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ORIGINAL RESEARCH

Artificial Intelligence-Enhanced Electrocardiography and Health Records to Predict Cardiac Arrest

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ABSTRACT

BACKGROUND Out-of-hospital cardiac arrest (OHCA) is a public health burden with the majority occurring in the general population for whom there is no firm strategy to predict risk.

OBJECTIVES The authors evaluated whether artificial intelligence enhanced electrocardiography (ECG) and clinical information from electronic health records (EHRs) can stratify risk of OHCA in the general population.

METHODS We use a case-control study design (matching on age and sex), to derive and temporally validate models to predict OHCA. To evaluate the potential use case of models in a real-world context, we evaluated the 2-year cumulative incidence of OHCA in individuals undergoing ECG in a health care system, while accounting for the competing risk of non-OHCA mortality.

RESULTS In the temporal validation cohort, discrimination of OHCA was highest for the multimodal ECG + EHR model (area under the receiver operating characteristic curve: 0.83; area under the precision recall curve: 0.44) followed by the EHR-only model and the ECG-only model (Bonferroni adjusted P for all pairwise comparisons <0.05). In the real-world cohort of individuals undergoing ECG, the EHR + ECG model flagged two-thirds (153 of 228) of those with incident OHCA over a 2-year period as high-risk. Using the ECG + EHR model, the 2-year cumulative incidence of OHCA was 2.4% (95% CI: 2.0%-2.8%) in individuals identified as high-risk compared with 0.5% (95% CI: 0.3%-0.8%) in individuals designated as low risk.

CONCLUSIONS In a large U.S. health care system, artificial intelligence-enhanced ECG and EHR data effectively discriminated individuals at risk of OHCA and identified those at clinically relevant risk of incident OHCA over a 2-year period. (JACC Adv. 2026;5:102787) © 2026 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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ABBREVIATIONS AND ACRONYMS

AI = artificial intelligence

AU-PRC = area under the precision recall curve

AU-ROC = area under the receiver operating characteristic curve

ECG = electrocardiogram

EHR = electronic health records

EMS = emergency medical services

OHCA = out-of-hospital cardiac arrest

UW = University of Washington

Sudden cardiac arrest is a public health crisis, responsible for more than 5 million deaths annually.[1] Defined as the unexpected and rapid loss of spontaneous circulation and cardiac mechanical activity, sudden cardiac arrest most commonly occurs in the context of out-of-hospital cardiac arrest (OHCA).[2] Most OHCA occurs in the general population, often among individuals with no known cardiovascular disease. Despite advances in resuscitation science, survival after OHCA is 10%.[3] Therefore, mitigating the public health burden of sudden cardiac arrest requires upstream identification of risk in the general population to enable preventive efforts.

Previously, we demonstrated the feasibility of evaluating OHCA at scale in the general population by establishing a unique linkage between a population-based emergency medical services (EMS) adjudicated OHCA registry and a longitudinal electronic health record (EHR) of approximately 1.5 million individuals.[4] Machine learning models incorporating structured EHR data including comorbid conditions, vital signs, routine electrocardiogram (ECG) measures, and medications demonstrated moderate discrimination of OHCA from controls.

Artificial intelligence (AI)-enhanced ECG analysis has emerged as another promising tool for estimating cardiovascular risk. AI-enhanced ECG analysis has been shown to predict several conditions salient to OHCA risk (eg structural heart disease, left ventricular ejection fraction, and arrhythmias), often by encoding waveform features not apparent to human readers.[5-7] Unsupervised deep learning models extend this potential, providing rich and compact representations of the ECG with potential to identify conditions—like OHCA—that are too rare to support the development of purpose-built AI models.[8]

In this study, leveraging our linkage of an EMS-adjudicated OHCA registry with a longitudinal health record of 1.7 million individuals, we apply a case-control design with temporal validation to evaluate models incorporating structured EHR data and AI-enhanced ECG analysis to predict OHCA in the general population. We further quantify the ability to stratify longitudinal OHCA incidence over a 2-year time period in a real-world cohort within a large U.S. health care system.

METHODS

STUDY COHORT. We assembled 3 distinct cohorts from the University of Washington (UW) (Seattle, Washington, USA) Medicine EHR: 1) a derivation cohort (OHCA 2013-2021); 2) a temporal validation cohort (OHCA 2022-2023); and 3) a real-world cohort (ECG recorded in 2021) (**Figure 1**). There was no individual-level overlap between the derivation cohort with either the 1) temporal validation cohort or 2) the real-world cohort. The study cohorts comprised individuals who sought care at UW Medicine between January 1, 2010, and December 31, 2023. UW Medicine is located in King County, Washington—a metropolitan region of approximately 2.3 million persons—and delivered care to approximately 1.7 million unique patients over the study period. OHCA cases within the UW Medicine were identified by cross-referencing all health encounters during the study period against a comprehensive registry of OHCA in King County and the City of Seattle (Supplemental Appendix).[3] OHCA cases with antecedent health care within UW Medicine were identified by matching by name (first, last) and date of birth. OHCA cases were considered if the date of arrest within the EMS registry was between January 1, 2013, and December 31, 2023. Exclusion criteria included age <18 or >90 years of age at the time of first health encounter, traumatic OHCA, or a history of cardiac arrest/cardiopulmonary resuscitation, or presence of an implantable cardioverter defibrillator at the time of first health care encounter (Supplemental Appendix).

The parent cohort from which our derivation cohort was derived has been previously described.[4] In brief, we identified 2366 OHCA cases between 2013 and 2021. The control population was selected from the remainder of individuals with health encounters within UW Medicine over the study period (additional details in the Supplemental Appendix). Control patients were matched to cases by age (by decade) and sex at a 1:10 case:control ratio. We then restricted the parent cohort to individuals with an available ECG before cardiac arrest (cases) or at any

