An Ensemble Deep Learning Algorithm for Structural Heart Disease Screening Using Electrocardiographic Images: PRESENT SHD

Online Supplement

SUPPLEMENTARY METHODS

Data Sources

The electronic health records (EHR) data was acquired during patient care at the hospital sites in the Yale New Haven Health System using Epic and was extracted from the Clarity database.[1,2] The YNHHS EHR data are linked to the CT death index to capture out-of-hospital mortality.

The Brazilian Longitudinal Study of Adult Health (ELSA-Brasil) study, a large multicenter prospective cohort study conducted in Brazil, enrolled,105 community-dwelling adults aged 35-74 years at their baseline visit during 2008-2010.[3,4] These participants represent active and retired civil servants from six higher education and research institutions in Brazilian state capitals in three geographical regions of the country: Southeast (Belo Horizonte, Rio de Janeiro, São Paulo and Vitória), South (Porto Alegre) and Northeast (Salvador).[5] The ELSA-Brasil study aimed to investigate the development and progression of chronic diseases and their determinants in the Brazilian adult population. Baseline data were collected using validated instruments, physical examinations, laboratory assessments, and imaging modalities.[3] Additionally, all participants underwent protocolized 12-lead ECG and echocardiogram.[3,4] To ascertain exposure status and to identify changes in baseline, ELSA-Brasil participants present for in-person follow-up visits every three to four years. Moreover, telephone interviews occur annually to obtain information on new diagnoses, hospitalization, and death with adjudicated clinical events based on expert medical record review.[3]

UK Biobank (UKB) is a prospective cohort of 502,468 community-dwelling adults aged 40-69 years recruited during 2006-2010.[3] A group of these participants accepted to participate in the third or fourth UKB study visit during which the participants underwent 12-lead electrocardiograms (ECGs) in 2014-2021. The UKB dataset is linked with the national EHR from the UK National Health Service predating UKB enrollment, enabling access to EHR diagnosis and procedure codes.[7,8] It is also linked to the national death index for complete capture of mortality data. We used data from UKB under research application #71033.

Signal Preprocessing

We used a standard preprocessing strategy to extract the signal waveform data from 12-lead ECGs, predominantly acquired using Philips PageWriter and GE MAC machines. We used linear interpolation to resample the ECGs that were obtained at 250Hz to align with a majority that were recorded at a sampling frequency of 500Hz as 10-second ECGs. Median pass filtering was done by subtracting a one-second median filter from the acquired signals to eliminate baseline drift. ECG signals were divided by a factor of 1000 and scaled to millivolts.

Model Evaluation on Novel ECG Formats

As a sensitivity analysis, we also evaluated the model on ECG images plotted in 4 novel formats that were not encountered by the model during training, including (a) Black-on-Red Standard: black ECG trace on red background grid plotted in standard clinical format, (b) Blue-on-Black Standard: blue ECG trace on black background grid plotted in standard clinical format, and (c) Black-on-black rhythm-on-top: black ECG trace plotted on black background with a single 10-second rhythm strip (lead I) above the 12 limb and precordial leads, and (d) Blue-on-red rhythm-on-top: blue

ECG trace plotted on red background in the rhythm-on-top layout (**Supplementary Figure 3.5**)."

Signal Model Development

For each image-based CNN, a corresponding signal-based CNN model was trained using the same disease labels and in the same training population as the image models. We evaluated multiple CNN architectures, experimenting with the number and size of convolutional layers as well as dropout and learning rates. The architecture with the highest AUROC for LVSD detection in the validation set was selected as the final architecture for training the individual disease detection models.[9,10] This architecture comprised an input layer with dimensions of (5000, 12, 1), representing a 10-second, 500 Hz, 12-lead ECG. The input layer was followed by 7 2-dimensional convolutional layers, progressively increasing the number of filters from 16 to 64 while incorporating varying kernel sizes (7x1, 5x1, and 3x1) to capture different levels of feature abstraction. A batch normalization layer, a ReLU activation layer, and a 2-dimensional max-pooling layer with different pool sizes (2x1 and 4x1) followed each convolutional layer. Next, the output of the 7th convolutional layer was used as the input for a fully connected network that included two dense layers. Each dense layer was followed by a batch normalization layer, a ReLU activation layer, and a dropout layer with a rate of 0.5. Finally, the model output was a dense layer with a single class and a sigmoid activation to generate the output probability of the label. The loss function was adjusted by calculating model weights using the effective number of samples class re-weighting approach to ensure that the learning is not impacted by the differential prevalence of positive and negative labels. The LVSD model was trained first and the weights from the optimal epoch were transferred to initialize the training for the models for sLVH and valve disease labels.

SUPPLEMENTARY REFERENCES.

1. Chishtie J, Sapiro N, Wiebe N, et al. Use of Epic Electronic health record system for health care research: Scoping review. *J Med Internet Res*. 2023;25:e51003.

2. Dhingra LS, Shen M, Mangla A, Khera R. Cardiovascular Care Innovation through Data-Driven Discoveries in the Electronic Health Record. *Am J Cardiol*. 2023;203:136–148.

3. Aquino EML, Barreto SM, Bensenor IM, et al. Brazilian Longitudinal Study of Adult Health (ELSA-Brasil): objectives and design. *Am J Epidemiol*. 2012;175:315–324.

4. Schmidt MI, Duncan BB, Mill JG, et al. Cohort profile: Longitudinal study of adult health (ELSA-brasil). *Int J Epidemiol*. 2015;44:68–75.

5. Aquino EML, Araujo MJ, Almeida M da CC, et al. Recrutamento de participantes no Estudo Longitudinal de Saúde do Adulto. *Rev Saúde Pública*. 2013;47:10–18.

6. Palmer LJ. UK Biobank: bank on it. *Lancet*. 2007;369:1980–1982.

7. Littlejohns TJ, Sudlow C, Allen NE, Collins R. UK Biobank: opportunities for cardiovascular research. *Eur Heart J*. 2019;40:1158–1166.

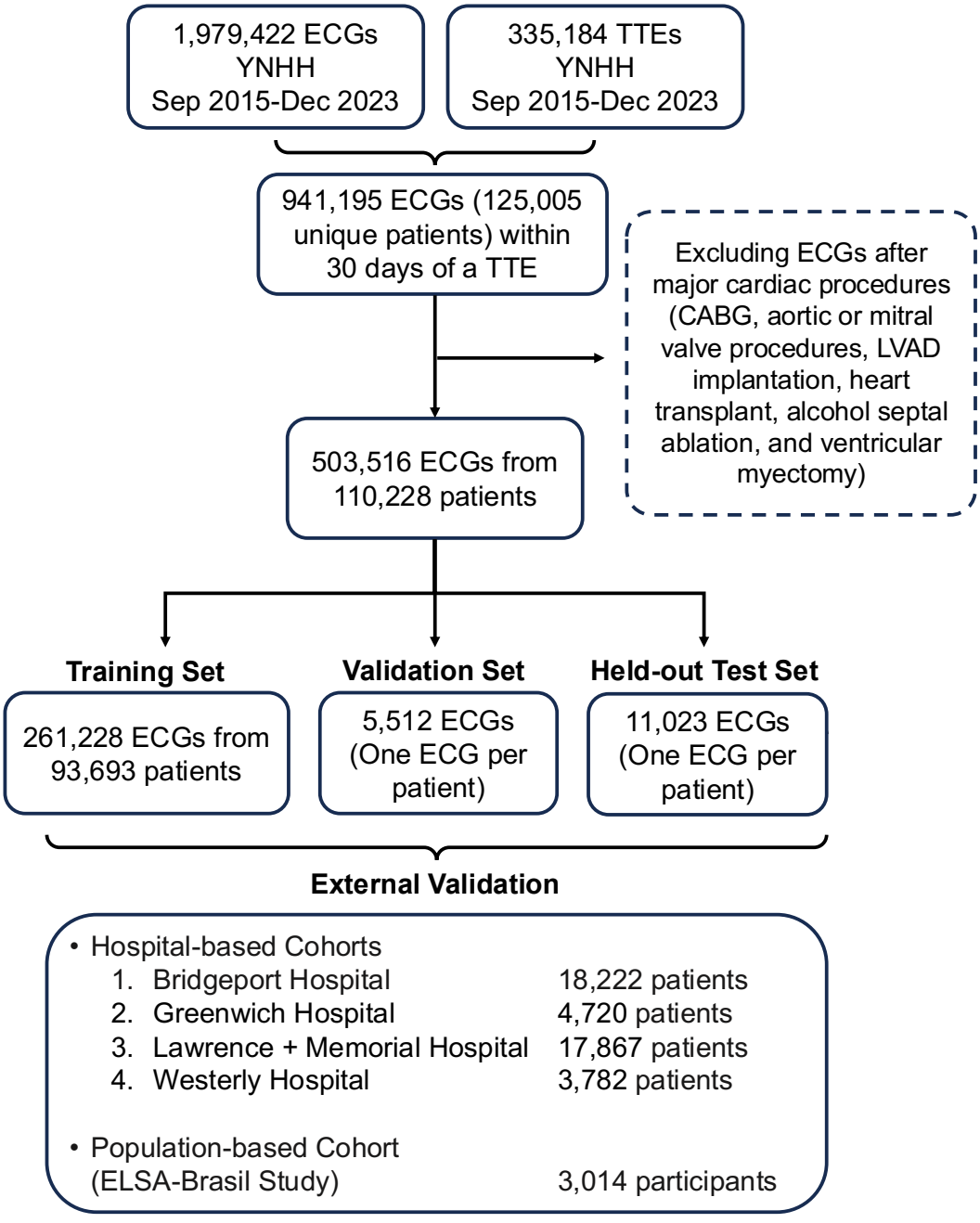
8. Raisi-Estabragh Z, Petersen SE. Cardiovascular research highlights from the UK Biobank: opportunities and challenges. *Cardiovasc Res*. 2020;116:e12–e15.

9. Sangha V, Mortazavi BJ, Haimovich AD, et al. Automated multilabel diagnosis on electrocardiographic images and signals. *Nat Commun*. 2022;13:1583.

