Supplementary Section S1 – STARD Checklist

Table S1 - STARD Checklist.

Section & Topic	No	Item	Reported on page #
TITLE OR ABSTRACT			
	1	Identification as a study of diagnostic accuracy using at least one measure of accuracy (such as sensitivity, specificity, predictive values, or AUC)	1
ABSTRACT			
	2	Structured summary of study design, methods, results, and conclusions (for specific guidance, see STARD for Abstracts)	1
INTRODUCTION			
	3	Scientific and clinical background, including the intended use and clinical role of the index test	2-3
	4	Study objectives and hypotheses	3
METHODS			
Study design	5	Whether data collection was planned before the index test and reference standard were performed (prospective study) or after (retrospective study)	4
Participants	6	Eligibility criteria	3, Supplement Section S2
	7	On what basis potentially eligible participants were identified (such as symptoms, results from previous tests, inclusion in registry)	3-5
	8	Where and when potentially eligible participants were identified (setting, location and dates)	Supplement Section S3
	9	Whether participants formed a consecutive, random or convenience series	3
Test methods	10a	Index test, in sufficient detail to allow replication	4
	10b	Reference standard, in sufficient detail to allow replication	4-5
	11	Rationale for choosing the reference standard (if alternatives exist)	2-3
	12a	Definition of and rationale for test positivity cut-offs or result categories of the index test, distinguishing pre-specified from exploratory	4
	12b	Definition of and rationale for test positivity cut-offs or result categories of the reference standard, distinguishing pre-specified from exploratory	5
	13a	Whether clinical information and reference standard results were available to the performers/readers of the index test	6
	13b	Whether clinical information and index test results were available to the assessors of the reference standard	6
Analysis	14	Methods for estimating or comparing measures of diagnostic accuracy	5-6
	15	How indeterminate index test or reference standard results were handled	5-6
	16	How missing data on the index test and reference standard were handled	5-6
	17	Any analyses of variability in diagnostic accuracy, distinguishing pre-specified from exploratory	n/a
	18	Intended sample size and how it was determined	6
RESULTS			
Participants	19	Flow of participants, using a diagram	Supplement Section S5 & S6
	20	Baseline demographic and clinical characteristics of participants	Table 1
	21a	Distribution of severity of disease in those with the target condition	6
	21b	Distribution of alternative diagnoses in those without the target condition	Table 1
	22	Time interval and any clinical interventions between index test and reference standard	5-6
Test results	23	Cross tabulation of the index test results (or their distribution) by the results of the reference standard	Table 2
	24	Estimates of diagnostic accuracy and their precision (e.g. 95% confidence intervals)	8, Table 2
	25	Any adverse events from performing the index test or the reference standard	7
DISCUSSION			
	26	Study limitations, including sources of potential bias, statistical uncertainty, and generalizability	12
	27	Implications for practice, including the intended use and clinical role of the index test	12
OTHER INFORMATION			
	28	Registration number and name of registry	3
	29	Where the full study protocol can be accessed	3
	30	Sources of funding and other support; role of funders	12

Supplementary Section S2 – Inclusion/Exclusion Criteria

Table S2 - Inclusion/Exclusion Criteria.

Inclusion	Exclusion
≥ 18 years of age	Prior documented history of myocardial infarction (MI)
Cardiovascular symptoms	Suspected acute myocardial infarction (AMI) at current presentation
Scheduled to undergo cardiac catheterization with coronary angiography (Group 2) or Computed Tomography Angiography (Group 4)	Prior coronary artery bypass grafting (CABG)
	Prior heart valve replacement
	Previous sustained or paroxysmal atrial or ventricular arrythmia
Ability to understand the requirements of the study and to provide written informed consent	Infiltrative myocardial disease (amyloid, sarcoid, right ventricular dysplasia)
	Presence of cardiac implantable electronic device (CIED), including implantable cardioverter defibrillator (ICD), pacemaker (PM), implantable loop recorders and other monitors
	Implantable Neuro-stimulators
	Congenital Heart Disease
	Pregnant or breast feeding
	Currently taking any Type IA, IC or III antiarrhythmics
	Any history of amiodarone use
	Clinically significant chest deformity (e.g., pectus excavatum or pectus carinatum)
	Breast implants
	Neuromuscular disease if the condition results in tremor or muscle fasciculations

Supplemental Section S3 – Clinical study sites and locations.