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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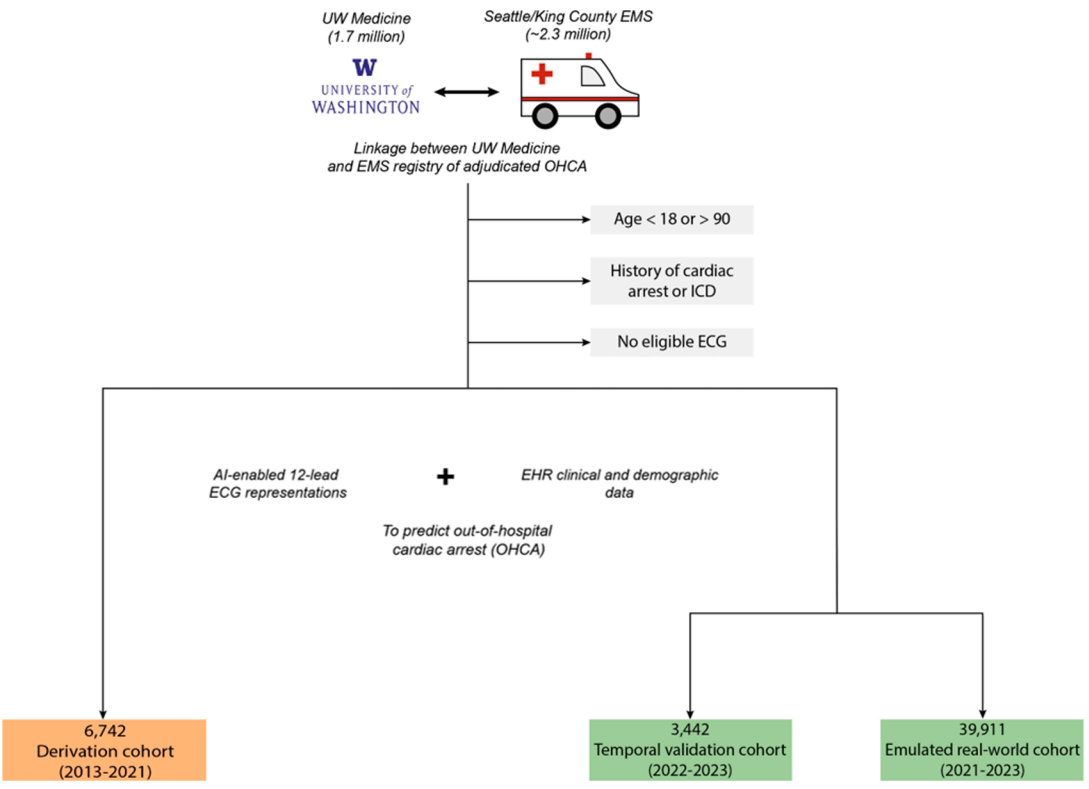
FIGURE 1 Overview of Study Cohorts



Shown is a conceptual overview of the study cohorts including: 1) initial linkage of University of Washington (UW) Medicine healthcare system and an emergency medical services (EMS) population-based registry of out-of-hospital cardiac arrest (OHCA); 2) exclusion criteria; and 3) delineation of derivation cohort, temporal validation cohort, and real-world cohort. ECG = electrocardiogram; EHR = electronic health record; ICD = implantable cardioverter-defibrillator.

point during the window of ascertainment (controls) yielding a derivation cohort of 6,472 individuals (993 cases, 5,479 controls). The temporal validation cohort was constructed using an analogous approach as the derivation cohort with the exception of using OHCA cases occurring in 2022 and 2023, resulting in 3,442 individuals with an available ECG (463 cases, 2,979 controls). Lastly, the real-world cohort was designed to evaluate the potential utility of deploying AI-enhanced ECG and EHR-base data during a baseline period to stratify incident OHCA over 2 years. This cohort comprised all individuals who underwent 12-lead ECG in 2021 at UW Medicine. We aimed to simulate the real-world circumstance where a health-system elects to "turn on" a clinical tool at a specified time with a harmonized "look-back" period. In addition to the exclusion criteria employed for the derivation and validation cohorts, we additionally excluded individuals who died in 2021 and individuals without documentation of vital status within the EHR over the ascertainment period (2022-2023) yielding a real-world cohort of 39,911 individuals.

Data collection and analyses were approved by the review boards at the UW and Public Health-Seattle & King County. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines were adhered to and are provided for this study (Supplemental Appendix).[9]

ASCERTAINMENT OF COVARIATES. The UW Medicine EHR includes data from over 60 sources including demographic data, diagnosis codes, and medication prescriptions. Covariates of interest included sociodemographic information, vital signs, comorbidities, habits, conventional ECG measures,

health care engagement metrics, and medication use (Supplemental Tables 1 and 2, and Supplemental Appendix).[4] For AI-ECG analysis, we extracted deep learning-derived vectors from the standard 12-lead ECGs (Supplemental Appendix). From each qualifying ECG tracing, we derived a 256-dimensional latent representation using a previously validated deep neural autoencoder.[8] This autoencoder was trained using over 35,000 ECGs from the fully external Mass General Brigham health care system and produces a representation of the ECG with sufficient information to reconstruct the ECG waveform with high accuracy ($r = 0.9916$).

The window of covariate ascertainment for cases was the first qualifying health visit until the day before the date of cardiac arrest. For controls, the window of ascertainment was the first qualifying health visit until the first instance of death (adjudicated using EHR documentation and the Washington State Death Index), date of last known health care contact within the EHR, or end of cohort study period. For the derivation cohort (OHCA cases 2013-2021), the window of ascertainment was January 1, 2010, to December 31, 2021. For the temporal validation cohort (OHCA cases 2022-2023), the window of ascertainment was January 1, 2019, to December 31, 2023. In both derivation and validation cohorts, the ECG most proximate to OHCA was selected, and for controls, a random ECG during the ascertainment window was selected. For the real-world cohort, the qualifying ECG was between January 1, 2021, and December 31, 2021, with the most proximate ECG to January 1, 2022 selected; the window of ascertainment for structured covariates was January 1, 2019, to December 31, 2023. There was missingness, as anticipated, for vital signs covariates (Supplemental Table 3) and these values were imputed in all cohorts (Supplemental Appendix).