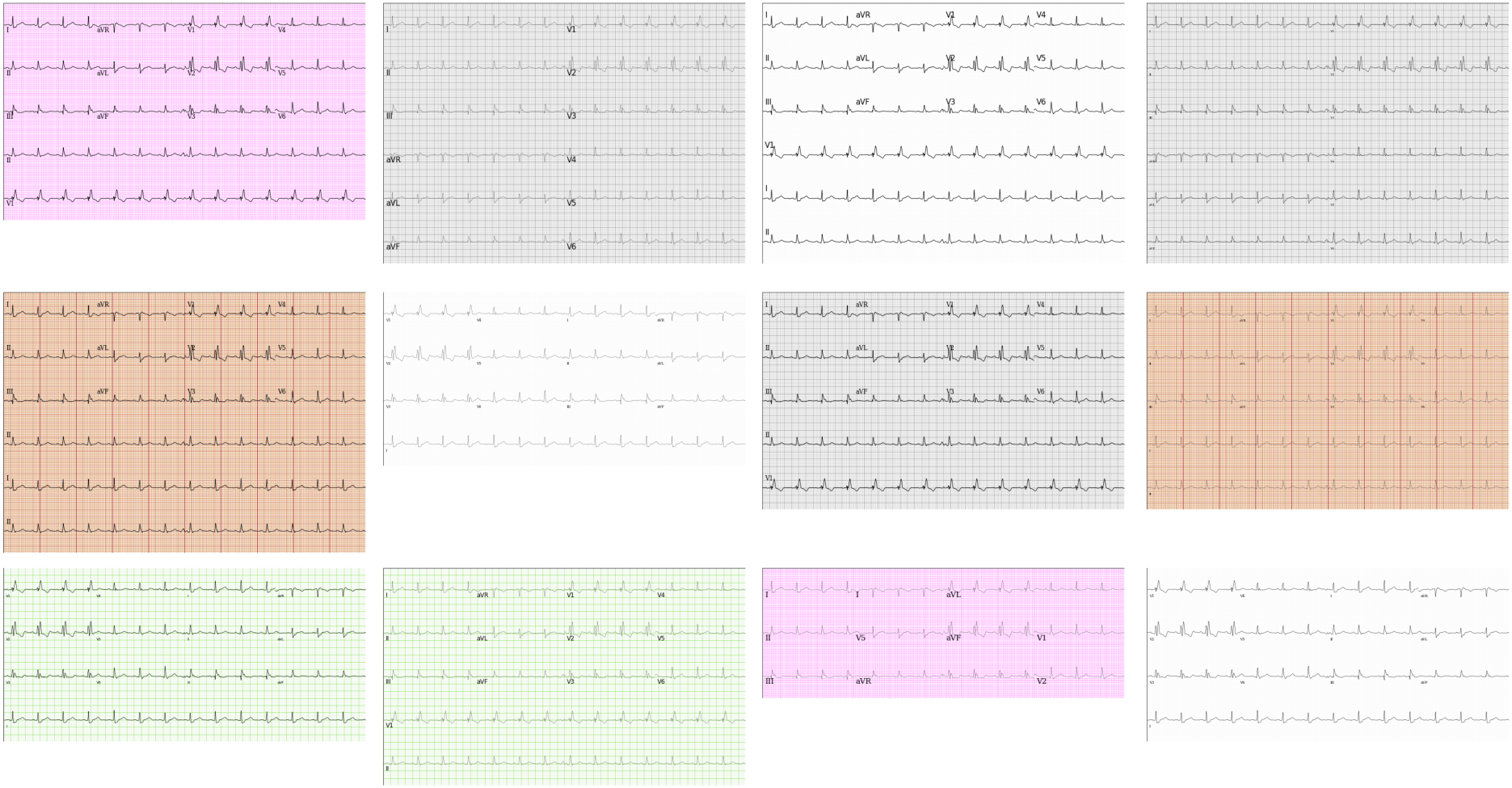
10. Khunte A, Sangha V, Oikonomou EK, et al. Detection of left ventricular systolic dysfunction from single-lead electrocardiography adapted for portable and wearable devices. *NPJ Digit Med*. 2023;6:124.

SUPPLEMENTARY FIGURES

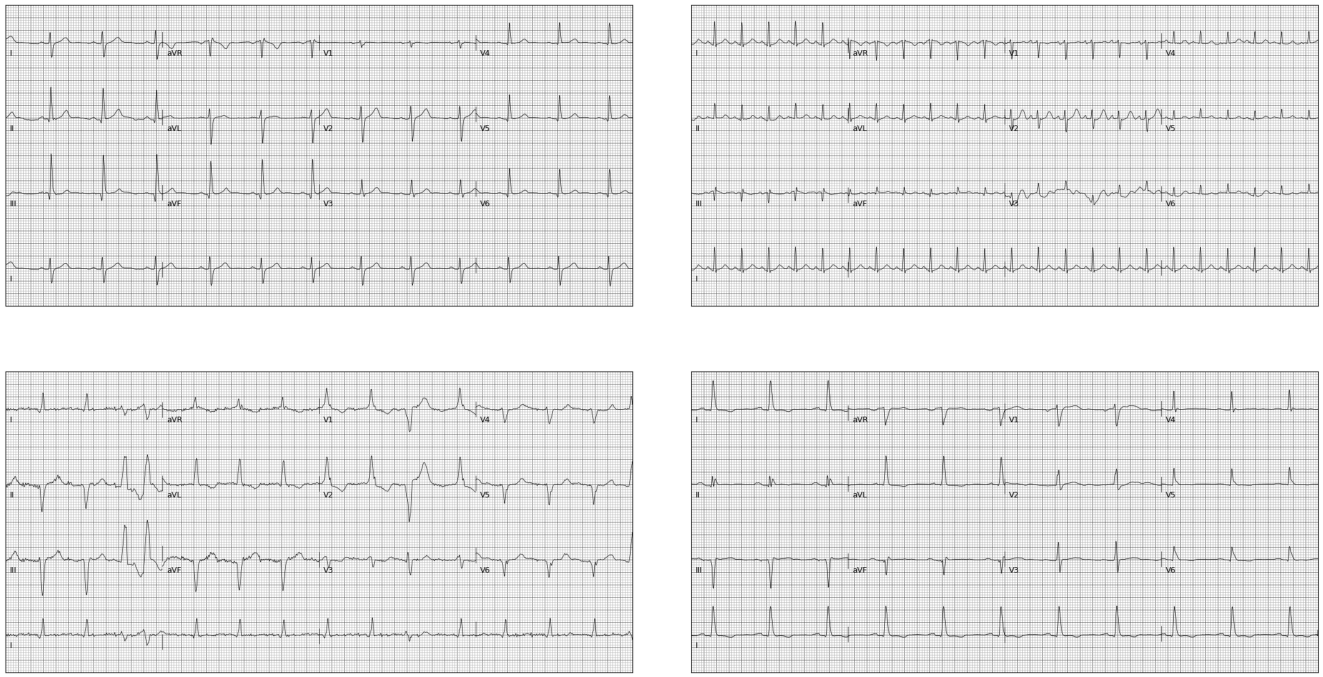
Supplementary Figure 1. Flow Diagram of study population and analysis. Abbreviations: ECG, electrocardiogram; TTE, transthoracic echocardiogram; YNHHS, Yale New Haven Health System.



Supplementary Figure 2. Examples of 12 variations in the electrocardiographic images used for convolutional neural network training.

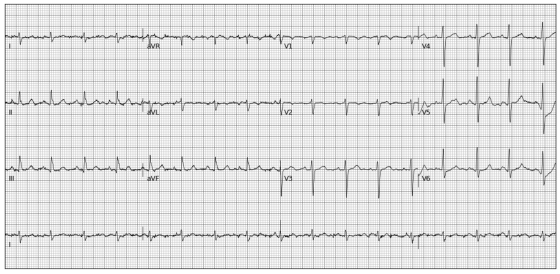


Supplementary Figure 3. Example of 4 electrocardiographic images plotted in the standard layout and used for model evaluation.

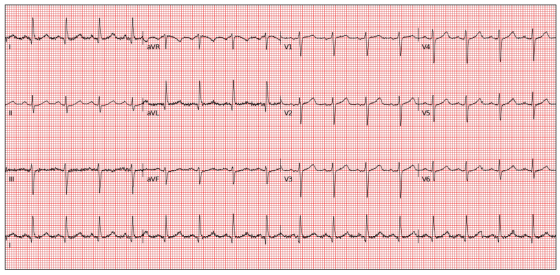


Supplementary Figure 4. Novel electrocardiogram formats used for model evaluation.
Abbreviations: ECG, electrocardiogram

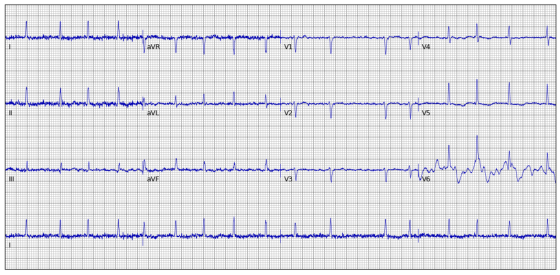
(A) Standard ECG format (presented here for reference)



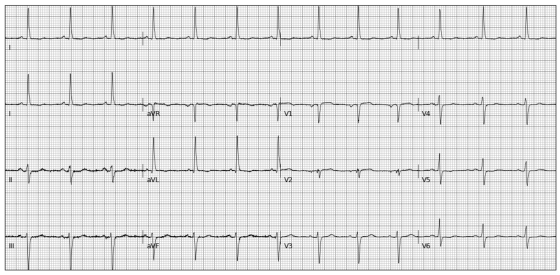
(B) Black-on-Red colors in standard ECG layout



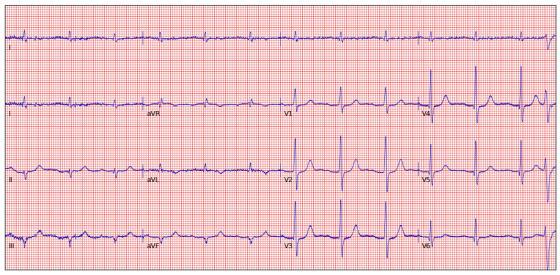
(C) Blue-on-Black colors in standard ECG layout



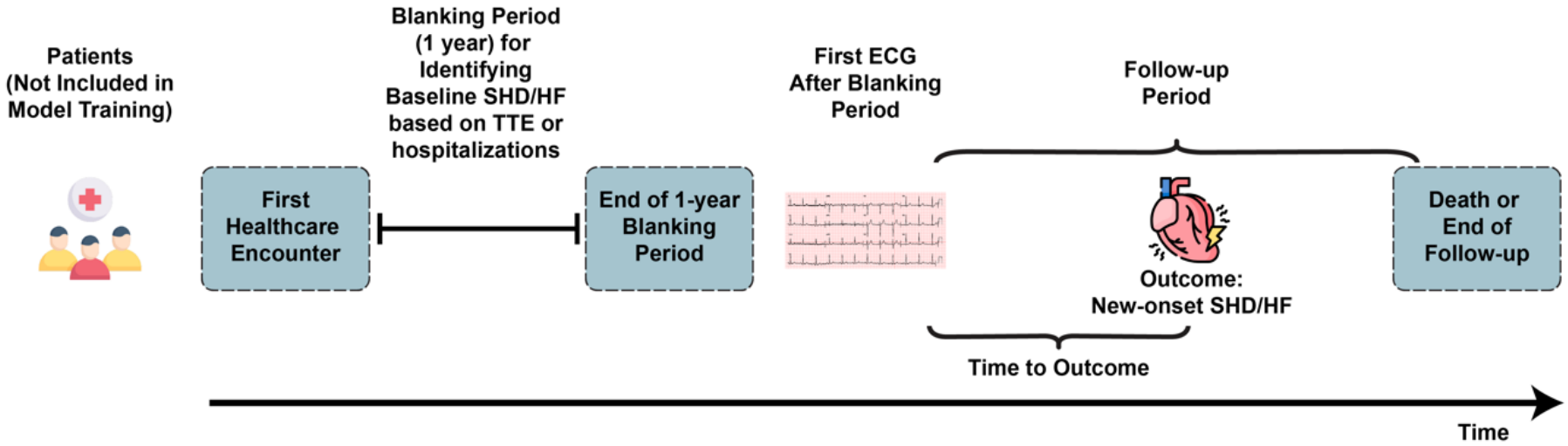
(D) Black-on-Black colors in rhythm-on-top layout



