American Heart Journal Plus: Cardiology Research and Practice 54 (2025) 100528

Contents lists available at ScienceDirect

American Heart Journal Plus: Cardiology Research and Practice

journal homepage: www.sciencedirect.com/journal/american-heart-journal-plus-cardiology-research-and-practice

Research paper

A multicenter pragmatic implementation study of AI-ECG-based clinical decision support software to identify low LVEF: Clinical trial design and methods

Francisco Lopez-Jimenez [a], Heather M. Alger [b,c,*], Zachi I. Attia [a], Barbara Barry [a], Ranee Chatterjee [d], Rowena Dolor [d], Paul A. Friedman [a], Stephen J. Greene [d,i], Jason Greenwood [a], Vinay Gundurao [b,c], Sarah Hackett [b,c], Prerak Jain [b,c], Anja Kinaszczuk [e], Ketan Mehta [b,c,1], Jason O'Grady [a], Ambarish Pandey [f], Christopher Pullins [g], Arjun R. Puranik [b,c], Mohan Krishna Ranganathan [b,c], David Rushlow [a], Mark Stampehl [h,1], Vinayak Subramanian [f], Kitzner Vassor [b,c], Xuan Zhu [a], Samir Awasthi [b,c]

[a] *Mayo Clinic, Rochester, MN, United States of America*
[b] *Anumana, Inc., Cambridge, MA, United States of America*
[c] *nference, Inc., Cambridge, MA, United States of America and Bengaluru, India*
[d] *Duke University School of Medicine, Durham, NC, United States of America*
[e] *Mayo Clinic, Jacksonville, FL, United States of America*
[f] *UT Southwestern Medical Center, Dallas, TX, United States of America*
[g] *Mayo Clinic Arrowhead, AZ, United States of America*
[h] *Novartis Pharmaceuticals Corp, East Hanover, NJ, United States of America*
[i] *Duke Clinical Research Institute, United States of America*

ARTICLE INFO

Keywords:
Electrocardiogram
Artificial intelligence
Left ventricular ejection fraction
Heart failure
Clinical decision support
Best practice alerts
Pragmatic implementation study

ABSTRACT

Background: Artificial intelligence (AI) enabled algorithms can detect or predict cardiovascular conditions using electrocardiogram (ECG) data. Clinical studies have evaluated ECG-AI algorithms, including a recent single-center study which evaluated outcomes when clinicians were provided with ECG-AI results. A Multicenter Pragmatic IMplementation Study of ECG-AI-Based Clinical Decision Support Software to Identify Low LVEF (AIM ECG-AI) will evaluate clinical impacts of clinical decision support software (CDSS) integrated within the electronic health record (EHR) to provide point-of-care ECG-AI results to clinicians during routine outpatient care.
Methods: AIM ECG-AI is a multicenter, cluster-randomized trial recruiting and randomizing clinicians to receive access to the CDSS (intervention) or provide usual care. Clinicians are recruited from 5 geographically distinct health systems and clustered at the care team level. AIM ECG-AI will evaluate clinical care provided during >32,000 eligible clinical encounters with adult patients with no history of low LVEF and who have a digital ECG documented within the health system's EHR, with 90 day follow up.
Results: Study data includes clinician surveys, study software metrics, and EHR data as a read-out for clinician decision-making. AIM ECG-AI will evaluate detection of left ventricular ejection fraction ≤40 % by echocardiography, with exploratory endpoints. Subgroup analyses will evaluate the health system, clinician, and patient-level characteristics associated with outcomes (NCT05867407).

Abbreviations: AE, Adverse events; AI, Artificial intelligence; AIM ECG-AI, A Multicenter Pragmatic IMplementation Study of ECG-AI-Based Clinical Decision Support Software to Identify Low LVEF; BNP, B-type natriuretic peptide; BPA, Best practice alert; CDS, Clinical decision support; EAGLE, ECG AI-Guided Screening for Low Ejection Fraction Study; ECG, Electrocardiogram; EF, Ejection fraction; EHR, Electronic health record; IT, Information technology; LVEF, Left ventricular ejection fraction; SAE, Severe adverse events; SaMD, Software as a medical device; SOC, Standard of care; TTE, Transthoracic echocardiography.

* Corresponding author at: Anumana, Inc., Cambridge, MA, United States of America
E-mail address: halger@anumana.ai (H.M. Alger).

[1] Indicates position held during the contribution to this work.

https://doi.org/10.1016/j.ahjo.2025.100528
Received 5 November 2024; Received in revised form 28 January 2025; Accepted 20 March 2025
Available online 21 March 2025

Conclusion: AIM ECG-AI is the first multisite clinical evaluation of an EHR-integrated, point-of-care CDSS to provide ECG-AI results in the clinical workflow. The findings will provide valuable insights for clinically focused software design to bring AI into routine clinical practice.

