM model achieved accuracy, sensitivity, and specificity values of 99.89%, 99.86%, and 99.93%, respectively, using a 2-lead ECG configuration (Ma et al. 2022). For acute coronary syndrome detection, individual studies reported maximum performance values using SVM/ANN and Graph-CNN models, each achieving 100% accuracy and sensitivity with 1-lead and 12-lead ECGs, respectively, whereas the highest reported specificity was observed with SVM using a single lead and ensemble subspace KNN/multilayer perceptron neural network models using 12-lead ECGs (Kumar et al. 2022; Duong et al. 2023; Shahnawaz et al. 2021; Olsson et al. 2002; Chaitanya and Sharma 2023; Chauhan et al. 2023). In heart failure detection, a Gabor-CNN model reported a maximum accuracy of 98.74% using a single lead, while CNN-LSTM models achieved upper-bound sensitivity and specificity values of 99.3% and 97.89%, respectively, under the same lead configuration (Jahmunah et al. Jul 2021; Lih et al. Mar 2020). Detection of cardiac arrest or flatline conditions showed comparatively lower peak performance, with CNN-LSTM models achieving a highest reported accuracy of 93.32% and sensitivity of 97.03% using a single lead, and morphology-based CNN-residual networks reporting a maximum specificity of 98.5% using 12-lead ECGs (Mousavi et al. 2020; Dwivedi et al. 2023). For hypertrophy detection, ensemble subspace KNN models reported upper-bound accuracy, sensitivity, and specificity values of 99.8%, 99%, and 100%, respectively, using a 12-lead ECG (Chaitanya and Sharma 2023). In heart valve disease detection, CNN models achieved the highest reported accuracy (99.74%), sensitivity (99.36%), and specificity (99.92%) using 12-lead ECGs in individual studies (Dai et al. 2021). Similarly, for heart muscle defect detection, SVM models with radial basis function kernels reported a maximum accuracy of 99.81%, while least-squares SVM models achieved the highest reported sensitivity (99.87%) and specificity (99.6%) using 12-lead ECGs (Han and Shi Jul 2019; Tripathy et al. 2019). For hypertrophy, heart valve disease, and heart muscle defect detection, the evidence from fewer lead configurations (using lead number <12 lead) was extremely sparse, rendering any evaluation of performance loss relative to 12-lead systems inconclusive. For conduction disorder detection, ResNet-based models reported upper-bound performance values, reaching 99.98% accuracy, 100% sensitivity, and 99.94% specificity using 12-lead ECGs in specific experimental settings (Faust et al. 2021). Also, among fewer-lead configurations, a CNN-ResNet model using 8-lead configuration reported accuracy and sensitivity of 99.69% and

95.81% (Xu et al. 2023). Scatter plots corresponding to Fig. 6–8 representing distribution of individual study results (i.e., accuracy, sensitivity and specificity) have been provided in Supplementary_Document_5 for additional insight.

In a limited number of studies (Table 1), the application of adaptive models, multi-task learning model and explainable DL frameworks has been explored for the detection conduction disorders, arrhythmias, acute coronary syndrome and heart failure, using 1-lead, 2-lead and 3-lead configuration. These methods achieved an accuracy above 97% in most cases (Bachtiger et al. 2022; Le et al. 2023; Ullah et al. 2021; Khunte et al. 2023; Park et al. 2020), with the exception of 93.14% and 94.29% reported in study (Wang et al. May 2021) and (Li et al. 2020a), respectively. However, the sensitivity and specificity achieved in these studies (Bachtiger et al. 2022; Le et al. 2023; Khunte et al. 2023; Wang et al. May 2021) were below 97% in most cases, with the exception reported in study (Ullah et al. 2021) and (Li et al. 2020a).