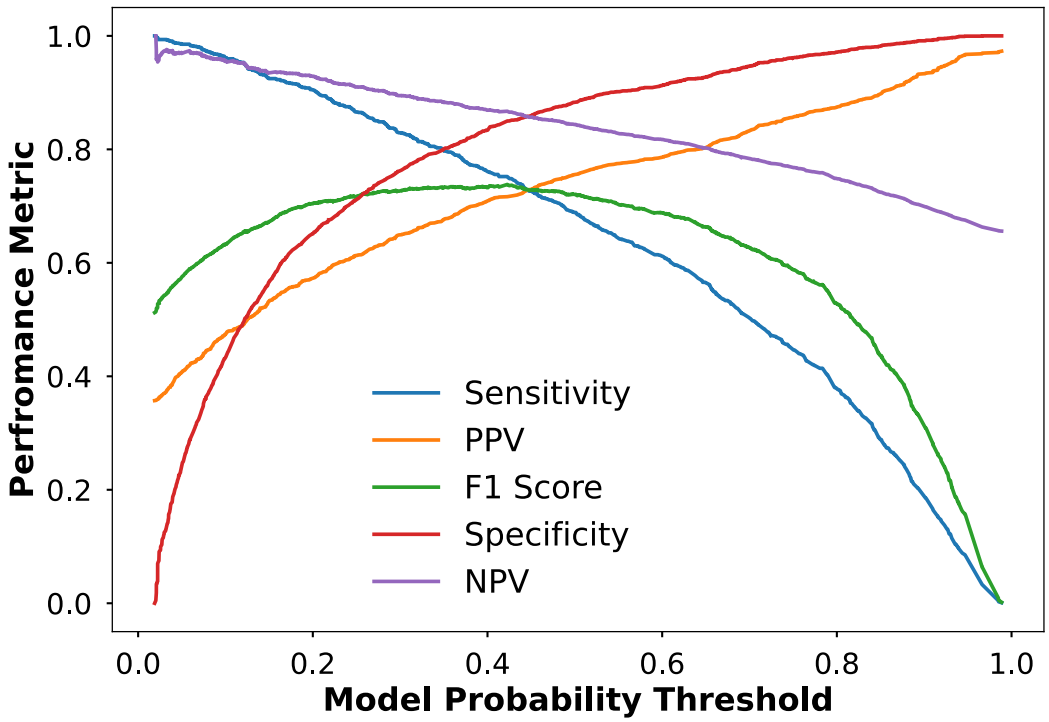
(E) Blue-on-Red colors in rhythm-on-top layout



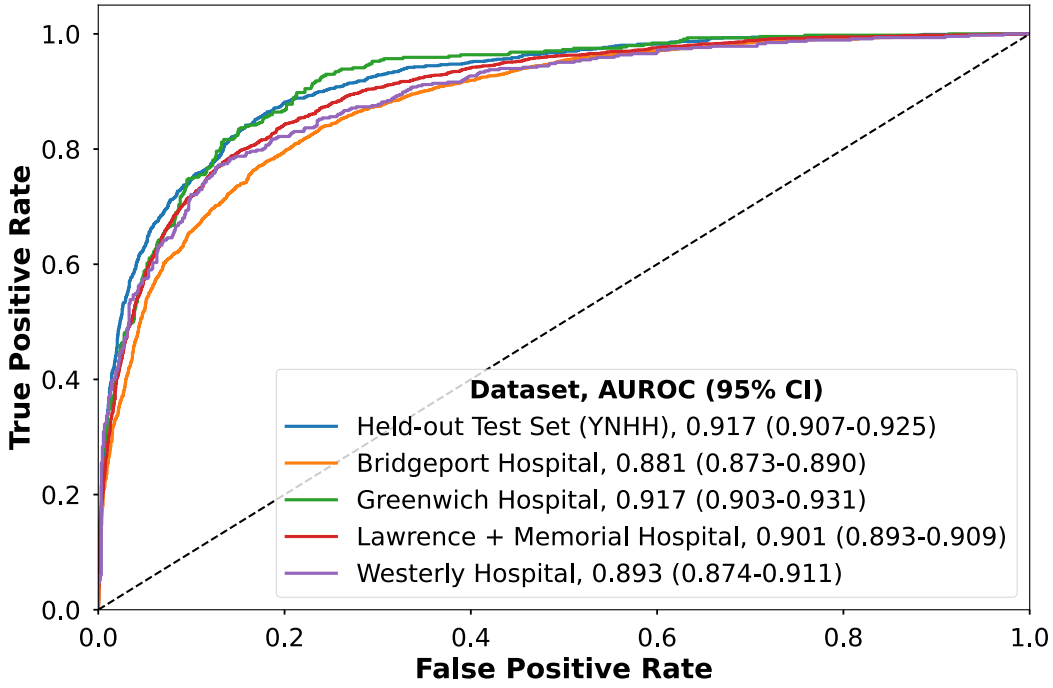
Supplementary Figure 5. Overview of methodology to identify individuals at risk of new-onset disease in the hospital-based validation sites.
Abbreviations: ECG, electrocardiograms; HF, heart failure; SHD, structural heart disease; TTE, transthoracic echocardiograms.



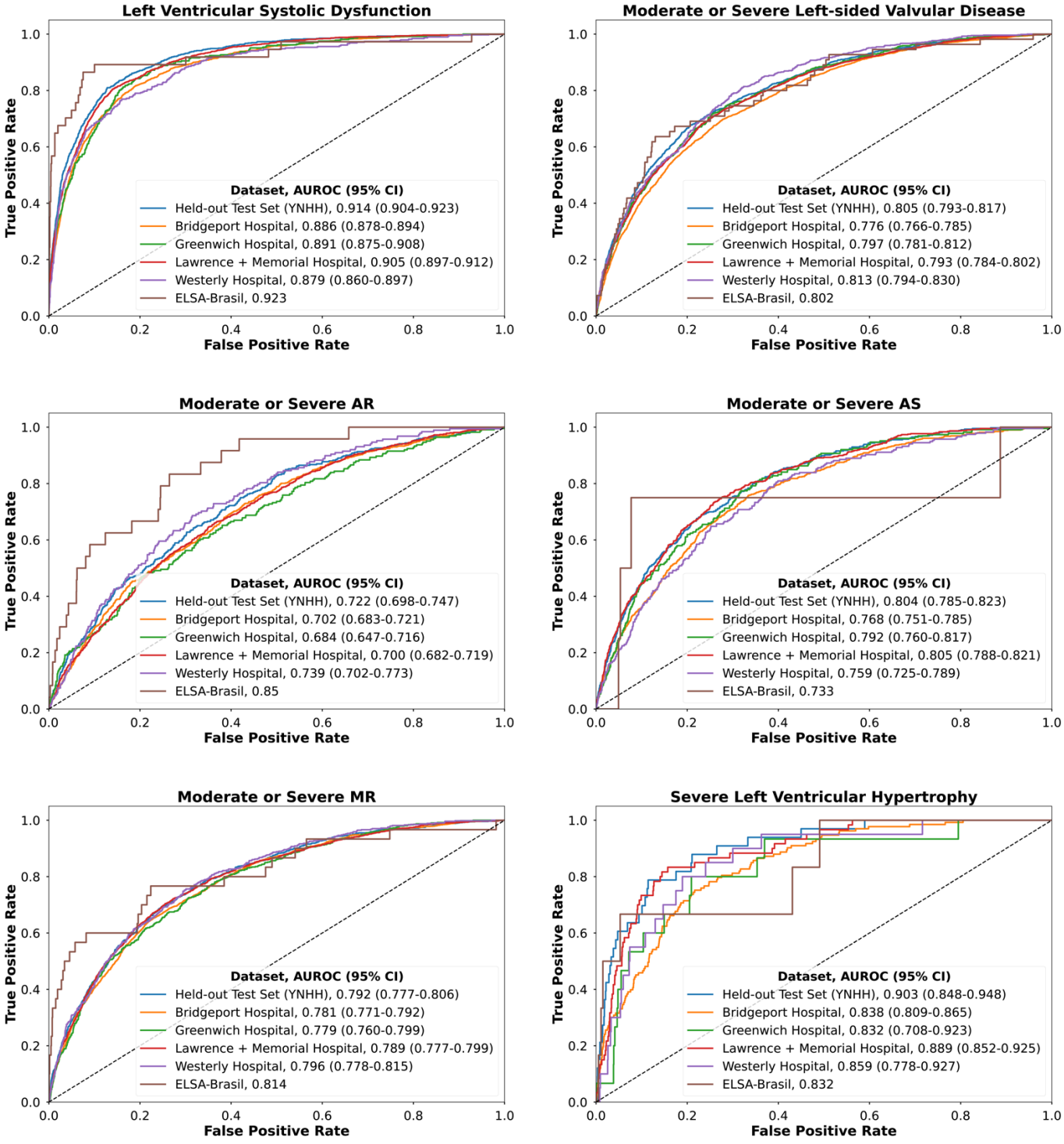
Supplementary Figure 6. PRESENT-SHD performance metrics across probability thresholds in the held-out test set.
Abbreviations: NPV, negative predictive value; PPV, positive predictive value.



Supplementary Figure 7. PRESENT-SHD performance for detection of structural heart disease including left ventricular systolic dysfunction, severe left-sided valve diseases, and severe left ventricular hypertrophy across study cohorts.



Supplementary Figure 8. Receiver operating characteristic curves for detecting individual structural heart disease across study cohorts.
Abbreviations: AR, aortic regurgitation; AS, aortic stenosis; AUROC, area under the receiver operating characteristic curve; sLVH, severe left ventricular hypertrophy; IVSd, interventricular septal diameter at end-diastole; LVDD, left ventricular diastolic dysfunction; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; NPV, negative predictive value; PPV, positive predictive value.



SUPPLEMENTARY TABLES

Supplementary Table 1. Diagnosis and procedure codes used to identify longitudinal outcomes.

Condition	ICD-10-CM codes
Heart Failure	'I11.0','I13.0','I13.2','I50','I50.0','I50.1','I50.9','Z95.81','I09.81'
Acute Myocardial Infarction	'I21', 'I22', 'I23', 'I24.0', 'I24.8', 'I24.9'
Stroke	'G45','G45.0','G45.1','G45.2','G45.3','G45.4','G45.8','G45.9', 'I63','I63.0','I63.1','I63.2','I63.3','I63.4','I63.5','I63.8','I63.9','I64', 'I65','I65.0','I65.1','I65.2','I65.3','I65.8','I65.9','I66','I66.0','I66.1', 'I66.2','I66.3','I66.4','I66.8','I66.9','I67.2','I69.3','I69.4'
Type 2 Diabetes Mellitus	'E11','E11.0','E11.1','E11.2','E11.3','E11.4','E11.5','E11.6', 'E11.7','E11.8','E11.9','O24.1'
Hypertension	'I10','I11','I11.0','I11.9','I12','I12.0','I12.9', 'I13','I13.0','I13.1','I13.2','I13.9','I67.4', 'O10','O10.0','O10.1','O10.2','O10.3','O10.9','O11'

Supplementary Table 2. Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis + Artificial Intelligence (TRIPOD + AI) checklist.