1. Introduction

An estimated 6.9 million U.S. adults have a Heart Failure (HF) diagnosis and the prevalence of heart failure is projected to increase to 11.4 million by 2050 [1]. In 2020, HF was associated with an estimated 1.1 million hospital discharges and the underlying cause of death for >85,000 individuals in 2021 [2].

Additionally, HF is classified by left ventricular ejection fraction (LVEF) with HF with reduced ejection fraction (HFrEF) defined by any LVEF at or below 40 % [3]. The 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure provides evidence-based recommendations for managing patients at each stage of HF; unimpeded progression to more severe classes of HF is associated with reduced survival [3].

Transthoracic echocardiography (TTE) is the standard clinical method to evaluate LVEF, however TTE can present a diagnostic barrier to access for some patients because of its cost, time, and inconvenience [4]. Patients can be screened for HF using blood biomarkers such as B-type natriuretic peptide (BNP) to establish presence or severity, however some conditions such as obesity can limit the diagnostic accuracy of BNP assays and the Guidelines recommend the use of these biomarkers to support decision-making, risk stratification, or establish prognosis [3].

In recent years, electrocardiography (ECG) informed by artificial intelligence (AI) has evolved as a low-cost solution to detect the presence of various cardiovascular conditions using a routine 12-lead clinical ECG. Specifically, ECG-AI has been used to low LVEF retrospectively [5], prospectively [6], and in a randomized clinical trial [7] with high accuracy, sensitivity, and specificity. Further, in a retrospective analysis of a patient population which presented to the Emergency Department with dyspnea, the ECG-AI algorithm model outperformed the standard NT-proBNP (N-terminal pro-B-type natriuretic peptide) assay to detect left ventricular systolic dysfunction [8]. To our knowledge, there are no prospective, multicenter, ethnically diverse randomized trials testing the effectiveness of implementing AI-ECG to detect LVEF.

At present, there are >900 AI and machine learning (ML) enabled medical devices listed on the US Food and Drug Administration's database [9]. The overwhelming majority of these devices are designed for use in radiology, with approximately 10 % of AI and ML devices intended for cardiology [10,11]. From those, validation in real world settings using randomized trials has been nearly non-existent [7]. This relative nascence of AI in caring for patients with cardiovascular risk factors and conditions underscores the urgent need to assess the effectiveness of AI in the clinical workflow in multicenter, multispecialty randomized implementation studies. The A Multicenter Pragmatic IMplementation Study of ECG-AI-Based Clinical Decision Support Software to Identify Low LVEF (AIM ECG-AI) study will begin to address this knowledge gap through a novel multicenter pragmatic implementation study designed to evaluate the impact of an EHR-workflow integrated clinical decision support software on patient outcomes across a diversity of care practices, geographies, and patient populations (NCT05867407).

2. Methods

2.1. Overview of the ECG Viewer study trial design

The AIM ECG-AI trial is a multicenter, cluster-randomized trial that will recruit and randomize clinicians to receive access to the intervention software or provide care-as-usual to evaluate the effectiveness of the intervention (e.g., access to Anumana's ECG Viewer Clinical Decision Support (CDS) tool and LEF ECG-AI results).

Approximately 790 (range: 600–1000) Primary Care and Cardiology clinicians will be recruited from 5 geographically distinct health systems and participants will be cluster-randomized at the care team level within each site to receive either intervention or provide care-as-usual in their ambulatory care practices. The trial is expected to evaluate the clinical care provided during >32,000 eligible clinical encounters and 90 days following the index encounter.

The study was designed to evaluate clinical decision making in general practice and cardiology practices, as these specialties may be the first clinical opportunity to detect and initiate treatment for otherwise asymptomatic patients at risk for reduced LVEF and HF.

To evaluate the study endpoints in the control and intervention groups, multiple data sources will be used to collect study data including participant surveys, electronic health record (EHR) data, and software performance data.

2.2. Study population

Similar to other recent studies designed to evaluate clinical decision-making [7,12], AIM ECG-AI will recruit and consent clinicians across the clinical care team (physicians, nurses, physician assistants); AIM ECG-AI will not recruit individual patients to participate in the study and patients will not have access to the CDS study software (Fig. 1). There will be no direct contact with individual patients during this study and the study has received a waiver of informed consent through a central institutional review board (IRB) review (WCG Clinical Services, Princeton, NJ).

Clinical encounters will be eligible for inclusion and evaluation in the study if the patient being cared for is an adult ≥18 years old with no known history of low LVEF or HF with a routine 10-s 12-lead digital ECG available. As the study will leverage EHR data as a readout of clinical decision-making, data from clinical encounters of patients who have declined to provide authorization for EHR-based research will be excluded from the AIM ECG-AI study.