STATISTICAL ANALYSIS. Descriptive statistics for OHCA cases and controls were compared using t-tests or chi-square tests as appropriate. Three OHCA classification models were created using least absolute shrinkage and selection operator: 1) an ECG-only model using the 256-dimensional ECG embedding plus conventional ECG intervals (PR interval, QRS duration, corrected QT interval, and heart rate); 2) an EHR-only model using 156 structured clinical features; and 3) a model combining ECG + EHR data. In the derivation cohort, data were split by subject into 70% training and 30% testing. Cross-validation (5-fold) was used to tune the regularization parameter within the training set and model performance was evaluated in the testing subset of the derivation cohort. For robust, independent validation, the temporal validation cohort was used and not involved in any aspect of model training, tuning or threshold selection. The AI-ECG model is publicly available.[10]

We first evaluated model performance in the temporal validation cohort using the area under the receiver operating characteristic curve (AU-ROC) and the area under the precision recall curve (AU-PRC). Model predicted probabilities were used to compute AU-ROC and AU-PRC and 95% CIs were obtained using bootstrap resamples of the validation set (n = 1,000 iterations). Comparisons of AU-ROC and AU-PRC were conducted using a nonparametric bootstrap test for 2 paired ROC or PRC curves, with Bonferroni correction for multiplicity. We then calculated model sensitivity, specificity, positive predictive value, negative predictive value and F1 scores at 3 prespecified operating points, selected a priori within the derivation cohort, to reflect discrete clinical use cases: 1) F1 score maximization, reflecting balanced positive predictive value and sensitivity; 2) a high-sensitivity threshold (99%), simulating use of the model as a broad screening tool; and 3) a high-specificity threshold (99%), reflecting a strategy to prioritize identification of high-risk individuals while minimizing false positives. Calibration was evaluated using the Brier score.

In secondary analyses, we evaluated model performance in the temporal validation cohort across 3 prespecified strata: 1) shockable vs nonshockable OHCA; 2) presence or absence of established cardiovascular disease (Supplemental Appendix); and 3) normal vs not normal ECG according to physician diagnostic interpretation. Down-sampling was used to account for case:control imbalance in subgroups. We also evaluated model performance in the temporal validation cohort when restricting cases to individuals with ECGs obtained within: 1) 6 months; and 2) 3 months before OHCA. For comparison of AU-ROC and AU-PRC in all secondary analyses, we did not adjust for multiplicity and thus present point estimates and 95% CIs. To further understand the relative importance of covariates and ECG waveforms contributing to OHCA prediction, we used SHapley Additive exPlanations,[11] absolute value of coefficients from the least absolute shrinkage and selection operator model (scaled in a harmonized manner), and latent space visualization analysis (Supplemental Text 8 in Supplemental Appendix). Given the established association of left ventricular ejection fraction and sudden cardiac arrest, we also

evaluated the performance of a validated AI-ECG algorithm predictive of left ventricular ejection fraction <50% to discriminate OHCA.[12]

Lastly, to evaluate the utility of the developed models to identify OHCA risk in the general population, we used cumulative incidence functions, accounting for the competing risk of non-OHCA mortality, to estimate the primary outcome of 2-year incidence of OHCA in the real-world cohort, stratified by model-predicted risk. Thresholds for delineating "high-risk" for each model were based on the F1 score maximization point in the derivation cohort. For time-to-event analyses, individuals contributed person-time from January 1, 2022. (ie time zero) to the earliest of OHCA, last known follow-up in the EHR, or December 31, 2023. Subdistribution HRs from competing-risk Fine-Gray models were used to estimate relative risks. In exploratory analyses, we: 1) evaluated cumulative incidence of OHCA in key subgroups including stratification by age, sex, and race/ethnicity; 2) evaluated the intraindividual SD of estimated OHCA probability for the subset of individuals in the real-world cohort who underwent >1 ECG in the ascertainment window; and 3) evaluated cumulative incidence of OHCA stratified by model predicted risk using a rolling baseline of the date of ECG acquisition as time zero with follow-up until OHCA, last known follow-up in the EHR, or December 31, 2023. A 2-tailed Gray $P < 0.017$ (0.05/3) was considered to indicate statistical significance to account for cumulative incidence comparisons in 3 models.

RESULTS

STUDY POPULATION. Baseline characteristics for the temporal validation cohort are shown in **Table 1** and baseline characteristics for the derivation cohort and real-world cohort are shown in Supplemental Tables 4 and 5. In the temporal validation cohort there were 463 individuals with OHCA (56 ± 16 years, 69% male) and 2,979 individuals without OHCA (62 ± 16 years, 70% male). In the temporal validation cohort, the median time from ECG to OHCA was 129 days (IQR: 45-389 days).

TABLE 1 Baseline Characteristics of Temporal Validation Cohort

	OHCA (n = 463)	Control (n = 2,979)	*P* Value
Socio-demographic covariates			
Age, y	56 ± 16	62 ± 16	<0.0001
Sex, n (%)			0.86
Male	320 (69)	2,075 (70)	
Female	143 (31)	904 (30)	
Race/ethnicity, n (%)			
American Indian or Alaskan Native	2 (0)	7 (0)	<0.0001
Asian	43 (9)	267 (9)	
Black	92 (20)	237 (8)	
Native Hawaiian or Pacific Islander	1 (0)	7 (0)	
White	284 (61)	2,264 (76)	
Other	41 (9)	197 (7)	
Vital sign covariates			
Heart rate, beats/min			
Minimum	70 ± 14	66 ± 14	<0.0001
Maximum	100 ± 16	89 ± 18	<0.0001
Mean	84 ± 11	76 ± 13	<0.0001
SBP, mm Hg			
Minimum	110 ± 19	115 ± 17	<0.0001
Maximum	153 ± 24	146 ± 22	<0.0001
Mean	131 ± 16	130 ± 15	0.24
DBP, mm Hg			
Minimum	63 ± 13	67 ± 13	<0.0001
Maximum	93 ± 16	87 ± 13	<0.0001
Mean	78 ± 10	77 ± 9	0.05
Respiratory rate, breaths/min			
Minimum	15 ± 2	15 ± 4	0.16
Maximum	21 ± 9	19 ± 9	0.0005
Mean	17 ± 2	17 ± 4	0.004
SpO_2, %			
Minimum	83 ± 22	90 ± 16	<0.0001
Maximum	100 ± 37	99 ± 1	0.18
Mean	97 ± 2	97 ± 2	0.0002
Weight, kg			
Minimum	78 ± 25	81 ± 22	0.01
Maximum	91 ± 36	89 ± 24	0.41
Mean	84 ± 26	85 ± 23	0.27
Electrocardiographic covariates			
PR interval, msec			
Minimum	149 ± 30	164 ± 38	<0.0001
Maximum	173 ± 44	175 ± 46	0.36
Mean	160 ± 32	170 ± 41	<0.0001