Section/Topic	Item	Development / evaluation[1]	Checklist item	Reported on page
TITLE				
Title	1	D;E	Identify the study as developing or evaluating the performance of a multivariable prediction model, the target population, and the outcome to be predicted	Pg 1
ABSTRACT				
Abstract	2	D;E	See TRIPOD+AI for Abstracts checklist	Pg 2
INTRODUCTION				
Background	3a	D;E	Explain the healthcare context (including whether diagnostic or prognostic) and rationale for developing or evaluating the prediction model, including references to existing models	Pg 6
	3b	D;E	Describe the target population and the intended purpose of the prediction model in the context of the care pathway, including its intended users (e.g., healthcare professionals, patients, public)	Pg 6
	3c	D;E	Describe any known health inequalities between sociodemographic groups	Pg 6,7
Objectives	4	D;E	Specify the study objectives, including whether the study describes the development or validation of a prediction model (or both)	Pg 7
METHODS				
Data	5a	D;E	Describe the sources of data separately for the development and evaluation datasets (e.g., randomised trial, cohort, routine care or registry data), the rationale for using these data, and representativeness of the data	Pg 7 and suppl.
	5b	D;E	Specify the dates of the collected participant data, including start and end of participant accrual; and, if applicable, end of follow-up	Pg 7 and suppl.
Participants	6a	D;E	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including the number and location of centres	Pg 7-8
	6b	D;E	Describe the eligibility criteria for study participants	Pg 7-8
	6c	D;E	Give details of any treatments received, and how they were handled during model development or evaluation, if relevant	N/A
Data preparation	7	D;E	Describe any data pre-processing and quality checking, including whether this was similar across relevant sociodemographic groups	Pg 8-9 and suppl.
Outcome	8a	D;E	Clearly define the outcome that is being predicted and the time horizon, including how and when assessed, the rationale for choosing this outcome, and whether the method of outcome assessment is consistent across sociodemographic groups	Pg 8-9, 11-12
	8b	D;E	If outcome assessment requires subjective interpretation, describe the qualifications and demographic characteristics of the outcome assessors	N/A
	8c	D;E	Report any actions to blind assessment of the outcome to be predicted	N/A
Predictors	9a	D	Describe the choice of initial predictors (e.g., literature, previous models, all available predictors) and any pre-selection of predictors before model building	Pg 8
	9b	D;E	Clearly define all predictors, including how and when they were measured (and any actions to blind assessment of predictors for the outcome and other predictors)	N/A
	9c	D;E	If predictor measurement requires subjective interpretation, describe the qualifications and demographic characteristics of the predictor assessors	Pg 8
Sample size	10	D;E	Explain how the study size was arrived at (separately for development and evaluation), and justify that the study size was sufficient to answer the research question. Include details of any sample size calculation	Pg 6
Missing data	11	D;E	Describe how missing data were handled. Provide reasons for omitting any data	Pg 7-8
Analytical methods	12a	D	Describe how the data were used (e.g., for development and evaluation of model performance) in the analysis, including whether the data were partitioned, considering any sample size requirements	Pg 11-12
	12b	D	Depending on the type of model, describe how predictors were handled in the analyses (functional form, rescaling, transformation, or any standardisation).	Pg 9-11
	12c	D	Specify the type of model, rationale[2], all model-building steps, including any hyperparameter tuning, and method for internal validation	Pg 9-11
	12d	D;E	Describe if and how any heterogeneity in estimates of model parameter values and model performance was handled and quantified across clusters (e.g., hospitals, countries). See TRIPOD-Cluster for additional considerations[3]	N/A
	12e	D;E	Specify all measures and plots used (and their rationale) to evaluate model performance (e.g., discrimination, calibration, clinical utility) and, if relevant, to compare multiple models	Pg 9-11
	12f	E	Describe any model updating (e.g., recalibration) arising from the model evaluation, either overall or for particular sociodemographic groups or settings	N/A
	12g	E	For model evaluation, describe how the model predictions were calculated (e.g., formula, code, object, application programming interface)	Pg 9-11
Class imbalance	13	D;E	If class imbalance methods were used, state why and how this was done, and any subsequent methods to recalibrate the model or the model predictions	N/A
Fairness	14	D;E	Describe any approaches that were used to address model fairness and their rationale	Pg 12
Model output	15	D	Specify the output of the prediction model (e.g., probabilities, classification). Provide details and rationale for any classification and how the thresholds were identified	Pg 12

[1] D=items relevant only to the development of a prediction model; E=items relating solely to the evaluation of a prediction model; D;E=items applicable to both the development and evaluation of a prediction model

[2] Separately for all model building approaches.

[3] TRIPOD-Cluster is a checklist of reporting recommendations for studies developing or validating models that explicitly account for clustering or explore heterogeneity in model performance (eg, at different hospitals or centres). Debray et al, BMJ 2023; 380: e071018 [DOI: 10.1136/bmj-2022-071018]

Training versus evaluation	16	D;E	Identify any differences between the development and evaluation data in healthcare setting, eligibility criteria, outcome, and predictors	N/A
Ethical approval	17	D;E	Name the institutional research board or ethics committee that approved the study and describe the participant-informed consent or the ethics committee waiver of informed consent	Pg 7
OPEN SCIENCE				
Funding	18a	D;E	Give the source of funding and the role of the funders for the present study	Pg 21
Conflicts of interest	18b	D;E	Declare any conflicts of interest and financial disclosures for all authors	Pg 19-20
Protocol	18c	D;E	Indicate where the study protocol can be accessed or state that a protocol was not prepared	Not prepared
Registration	18d	D;E	Provide registration information for the study, including register name and registration number, or state that the study was not registered	N/A
Data sharing	18e	D;E	Provide details of the availability of the study data	Pg 21
Code sharing	18f	D;E	Provide details of the availability of the analytical code[4]	Pg 21
PATIENT & PUBLIC INVOLVEMENT				
Patient & Public Involvement	19	D;E	Provide details of any patient and public involvement during the design, conduct, reporting, interpretation, or dissemination of the study or state no involvement.	N/A
RESULTS				
Participants	20a	D;E	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	Suppl.
	20b	D;E	Report the characteristics overall and, where applicable, for each data source or setting, including the key dates, key predictors (including demographics), treatments received, sample size, number of outcome events, follow-up time, and amount of missing data. A table may be helpful. Report any differences across key demographic groups.	Suppl.
	20c	E	For model evaluation, show a comparison with the development data of the distribution of important predictors (demographics, predictors, and outcome).	Suppl.
Model development	21	D;E	Specify the number of participants and outcome events in each analysis (e.g., for model development, hyperparameter tuning, model evaluation)	Pg 13-14
Model specification	22	D	Provide details of the full prediction model (e.g., formula, code, object, application programming interface) to allow predictions in new individuals and to enable third-party evaluation and implementation, including any restrictions to access or re-use (e.g., freely available, proprietary)[5]	Pg 13-15
Model performance	23a	D;E	Report model performance estimates with confidence intervals, including for any key subgroups (e.g., sociodemographic). Consider plots to aid presentation.	Pg 14-15
	23b	D;E	If examined, report results of any heterogeneity in model performance across clusters. See TRIPOD Cluster for additional details[3].	N/A
Model updating	24	E	Report the results from any model updating, including the updated model and subsequent performance	N/A
DISCUSSION				
Interpretation	25	D;E	Give an overall interpretation of the main results, including issues of fairness in the context of the objectives and previous studies	Pg 16
Limitations	26	D;E	Discuss any limitations of the study (such as a non-representative sample, sample size, overfitting, missing data) and their effects on any biases, statistical uncertainty, and generalizability	Pg 18
Usability of the model in the context of current care	27a	D	Describe how poor quality or unavailable input data (e.g., predictor values) should be assessed and handled when implementing the prediction model	Pg 19
	27b	D	Specify whether users will be required to interact in the handling of the input data or use of the model, and what level of expertise is required of users	N/A
	27c	D;E	Discuss any next steps for future research, with a specific view to applicability and generalizability of the model	Pg 19

From: Collins GS, Moons KGM, Dhiman P, et al. *BMJ* 2024;385:e078378. doi:10.1136/bmj-2023-078378

[4] This relates to the analysis code, for example, any data cleaning, feature engineering, model building, evaluation.
[5] This relates to the code to implement the model to get estimates of risk for a new individual.

Supplementary Table 3. Demographic and clinical characteristics of the model development population (including training and validation sets).
Abbreviations: AR, aortic regurgitation; AS, aortic stenosis; ECG, electrocardiogram; IQR, interquartile range; LVSD, left ventricular systolic dysfunction; SHD, structural heart disease; sLVH, severe left ventricular hypertrophy; MR, mitral regurgitation

Characteristic*	Train Set (ECG Level)	Train Set (Patient Level)	Internal Validation Set
Number	261,228	93,693	5,512
Age (years)	67.8 [56.1-78.3]	66.4 [54.1-77.3]	66.5 [54.1-77.4]
Female Sex	125735 (48.1%)	47153 (50.3%)	2794 (50.7%)
Race and Ethnicity			
White	172972 (66.2%)	61656 (65.8%)	3612 (65.5%)
Black	38938 (14.9%)	12630 (13.4%)	753 (13.7%)
Hispanic	20941 (8.0%)	7346 (7.8%)	408 (7.4%)
Others	28377 (10.9%)	12061 (12.9%)	739 (13.4%)
SHD	59005 (22.6%)	17805 (19.0%)	1091 (19.8%)
Indeterminate	119837 (45.9%)	40952 (43.7%)	2344 (42.5%)
LVSD (LVEF <40%)	25162 (9.6%)	6601 (7.0%)	390 (7.1%)
Indeterminate	4705 (1.8%)	1424 (1.5%)	82 (1.5%)
Moderate or Severe Left-sided Valvular Disease	42170 (16.1%)	13397 (14.3%)	819 (14.9%)
Indeterminate	91537 (35.0%)	30510 (32.6%)	1745 (31.7%)
Moderate or Severe AR	10271 (3.9%)	3446 (3.7%)	214 (3.9%)
Indeterminate	28423 (10.9%)	8806 (9.4%)	539 (9.8%)
Moderate or Severe AS	10270 (3.9%)	3389 (3.6%)	202 (3.7%)
Indeterminate	84492 (32.3%)	28143 (30.0%)	1614 (29.3%)
Moderate or Severe MR	27347 (10.5%)	8399 (9.0%)	503 (9.1%)
Indeterminate	21087 (8.1%)	6428 (6.9%)	387 (7.0%)
Severe Left-sided Valvular Disease	6193 (2.4%)	2060 (2.2%)	128 (2.3%)
Indeterminate	108234 (41.4%)	35658 (38.1%)	2064 (37.4%)
Severe AR	348 (0.1%)	109 (0.1%)	10 (0.2%)
Indeterminate	28423 (10.9%)	8806 (9.4%)	539 (9.8%)
Severe AS	3123 (1.2%)	1132 (1.2%)	70 (1.3%)
Indeterminate	84492 (32.3%)	28143 (30.0%)	1614 (29.3%)
Severe MR	2672 (1.0%)	813 (0.9%)	44 (0.8%)
Indeterminate	21087 (8.1%)	6428 (6.9%)	387 (7.0%)
sLVH	975 (0.4%)	276 (0.3%)	29 (0.5%)
Indeterminate	118906 (45.5%)	37952 (40.5%)	2233 (40.5%)

Footnote: Missing values were considered ‘indeterminate’ for individual SHD components. For composite SHD, the label was considered positive if any of the SHD components was flagged positive, negative is all SHD components were flagged negative, and ‘indeterminate’ otherwise.

Supplementary Table 4. Demographic and clinical characteristics of the held-out test set and the external validation cohorts.