2.3. Recruitment and randomization

Clinicians will be invited to participate in the AIM ECG-AI study through one or more channels: invitation email, informational presentation, or peer-to-peer conversation. Those clinicians interested in participating will consent to participate through a digital platform (e-consent) and will receive a pre-study survey. Clinicians in the intervention group will receive an additional consent form and additional training on the study software following cluster randomization into the intervention group.

As multiple healthcare providers may be involved in a single clinical encounter, the AIM ECG-AI Study will randomize clinicians at the care team level to ensure that clinicians within the same care team are not randomized to different care groups. To ensure balance across randomization groups, care teams will also be randomized based on team size (large vs. small) and specialty for sites enrolling both general medicine and cardiology clinicians. Invitees who decline to participate will not impact the participation of their colleagues, as access to the

study software will be controlled at the individual user level in the intervention group and control clinicians will provide care-as-usual.

2.4. Intervention

The AIM ECG-AI Study is a 2-arm cluster-randomized trial with an Intervention group and a care-as-usual Control group conducted at 5 healthcare systems within the United States (US). Clinicians randomized to the intervention group will receive access to the study software which includes Anumana's ECG Viewer and LEF ECG-AI Algorithm.

The ECG Viewer is a point-of-care, EHR-integrated user interface to provide a visualization of the ECG-AI algorithm results, a digitized ECG, and summary results table for all ECGs available in the EHR with minimally necessary patient data (Fig. 2).

The LEF ECG-AI algorithm is a software as a medical device (SaMD) which ingests digital ECG data as its sole input to provide a binary detection of low left ventricular ejection fraction. The ECG-AI can be used to evaluate concurrent or previously collected ECG data. Predecessors of this algorithm have been previously evaluated and model performance reported in several clinical studies (Table 1). The algorithm used in these previous studies provided the foundation for the ECG-AI algorithm that is used in the AIM ECG-AI Study and displayed on the ECG Viewer CDSS (Intervention). This algorithm, Anumana's LEF ECG-AI algorithm, received FDA clearance in 2023 with a reported sensitivity and specificity of 84.5 % and 83.6 %, respectively [13]. The LEF ECG-AI model will remain fixed during the duration of the AIM ECG-AI study and no further re-training or adjustments will be made to the model, to reduce the risk of introducing additional variables or biases into the final dataset.

In close collaboration with each study site's information technology (IT) team, the ECG Viewer software is either installed on premise or on a cloud environment as a Docker container to seamlessly integrate within the site's IT platform. The intervention software is deployed system-wide at each participating healthcare system, allowing a single, centralized installation to be available to providers throughout the system, regardless of the geographic location. This deployment-at-scale approach requires substantial upfront technical collaboration, but allows participating clinicians to seamlessly access the intervention software at point-of-care without additional technical and administrative burden or software access restrictions. The study software will be thoroughly tested and approved during a feasibility phase prior to the observational phase of the study.

Clinicians in the SOC group do not receive the BPA and are not given access to the Intervention software or results. Clinicians in the intervention group will be given access to the study software and will receive a best practice alert (BPA) notification (Fig. 3) for each eligible encounter with an actionable result (e.g., positive finding from the LEF ECG-AI algorithm). The BPA will fire upon opening the patient chart indicating an "AI-Enabled Low Ejection Fraction (EF) Screening Result Available" in the clinical workflow.

Following the initial software training, Intervention group participants will not be required to open the BPA or the study software at any point during the observational period of the study. To account for those Intervention group participants who do not interact with the study software, subgroup analyses are planned to evaluate clinical behaviors and decision making among low-adopters and high-adopters, as was previously described [14].

2.5. Data Collection

To evaluate the primary and exploratory outcomes for the AIM ECG-AI study (Table 2), data from multiple sources must be collected for each participating clinician and eligible encounter, including survey data, EHR data, and software performance data. Data will only be collected following eligible encounters with patients with no known history of heart failure or left ventricular ejection fraction ≤40 %.

Participating clinicians will be asked to complete pre-study and post-study online surveys. To support clinician engagement and reduce attrition due to data burden, clinicians will not be required to manually input any data about eligible clinical encounters. Instead, clinical