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PREDICTION OF OUT-OF-THOSPITAL CARDIAC ARREST. In the temporal validation cohort, discrimination of OHCA was highest for the multimodal ECG + EHR model (AU-ROC: 0.83; 95% CI: 0.81-0.85, AU-PRC: 0.44; 95% CI: 0.40-0.49) followed by EHR-only (AU-ROC: 0.80; 95% CI: 0.78-0.83, AU-PRC: 0.41; 95% CI: 0.37-0.45) and ECG-only (AU-ROC: 0.76; 95% CI: 0.74-0.70, AU-PRC: 0.34; 95% CI: 0.30-0.38) (**Figure 2**, Supplemental Table 6) (Bonferroni-adjusted *P* for all pairwise AUC-ROC and AUC-PRC comparisons <0.05). **Table 2** summarizes detailed performance metrics at 3 clinically relevant thresholds. The distribution of predicted OHCA probabilities in cases and controls in the temporal validation cohort are shown in Supplemental Figure 1. Model calibration in the temporal validation cohort appeared reasonable (Supplemental Table 7). Discrimination indices in the derivation cohort were

TABLE 1 Continued

	OHCA (n = 463)	Control (n = 2,979)	*P* Value
QRS duration, ms			
Minimum	91 ± 20	94 ± 22	0.000
Maximum	105 ± 28	100 ± 25	0.001
Mean	97 ± 22	97 ± 23	0.90
QT corrected, ms			
Minimum	437 ± 37	431 ± 38	0.006
Maximum	481 ± 48	449 ± 44	<0.0001
Mean	458 ± 31	440 ± 36	<0.0001
Clinical comorbidities			
Hypertension, n (%)	325 (70)	1,851 (62)	0.001
Diabetes mellitus, n (%)	161 (35)	791 (27)	0.0002
Hyperlipidemia, n (%)	263 (57)	1,712 (57)	0.83
Heart failure, n (%)	171 (37)	493 (17)	<0.0001
Coronary heart disease, n (%)	175 (38)	731 (25)	<0.0001
Valvular heart disease, n (%)	125 (27)	464 (16)	<0.0001
Stroke or TIA, n (%)	107 (23)	413 (14)	<0.0001
Myocardial infarction, n (%)	126 (27)	361 (12)	<0.0001
Peripheral arterial disease, n (%)	137 (30)	589 (20)	<0.0001
Cerebral atherosclerosis, n (%)	142 (31)	628 (21)	<0.0001
Chronic kidney disease, n (%)	147 (32)	506 (17)	<0.0001
Renal failure, n (%)	134 (29)	492 (17)	<0.0001
Substance use disorder, n (%)	237 (51)	309 (10)	<0.0001
Depression, n (%)	238 (51)	890 (30)	<0.0001
Obstructive sleep apnea, n (%)	38 (8)	155 (5)	0.01
Cardiac arrhythmias, n (%)	109 (24)	409 (14)	<0.0001
Ventricular tachycardia, n (%)	20 (4)	68 (2)	0.015
Atrial fibrillation, n (%)	105 (23)	545 (18)	0.03
Palpitations, n (%)	104 (22)	472 (16)	0.0005
Syncope, n (%)	114 (25)	400 (13)	<0.0001
Cirrhosis, n (%)	161 (35)	499 (17)	<0.0001
Gastrointestinal bleeding, n (%)	42 (9)	104 (3)	<0.0001
Peptic ulcer without bleeding, n (%)	36 (8)	84 (3)	<0.0001
Smoking, n (%)	294 (63)	1,021 (34)	<0.0001
Pulmonary disease, n (%)	195 (42)	826 (28)	<0.0001
Obesity, n (%)	151 (33)	882 (30)	0.21
Weight loss, n (%)	125 (27)	438 (15)	<0.0001
Anemia, n (%)	233 (50)	815 (27)	<0.0001
HIV, n (%)	20 (4)	51 (2)	0.0005
Alcohol abuse, n (%)	182 (39)	332 (11)	<0.0001
Autoimmune conditions, n (%)	21 (5)	197 (7)	0.11
Coagulopathy, n (%)	105 (23)	404 (14)	<0.0001
Dementia, n (%)	43 (9)	194 (7)	0.04
Hypothyroidism, n (%)	53 (11)	448 (15)	0.05
Neurological disorders, n (%)	147 (32)	434 (15)	<0.0001
Paralysis, n (%)	57 (12)	170 (6)	<0.0001
Epilepsy, n (%)	87 (19)	199 (7)	<0.0001
Psychoses, n (%)	188 (41)	447 (15)	<0.0001
Pulmonary circulation disease, n (%)	66 (14)	162 (5)	<0.0001
Any malignancy, n (%)	66 (14)	527 (18)	0.08
Fluid and electrolyte disorders, n (%)	326 (70)	1,091 (37)	<0.0001

Values are mean ± SD or n (%).

Bpm = beats per minute; DBP = diastolic blood pressure; OHCA = out-of-hospital cardiac arrest; SBP = systolic blood pressure; SpO_2 = oxygen saturation; TIA = transient ischemic attack.

similar and are summarized in Supplemental Figure 2.

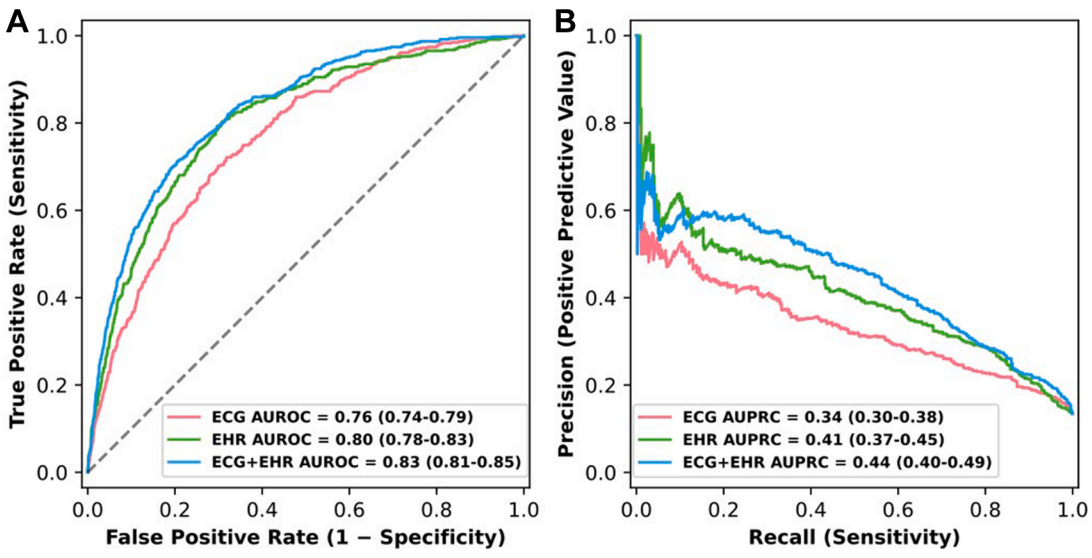
In secondary analysis, we identified consistent model performance in key subgroups including shockable vs nonshockable OHCA, the presence or absence of prevalent cardiovascular disease, and ECGs interpreted clinically as normal or not normal (Supplemental Figure 3, Supplemental Tables 8 to 10). Model performance also remained consistent in the temporal validation set when restricting ECGs to those within 6 months or within 3 months of OHCA (Supplemental Figure 4).