Abbreviations: AR, aortic regurgitation; AS, aortic stenosis; ECG, electrocardiogram; IQR, interquartile range; LVSD, left ventricular systolic dysfunction; SHD, structural heart disease; sLVH, severe left ventricular hypertrophy; MR, mitral regurgitation

	Held-out Test Set	Bridgeport Hospital	Greenwich Hospital	Lawrence + Memorial Hospital	Westerly Hospital	ELSA-Brasil
Number	11,023	18,222	4,720	17,867	3,782	3,014
Age (years)	66.3 [53.7-77.4]	68.5 [56.0-80.0]	74.0 [59.9-84.5]	68.7 [57.3-79.5]	73.3 [62.2-82.4]	62.0 [57.0-67.0]
Female Sex	5501 (49.9%)	9210 (50.5%)	2316 (49.1%)	8634 (48.3%)	1821 (48.1%)	1596 (53.0%)
Race and Ethnicity						
White	7264 (65.9%)	10420 (57.2%)	3110 (65.9%)	12944 (72.4%)	3181 (84.1%)	1661 (55.1%)
Black	1474 (13.4%)	3472 (19.1%)	182 (3.8%)	1184 (6.6%)	56 (1.5%)	455 (15.1%)
Hispanic	897 (8.1%)	2849 (15.6%)	504 (10.7%)	1271 (7.1%)	53 (1.4%)	-
Pardo	-	-	-	-	-	753 (25.0%)
Others	1388 (12.6%)	1481 (8.1%)	924 (19.6%)	2468 (13.8%)	492 (13.0%)	145 (4.8%)
SHD	2085 (18.9%)	4167 (22.9%)	1130 (23.9%)	3601 (20.2%)	1024 (27.1%)	88 (2.9%)
Indeterminate	4820 (43.7%)	9278 (50.9%)	2449 (51.9%)	6420 (35.9%)	1939 (51.3%)	26 (0.9%)
LVSD (LVEF <40%)	821 (7.4%)	1772 (9.7%)	368 (7.8%)	1466 (8.2%)	386 (10.2%)	37 (1.2%)
Indeterminate	163 (1.5%)	307 (1.7%)	414 (8.8%)	137 (0.8%)	168 (4.4%)	2 (0.1%)
Moderate or Severe Left-sided Valvular Disease	1569 (14.2%)	3053 (16.8%)	924 (19.6%)	2640 (14.8%)	818 (21.6%)	55 (1.8%)
Indeterminate	3597 (32.6%)	6979 (38.3%)	1243 (26.3%)	4537 (25.4%)	1611 (42.6%)	27 (0.9%)
Moderate or Severe AR	392 (3.6%)	688 (3.8%)	224 (4.7%)	694 (3.9%)	188 (5.0%)	24 (0.8%)
Indeterminate	997 (9.0%)	2436 (13.4%)	472 (10.0%)	1204 (6.7%)	277 (7.3%)	12 (0.4%)
Moderate or Severe AS	426 (3.9%)	714 (3.9%)	226 (4.8%)	607 (3.4%)	236 (6.2%)	4 (0.1%)
Indeterminate	3312 (30.0%)	5958 (32.7%)	1167 (24.7%)	4343 (24.3%)	1252 (33.1%)	9 (0.3%)
Moderate or Severe MR	958 (8.7%)	2104 (11.5%)	627 (13.3%)	1670 (9.3%)	537 (14.2%)	30 (1.0%)
Indeterminate	759 (6.9%)	1222 (6.7%)	310 (6.6%)	823 (4.6%)	170 (4.5%)	15 (0.5%)
Severe Left-sided Valvular Disease	279 (2.5%)	400 (2.2%)	81 (1.7%)	281 (1.6%)	81 (2.1%)	0 (0%)
Indeterminate	4166 (37.8%)	8318 (45.6%)	1560 (33.1%)	5407 (30.3%)	2054 (54.3%)	0 (0%)
Severe AR	15 (0.1%)	27 (0.1%)	7 (0.1%)	12 (0.1%)	1 (0.0%)	0 (0%)
Indeterminate	997 (9.0%)	2436 (13.4%)	472 (10.0%)	1204 (6.7%)	277 (7.3%)	0 (0%)
Severe AS	155 (1.4%)	220 (1.2%)	47 (1.0%)	167 (0.9%)	59 (1.6%)	0 (0%)
Indeterminate	3312 (30.0%)	5958 (32.7%)	1167 (24.7%)	4343 (24.3%)	1252 (33.1%)	0 (0%)

Severe MR	104 (0.9%)	146 (0.8%)	28 (0.6%)	94 (0.5%)	19 (0.5%)	0 (0%)
Indeterminate	759 (6.9%)	1222 (6.7%)	310 (6.6%)	823 (4.6%)	170 (4.5%)	0 (0%)
sLVH	33 (0.3%)	133 (0.7%)	15 (0.3%)	60 (0.3%)	20 (0.5%)	6 (0.2%)
Indeterminate	4446 (40.3%)	8814 (48.4%)	2979 (63.1%)	5991 (33.5%)	2152 (56.9%)	0 (0%)

Footnote: Missing values were considered ‘indeterminate’ for individual SHD components. For composite SHD, the label was considered positive if any of the SHD components was flagged positive, negative is all SHD components were flagged negative, and ‘indeterminate’ otherwise.

Supplementary Table 5. Model performance on novel electrocardiogram formats not encountered during training.

Novel Image Format	Key Novel Features	PRESENT-SHD AUROC (95% CI)	PRESENT-SHD AUPRC (95% CI)
Black-on-Red Standard	**1. Novel background grid color (red)** **2. Standard ECG trace color** **3. Standard ECG layout**	0.884 (0.877-0.893)	0.806 (0.789-0.822)
Blue-on-Black Standard	**1. Standard background grid color** **2. Novel ECG trace color (blue)** **3. Standard ECG lead layout**	0.885 (0.877-0.893)	0.807 (0.788-0.821)
Black-on-Black Rhythm-on-top	**1. Standard background grid color** **2. Standard ECG trace color** **3. Novel ECG lead layout (rhythm strip on top of the 12 limb and precordial leads)**	0.883 (0.875-0.892)	0.802 (0.785-0.818)
Blue-on-Red Rhythm-on-top	**1. Novel background grid color (red)** **2. Novel ECG trace color (blue)** **3. Novel ECG lead layout (rhythm strip on top of the 12 limb and precordial leads)**	0.883 (0.874-0.892)	0.803 (0.785-0.820)

Supplementary Table 6. Model discrimination in subsets of the held-out test set where transthoracic echocardiograms were performed before, after, or on the same day as the electrocardiogram.
Abbreviations: AUPRC, area under the precision-recall curve; AUROC, area under the receiver operating characteristic curve; ECG, electrocardiogram; TTE, transthoracic echocardiogram.

Subset of interest	Number of patients	AUROC
TTE performed within 30 days before the ECG	2745	0.885
TTE performed on the same day as the ECG	1671	0.882
TTE performed within 30 days after the ECG	6607	0.885

Supplementary Table 7. Performance for detection of structural heart diseases for convolutional neural network model for structural heart disease in the held-out test set.

Performance metric	Convolutional Neural Network for Structural Heart Disease Detection	PRESENT-SHD (Mentioned for reference)
AUROC	0.856 (0.846-0.866)	0.886 (0.877-0.894)
AUPRC	0.774 (0.758-0.792)	0.807 (0.791-0.823)
Diagnostic OR	10.94 (9.41-12.76)	17.2 (14.7-20.1)
Sensitivity	89.3% (88.0-90.6)	89.8% (89.0-90.5)
Specificity	56.6% (55.1-58.3)	66.2% (65.0-67.4)
PPV	51.0% (49.4-52.4)	57.4% (56.1-58.6)
NPV	91.3% (90.1-92.3)	92.8% (92.1-93.4)
F1 score	0.649	0.7

Supplementary Table 8. Performance for detection of structural heart diseases for extreme gradient boosting model variations in the held-out test set.
Abbreviations: AUROC, area under the receiver operating characteristic curve; CNN, convolutional neural network; SHD, structural heart disease; XGBoost, extreme gradient boosting.

Model Variation	XGBoost Model Input Features	AUROC (95% CI)
Variation 1 (without age, sex, or CNNs for individual valve diseases)	**1. LVSD CNN probability** **2. Moderate/Severe Valve Disease CNN Probability** **3. sLVH CNN Probability**	0.869 (0.859-0.878)
Variation 2 (without CNNs for individual valve diseases)	**1. Age** **2. Sex** **3. LVSD CNN probability** **4. Moderate/Severe Valve Disease CNN Probability** **5. sLVH CNN Probability**	0.885 (0.876-0.893)

Supplementary Table 9. Model performance characteristics for signal-based ensemble model for detection of structural heart disease across the held-out test set and external validation cohorts.
Abbreviations: AUPRC, area under the precision recall curve; AUROC, area under the receiver operating characteristic curve; NPV, negative predictive value; PPV, positive predictive value.

Cohort Type	Site Name	Total Number	Diagnostic OR	AUROC	AUPRC	F1 Score	Prevalence	Sensitivity	Specificity	PPV	NPV
Held-out test set	**Yale New Haven Hospital**	6203	19.9 (16.9-23.5)	0.894 (0.885-0.902)	0.823 (0.806-0.838)	0.701	33.60%	91.6% (90.9-92.3)	64.7% (63.6-65.9)	56.8% (55.6-58.0)	93.8% (93.2-94.4)
External validation – Hospital sites	**Bridgeport Hospital**	8944	16.6 (14.5-19.0)	0.868 (0.861-0.875)	0.852 (0.842-0.862)	0.757	46.60%	93.6% (93.1-94.1)	53.0% (52.0-54.0)	63.5% (62.5-64.5)	90.5% (89.9-91.1)
	Greenwich Hospital	2271	36.7 (26.3-51.2)	0.908 (0.897-0.920)	0.903 (0.887-0.918)	0.808	49.80%	96.4% (95.6-97.1)	58.0% (56.0-60.0)	69.5% (67.6-71.3)	94.2% (93.2-95.1)
	Lawrence + Memorial Hospital	11447	19.2 (16.6-22.1)	0.880 (0.874-0.887)	0.783 (0.769-0.797)	0.643	31.50%	94.1% (93.6-94.5)	54.8% (53.8-55.7)	48.8% (47.9-49.7)	95.3% (94.9-95.6)
	Westerly Hospital	1843	21.6 (15.6-29.8)	0.895 (0.882-0.910)	0.916 (0.901-0.928)	0.813	55.60%	95.4% (94.5-96.4)	50.9% (48.6-53.2)	70.8% (68.8-72.9)	89.9% (88.5-91.2)
External validation – Population-based cohort	**ELSA-Brasil**	2988	9.4 (5.5-16.1)	0.854 (0.806-0.895)	0.335 (0.234-0.442)	0.136	2.90%	80.7% (79.3-82.1)	69.3% (67.7-71.0)	7.4% (6.5-8.3)	99.2% (98.8-99.5)

Supplementary Table 10. Performance metrics for detecting structural heart disease across key demographic subgroups in Bridgeport Hospital.
Abbreviations: AUPRC, area under the precision-recall curve; AUROC, area under the receiver operating characteristic curve; NPV, negative predictive value; PPV, positive predictive value.

Subgroup	Total Number	Diagnostic OR	AUROC	AUPRC	F1 Score	Prevalence	Sensitivity	Specificity	PPV	NPV
Overall	8944	14.8 (12.9-16.9)	0.854 (0.847-0.862)	0.834 (0.823-0.845)	0.751	46.60%	93.2% (92.6-93.7)	52.0% (51.0-53.1)	62.9% (61.9-63.9)	89.7% (89.1-90.3)
Age ≥ 65 years	5139	9.4 (7.3-12.2)	0.798 (0.786-0.810)	0.853 (0.840-0.866)	0.777	60.30%	97.7% (97.3-98.1)	18.3% (17.2-19.3)	64.5% (63.2-65.8)	83.8% (82.8-84.8)
Age < 65 years	3805	13.6 (11.4-16.2)	0.859 (0.846-0.873)	0.756 (0.732-0.780)	0.671	28.10%	80.1% (78.8-81.3)	77.2% (75.8-78.5)	57.8% (56.2-59.3)	90.8% (89.9-91.8)
Female Sex	4528	11.9 (9.9-14.2)	0.833 (0.821-0.844)	0.794 (0.776-0.812)	0.729	44.70%	91.7% (90.9-92.6)	51.6% (50.2-53.1)	60.5% (59.1-62.0)	88.6% (87.6-89.5)
Male Sex	4416	18.9 (15.4-23.2)	0.875 (0.865-0.885)	0.867 (0.853-0.882)	0.772	48.50%	94.5% (93.8-95.2)	52.4% (51.0-53.9)	65.2% (63.8-66.6)	91.0% (90.1-91.8)
Non-Hispanic White	5010	13.8 (11.5-16.7)	0.839 (0.828-0.850)	0.846 (0.831-0.860)	0.776	53.30%	94.7% (94.1-95.3)	43.5% (42.2-44.9)	65.7% (64.4-67.0)	87.8% (86.9-88.7)
Non-Hispanic Black	1754	11.6 (8.8-15.2)	0.847 (0.827-0.864)	0.813 (0.784-0.838)	0.713	41.50%	90.4% (89.0-91.8)	55.2% (52.8-57.5)	58.9% (56.6-61.2)	89.0% (87.5-90.5)
Hispanic	1355	15.9 (11.5-21.8)	0.875 (0.854-0.893)	0.826 (0.798-0.855)	0.725	38.00%	89.7% (88.1-91.3)	64.5% (62.0-67.1)	60.8% (58.2-63.4)	91.1% (89.6-92.6)
Others	825	18.6 (11.6-30.1)	0.863 (0.835-0.888)	0.765 (0.711-0.813)	0.665	30.80%	91.7% (89.9-93.6)	62.7% (59.4-66.0)	52.2% (48.8-55.7)	94.5% (92.9-96.0)

Supplementary Table 11. Performance metrics for detecting structural heart disease across key demographic subgroups in Greenwich Hospital.
Abbreviations: AUPRC, area under the precision-recall curve; AUROC, area under the receiver operating characteristic curve; NPV, negative predictive value; PPV, positive predictive value.