4 Discussion

This systematic review provides a comprehensive evaluation of the advancements and persisting challenges in the research of clinically aligned fewer-lead AI-ECG approaches for CVD detection. The extensive volume of research identified (Fig. 2) and the research trend over the past decade (Fig. 3), particularly from 2019 to 2023, highlights several key implications. One of the key implication is that researchers are actively and diligently addressing the limitations of traditional 12-lead ECG, and portable/wearable AI-ECGs. Another critical implication is that researchers are pursuing continuous efforts in investigating AI-ECG's potential through fewer clinically aligned ECG lead(s) to revolutionise cardiovascular diagnostics by bridging the gap between AI technologies and clinical applicability. To elaborate, research has progressed from reliance on traditional 12-lead ECGs requiring trained professionals to portable/wearable AI-ECGs, which are compatible with both trained and untrained users but are not yet fully clinically aligned (Topol 2019). More recently, research is evolving toward clinically aligned fewer-lead AI-ECGs, maintaining compatibility for both trained and untrained users, and offering and applicability in both self-care and clinical environments. This suggest that enhancing AI-ECG with fewer clinically aligned lead(s) is emerging as a significant and increasingly prominent area of study (Elias et al. 2024).

The focus of clinically aligned fewer-lead AI-ECG research has predominantly been on life-threatening CVDs (e.g., arrhythmias, acute coronary syndromes, and conduction disorders), with comparatively less emphasis on slower-progressing CVDs (e.g., coronary artery disease, cardiomyopathy, heart valve disease, myocardial defects, and hypertrophy) (Fig. 4, and Supplementary Document 1 Table S8). Life threatening CVDs require accurate and prompt diagnosis for preventing potentially fatal outcomes such as sudden cardiac arrest or significant impairment of heart function (Bonow et al. 2011; Nahar et al. 2013; Mohan et al. 2019), which may explain the concentrated research efforts in this area (Cho et al. 2020; Harrison and Kennedy Nov 2005; Heo et al. 2020; Liu et al. 2022; Zhao et al. 2020; Gibson et al. 2022; Wu et al. 2022a, 2022b Gustafsson et al. 2022; Tseng et al. 2023; Choi et al. 2022). In contrast, slow progressing CVDs present with less acute symptoms, allowing for more time in the diagnostic process (Sheikh Beig Goharrizi et al. 2023; Lee et al. 2020; Togo et al. 2023; Yang et al. 2023; Deng et al. 2020; Terzi and Arikan 2024). Also, some of

these conditions might require more complex imaging techniques or invasive procedures, such as an angiogram, for definitive diagnosis (Bonow et al. 2011; Nahar et al. 2013; Mohan et al. 2019). These reasons could explain the relatively lower research focus on slower-progressing CVDs. However, if left undetected or untreated, many slower-progressing CVDs can evolve into severe or life-threatening conditions—for instance, prolonged coronary artery disease may lead to myocardial infarction (Bonow et al. 2011; Nahar et al. 2013; Mohan et al. 2019). Since AI can explore subtle and previously underutilised information in ECG signals that may be imperceptible to human interpretation, it has the potential to serve as an effective screening tool for a broader spectrum of CVDs, facilitating timely referral for further confirmatory investigations using imaging modalities such as echocardiography, cardiac MRI, or angiography (Topol 2019; Elias et al. 2024). Therefore, rather than focusing solely on life-threatening conditions, researchers should aim to develop clinically aligned fewer-lead AI-ECG approaches that could detect a wide range of CVDs.