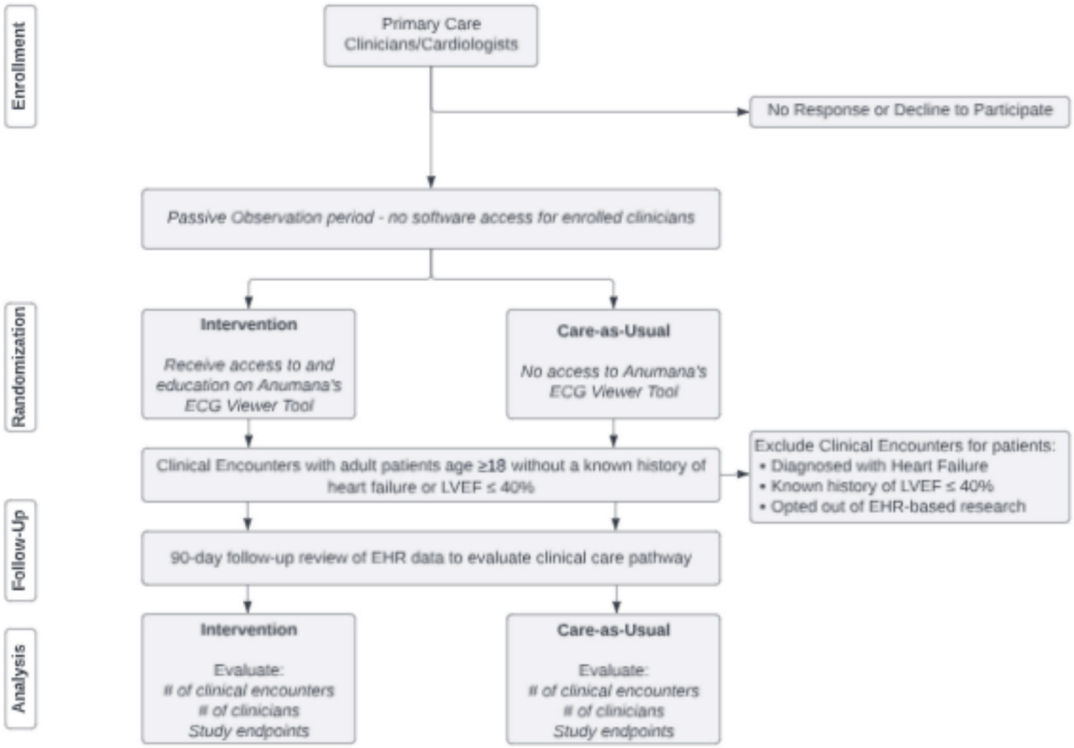

Fig. 1. CONSORT Diagram.

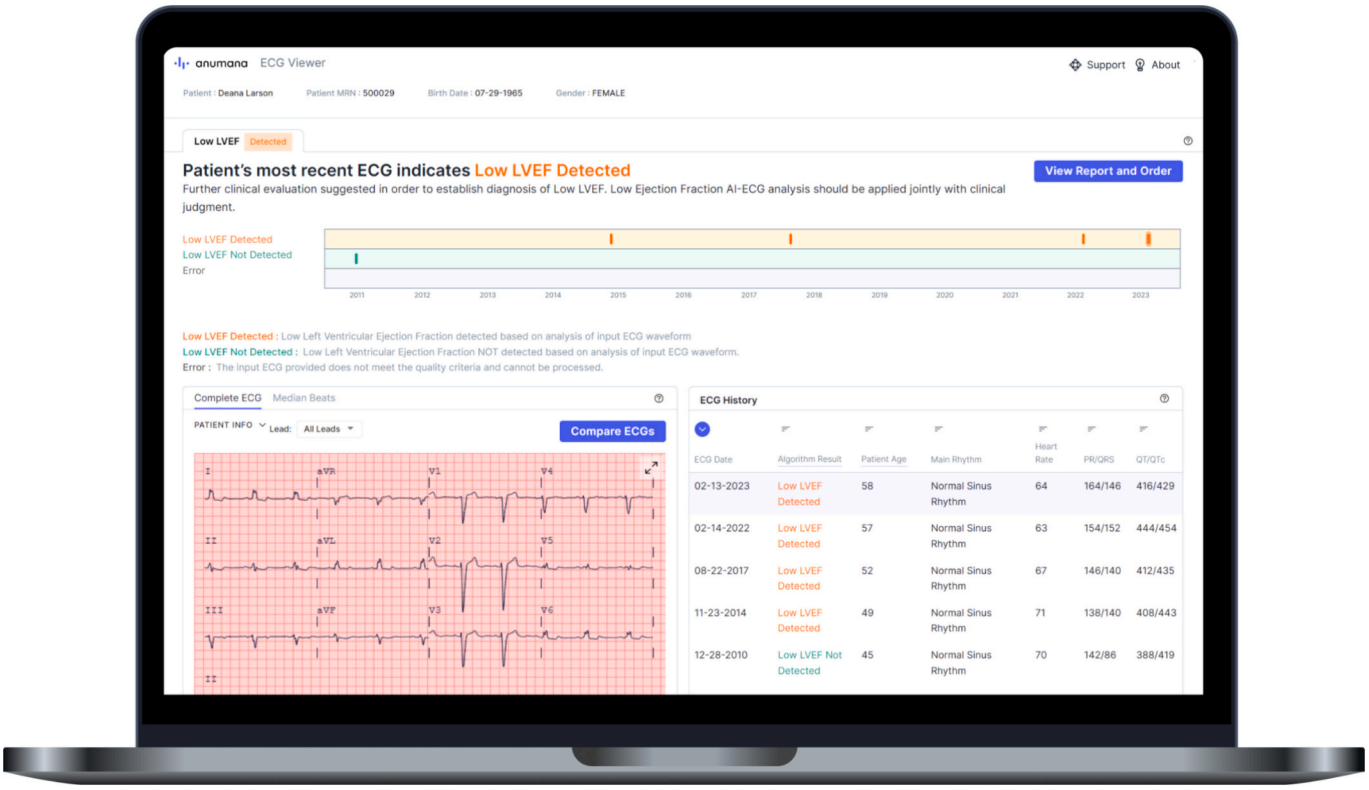

Fig. 2. ECG Viewer User Interface.