Subgroup	Total Number	Diagnostic OR	AUROC	AUPRC	F1 Score	Prevalence	Sensitivity	Specificity	PPV	NPV
Overall	2271	30.6 (22.2-42.1)	0.900 (0.888-0.913)	0.894 (0.878-0.910)	0.798	49.80%	96.0% (95.2-96.8)	55.9% (53.9-58.0)	68.3% (66.4-70.2)	93.4% (92.4-94.4)
Age ≥ 65 years	1440	11.8 (6.8-20.4)	0.829 (0.807-0.851)	0.904 (0.887-0.921)	0.822	67.20%	98.3% (97.7-99.0)	16.5% (14.6-18.4)	70.7% (68.4-73.1)	83.0% (81.0-84.9)
Age < 65 years	831	23.6 (15.0-37.0)	0.907 (0.881-0.934)	0.790 (0.733-0.839)	0.659	19.50%	82.1% (79.5-84.7)	83.7% (81.2-86.2)	55.0% (51.6-58.3)	95.1% (93.6-96.5)
Female Sex	1139	28.5 (17.9-45.4)	0.889 (0.870-0.907)	0.873 (0.846-0.898)	0.776	47.40%	96.1% (95.0-97.2)	53.6% (50.7-56.5)	65.1% (62.4-67.9)	93.9% (92.5-95.3)
Male Sex	1132	33.2 (21.3-51.7)	0.911 (0.894-0.927)	0.912 (0.891-0.931)	0.82	52.10%	95.9% (94.8-97.1)	58.5% (55.6-61.4)	71.6% (68.9-74.2)	93.0% (91.5-94.5)
Non-Hispanic White	1440	27.4 (17.9-41.8)	0.884 (0.866-0.901)	0.907 (0.888-0.925)	0.827	58.80%	96.9% (96.0-97.8)	46.5% (43.9-49.0)	72.1% (69.7-74.4)	91.4% (89.9-92.8)
Non-Hispanic Black	77	12.2 (3.6-41.3)	0.887 (0.799-0.951)	0.903 (0.814-0.964)	0.773	49.40%	89.5% (82.6-96.3)	59.0% (48.0-70.0)	68.0% (57.6-78.4)	85.2% (77.3-93.1)
Hispanic	235	112.4 (26.4-477.8)	0.920 (0.882-0.949)	0.887 (0.832-0.936)	0.816	41.30%	97.9% (96.1-99.8)	70.3% (64.4-76.1)	69.9% (64.0-75.7)	98.0% (96.2-99.8)
Others	519	19.8 (10.8-36.3)	0.899 (0.869-0.927)	0.809 (0.749-0.859)	0.659	28.70%	91.3% (88.8-93.7)	65.4% (61.3-69.5)	51.5% (47.2-55.8)	94.9% (93.0-96.8)

Supplementary Table 12. Performance metrics for detecting structural heart disease across key demographic subgroups in Lawrence + Memorial Hospital.
Abbreviations: AUPRC, area under the precision-recall curve; AUROC, area under the receiver operating characteristic curve; NPV, negative predictive value; PPV, positive predictive value.

Subgroup	Total Number	Diagnostic OR	AUROC	AUPRC	F1 Score	Prevalence	Sensitivity	Specificity	PPV	NPV
Overall	11447	16.0 (14.0-18.2)	0.871 (0.864-0.878)	0.771 (0.757-0.784)	0.643	31.50%	92.5% (92.0-93.0)	56.4% (55.5-57.3)	49.3% (48.4-50.3)	94.3% (93.8-94.7)
Age ≥ 65 years	6165	11.7 (9.1-15.0)	0.822 (0.812-0.832)	0.795 (0.779-0.810)	0.673	45.50%	97.6% (97.2-98.0)	22.5% (21.4-23.5)	51.3% (50.0-52.5)	91.7% (91.0-92.4)
Age < 65 years	5282	13.1 (11.0-15.7)	0.861 (0.845-0.875)	0.653 (0.619-0.686)	0.537	15.00%	74.5% (73.4-75.7)	81.8% (80.8-82.8)	42.0% (40.6-43.3)	94.8% (94.2-95.4)
Female Sex	5634	13.5 (11.3-16.1)	0.858 (0.848-0.868)	0.737 (0.715-0.758)	0.63	30.50%	91.1% (90.3-91.8)	56.9% (55.6-58.2)	48.1% (46.8-49.4)	93.6% (92.9-94.2)
Male Sex	5813	19.1 (15.7-23.3)	0.884 (0.876-0.893)	0.800 (0.782-0.817)	0.657	32.40%	93.8% (93.2-94.4)	55.9% (54.6-57.2)	50.5% (49.2-51.8)	94.9% (94.4-95.5)
Non-Hispanic White	8085	15.9 (13.5-18.7)	0.869 (0.861-0.876)	0.787 (0.772-0.801)	0.658	34.80%	93.7% (93.2-94.3)	51.5% (50.4-52.6)	50.7% (49.7-51.8)	93.9% (93.4-94.4)
Non-Hispanic Black	776	14.0 (8.7-22.4)	0.879 (0.851-0.905)	0.766 (0.707-0.819)	0.615	27.20%	89.6% (87.4-91.7)	61.9% (58.5-65.4)	46.8% (43.3-50.3)	94.1% (92.4-95.7)
Hispanic	882	19.4 (11.8-31.8)	0.885 (0.856-0.911)	0.692 (0.616-0.762)	0.58	19.50%	88.4% (86.3-90.5)	71.8% (68.9-74.8)	43.2% (39.9-46.5)	96.2% (95.0-97.5)
Others	1704	13.0 (9.5-17.7)	0.851 (0.830-0.871)	0.686 (0.640-0.729)	0.588	23.90%	87.3% (85.7-88.8)	65.4% (63.2-67.7)	44.3% (41.9-46.6)	94.2% (93.1-95.3)

Supplementary Table 13. Performance metrics for detecting structural heart disease across key demographic subgroups in Westerly Hospital.
Abbreviations: AUPRC, area under the precision-recall curve; AUROC, area under the receiver operating characteristic curve; NPV, negative predictive value; PPV, positive predictive value.

Subgroup	Total Number	Diagnostic OR	AUROC	AUPRC	F1 Score	Prevalence	Sensitivity	Specificity	PPV	NPV
Overall	1843	19.9 (14.5-27.3)	0.887 (0.874-0.902)	0.906 (0.890-0.922)	0.81	55.60%	95.1% (94.1-96.1)	50.5% (48.3-52.8)	70.6% (68.6-72.7)	89.2% (87.8-90.6)
Age ≥ 65 years	1282	16.3 (9.2-29.1)	0.847 (0.827-0.869)	0.916 (0.899-0.933)	0.833	67.60%	98.4% (97.7-99.1)	21.2% (18.9-23.4)	72.2% (69.8-74.7)	86.3% (84.4-88.2)
Age < 65 years	561	14.3 (9.2-22.4)	0.885 (0.853-0.914)	0.810 (0.759-0.857)	0.683	28.20%	77.2% (73.7-80.7)	80.9% (77.6-84.1)	61.3% (57.3-65.3)	90.1% (87.6-92.5)
Female Sex	895	19.6 (12.4-31.1)	0.879 (0.856-0.900)	0.890 (0.863-0.913)	0.797	53.60%	95.2% (93.8-96.6)	49.6% (46.4-52.9)	68.6% (65.6-71.7)	90.0% (88.0-91.9)
Male Sex	948	20.3 (13.2-31.3)	0.895 (0.875-0.914)	0.918 (0.896-0.938)	0.822	57.40%	95.0% (93.7-96.4)	51.5% (48.3-54.7)	72.5% (69.7-75.4)	88.5% (86.5-90.5)
Non-Hispanic White	1527	19.7 (13.9-28.1)	0.884 (0.867-0.902)	0.916 (0.900-0.932)	0.831	60.20%	95.5% (94.5-96.6)	47.9% (45.4-50.4)	73.6% (71.3-75.8)	87.7% (86.0-89.3)
Non-Hispanic Black	23	14.0 (1.3-147.4)	0.750 (0.526-0.938)	0.619 (0.326-0.888)	0.7	34.80%	87.5% (74.0-101.0)	66.7% (47.4-85.9)	58.3% (38.2-78.5)	90.9% (79.2-102.7)
Hispanic	28	10.7 (1.0-109.8)	0.886 (0.741-1.000)	0.612 (0.316-1.000)	0.556	21.40%	83.3% (69.5-97.1)	68.2% (50.9-85.4)	41.7% (23.4-59.9)	93.8% (84.8-102.7)
Others	265	15.1 (6.6-34.5)	0.890 (0.847-0.928)	0.843 (0.777-0.900)	0.664	34.00%	92.2% (89.0-95.4)	56.0% (50.0-62.0)	51.9% (45.9-57.9)	93.3% (90.3-96.3)

Supplementary Table 14. Performance metrics for detecting structural heart disease across key demographic subgroups in Brazilian Longitudinal Study of Adult Health.
Abbreviations: AUPRC, area under the precision-recall curve; AUROC, area under the receiver operating characteristic curve; NPV, negative predictive value; PPV, positive predictive value.