Table S3 - Clinical study sites and locations.

Site Name	Location	Site Used in Development	Site Used in Validation
Atlanta Heart Specialists	Tucker, GA	Yes	Yes
Cone Health Heart and Vascular Center	Greensboro, NC	Yes	Yes
Novant Health New Hanover Regional Medical Center	Wilmington, NC	Yes	Yes
Rochester General Hospital	Rochester, NY	Yes	Yes
Bryan Heart	Lincoln, NE	Yes	Yes
Piedmont Healthcare	Atlanta, GA	Yes	Yes
Austin Heart	Austin, TX	Yes	Yes
Cardiovascular Associates of the Southeast	Birmingham, AL	Yes	No
Sentara Hospital and Medical Group	Norfolk, VA	Yes	Yes
North Georgia Medical Center	Gainesville, GA	Yes	No
Jacobs Institute	Buffalo, NY	Yes	No
Lexington Medical Center Heart & Vascular	West Columbia, SC	Yes	Yes
Ochsner Medical Foundation	Jefferson, LA	Yes	No
Advent Health Tampa	Tampa, FL	No	Yes
Cardiovascular Institute of the South (Houma)	Houma, LA	Yes	Yes
Cardiovascular Institute of the South (Lafayette)	Lafayette, LA	Yes	Yes
Jackson Heart Clinic	Jackson, MS	Yes	Yes
Oklahoma Heart Hospital	Oklahoma City, OK	Yes	Yes
WellStar Research Institute	Marietta, GA	Yes	Yes
Cardiology Associates of North Mississippi	Tupelo, MS	Yes	Yes
Medical University of South Carolina	Charleston, SC	No	Yes
Minneapolis Heart	Minneapolis, MN	No	Yes
Alamance Regional Medical Center	Burlington, NC	No	Yes
Lundquist Institute	Torrance, CA	No	Yes