As a benchmark, a previously validated AI-ECG model to predict left ventricular systolic dysfunction demonstrated poor discrimination for OHCA in the temporal validation cohort (AU-ROC: 0.68; 95% CI: 0.65-0.70, AU-PRC: 0.23; 95% CI: 0.20-0.27) (Supplemental Figure 5).

FEATURE IMPORTANCE FOR OHCA PREDICTION IN ECG AND EHR MODELS. To further understand which components of the ECG and EHR models were most salient to OHCA prediction, we employed feature importance analysis in the ECG-only, EHR-only, and ECG + EHR models (Supplemental Figure 6 and Supplemental Table 11). In the ECG-only model, we observed substantial influence from both AI-defined representations and conventional ECG metrics (QTc and heart rate). In an exploratory analysis, we observed only modest correlation between the most contributory AI-defined representations and conventional ECG metrics (Supplemental Figure 7). In the EHR-only model, the most influential features were fluid and electrolyte disorder, heart failure, and substance use disorder. In the ECG + EHR model, both structured EHR data (eg fluid and electrolyte disorders, substance abuse disorder, and heart failure) and ECG parameters (AI-representations and mean corrected QT interval) were identified as key contributors. To further understand the components of the ECG waveforms reflected in AI-representations predictive of OHCA, we evaluated representative reconstructions of the ECG waveform across the spectrum of AI-ECG predicted OHCA risk (Supplemental Figure 8). ECG waveforms associated with higher OHCA risk generally had lower QRS amplitudes in all ECG leads and smaller T-wave amplitudes.

MODEL PERFORMANCE FOR OHCA INCIDENCE IN A REAL-WORLD COHORT. We next evaluated the 2-year cumulative incidence of OHCA, accounting for competing mortality, using risk designations derived from ECG-only, EHR-only, and ECG + EHR models in our real-world cohort of individuals with an ECG performed over the course of 1 year (**Figure 3**). The

FIGURE 2 Model Discrimination of Out-of-Hospital Cardiac Arrest in Temporal Validation Cohort



(A) Area under receiver operating characteristic curve (AU-ROC) curves and (B) area under the precision–recall curve (AU-PRC) for the ECG-only, EHR-only, and ECG + EHR models. AU-ROC and AU-PRC values are shown with 95% CIs obtained via bootstrap resampling. Abbreviations as in Figure 1.

median time between contributing ECG and start of follow-up time was 152 days (IQR: 67-250). The distribution of predicted OHCA probabilities for individuals with OHCA vs no OHCA are shown in Supplemental Figure 9 in Supplemental Appendix. Model calibration across all 3 models appeared reasonable in the real-world cohort (Supplemental Table 7). All 3 models demonstrated a higher incidence of OHCA among individuals identified as high-risk compared to low-risk (Gray *P* for comparison of cumulative incidence <0.001 for all). For example, using the ECG + EHR model, the 2-year cumulative incidence of OHCA, accounting for the competing risk of other mortality, was 2.4% (95% CI: 2.0%-2.8%) in the high-risk stratum compared to 0.5% (95% CI: 0.3% to 0.8%) in the low-risk stratum. In the real-world cohort, of 228 individuals with incident OHCA over a 2-year period, the EHR + ECG model flagged approximately two-thirds of these individuals as high-risk (153 of 228). Performance metrics for OHCA prediction in the ECG-only, EHR-only, and ECG + EHR models in the real-world cohort are shown in Supplemental Table 12.

In exploratory analyses, we evaluated the 2-year cumulative incidence of OHCA stratified by age, sex, and race/ethnicity with similar findings