Subgroup	Total Number	Diagnostic OR	AUROC	AUPRC	F1 Score	Prevalence	Sensitivity	Specificity	PPV	NPV
Overall	2988	11.4 (6.0-21.5)	0.853 (0.811-0.897)	0.354 (0.253-0.460)	0.121	2.90%	87.5% (86.3-88.7)	61.9% (60.2-63.6)	6.5% (5.6-7.4)	99.4% (99.1-99.7)
Age ≥ 65 years	1087	7.0 (2.5-19.7)	0.813 (0.741-0.885)	0.364 (0.223-0.501)	0.123	4.50%	91.8% (90.2-93.5)	38.4% (35.5-41.3)	6.6% (5.1-8.1)	99.0% (98.4-99.6)
Age < 65 years	1901	13.7 (6.0-31.2)	0.860 (0.781-0.926)	0.366 (0.225-0.548)	0.119	2.10%	82.1% (80.3-83.8)	75.0% (73.0-76.9)	6.4% (5.3-7.5)	99.5% (99.2-99.8)
Female Sex	1584	6.5 (2.8-15.1)	0.809 (0.725-0.885)	0.214 (0.097-0.382)	0.083	2.10%	78.8% (76.8-80.8)	63.6% (61.3-66.0)	4.4% (3.4-5.4)	99.3% (98.9-99.7)
Male Sex	1404	19.0 (6.8-53.0)	0.877 (0.819-0.923)	0.449 (0.315-0.584)	0.157	3.90%	92.7% (91.4-94.1)	59.9% (57.3-62.5)	8.6% (7.1-10.1)	99.5% (99.1-99.9)
Non-Hispanic White	1644	29.1 (7.0-121.1)	0.889 (0.830-0.939)	0.381 (0.239-0.532)	0.106	2.40%	94.9% (93.8-95.9)	61.1% (58.8-63.5)	5.6% (4.5-6.7)	99.8% (99.6-100.0)
Non-Hispanic Black	451	9.8 (2.9-33.4)	0.876 (0.795-0.948)	0.527 (0.342-0.723)	0.192	5.50%	88.0% (85.0-91.0)	57.3% (52.7-61.8)	10.8% (7.9-13.6)	98.8% (97.8-99.8)
Hispanic	748	5.3 (2.1-13.7)	0.770 (0.651-0.863)	0.220 (0.088-0.408)	0.116	3.10%	73.9% (70.8-77.1)	65.2% (61.8-68.7)	6.3% (4.6-8.1)	98.7% (98.0-99.5)
Others	145	N/A	0.917	0.077	0.041	0.70%	100.0% (100.0-100.0)	67.4% (59.7-75.0)	2.1% (-0.2-4.4)	100.0% (100.0-100.0)

Supplementary Table 15. Performance metrics for PRESENT-SHD for detecting structural heart disease in simulated screening cohorts with varying prevalence.
Abbreviations: AR, aortic regurgitation; AS, aortic stenosis; MR, mitral regurgitation; LVSD, left ventricular systolic dysfunction; sLVH, severe left ventricular hypertrophy; NPV, negative predictive value; PPV, positive predictive value; SHD, structural heart disease; SVD, severe valvular disease.

Simulated Prevalence	F1 Score	PPV	NPV
40%	0.747	63.0%	90.7%
33.6%*	0.700	57.3%	92.8%
20%	0.553	39.9%	96.3%
10%	0.364	22.8%	98.3%
5%	0.216	12.3%	99.2%
2.5%	0.119	6.4%	99.6%
1%	0.051	2.6%	99.8%

* Prevalence in the held-out test set

Supplementary Table 16. Performance metrics for convolutional neural network for detecting left ventricular systolic dysfunction in the held-out test set and across external validation cohorts.
Abbreviations: AUPRC, area under the precision-recall curve; AUROC, area under the receiver operating characteristic curve; NPV, negative predictive value; PPV, positive predictive value.

Cohort Type	Site Name	Total Number	Diagnostic OR	AUROC	AUPRC	F1 Score	Prevalence	Sensitivity	Specificity	PPV	NPV
Held-out test set	**Yale New Haven Hospital**	10860	27.2 (21.7-34.0)	0.914 (0.904-0.923)	0.543 (0.507-0.579)	0.377	7.60%	89.2% (88.6-89.7)	76.8% (76.0-77.6)	23.9% (23.1-24.7)	98.9% (98.7-99.1)
External validation – Hospital sites	**Bridgeport Hospital**	17915	18.8 (16.1-22.1)	0.886 (0.878-0.895)	0.517 (0.494-0.543)	0.369	9.90%	90.2% (89.7-90.6)	67.2% (66.5-67.9)	23.2% (22.6-23.8)	98.4% (98.2-98.6)
	Greenwich Hospital	4306	22.2 (15.6-31.7)	0.891 (0.874-0.907)	0.508 (0.455-0.556)	0.354	8.50%	90.5% (89.6-91.4)	70.0% (68.7-71.4)	22.0% (20.8-23.2)	98.7% (98.4-99.1)
	Lawrence + Memorial Hospital	17730	24.5 (20.5-29.2)	0.905 (0.897-0.912)	0.534 (0.509-0.562)	0.362	8.30%	90.5% (90.0-90.9)	72.1% (71.4-72.7)	22.6% (22.0-23.2)	98.8% (98.7-99.0)
	Westerly Hospital	3614	16.6 (12.2-22.7)	0.879 (0.860-0.898)	0.544 (0.491-0.594)	0.401	10.70%	87.6% (86.5-88.6)	70.2% (68.7-71.7)	26.0% (24.6-27.5)	97.9% (97.5-98.4)
External validation – Population-based cohort	**ELSA-Brasil**	3012	75.7 (29.2-196.1)	0.923	0.485	0.212	1.20%	86.5% (85.3-87.7)	92.2% (91.2-93.2)	12.1% (11.0-13.3)	99.8% (99.7-100.0)

Supplementary Table 17. Performance metrics for convolutional neural network for detecting moderate or severe left-sided valvular disease in the held-out test set and across external validation cohorts.
Abbreviations: AUPRC, area under the precision-recall curve; AUROC, area under the receiver operating characteristic curve; NPV, negative predictive value; PPV, positive predictive value.

Cohort Type	Site Name	Total Number	Diagnostic OR	AUROC	AUPRC	F1 Score	Prevalence	Sensitivity	Specificity	PPV	NPV
Held-out test set	**Yale New Haven Hospital**	7426	8.4 (7.0-9.9)	0.805 (0.794-0.817)	0.536 (0.510-0.564)	0.471	21.10%	89.8% (89.1-90.5)	48.7% (47.5-49.8)	31.9% (30.9-33.0)	94.7% (94.2-95.2)
External validation – Hospital sites	**Bridgeport Hospital**	11243	7.2 (6.3-8.2)	0.776 (0.766-0.786)	0.555 (0.536-0.575)	0.522	27.20%	91.3% (90.7-91.8)	40.8% (39.9-41.7)	36.5% (35.6-37.4)	92.6% (92.1-93.1)
	Greenwich Hospital	3477	8.3 (6.4-10.9)	0.797 (0.779-0.813)	0.579 (0.545-0.615)	0.512	26.60%	93.1% (92.2-93.9)	38.2% (36.6-39.8)	35.3% (33.7-36.9)	93.8% (93.0-94.6)
	Lawrence + Memorial Hospital	13330	7.6 (6.6-8.8)	0.793 (0.784-0.802)	0.494 (0.475-0.514)	0.424	19.80%	91.7% (91.3-92.2)	40.7% (39.9-41.5)	27.6% (26.9-28.4)	95.2% (94.9-95.6)
	Westerly Hospital	2171	13.5 (9.4-19.5)	0.813 (0.794-0.830)	0.709 (0.677-0.741)	0.637	37.70%	96.0% (95.1-96.8)	36.3% (34.3-38.3)	47.7% (45.6-49.8)	93.7% (92.7-94.7)
External validation – Population-based cohort	**ELSA-Brasil**	2987	8.8 (2.7-28.1)	0.802	0.111	0.051	1.80%	94.5% (93.7-95.4)	33.6% (31.9-35.3)	2.6% (2.0-3.2)	99.7% (99.5-99.9)

Supplementary Table 18. Performance metrics for convolutional neural network for detecting moderate or severe aortic regurgitation in the held-out test set and across external validation cohorts.
Abbreviations: AUPRC, area under the precision-recall curve; AUROC, area under the receiver operating characteristic curve; NPV, negative predictive value; PPV, positive predictive value.

Cohort Type	Site Name	Total Number	Diagnostic OR	AUROC	AUPRC	F1 Score	Prevalence	Sensitivity	Specificity	PPV	NPV
Held-out test set	**Yale New Haven Hospital**	10026	4.8 (3.4-6.8)	0.722 (0.695-0.749)	0.109 (0.088-0.135)	0.097	3.90%	91.3% (90.8-91.9)	31.3% (30.4-32.2)	5.1% (4.7-5.6)	98.9% (98.7-99.1)
External validation – Hospital sites	**Bridgeport Hospital**	15786	4.3 (3.3-5.5)	0.702 (0.683-0.722)	0.097 (0.085-0.112)	0.107	4.40%	90.3% (89.8-90.7)	31.5% (30.7-32.2)	5.7% (5.3-6.0)	98.6% (98.4-98.8)
	Greenwich Hospital	4248	3.2 (2.1-5.0)	0.684 (0.650-0.719)	0.128 (0.099-0.170)	0.119	5.30%	89.7% (88.8-90.6)	27.0% (25.7-28.3)	6.4% (5.7-7.1)	97.9% (97.5-98.4)
	Lawrence + Memorial Hospital	16663	4.6 (3.5-6.0)	0.700 (0.680-0.719)	0.091 (0.080-0.104)	0.1	4.20%	91.8% (91.4-92.2)	29.0% (28.3-29.7)	5.3% (5.0-5.7)	98.8% (98.6-98.9)
	Westerly Hospital	3505	7.3 (3.6-14.9)	0.739 (0.706-0.772)	0.127 (0.104-0.161)	0.125	5.40%	95.7% (95.1-96.4)	24.5% (23.1-25.9)	6.7% (5.9-7.5)	99.0% (98.7-99.3)
External validation – Population-based cohort	**ELSA-Brasil**	3002	inf (nan-inf)	0.85	0.078	0.018	0.80%	100.0% (100.0-100.0)	14.4% (13.1-15.7)	0.9% (0.6-1.3)	100.0% (100.0-100.0)

Supplementary Table 19. Performance metrics for convolutional neural network for detecting moderate or severe aortic stenosis in the held-out test set and across external validation cohorts.
Abbreviations: AUPRC, area under the precision-recall curve; AUROC, area under the receiver operating characteristic curve; NPV, negative predictive value; PPV, positive predictive value.

Cohort Type	Site Name	Total Number	Diagnostic OR	AUROC	AUPRC	F1 Score	Prevalence	Sensitivity	Specificity	PPV	NPV
Held-out test set	**Yale New Haven Hospital**	7711	8.0 (6.0-10.7)	0.804 (0.782-0.822)	0.206 (0.175-0.244)	0.178	5.50%	87.6% (86.8-88.3)	53.3% (52.2-54.4)	9.9% (9.2-10.5)	98.7% (98.4-98.9)
External validation – Hospital sites	**Bridgeport Hospital**	12264	5.7 (4.6-7.0)	0.768 (0.751-0.785)	0.175 (0.156-0.201)	0.172	5.80%	84.9% (84.2-85.5)	50.5% (49.6-51.3)	9.6% (9.1-10.1)	98.2% (97.9-98.4)
	Greenwich Hospital	3553	8.5 (5.4-13.5)	0.792 (0.763-0.818)	0.199 (0.163-0.248)	0.187	6.40%	90.7% (89.8-91.7)	46.7% (45.0-48.3)	10.4% (9.4-11.4)	98.7% (98.3-99.0)
	Lawrence + Memorial Hospital	13524	7.6 (5.8-9.9)	0.805 (0.788-0.822)	0.178 (0.154-0.205)	0.133	4.50%	90.0% (89.4-90.5)	45.8% (45.0-46.7)	7.2% (6.8-7.7)	99.0% (98.8-99.1)
	Westerly Hospital	2530	6.0 (3.9-9.3)	0.759 (0.729-0.789)	0.243 (0.205-0.302)	0.232	9.30%	90.3% (89.1-91.4)	39.3% (37.4-41.2)	13.3% (11.9-14.6)	97.5% (96.9-98.1)
External validation – Population-based cohort	**ELSA-Brasil**	3005	2.5 (0.3-23.9)	0.733	0.008	0.004	0.10%	75.0% (73.5-76.5)	45.3% (43.5-47.1)	0.2% (0.0-0.3)	99.9% (99.8-100.0)

Supplementary Table 20. Performance metrics for convolutional neural network for detecting moderate or severe mitral regurgitation in the held-out test set and across external validation cohorts.
Abbreviations: AUPRC, area under the precision-recall curve; AUROC, area under the receiver operating characteristic curve; NPV, negative predictive value; PPV, positive predictive value.