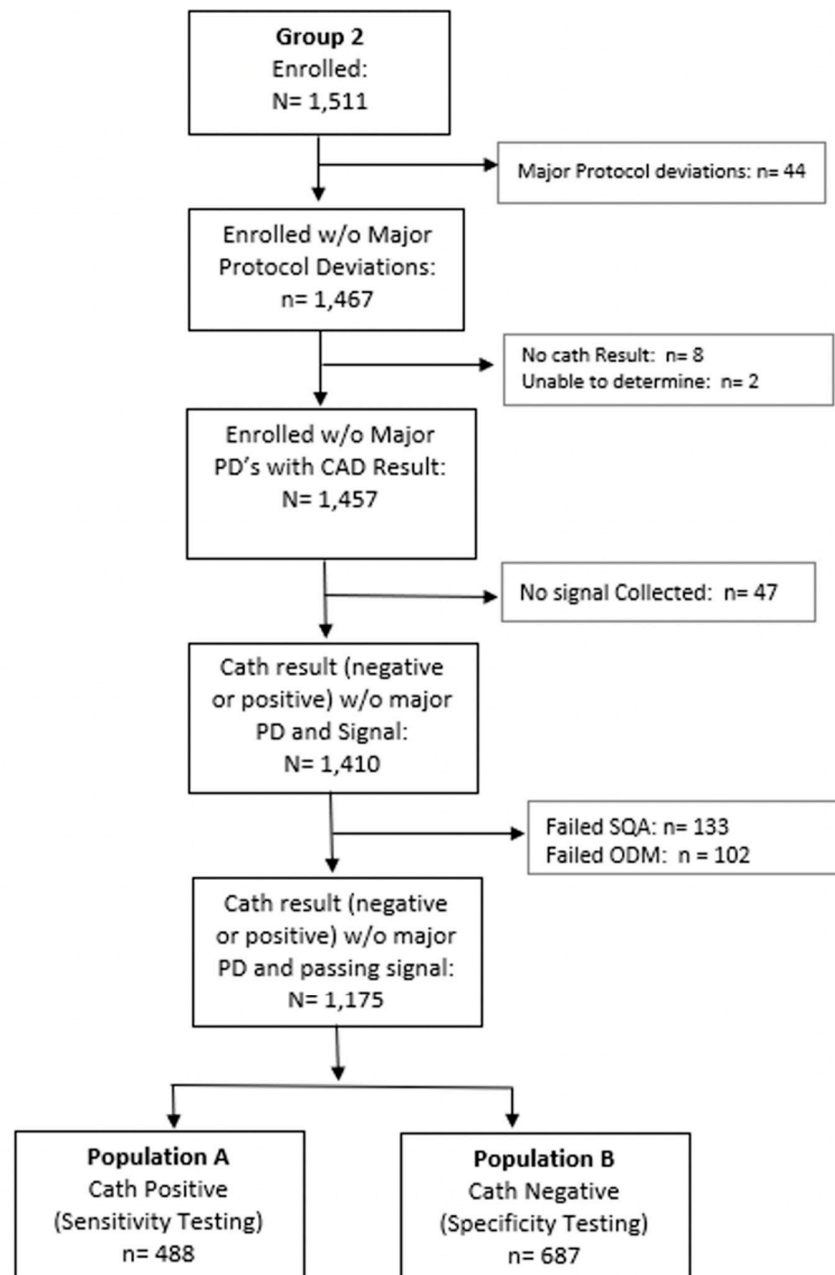# Supplemental Section S4 – CONSORT Flow for IDENTIFY Group 2

Figure S1 - CONSORT Flow for IDENTIFY Group 2.

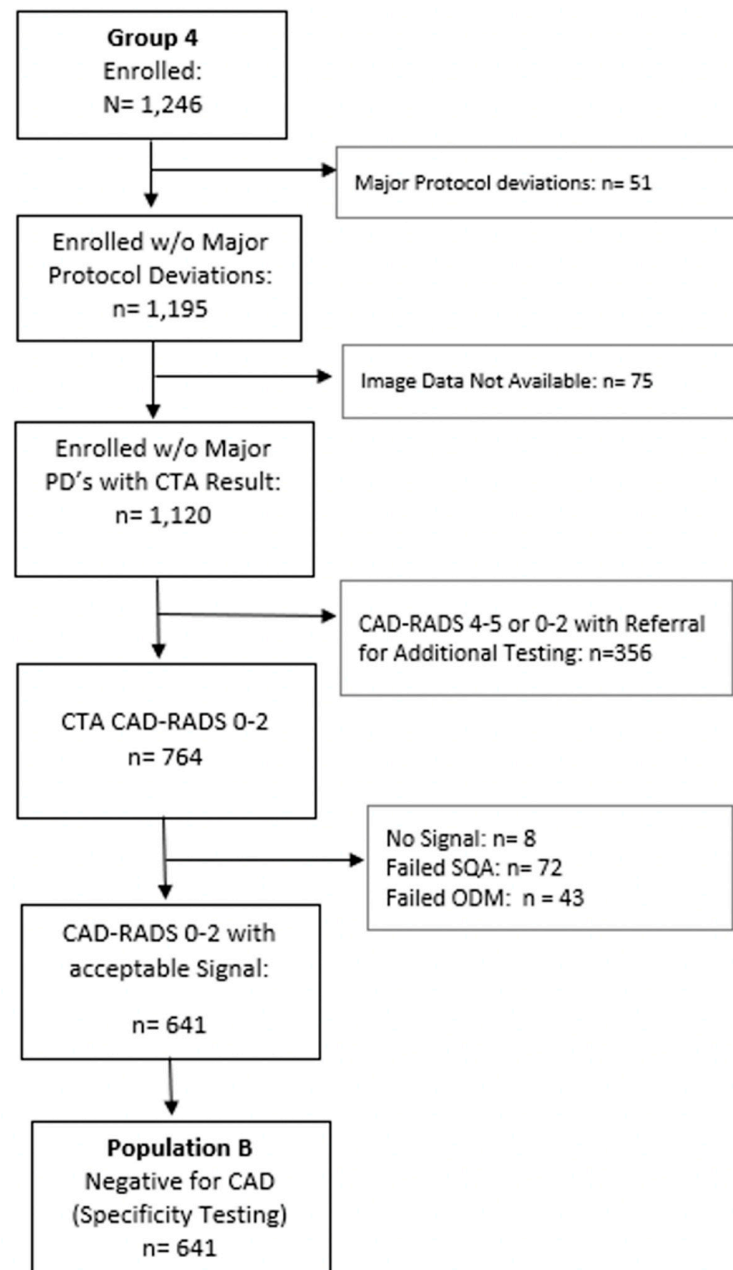# Supplemental Section S5 – CONSORT Flow for IDENTIFY Group 4