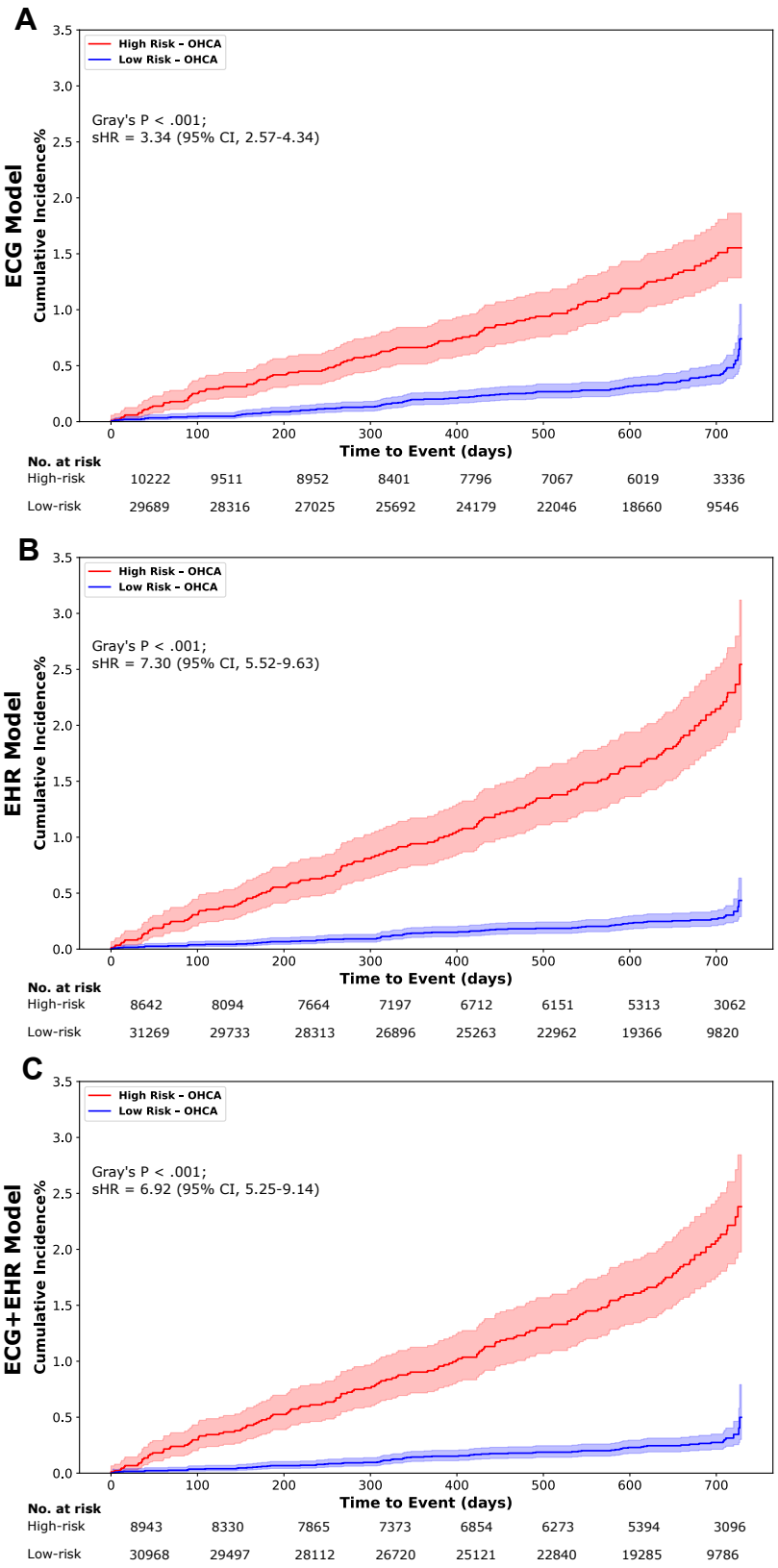
TABLE 2 Model Performance for Prediction of out of Hospital Cardiac Arrest in Temporal Validation Cohort

	ECG Model			EHR Model			ECG + EHR Model		
	F1-Score Threshold	99% Specificity	99% Sensitivity	F1-Score Threshold	99% Specificity	99% Sensitivity	F1-Score Threshold	99% Specificity	99% Sensitivity
Accuracy	0.76	0.87	0.21	0.79	0.87	0.31	0.80	0.87	0.33
PPV[a]	0.30	0.53	0.14	0.35	0.63	0.16	0.36	0.57	0.16
Sensitivity	0.58	0.05	0.99	0.64	0.10	0.97	0.69	0.11	0.99
F1-Score	0.39	0.09	0.25	0.45	0.17	0.27	0.48	0.19	0.28
NPV[a]	0.92	0.87	0.99	0.94	0.88	0.97	0.94	0.88	0.99
Specificity	0.79	0.99	0.09	0.81	0.99	0.20	0.81	0.99	0.22

[a]Some measures of model performance including PPV and NPV are sensitive to underlying disease incidence. Estimates provided for the case control cohort do not reflect anticipated performance in the general population where incidence of out-of-hospital cardiac arrest is lower.

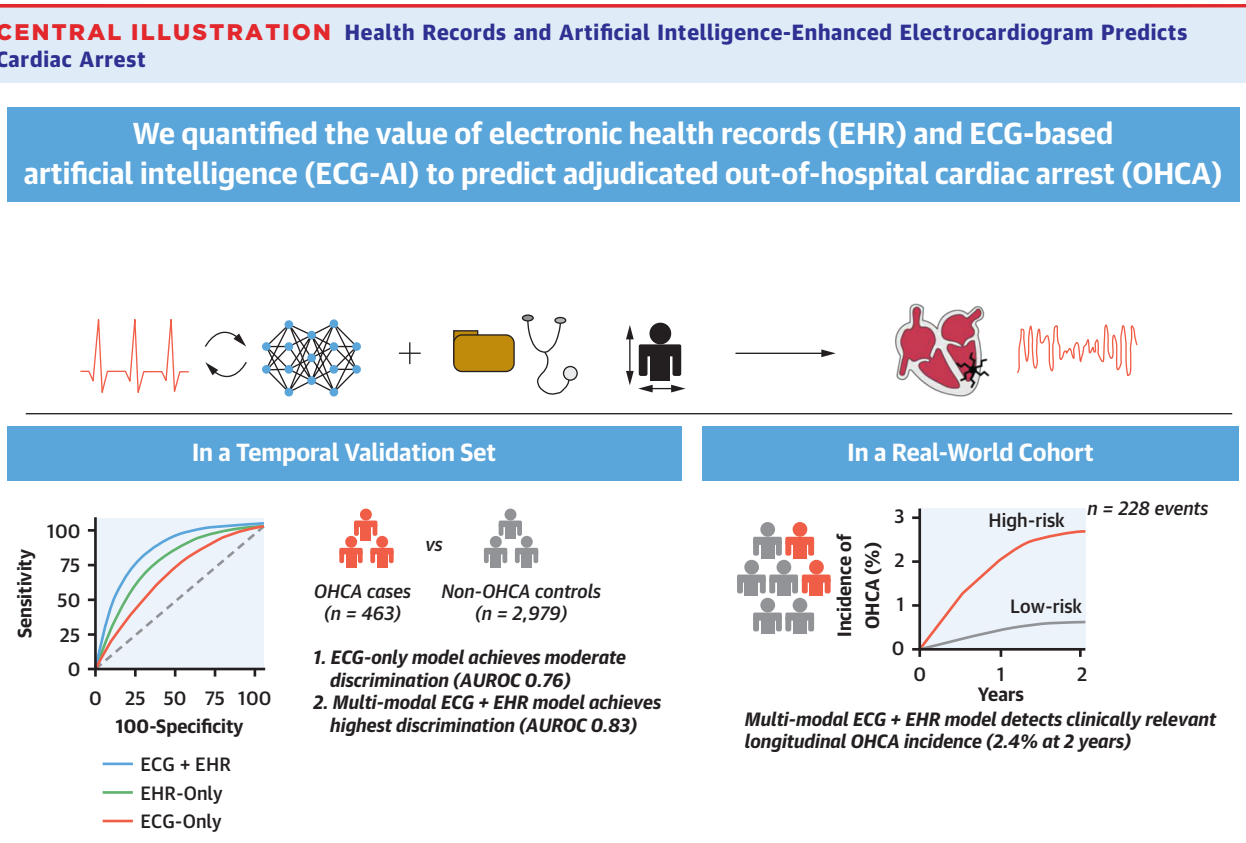
ECG = electrocardiogram; EHR = electronic health record; NPV = negative predictive value; PPV = positive predictive value.