encounter data are automatically abstracted from the EHR to evaluate study endpoints including diagnoses and echocardiogram orders made following the index encounter and 12-weeks later as a readout of clinician decision making. Software performance metrics will be collected at each eligible encounter, including use of the study software features among Intervention group participants. All data will be aggregated and deidentified for analysis.

2.6. Endpoints

Outcomes of interest in the AIM ECG-AI study are shown in Table 2. The primary outcome of the AIM ECG-AI study is to evaluate the detection of LVEF $\leq$40 % by echocardiography at 90-days post clinical encounter, per patient, compared to care-as-usual (control arm). Data for the primary outcome will be abstracted from the site's EHR data after the 90-day readout period. Should participating clinicians in both Intervention and Control groups determine that an echocardiogram is necessary based on their clinical-decision making, they will submit the echocardiogram order according to the clinical site's standard clinical workflow without specific indication that the echocardiogram has been ordered as a part of the AIM ECG-AI study. Cardiologists and sonographers will complete and document the echocardiogram output according to the site's standard assessment methodology without knowledge of the AIM ECG-AI study or the LEF ECG-AI result; Ordering clinicians will receive the results as usual. Participating clinicians have no additional data collection or reporting requirements for the AIM ECG-AI study primary endpoint analysis following receipt of the echocardiography report. At the end of the 90-day readout period, data from the echocardiography report will be abstracted from the EHR by a clinical research coordinator.

Exploratory endpoints will be evaluated in two categories: Clinical outcomes and Intervention software CDS outcomes. Clinical outcomes data will be collected as described for the primary endpoint; participating clinicians will not be required to manually upload any clinical outcomes data, as these will be abstracted from the EHR by a clinical research coordinator. Software related data, including software-based study survey data, will be linked to clinical encounter data through a deidentified encounter ID associated with the participating provider. No identifiable patient data will be uploaded into the electronic data capture (EDC) system.

Adverse events (AE) and severe adverse events (SAE) will also be reported throughout the duration of the study, as applicable. AIM ECG-AI is a minimal risk study and AE/SAE are not anticipated. If any AE/SAE occur during the course of the study, participants are asked to notify the Site PI or designee to report the event within 24 h of knowledge of the event.

At the completion of the study, subgroup analyses will be conducted to evaluate the impact of the Intervention software by factors such as clinical setting, clinician factors, and patient factors.

3. Discussion

In recent years, the power and promise of AI in healthcare has become apparent through investigational and commercialization of tools focused on many aspects of clinical practice and condition areas. However, the use of AI in healthcare is also the subject of a national call

Table 1
Performance of AI-ECG to detect low LVEF in several patient populations.

Study Population	Area under the curve (AUC)	Sensitivity	Specificity	Diagnostic Odds Ratio
Retrospective detection of LVEF ≤35 % [5]	0.93	86 %	88 %	37.88
Prospective detection of LVEF ≤35 % [6]	0.918	82.5 %	86.5 %	30.25
Retrospective detection of LVEF ≤35 % [16]	0.82	26.9 %	97.4 %	13.7
Retrospective detection of LVEF ≤40 % in the general population [17]	0.97	90.0 %	92.0 %	122.28
Retrospective detection of LVEF ≤40 % in a high-risk population [17]	0.97	92.0 %	93.0 %	175.24
Retrospective detection of LVEF ≤35 % in dyspnea population [8]	0.89	73.8 %	87.3 %	19.4
Retrospective detection of cardiomyopathies (LVEF ≤35 %) in pregnancy and the peripartum period [18]	0.92	70.1 %	95.8 %	53.50
Retrospective detection of LVEF ≤45 % in dilated cardiomyopathy population [19]	0.96	98.8 %	44.8 %	66.29
Retrospective detection of LVEF ≤35 % in cardiac intensive care unit population [20]	0.83	75.1 %	76.1 %	9.61
Retrospective detection of left ventricular dysfunction in immune mediated necrotizing myopathy [21]	0.74	80.0 %	62.8 %	0.93
Retrospective detection of LVEF ≤40 % in a Chagas patient population [22]	0.92	70.1 %	95.8 %	13.2

for focused attention on the judicious use of AI technologies, as highlighted by the 2023 U.S. Presidential Executive Order #14110 on the Safe, Secure, and Trustworthy Development and Use of Artificial Intelligence [15].