Clinically aligned AI-ECGs utilising 12-lead configuration are capable of detecting all types of CVDs, whereas most conditions, excluding heart muscle defects, can be identified using single-lead configurations (e.g., leads I, II, V3, or V5). Additionally, two- and three-lead configurations (e.g., [Lead I, Lead II] and [Lead II, Lead aVR]) have demonstrated effectiveness for detecting specific types of CVDs (Fig. 5a and Supplementary Document 1 Table S9). These observations suggest that the diagnostic strength of the 12-lead configuration stems from its ability to capture electrical activity from multiple spatial orientations of the heart, providing a comprehensive perspective essential for identification of complex and varied cardiac conditions (Bonow et al. 2011; Nahar et al. 2013; Garcia 2014; Mohan et al. 2019; Zhang et al. 2023). Consequently, in the pursuit of identifying clinically aligned fewer-lead configurations, it is crucial to direct research attention toward two foundational aspects. First, cardiac electrophysiological insights, i.e., the relationship between the spatial orientation of CVDs' origin within the heart and the leads capturing corresponding electrical activity. For example, the septal wall of the heart—supplied by the left anterior descending artery—is optimally represented by leads V1 and V2, while the inferior wall—typically perfused by the right coronary artery—is reflected in leads II, III, and aVF. These associations highlight the importance of selecting leads that are electrophysiologically aligned with the site of cardiac events, especially when aiming to reduce the number of leads, in order to preserve diagnostic accuracy (Bonow et al. 2011; Nahar et al. 2013; Garcia 2014; Mohan et al. 2019; Zhang et al. 2023; Hirota et al. 2023; Xiong et al. 2023; Chang et al. 2012; Malmivuo and Plonsey 1975; Levkov 1987; Maheshwari et al. 2016). Second, the interdependence and derivability of ECG leads must be considered when aiming to reduce lead numbers. For instance, aVR, aVL, and aVF, are not independently recorded but mathematically derived from the electrodes used for leads I, II, and III. This inherent redundancy in the standard 12-lead ECG system suggests that specific signals can be computationally reconstructed, thereby supporting the development of reduced-lead configurations without substantial loss of diagnostic information (Bonow et al. 2011; Nahar et al. 2013; Garcia 2014; Mohan et al. 2019; Zhang et al. 2023; Hirota et al. 2023; Xiong et al. 2023; Chang et al. 2012; Malmivuo and Plonsey 1975; Levkov 1987; Maheshwari et al. 2016). Despite the potential of these two considerations, lead selection in existing studies (Fig. 5b and Supplementary Document 1 Table S9–S10) has predominantly been guided by cardiologist preferences, wearable device compatibility, and detection accuracy, with limited emphasis on cardiac electrophysiology, and the interdependence of leads. Importantly, while these

practical considerations facilitate rapid acquisition, user compliance, and device feasibility, they do not inherently guarantee optimal physiological coverage of disease-specific electrical activity. For example, the frequent selection of leads I and II reflects ease of acquisition and clinical familiarity rather than deliberate targeting of specific myocardial regions, whereas limb-lead dominance in wearable-compatible systems prioritises electrode simplicity over spatial resolution of ventricular depolarisation. Similarly, the selection of chest leads V1-V6 in ambulatory or post-surgical contexts is often driven by placement constraints, rather than systematic alignment with the electrophysiological origin of the underlying pathology. As a result, lead configurations optimised primarily for practicality may inadequately capture disease-specific electrical signatures, particularly for CVDs with heterogeneous or regionally distinct substrates. Notably, research has primarily focused on myocardial infarction (MI), particularly acute (AMI) and inferior (IMI) myocardial infarctions, where clearer spatial lead–pathology associations exist, while other CVDs and their spatial origin within the heart remain comparatively unexplored (Xiong et al. 2023; Chang et al. 2012; Hernandez et al. 2018). These disparities suggest the need for a more balanced exploration of fewer-lead configurations considering clinical preferences, device suitability and most importantly cardiac electrophysiology, and lead interdependencies. This balanced exploration could enhance fewer-lead configurations, enabling them to detect a wider range of CVDs comparable to the 12-lead configuration. Though, in less favourable scenarios, universal detection of all CVDs using same fewer-lead configuration may not be feasible, achieving this balance could pave the way for an optimised clinically aligned fewer-lead approach tailored to the detection of group of related CVDs (Lai et al. 2021; Topol 2019; Elias et al. 2024; Leur et al. 2021).

Achieving high detection accuracy, sensitivity, and specificity is critically important for AI-ECG approaches for detecting diverse CVDs due to the potential life-or-death implications associated with these conditions (Scholz et al. 2018; Fan et al. 2021). Across the reviewed literature, individual studies have reported upper-bound performance values approaching 97–100% for specific CVDs, AI methods, and ECG lead configurations (Figs. 6, 7 and 8). However, these values should be interpreted with caution, as they frequently reflect best-case experimental conditions, including the use of curated, single-source or differing datasets, differing disease labels and validation strategies, and limited population diversity. Consequently, the results presented in Figs. 6, 7 and 8 should not be interpreted as evidence of comparative superiority between AI models or ECG lead configurations, but rather as illustrative performance limits observed under study-specific conditions. Additionally, the widespread reuse of a small number of benchmark datasets across multiple studies highlights a risk of evidence redundancy and reinforces the importance of external validation using independent, multi-center, and clinically diverse ECG datasets to establish generalisable AI-ECG performance. In contrast, the mean ± SD values reported in this review provide a descriptive overview of central tendencies and variability across a heterogeneous body of studies, highlighting substantial dispersion in performance across disease types, AI architectures, and lead configurations. This variability underscores persistent challenges related to overfitting, dataset bias, and limited external validation, which remain key barriers to the clinical generalisability of AI-ECG systems. While conventional 12-lead ECG configurations enable comprehensive assessment of a wide spectrum of CVDs, the reviewed evidence suggests that clinically aligned fewer-lead configurations (e.g., 1-lead, 2-lead, and 3-lead ECGs) can achieve performance levels comparable to 12-lead systems for specific condi-