FIGURE 3 **Incidence of Out-of-Hospital Cardiac Arrest in a Real-World Cohort**



Shown is the 2-year cumulative incidence (%) of out-of-hospital cardiac arrest (OHCA), accounting for competing risk of non-OHCA mortality, stratified by low-vs high-risk status using AI-enhanced electrocardiography (ECG) and electronic health records (EHR) models: (A) ECG model, (B) EHR model and (C) ECG + EHR model. Subdistribution HR (sHR) with 95% CIs and Gray's test are displayed on each plot to indicate statistical significance and relative risk for high-risk vs low-risk strata.

CENTRAL ILLUSTRATION **Health Records and Artificial Intelligence-Enhanced Electrocardiogram Predicts Cardiac Arrest**



Sharma S, et al. JACC Adv. 2026;5(6):102787.

Models incorporating structured electronic health records and artificial intelligence (AI)-enhanced electrocardiogram (ECG) analysis in the general population effectively discriminated individuals with out-of-hospital cardiac arrest (OHCA) from those without. In a real-world cohort of individuals undergoing routine ECG, multimodal models incorporating health records data and AI-enhanced ECG effectively stratified incident risk of OHCA. AUROC = area under receiver operating characteristic curve; EHR = electronic health record.

regarding risk stratification across all models (Supplemental Figure 10). In additional exploratory analysis, in the subset of individuals who had more than 1 ECG over the course of 1 year, we observed minimal intraindividual SD of predicted OHCA risk in both the ECG-only model and the ECG + EHR model (Supplemental Figure 11). Finally, in sensitivity analysis incorporating a rolling baseline with date of ECG acquisition as cohort entry, we observed similar stratification of OHCA risk across all models (Supplemental Figure 12).

DISCUSSION

In a large U.S. health care system, we show that models incorporating AI-enhanced ECG analysis and EHR data discriminate individuals in the general population at risk for OHCA (**Central Illustration**). In a real-world cohort of individuals undergoing 12-lead ECG, AI-enhanced ECG analysis and EHR data identified clinically relevant incidence of OHCA over a 2-year period.

Our study has 3 key findings. First, stratification of longitudinal OHCA risk in the general population is feasible. Previous studies in the general population have focused on conventional cardiovascular risk factors and showed lower discrimination of OHCA risk when compared to the models evaluated in this study.[11,13] When considering actionable clinical deployment, an OHCA risk model should identify salient risk over a relevant timeline. To that end, in our real-world cohort of all individuals undergoing ECG over a 1-year period, we show that individuals designated as high-risk by a model incorporating AI-enhanced ECG analysis and EHR data had an OHCA incidence of ~1% per year over the subsequent 2-year period, which represents a 10- to 20-fold enrichment over the general population and a rate

comparable to actionable thresholds for sudden cardiac death primary prevention in guidelines for structural heart disease.[14] In this instance, we would estimate needing to flag 100 individuals as "high-risk" to identify 1 OHCA event over 1 year. In the real-world cohort, two-thirds of individuals destined to have OHCA over the 2 years after an ECG were successfully flagged as "high-risk" by the combined EHR-ECG model.

With respect to generalizability, given that our models incorporated data from ECGs, our real-world cohort reflected individuals undergoing ECG who may differ from individuals not undergoing ECG. Despite potential selection bias, the incidence of OHCA in our real-world cohort (~0.37% per year) was comparable to incidence rates of OHCA in previous general population-based cohorts, providing support for generalizability.[1] We view the findings of our study as necessary and foundational to justify future prospective evaluation of these models in an unselected general population cohort. We would further emphasize that effective stratification of OHCA risk represents a requisite, *first-step* in considering prevention strategies in the general population. Future work is warranted to better define the discrete clinical pathways that a "high-risk" flag may motivate. Potential considerations include the implementation of individually tailored efforts to modify OHCA risk (eg address reversible mechanisms of QT prolongation or electrolyte aberration) or intensified rhythm surveillance with validated wearable technologies capable of detecting pulselessness and activation of EMS systems.[15] Ultimately, clinical deployment of screening algorithms for OHCA in the general population will need to directly address the potential for false positivity and implications of testing and anxiety that such alerts may trigger.

Second, optimal approaches to estimation of OHCA risk should reflect its complex nature, including contributions from myriad cardiovascular and noncardiovascular factors detectable by AI-enhanced ECG and EHR data. Previous studies of OHCA epidemiology in the general population focused predominantly on White men, and suggested coronary heart disease as etiological in 75% to 80% of individuals.[16-18] More recent studies have highlighted an evolving epidemiology of OHCA, identifying prevalent cardiovascular disease in only one-third to one-half of individuals and emphasizing key contributions of noncardiovascular comorbidities.[19,20] In our study, feature-importance analysis identified a range of conditions (eg fluid and electrolyte disorders), conventional ECG parameters (eg prolonged QT interval), and AI-enhanced ECG representations (ie complex waveform features) as salient for OHCA risk prediction. Model performance was robust across key subgroups including individuals without known cardiovascular disease and individuals in whom ECG analysis was interpreted as normal, providing strong evidence that model performance is not driven solely by overt ECG abnormalities and underscoring the added value of AI-enabled ECG analysis. Our findings support ongoing efforts to expand the formulation of OHCA risk beyond conventional cardiovascular risk factors and frame the importance of considering personalized risk assessment and modification.