In alignment with this national focus, the AIM ECG-AI study will be the first multisite clinical evaluation of the effectiveness of an EHR-integrated, point-of-care CDS software to provide ECG-AI results to clinicians within the clinical workflow. Specifically, AI enabled algorithms can effectively detect several cardiovascular conditions using ECG waveforms as the sole data input. The validity of these algorithms has been evaluated in several investigational studies, including a recent single-center study which evaluated clinical outcomes when primary care clinicians were emailed ECG-AI results for low LVEF [7]. In the EAGLE study, when participating clinicians were provided ECG-AI results by email, new diagnoses of low left ventricular ejection fraction were greater than care-as-usual, despite an equivalent rate of ordering echocardiograms in both intervention and control groups. The present study aims to expand on the results of the EAGLE study by providing the ECG-AI results for the LEF ECG-AI algorithm at point of care using Anumana's novel ECG Viewer CDS software. Additionally, the AIM ECG-AI investigators strive to demonstrate transferability of the results by evaluating the impact of the intervention across clinical specialties (e.g., cardiology and primary care) and across five geographically distinct clinical sites. The findings will provide valuable insights for the growing field of clinically-focused software designed to bring AI into routine clinical practice.

This pragmatic approach requires the integration of several unique data sources into a single deidentified study dataset to evaluate primary and exploratory outcomes. Similar to the EAGLE study design, AIM ECG-AI will evaluate the detection of LVEF ≤40 % by echocardiography at 90-days post clinical encounter in the control and intervention groups. The intervention software is designed to integrate within a clinical workflow, providing a just-in-time alert to clinicians for actionable results without additional significant burden. We project that the observation period will complete in August 2025 with 90-day data readout and primary analyses available in early 2026. Analysis of exploratory endpoints and subgroup analyses may be presented later in 2026.

A limitation of this study is its pragmatic design to evaluate the natural course of clinical decision making among participants. Following the initial software training, clinicians randomized to the Intervention group are not required to access the study software at any time during the duration of the Observational phase of the study. Those "Low Adopters" of the software could bias the results towards the null hypothesis of no significant effect between the intervention and control groups. To address this potential concern, the study design includes subgroup analyses comparing outcomes among Low Adopters and High Adopters in the Intervention Group. Additionally, the inclusion and exclusion criteria may provide a limitation to the generalizability of the study results. Similar to the EAGLE study [4], clinical encounters must include 10-s, 12 Lead ECG waveform data to be eligible for inclusion in the AIM ECG-AI study dataset. While this is a relatively inexpensive and routine test, it may not be broadly available among all symptomatic patients which could present a bias in the baseline dataset.

In conclusion, the AIM ECG-AI study will provide important evidence of whether an EHR-integrated, point-of-care CDS software using ECG-AI to detect LVEF will increase the detection of patients with LVEF compared to standard of care across geographically diverse clinical settings. The results of the AIM ECG-AI Study will further inform the growing field of the use, applicability, and integration of AI in the clinical workflow.

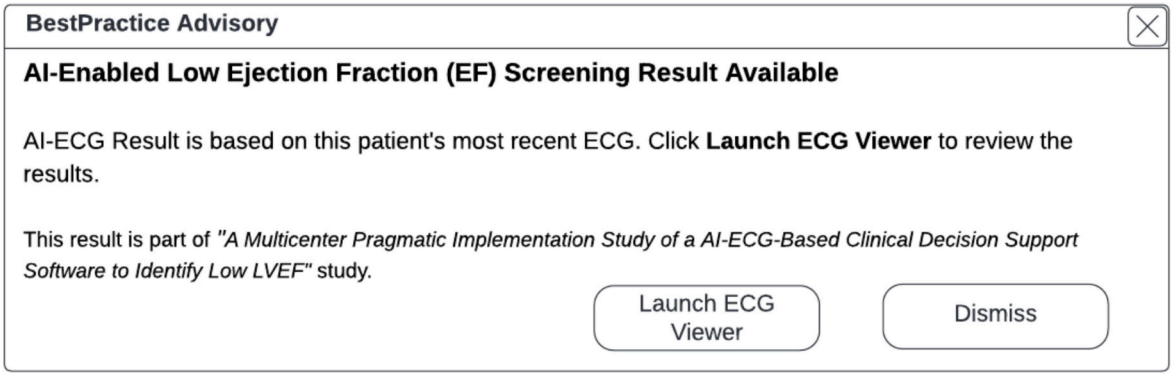

Fig. 3. Sample Best Practice Alert Display.

Table 2
AIM ECG-AI Study Endpoints.