tions under controlled settings (Figs. 6, 7 and 8). In addition, evaluation of performance using fewer-lead configurations in individual studies indicates that for some CVDs, metrics such as accuracy, sensitivity, and specificity remain high even with 1-lead or 2-lead configuration. However, for other conditions, including hypertrophy, heart valve disease, and heart muscle defects, evidence from fewer-lead configurations is sparse, making it difficult to determine potential performance trade-offs. Importantly, this observation does not imply universal equivalence across all CVDs but rather indicates the potential feasibility of fewer-lead approaches when disease-specific electrophysiological signatures are appropriately captured and leveraged by advanced AI models. However, employing different DL methods and lead configurations for accurate detection of different CVDs in every instance is not feasible, as it would require a labor-intensive, non-automated process that limits scalability and efficiency (Bachtiger et al. 2022; Le et al. 2023; Ullah et al. 2021; Khunte et al. 2023; Park et al. 2020; Wang et al. 2021). This challenge underscores the need for application of advanced adaptive DL methods [such as federated learning (Pfitzner et al. 2021; Antunes et al. 2022), domain adaptation (Guan and Liu 2021), attention-based model (Gonçalves et al. 2022)], which are capable of dynamically adjusting or switching among lead configurations or appropriate methods. In addition, advanced multitask learning methods (such as MTL-CNN, MTN-LSTM, MTL-CNN-GRU (gated recurrent unit) (Mahmoud et al. 2020)) can be leveraged to simultaneously select among specific lead configuration and DL method it is trained on to detect various CVDs. Moreover, the incorporation of explainable DL models [such as gradient-weighted class activation mapping (Grad-CAM) (Le et al. 2023), local interpretable model-agnostic explanations (LIME) (Abdullah et al. 2024; Meng et al. 2024), SHapley Additive exPlanations (SHAP) (Martino and Delmastro 2023), and concept bottleneck models (CBMs) (Sawada and Nakamura 2022; Li et al. 2020b), etc.] could further enhance the interpretability and generalisability of fewer lead configurations results, providing clinicians with a more transparent understanding of the AI-driven diagnostic process. More recently, the emergence of ECG foundation models and lead-agnostic or channel-adaptive self-supervised learning frameworks has shown promise in learning generalisable representations that can adapt to clinically aligned fewer-lead ECG configurations (Oh et al. 2022; Monachino et al. 2507). While some studies (Table 1) have investigated the potentials of adaptive DL methods, multitask learning DL methods and explainable DL models, their application remains limited in the context of exploring diverse methods for achieving high accuracy, sensitivity, and specificity across a range of CVDs. Further exploration of these advanced DL methods together with clinically aligned fewer lead configurations has the potential to significantly enhance the reliability and confidence of AI-ECG. This advancement would facilitate their seamless integration into clinical practice, ultimately improving patient outcomes and advancing the standard of care for cardiovascular health.

Overall, the limited detected CVD types, inconsistencies in diagnostic performance across studies, insufficient incorporation of cardiac electrophysiological insights, limited understanding of lead interdependency, diverse application of DL methods with limited adoption of advanced multi-task learning and adaptive approaches, and the limited implementation of explainable DL models to enhance detection result interpretability—particularly for fewer-lead configurations—underscore the challenges in achieving generalisability. These highlight the need for standardised benchmarks for the development of a clinically aligned fewer-lead AI-ECG systems. Future research should prioritise addressing these gaps by focusing on areas such as the incorporation of cardiac electrophysiological insights and

lead interdependency into DL models, as well as the integration of advanced multi-task learning, adaptive approaches, and explainable methods. These efforts would help standardise methodologies to minimise inconsistencies in diagnostic performance, expand the range of detectable CVD types, and enhance interpretability and generalisability. Along with this future research should also consider optimising the trade-off between clinically aligned lead placement and design constraints of wearable/portable ECG devices to enhance the usability and scalability for point-of-care applications. This can be done by inventing a new device or tailoring existing devices such as the most recent advancement stethoscope-based AI-ECG (Bachtiger et al. 2022). Furthermore, future research should consider the least favourable scenario, where detecting all types of CVDs using the same fewer lead configuration may not be possible, even with the development of advanced DL methods. In such a scenario, future research should consider developing multiple devices, each targeting a group of related CVDs (Topol 2019; Elias et al. 2024; Leur et al. 2021).