Figure S2 - CONSORT Flow for IDENTIFY Group 4

Supplemental Section S6 – Relevance of CAD Score Beyond Binary Results

The test-negative and test-positive ranges of the CAD Score were divided into tertiles (i.e., three ranges, each with an equal number of subjects). For this analysis, the Group 2 subjects in Population B were excluded, due to the minimal effect on specificity (Group 4 specificity of 60% is not substantially affected when including the Group 2 subjects, reducing only to 58%).

The negative and positive likelihood ratios were calculated for each tertile assuming that the score range represents the entire test-negative or test-positive range, respectively.

The results with the unmodified thresholds are show in Table 4. The following tables reflect the adjustment of the female threshold described in the discussion.

Table S4 – Score ranges and likelihood ratios for test-negative and test-positives for each tertile.

Test-Negative		
Tertile	Score Range	Negative Likelihood Ratio
Tertile 1	(-0.401, -0.122)	0.129
Tertile 2	(-0.121, -0.058)	0.220
Tertile 3	(-0.057, -0.001)	0.340
Test-Positive		
Tertile	Score Range	Positive Likelihood Ratio
Tertile 1	(0.000, 0.100)	1.446
Tertile 2	(0.101, 0.199)	1.913
Tertile 3	(0.200, 0.644)	2.888

Supplemental Section S7 – Comparison Between Development and Validation Key Demographics

Table S5 – Comparison of Population A

Characteristic	Development (n=641)	Validation (n=488)	p-value
Age at consent			
Mean ± SD	64.9 ± 9.6	66.1 ± 9.2	0.0344
<65	43.7% (280/641)	40.6% (198/488)	0.3240
≥65	56.3% (361/641)	59.4% (290/488)	
Sex			
Female	26.7% (171/641)	30.9% (151/488)	0.1321
Male	73.3% (470/641)	69.1% (337/488)	
BMI			
Mean ± SD	30.9 ± 6.2	30.7 ± 6.1	0.5888
<30	45.7% (293/641)	50.5% (246/487)	<0.05
≥30	54.3% (348/641)	49.5% (241/487)	
Hypertension	78.6% (504/641)	77.9% (380/488)	0.8155
Diabetes	34.5% (221/641)	38.9% (190/488)	0.1390
Hypercholesterolemia/ Hyperlipidemia	76.6% (491/641)	83.6% (408/488)	0.0048