AIM ECG-AI Study - Primary Endpoints
● Detection of LVEF ≤40 % by echocardiography at 90-days post clinical encounter, per patient, compared to care-as-usual (control arm)

AIM ECG-AI Study - Exploratory Endpoints	
Clinical Outcomes	Software Usability Outcomes
● Diagnostic yield of LVEF ≤40 % as detected by echocardiography ● Diagnostic yield of LVEF ≤40 % as detected by any modality of EF measurement (including cardiac MRI, cardiac CT, cardiac catheterization, nuclear imaging) ● Heart failure diagnoses, including mid-range ejection fraction, and heart failure treatment initiation ● Time to event analyses ● Incidence of cardiometabolic and cardiovascular conditions ● All-cause, cardiovascular, and HF hospitalizations ● All-cause, cardiovascular, and HF mortality	● User engagement with the software, including session counts and click counts. ● Percent of notification prompts that are accepted or dismissed, at the clinician level. ● Clinician experience with software (survey-based) ○ Cognitive behavioral, and contextual factors related to clinician satisfaction, acceptance, and use of the software ○ Rejected, modified, or ignored recommendation explanations ○ Barriers and facilitators to use

AIM ECG-AI Study - Safety Endpoints
● Incidences and event rates of study-related adverse events (AE), compared to control arm ● Incidences and event rates of study-related Severe Adverse Events (SAE), compared to control arm

CRediT authorship contribution statement

Francisco Lopez-Jimenez: Writing – review & editing, Methodology, Investigation, Conceptualization. **Heather M. Alger:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Investigation, Conceptualization. **Zachi I. Attia:** Investigation. **Barbara Barry:** Investigation. **Ranee Chatterjee:** Investigation. **Rowena Dolor:** Investigation. **Paul A. Friedman:** Investigation. **Stephen J. Greene:** Investigation. **Jason Greenwood:** Investigation. **Vinay Gundurao:** Software. **Sarah Hackett:** Project administration, Methodology, Investigation, Conceptualization. **Prerak Jain:** Software. **Anja Kinaszczuk:** Investigation. **Ketan Mehta:** Software. **Jason O'Grady:** Investigation. **Ambarish Pandey:** Investigation. **Christopher Pullins:** Investigation. **Arjun R. Puranik:** Formal analysis, Methodology, Project administration. **Mohan Krishna Ranganathan:** Software. **David Rushlow:** Investigation. **Mark Stampehl:** Investigation. **Vinayak Subramanian:** Investigation, Project administration, Writing – review & editing. **Kitzner Vassor:** Software. **Xuan Zhu:** Investigation. **Samir Awasthi:** Writing – review & editing, Supervision, Project administration, Methodology, Investigation, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: The AIM ECG-AI Study is sponsored by Anumana, Inc.

Acknowledgements

The AIM ECG-AI Study is sponsored by Anumana, Inc.

References

[1] K.E. Joynt Maddox, M.S.V. Elkind, H.J. Aparicio, et al., Forecasting the burden of cardiovascular disease and stroke in the United States through 2050—prevalence of risk factors and disease: a presidential advisory from the American Heart Association, Circulation. Published online June 4 (2024), https://doi.org/10.1161/CIR.0000000000001256.

[2] S.S. Martin, A.W. Aday, Z.I. Almarzooq, et al., 2024 heart disease and stroke statistics: a report of US and global data from the American Heart Association, Circulation 149 (8) (2024) E347–E913, https://doi.org/10.1161/CIR.0000000000001209.

[3] P.A. Heidenreich, B. Bozkurt, D. Aguilar, et al., 2022 AHA/ACC/HFSA guideline for the Management of Heart Failure: a report of the American College of Cardiology/American Heart Association joint committee on clinical practice guidelines, J. Am. Coll. Cardiol. 79 (17) (2022) e263–e421, https://doi.org/10.1016/J.JACC.2021.12.012.

[4] X. Yao, R.G. McCoy, P.A. Friedman, et al., ECG AI-guided screening for low ejection fraction (EAGLE): rationale and design of a pragmatic cluster randomized trial, Am. Heart J. 219 (2020) 31–36, https://doi.org/10.1016/j.ahj.2019.10.007.

[5] Z.I. Attia, S. Kapa, F. Lopez-Jimenez, et al., Screening for cardiac contractile dysfunction using an artificial intelligence–enabled electrocardiogram, Nat. Med. 25 (1) (2019) 70–74, https://doi.org/10.1038/s41591-018-0240-2.

[6] Z.I. Attia, S. Kapa, X. Yao, et al., Prospective validation of a deep learning electrocardiogram algorithm for the detection of left ventricular systolic dysfunction, J. Cardiovasc. Electrophysiol. 30 (5) (2019) 668–674, https://doi.org/10.1111/jce.13889.

[7] X. Yao, D.R. Rushlow, J.W. Inselman, et al., Artificial intelligence–enabled electrocardiograms for identification of patients with low ejection fraction: a pragmatic, randomized clinical trial, Nat. Med. 27 (5) (2021) 815–819, https://doi.org/10.1038/s41591-021-01335-4.