A limitation of this review is that the literature search was conducted up to December 2023. Nevertheless, given the rapidly accelerating publication trend in this field of research, the comprehensive search strategy, eligibility criteria, and synthesis framework presented here provide a reproducible foundation that can inform future updated systematic reviews. In addition, to assess the extent of recent publications and to verify whether emerging studies remain consistent with the findings identified in this review, a scoping check using the same search terms was conducted (on 18 March 2026) separately for the years 2024 and 2025 across major databases. The search identified a substantial volume of research in 2024 (832 records in Embase, 576 in PubMed, 273 in CINAHL, 673 in Scopus, and 889 in Web of Science) and 2025 (1195 records in Embase, 883 in PubMed, 421 in CINAHL, 939 in Scopus, and 1079 in Web of Science). Incorporating additional eligible records from this extensive search would require a full re-execution of the PRISMA workflow, including screening, eligibility assessment, data extraction, and synthesis, which would be highly time-intensive within the present study framework. Still, this scoping check further highlights the accelerating research activity in this field, which is aligned with our current review findings. Furthermore, exploration of some promising studies (Li et al. 2025; Nolin-Lapalme et al. 2025; Tian et al. 2024; Coppola et al. 2024; Ding et al. 2025) from 2024 and 2025 reinforces and extends the key findings of this review. Specifically, recent studies utilise self-supervised learning and adaptive frameworks, including attention mechanisms and multi-scale feature extraction in hybrid deep learning architectures (Li et al. 2025), large-scale ECG foundation models such as DeepECG-SL and DeepECG-SSL (Nolin-Lapalme et al. 2025), knowledge-enhanced explainable foundation models (Tian et al. 2024), self-supervised foundation models such as HuBERT-ECG (Coppola et al. 2024), and cross-modal learning frameworks (Ding et al. 2025). These approaches demonstrate strong generalisability and consistently high diagnostic performance across multiple external datasets and a range of cardiovascular diseases, which directly aligns with the findings of this review. In addition, the use of masked lead modelling (Monachino et al. 2507) highlights a growing shift toward lead-agnostic and flexible architectures, supporting our finding regarding the feasibility of clinically aligned fewer-lead configurations without substantial loss of diagnostic information, while also addressing the impracticality of disease-specific models and lead configurations. However, despite adopting generalisability-enhancing methods, most studies continue to rely predominantly on benchmark publicly available 12-lead ECG datasets and controlled experimental settings, and they do not systematically evaluate performance trade-offs asso-

ciated with lead reduction. This limited evaluation and validation on clinically aligned fewer-lead or wearable-compatible configurations reflect the same limitations identified in this review regarding external validation and real-world generalisability. In addition, these studies highlight ongoing challenges in interpretability due to the limited integration of explicit cardiac electrophysiological knowledge and lead interdependency in model design—an issue consistently emphasised in our findings. Furthermore, the use of general-purpose large language models (e.g., GPT-4, GPT-4o, and Gemini) (Coppola et al. 2024) for ECG interpretation and explainability shows weaker agreement with clinicians, highlighting limitations in reliability and the need for clinical alignment (Gunay et al. 2024; Huang et al. 2025), which is also consistent with our review findings. Also, another limitation of this review is that heterogeneity in datasets, disease phenotypes, classification objectives, and evaluation protocols excludes fair quantitative comparison of algorithmic performance across studies to establish ranking among algorithms and/or lead configurations.