Table S6 – Comparison of Population B

Characteristic	Development (n=513)	Validation (n=641)*	p-value
Age at consent			
Mean ± SD	55.0 ± 12.0	54.7 ± 11.3	0.6630
<65	77.0% (395/513)	78.3% (502/641)	0.6432
>=65	23.0% (118/513)	21.7% (139/641)	
Sex			
Female	64.5% (331/513)	64.1% (411/641)	0.9359
Male	35.5% (182/513)	35.9% (230/641)	
BMI			
Mean ± SD	31.3 ± 6.6	32.4 ± 7.1	0.0071
<30	47.8% (245/513)	41.3% (265/641)	0.0339
>=30	52.2% (268/513)	58.7% (376/641)	
Hypertension	60.0% (308/513)	59.3% (380/641)	0.8415
Diabetes	15.8% (81/513)	19.2% (123/641)	0.1537
Hypercholesterolemia/ Hyperlipidemia	52.6% (270/513)	58.5% (375/641)	0.0528

* CCTA (Group 4) only, since subjects without CAD from ICA were not used in training.

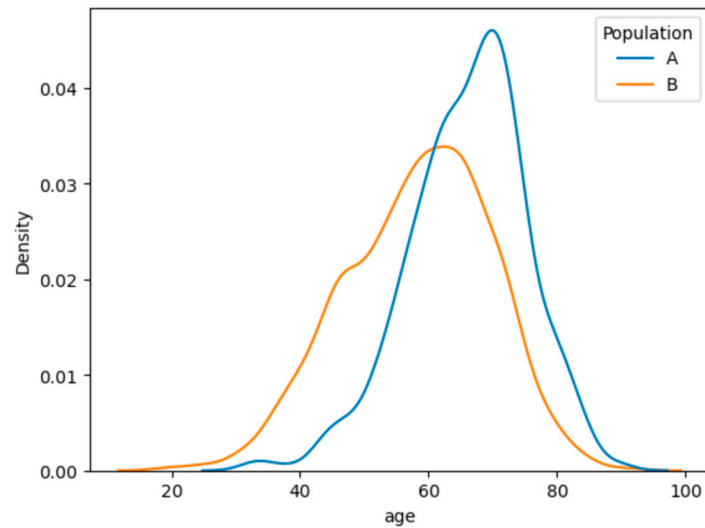# Supplementary Section S8 – Distribution of Age and BMI in the Validation Population
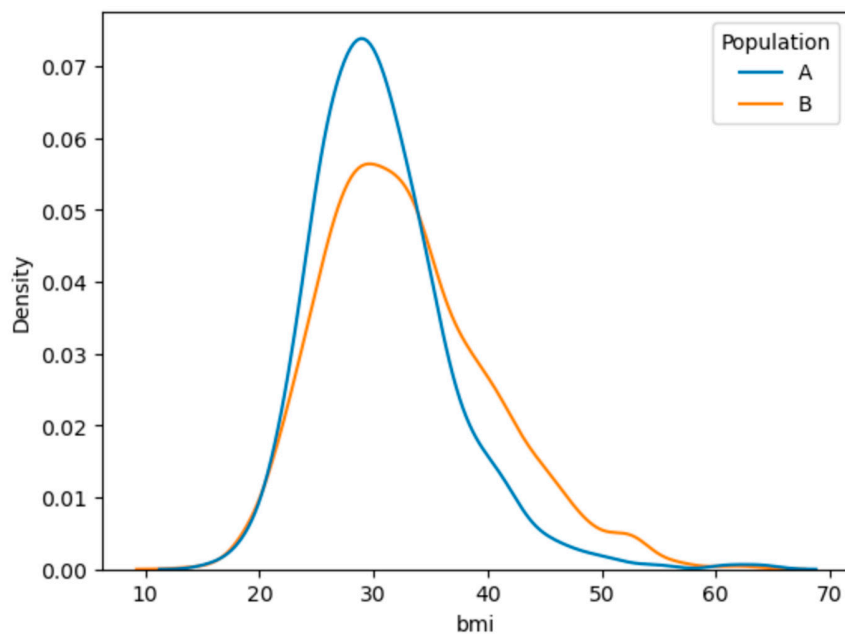

Figure S3 – Distribution of Age

Figure S4 – Distribution of BMI