Third, AI-enhanced ECG analysis could facilitate scalable OHCA risk evaluation in the general population. We demonstrate that the discrimination of our ECG-only model was only modestly lower than our EHR model incorporating 156 features. Both conventional ECG parameters and AI-enhanced ECG features contributed to OHCA prediction. As a low-cost, widely implemented diagnostic test, the ECG is an appealing method for risk assessment in diverse health care settings including resource-constrained communities without access to robust EHR platforms. To this end, we emphasize the AI-ECG model used in our study is publicly available.[8]

STUDY LIMITATIONS. Our study has limitations. First, these data reflect care within a large U.S. health care system and generalizability to other communities with differing comorbidity and demographic distributions is unknown. Geographic external validation is warranted. Second, study cohorts were restricted to individuals undergoing ECG evaluation, who may differ from individuals not undergoing ECG (Supplemental Table 13). As acknowledged, model performance in an unselected general population cohort will require prospective evaluation. Third, OHCA events without an EMS resuscitation attempt were not included in this study and could have led to misclassification of controls. Fourth, comorbidities were defined using validated billing codes yet misclassification is possible. Fifth, the real-world cohort excluded individuals who died within the same calendar year as ECG acquisition; incidence estimates do not reflect individuals at higher risk of near term mortality. Sixth, ECG representations in this study were derived using an externally trained autoencoder. Additional supervised training methods specific to OHCA (eg, modifying upstream autoencoder weights) could yield additional improvements in predictive performance and warrants further investigation. Seventh, ECG analysis employed the latest available ECG in a given cohorts

window of ascertainment. Future work could evaluate the predictive value of incorporating inputs and changes across serial ECGs. Eighth, the EHR model evaluated included a broad set of clinical features; future work identifying a more parsimonious set of features that retain predictive performance could enhance translational relevance. Finally, AI-enhanced ECG representations could reflect biases linked to demographics and healthcare patterns. Future evaluations incorporating fairness and bias evaluation will be the key before clinical implementation.

CONCLUSIONS

In a large U.S. health care system, AI-enhanced ECG and EHR data discriminated individuals at risk of OHCA in the general population. In a real-world cohort, individuals designated as high-risk had a clinically relevant 2-year incidence of OHCA. Future prospective studies are warranted to further establish the potential utility of such approaches for risk stratification of OHCA in the general population.

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REFERENCES

1. Hayashi M, Shimizu W, Albert CM. The spectrum of epidemiology underlying sudden cardiac death. *Circ Res*. 2015;116(12):1887-1906.

2. Myat A, Song KJ, Rea T. Out-of-hospital cardiac arrest: current concepts. *Lancet (London, England)*. 2018;391(10124):970-979.

3. McBride O, Poel A, Counts CR, et al. Temporal patterns in out-of-hospital cardiac arrest incidence and outcome. *JAMA Cardiol*. 2025;10(9):922-931.

4. Perry J, Brody JA, Fong C, et al. Predicting out-of-hospital cardiac arrest in the general population using electronic health records. *Circulation*. 2024;150(2):102-110.

5. Ulloa-Cerna AE, Jing L, Pfeifer JM, et al. rECHOmmend: an ECG-based machine learning approach for identifying patients at increased risk of undiagnosed structural heart disease detectable by echocardiography. *Circulation*. 2022;146(1):36-47.

6. Devkota A, Prajapati R, El-Wakeel A, Adjeroh D, Patel B, Gyawali P. AI analysis for ejection fraction estimation from 12-lead ECG. *Sci Rep*. 2025;15(1):13502.

7. Sau A, Pastika L, Sieliwonczyk E, et al. Artificial intelligence-enabled electrocardiogram for mortality and cardiovascular risk estimation: a model development and validation study. *Lancet Digit Health*. 2024;6(11):e791-e802.

8. Friedman SF, Khurshid S, Venn RA, et al. Unsupervised deep learning of electrocardiograms enables scalable human disease profiling. *NPJ Digit Med*. 2025;8(1):23.

9. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The strengthening the reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet (London, England)*. 2007;370(9596):1453-1457.

10. Sharma S, Boyle PM. ECG Risk Model Inference [software]. Version 1.0.0 *Zenodo*. 2026. https://doi.org/10.5281/zenodo.20033780

11. Deo R, Norby FL, Katz R, et al. Development and validation of a sudden cardiac death prediction model for the general population. *Circulation*. 2016;134(11):806-816.

12. Nolin-Lapalme A, Sowa A, Delfrate J, et al. Foundational models for generalizable electrocardiogram interpretation: comparison of supervised and self-supervised electrocardiogram foundational models. *Eur Heart J*. 2026. https://doi.org/10.1093/eurheartj/ehaf1119

13. Bogle BM, Ning H, Goldberger JJ, Mehrotra S, Lloyd-Jones DM. A simple community-based risk-prediction score for sudden cardiac death. *Am J Med*. 2018;131(5):532-539.e535.

14. Al-Khatib SM, Stevenson WG, Ackerman MJ, et al. 2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: executive summary: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines and the Heart Rhythm Society. *J Am Coll Cardiol*. 2018;72(14):e91-e220.

15. Shah K, Wang A, Chen Y, et al. Automated loss of pulse detection on a consumer smartwatch. *Nature*. 2025;642(8066):174-181.

16. de Vreede-Swagemakers JJ, Gorgels AP, Dubois-Arbouw WI, et al. Out-of-hospital cardiac arrest in the 1990's: a population-based study in the maastricht area on incidence, characteristics

and survival. *J Am Coll Cardiol*. 1997;30(6):1500–1505.

17. Margey R, Roy A, Tobin S, et al. Sudden cardiac death in 14- to 35-year olds in Ireland from 2005 to 2007: a retrospective registry. *Europace*. 2011;13(10):1411–1418.

18. Myerburg RJ, Junttila MJ. Sudden cardiac death caused by coronary heart disease. *Circulation*. 2012;125(8):1043–1052.

19. Skjelbred T, Warming PE, Krøll J, et al. Sudden cardiac death as first manifestation of cardiovascular disease: a nationwide study of 54,028 deaths. *JACC Clin Electrophysiol*. 2025;11(5):881–890.

20. Tseng ZH, Olgin JE, Vittinghoff E, et al. Prospective countywide surveillance and autopsy characterization of sudden cardiac death: POST SCD study. *Circulation*. 2018;137(25):2689–2700.

KEY WORDS artificial intelligence, cardiac arrest, electrocardiogram

APPENDIX For an expanded Methods section as well as supplemental tables and figures, please see the online version of this paper.