[8] D. Adedinsewo, R.E. Carter, Z. Attia, et al., Artificial intelligence-enabled ECG algorithm to identify patients with left ventricular systolic dysfunction presenting to the emergency department with dyspnea, Circ. Arrhythm. Electrophysiol. 13 (8) (2020) E008437, https://doi.org/10.1161/CIRCEP.120.008437.

[9] U.S. Food, Drug Administration, Artificial Intelligence and Machine Learning (AI/ML)-Enabled Medical Devices. https://www.fda.gov/medical-devices/software-medical-device-samd/artificial-intelligence-and-machine-learning-aiml-enabled-medical-devices, 2024. (Accessed 8 September 2024).

[10] U.J. Muehlematter, C. Bluethgen, K.N. Vokinger, FDA-cleared artificial intelligence and machine learning-based medical devices and their 510(k) predicate networks, Lancet Digit Health. 5 (9) (2023) e618–e626, https://doi.org/10.1016/S2589-7500(23)00126-7.

[11] G. Joshi, A. Jain, S.R. Araveeti, S. Adhikari, H. Garg, M. Bhandari, FDA-approved artificial intelligence and machine learning (AI/ML)-enabled medical devices: an updated landscape, Electronics (Basel). 13 (3) (2024) 498, https://doi.org/10.3390/electronics13030498.

[12] A. Mukhopadhyay, H.R. Reynolds, L.M. Phillips, et al., Cluster-randomized trial comparing ambulatory decision support tools to improve heart failure care, J Am Coll Cardiol. Published online (2023), https://doi.org/10.1016/J.JACC.2023.02.005.

[13] Anumana, Inc. Anumana 510K Summary Low Ejection Fraction AI ECG Algorithm K232699. Available at: https://www.accessdata.fda.gov/cdrh_docs/pdf23/K232699.pdf. Accessed January 16, 2025.

[14] D.R. Rushlow, I.T. Croghan, J.W. Inselman, et al., Clinician adoption of an artificial intelligence algorithm to detect left ventricular systolic dysfunction in primary care, Mayo Clin. Proc. 97 (11) (2022) 2076–2085, https://doi.org/10.1016/j.mayocp.2022.04.008.

[15] J. Biden, Executive Order on the Safe, Secure, and Trustworthy Development and Use of Artificial Intelligence. https://www.whitehouse.gov/briefing-room/presidential-actions/2023/10/30/executive-order-on-the-safe-secure-and-trustworthy-development-and-use-of-artificial-intelligence/.

[16] I.Z. Attia, A.S. Tseng, E.D. Benavente, et al., External validation of a deep learning electrocardiogram algorithm to detect ventricular dysfunction, Int. J. Cardiol. 329 (2021) 130–135, https://doi.org/10.1016/j.ijcard.2020.12.065.

[17] A.H. Kashou, J.R. Medina-Inojosa, P.A. Noseworthy, et al., Artificial intelligence-augmented electrocardiogram detection of left ventricular systolic dysfunction in the general population, Mayo Clin. Proc. 96 (10) (2021) 2576–2586, https://doi.org/10.1016/J.MAYOCP.2021.02.029.

[18] D.A. Adedinsewo, P.W. Johnson, E.J. Douglass, et al., Detecting cardiomyopathies in pregnancy and the postpartum period with an electrocardiogram-based deep learning model, European Heart Journal - Digital Health. 2 (4) (2021) 586–596, https://doi.org/10.1093/ehjdh/ztab078.

[19] S. Shrivastava, M. Cohen-Shelly, Z.I. Attia, et al., Artificial intelligence-enabled electrocardiography to screen patients with dilated cardiomyopathy, Am. J. Cardiol. 155 (2021) 121–127, https://doi.org/10.1016/j.amjcard.2021.06.021.

[20] J.C. Jentzer, A.H. Kashou, F. Lopez-Jimenez, et al., Mortality risk stratification using artificial intelligence-augmented electrocardiogram in cardiac intensive care unit patients, Eur. Heart J. Acute Cardiovasc. Care 10 (5) (2021) 532–541, https://doi.org/10.1093/ehjacc/zuaa021.

[21] C.J. Klein, I. Ozcan, Z.I. Attia, et al., Electrocardiogram-artificial intelligence and immune-mediated necrotizing myopathy: predicting left ventricular dysfunction and clinical outcomes, Mayo Clin Proc Innov Qual Outcomes. 6 (5) (2022) 450–457, https://doi.org/10.1016/j.mayocpiqo.2022.08.003.

[22] Brito BO de F, Attia ZI, Martins LNA, et al. Left ventricular systolic dysfunction predicted by artificial intelligence using the electrocardiogram in Chagas disease patients–the SaMi-trop cohort. PLoS Negl. Trop. Dis. 2021;15(12). doi:https://doi.org/10.1371/journal.pntd.0009974.