Cohort Type	Site Name	Total Number	Diagnostic OR	AUROC	AUPRC	F1 Score	Prevalence	Sensitivity	Specificity	PPV	NPV
Held-out test set	**Yale New Haven Hospital**	10264	7.2 (5.9-8.9)	0.792 (0.778-0.806)	0.312 (0.285-0.343)	0.257	9.30%	88.5% (87.9-89.1)	48.4% (47.5-49.4)	15.0% (14.3-15.7)	97.6% (97.3-97.9)
External validation – Hospital sites	**Bridgeport Hospital**	17000	7.1 (6.1-8.3)	0.781 (0.771-0.790)	0.343 (0.323-0.365)	0.3	12.40%	90.9% (90.4-91.3)	41.6% (40.9-42.4)	18.0% (17.5-18.6)	97.0% (96.7-97.3)
	Greenwich Hospital	4410	6.9 (5.2-9.2)	0.779 (0.760-0.797)	0.369 (0.333-0.409)	0.327	14.20%	91.5% (90.7-92.4)	38.9% (37.5-40.4)	19.9% (18.7-21.1)	96.5% (96.0-97.1)
	Lawrence + Memorial Hospital	17044	6.9 (5.9-8.1)	0.789 (0.778-0.799)	0.305 (0.282-0.327)	0.254	9.80%	89.8% (89.4-90.3)	43.9% (43.1-44.6)	14.8% (14.3-15.3)	97.5% (97.3-97.8)
	Westerly Hospital	3612	10.0 (6.8-14.7)	0.796 (0.780-0.816)	0.407 (0.366-0.453)	0.338	14.90%	94.6% (93.9-95.3)	36.4% (34.8-38.0)	20.6% (19.3-21.9)	97.5% (97.0-98.0)
External validation – Population-based cohort	**ELSA-Brasil**	2999	5.7 (2.0-16.3)	0.814	0.194	0.031	1.00%	86.7% (85.5-87.9)	46.6% (44.9-48.4)	1.6% (1.2-2.1)	99.7% (99.5-99.9)

Supplementary Table 21. Performance metrics for convolutional neural network for detecting severe left ventricular hypertrophy in the held-out test set and across external validation cohorts.
Abbreviations: AUPRC, area under the precision-recall curve; AUROC, area under the receiver operating characteristic curve; NPV, negative predictive value; PPV, positive predictive value.

Cohort Type	Site Name	Total Number	Diagnostic OR	AUROC	AUPRC	F1 Score	Prevalence	Sensitivity	Specificity	PPV	NPV
Held-out test set	**Yale New Haven Hospital**	6577	20.4 (6.2-66.8)	0.903 (0.848-0.946)	0.065 (0.037-0.131)	0.028	0.50%	90.9% (90.2-91.6)	67.1% (65.9-68.2)	1.4% (1.1-1.7)	99.9% (99.9-100.0)
External validation – Hospital sites	**Bridgeport Hospital**	9408	11.3 (6.7-19.1)	0.838 (0.809-0.866)	0.090 (0.063-0.136)	0.06	1.40%	88.0% (87.3-88.6)	60.8% (59.8-61.8)	3.1% (2.8-3.5)	99.7% (99.6-99.8)
	Greenwich Hospital	1741	9.0 (2.5-31.9)	0.832 (0.702-0.919)	0.072 (0.018-0.222)	0.043	0.90%	80.0% (78.1-81.9)	69.1% (66.9-71.3)	2.2% (1.5-2.9)	99.7% (99.5-100.0)
	Lawrence + Memorial Hospital	11876	12.1 (5.5-26.7)	0.889 (0.851-0.924)	0.064 (0.031-0.127)	0.024	0.50%	88.3% (87.8-88.9)	61.6% (60.7-62.4)	1.2% (1.0-1.3)	99.9% (99.8-100.0)
	Westerly Hospital	1630	31.5 (4.2-235.7)	0.859 (0.772-0.926)	0.067 (0.036-0.137)	0.058	1.20%	95.0% (93.9-96.1)	62.4% (60.0-64.7)	3.0% (2.2-3.9)	99.9% (99.7-100.1)
External validation – Population-based cohort	**ELSA-Brasil**	3014	4.0 (0.7-22.0)	0.832	0.035	0.008	0.20%	66.7% (65.0-68.3)	66.8% (65.1-68.5)	0.4% (0.2-0.6)	99.9% (99.8-100.0)

Supplementary Table 22. Baseline demographic and clinical characteristics of individuals without structural heart disease or heart failure included for the assessment of PRESENT-SHD for prediction of new-onset disease.

Characteristic	Yale New Haven Hospital	Bridgeport Hospital	Greenwich Hospital	Lawrence + Memorial Hospital	Westerly Hospital	UK Biobank
Number	127,547	46,883	26,835	28,344	3,930	41,800
Age (years)	53 [37-67]	53 [38-67]	59 [45-74]	59 [43-72]	63 [51-74]	65 [59-71]
Sex	73031 (57.3%)	27588 (58.8%)	15443 (57.5%)	16314 (57.6%)	2138 (54.4%)	21671 (51.8%)
Race/Ethnicity						
White	75450 (60.7%)	19597 (42.8%)	19002 (72.8%)	20609 (74.4%)	3596 (92.8%)	40359 (96.8%)
Black	24481 (19.7%)	11519 (25.1%)	1356 (5.2%)	2448 (8.8%)	71 (1.8%)	300 (0.7%)
Hispanic	20217 (16.3%)	13814 (30.1%)	4848 (18.6%)	3724 (13.4%)	127 (3.3%)	-
Others	4062 (3.3%)	905 (2.0%)	900 (3.5%)	908 (3.3%)	81 (3.1%)	1028 (3.4%)
Hypertension	56313 (44.2%)	21259 (45.3%)	10705 (39.9%)	14437 (50.9%)	2289 (58.2%)	5941 (14.2%)
Type-2 Diabetes Mellitus	21355 (16.7%)	9776 (20.9%)	3830 (14.3%)	5485 (19.4%)	855 (21.8%)	1224 (2.9%)
New-onset SHD/HF Outcome	5353 (4.2%)	3507 (7.5%)	1493 (5.6%)	2290 (8.1%)	298 (7.6%)	413 (1.0%)
TTE-defined SHD	4178 (3.3%)	2880 (6.1%)	1021 (3.8%)	1810 (6.4%)	221 (5.6%)	-
HF Hospitalization	1751 (1.4%)	1229 (2.6%)	761 (2.8%)	876 (3.1%)	138 (3.5%)	44 (0.1%)
Aortic Valve Repair/Replacement	518 (0.4%)	172 (0.4%)	48 (0.2%)	72 (0.3%)	10 (0.3%)	228 (0.5%)
Mitral Valve Repair/Replacement	199 (0.2%)	55 (0.1%)	20 (0.1%)	27 (0.1%)	4 (0.1%)	264 (0.6%)
Follow-up (years)	4.0 [1.7-6.4]	4.2 [2.4-6.2]	4.7 [2.7-6.5]	2.5 [1.1-4.1]	2.4 [0.8-4.0]	3.0 [2.1-4.5]

Supplementary Table 23. Performance metrics for risk stratification of new-onset structural heart disease or heart failure in individuals at risk in the Yale New Haven Hospital and external validation sites.

Model	Covariates	YNHH	Bridgeport Hospital	Greenwich Hospital	Lawrence + Memorial Hospital	Westerly Hospital	UK Biobank
Harrell's C-statistic	Model Probability	0.823 (0.817-0.828)	0.831 (0.819-0.844)	0.851 (0.841-0.861)	0.832 (0.824-0.840)	0.820 (0.796-0.845)	0.754 (0.728-0.780)
Cox Proportional Hazard Model	Per 0.1 increase	1.46 (1.45-1.48)	1.48 (1.45-1.51)	1.51 (1.48-1.54)	1.49 (1.47-1.51)	1.47 (1.42-1.53)	1.58 (1.51-1.64)
	Per 0.1 increase + Age + Sex	1.36 (1.35-1.38)	1.43 (1.39-1.47)	1.42 (1.38-1.47)	1.43 (1.4-1.45)	1.43 (1.36-1.51)	1.45 (1.38-1.52)
	Positive Screen	8.16 (7.69-8.66)	8.65 (7.41-10.09)	14.92 (12.31-18.08)	9.34 (8.4-10.39)	9.16 (6.65-12.63)	4.2 (3.42-5.17)
	Positive Screen + Age + Sex	4.28 (3.95-4.64)	5.11 (4.18-6.26)	6.14 (4.8-7.85)	4.6 (4.01-5.28)	5.03 (3.39-7.47)	2.39 (1.87-3.04)
	Positive Screen + Age + Sex + HTN + T2DM	4.04 (3.73-4.37)	4.73 (3.87-5.78)	5.55 (4.34-7.1)	4.21 (3.68-4.83)	4.72 (3.18-7.01)	2.34 (1.84-2.99)
Fine-Gray Subdistribution Hazard Model	Positive Screen + Age + Sex + Competing Risk of Death	4.24 (3.88-4.64)	5.07 (4.03-6.37)	6.25 (4.76-8.21)	4.56 (3.93-5.29)	5.09 (3.39-7.63)	2.62 (2.07-3.32)
	Positive Screen + Age + Sex + HTN + T2DM + Competing Risk of Death	3.99 (3.66-4.36)	4.69 (3.74-5.88)	5.64 (4.29-7.41)	4.18 (3.61-4.84)	4.77 (3.20-7.13)	2.56 (2.02-3.25)

Supplementary Table 24. Cumulative hazard across for new-onset structural heart disease or heart failure over median follow-up time across the cohort.

Cohort	Median Follow-up Time (years)	Cumulative Hazard for New-onset SHD/HF
Yale New Haven Hospital	4.0 [1.7-6.4]	0.015
Bridgeport Hospital	4.2 [2.4-6.2]	0.022
Greenwich Hospital	4.7 [2.7-6.5]	0.010
Lawrence + Memorial Hospital	2.5 [1.1-4.1]	0.021
Westerly Hospital	2.4 [0.8-4.0]	0.018
UK Biobank	3.0 [2.1-4.5]	0.004

Supplementary Table 25. Age- and sex-adjusted Cox proportional hazard models for the prediction of new-onset structural heart disease or heart failure across model output probabilities in individuals at risk in the Yale New Haven Hospital and external validation sites.

Model output probability bins	YNHH	Bridgeport Hospital	Greenwich Hospital	Lawrence + Memorial Hospital	Westerly Hospital	UK Biobank
0-0.2	Reference	Reference	Reference	Reference	Reference	Reference
0.2-0.4	3.55 (3.25-3.88)	3.88 (3.09-4.86)	5.52 (4.22-7.23)	3.86 (3.31-4.49)	4.53 (2.92-7.01)	1.88 (1.43-2.47)
0.4-0.6	5.53 (5-6.12)	6.55 (5.12-8.37)	9.45 (7.08-12.61)	6.25 (5.29-7.39)	7.49 (4.63-12.09)	3.86 (2.79-5.34)
0.6-0.8	7.56 (6.79-8.42)	9.85 (7.64-12.71)	16.68 (12.31-22.6)	10.52 (8.84-12.51)	11.74 (7.04-19.58)	7.49 (5.18-10.84)
0.8-1.0	12.87 (11.47-14.44)	18.72 (14.42-24.32)	25.24 (18.39-34.63)	20.15 (16.82-24.14)	27.79 (16.76-46.07)	13.7 (8.2-22.9)