5 Conclusion

This systematic review provides a comprehensive synthesis of current research on clinically aligned fewer-lead AI-enabled ECG (AI-ECG) systems for cardiovascular disease (CVD) detection. The findings reveal a rapidly growing body of research work, comprising 316 published studies, aimed at addressing the limitations of both the traditional 12-lead ECG and portable/wearable AI-ECGs by advancing towards clinically aligned fewer-lead configurations. While AI-ECG utilising 12-lead configurations can detect a broad spectrum of CVDs, fewer-lead systems have shown remarkable potential in detecting specific conditions, such as arrhythmias, acute coronary syndromes, and conduction disorders, often achieving diagnostic performance metrics approaching those of 12-lead configurations. However, research remains limited in addressing slower-progressing and diagnostically demanding (e.g., imaging-dependent and invasively diagnosed) CVDs such as coronary artery disease and cardiomyopathies. The disproportionate focus on acute conditions highlights the need to expand diagnostic coverage, particularly to include CVDs that may initially present with subtle symptoms. The review also identifies two underexplored but crucial considerations in designing clinically aligned fewer-lead configurations: (i) cardiac electrophysiological insights, i.e., the relationship between the spatial orientation of CVDs' origin within the heart and the leads capturing corresponding electrical activity, and (ii) the inherent interrelationship among leads. Existing research has often overlooked these foundational considerations, yet a physiologically grounded approach could enhance diagnostic coverage and preserve clinical relevance. Furthermore, while there are many existing DL models that demonstrated diagnostic performance of 97–100% in terms of accuracy, sensitivity, and specificity, their limited use of adaptive and multi-task learning approaches hinders potential for intelligent selection of lead configurations and appropriate methods. Moreover, explainable AI models remain underutilised in existing studies, despite their potential to enhance generalisability, interpretability, and clinical trust in AI-ECG systems. This systematic review also offers potential solutions by highlighting the need for integrating innovative methodologies to overcome these challenges. Incorporating cardiac electrophysiological insights and lead interdependency information into DL training processes can enhance diagnostic performance across diverse CVDs. Integration of advanced adaptive

and multi-task learning frameworks could dynamically adjust most appropriate DL methods and lead arrangements selection. Also, incorporation of explainable AI models remains an urgent priority to improve transparency and foster clinician trust, a crucial step toward bridging the gap between AI-driven diagnostics and clinical decision-making. Additionally, future research should address the design constraints of wearable and portable devices by optimising the trade-off between clinically aligned lead configurations and usability. Efforts should also explore tailored systems for specific CVD types or groups, as the development of universal fewer-lead configurations may not be practical. This approach may involve creating multiple specialised devices, each targeting a group of related CVDs. By addressing these gaps and prioritising these future directions, this research field can move closer to developing clinically robust, scalable, and commercially viable clinically aligned fewer-lead AI-ECGs. Such advancements have the potential to revolutionise cardiovascular care, making it more accessible, interpretable, and effective, particularly in clinical settings, resource-constrained settings and home-based applications.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s10462-026-11577-8.

Author contributions TS, TH, AKMA, AK, and MAM are responsible for the entirety of the work and the final decision to submit the manuscript; study concept and design: all authors; information extraction, processing, and analysis: TS and TH.; critical review and interpretation of data: TS, TH, AKMA, AK, and MAM; drafting of the manuscript: TS; critical revision of the manuscript: all authors; All authors have read and agreed to the published version of the manuscript.

Funding Open Access funding enabled and organized by CAUL and its Member Institutions. This work was supported and funded by the Deanship of Scientific Research at Imam Mohammad Ibn Saud Islamic University (IMSIU) (grant number IMSIU-DDRSP2601).

Data availability No datasets were generated or analysed during the current study.

Declarations

Conflict of interest The authors declare no competing interests.

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Authors and Affiliations

Tasriva Sikandar[1] · Md. Tariq Hasan[2] · AKM Azad[3] · Asaduzzaman Khan[1] · Mohammad Ali Moni[2,4]

✉ AKM Azad
kazad@imamu.edu.sa

✉ Mohammad Ali Moni
mmoni@csu.edu.au

[1] Faculty of Health and Behavioural Sciences, The University of Queensland, St Lucia, QLD 4072, Australia

[2] Rural Health Research Institute, Charles Sturt University, Orange, NSW 2800, Australia

[3] Department of Mathematics and Statistics, College of Science, Imam Mohammad Ibn Saud Islamic University (IMSIU), 13318 Riyadh, Saudi Arabia

[4] AI & Cyber Futures Centre, Charles Sturt University, NSW 2795 Bathurst, Australia