

## SUPPLEMENTAL MATERIAL

**Supplemental Table 1.** Heart Failure Classification<sup>a</sup>

Cardiac Score	ARIC Questions	JHS Variables
Prior coronary heart disease (1 point)	Positive response to “Has a doctor ever said you had a heart attack?”	Positive history or response to any of the questions (Note: Verified that the JHS derived variable CHDhx=1 can be substituted for items a-e below): PFHA4A: Has doctor said you had heart attack (missing at exam 2)? MHXA16/17: Saw a doctor because of chest pain? What did the doctor say it was? (H=Heart Attack) MHXA30/31: Saw a doctor because of this pain? What did the doctor say it was? (H=Heart Attack) MHXA32: Hospitalized for heart attack a week+? MI from ECG (missing at exam 2) MHXA52A: Have a coronary bypass? MHXA54A: Ever had angioplasty of coronary arteries?
Prior angina pectoris (1 point)	Positive response to all: <ul style="list-style-type: none"> <li>• “Have you ever had any pain or discomfort in your chest?”</li> <li>• “Do you get it when you walk uphill or hurry?” or “Do you get it when you walk at an ordinary pace on the level?”</li> </ul> Response of “stop or slow down” to “What do you do if you get it while you are walking?” Response of “relieved” to “If you stand still, what happens?” Response of “10 minutes or less” to “How soon?”	Positive response to either series of questions: 1) MHXA16:/17 Saw a doctor because of chest pain? What did the doctor say it was? (A=Angina) <i>or</i> 2) Positive response to <u>ALL</u> of the questions: MHXA8: Ever had any pain/discomfort in chest? MHXA9: ‘Chest pain walking up hill?’ <i>or</i> MHXA10: ‘Chest pain walking at ordinary pace on level?’ MHXA11: What do you do if you get chest pain while you are walking? Response=S (Stop or slow down) MHXA12: If you stand still, what happens? Response=R (Relieved) MHXA13: Time required for relief of chest pain. Response=L (10 min or less)
Swollen legs at end of day (1 point)	Positive response to both: <ul style="list-style-type: none"> <li>• “Have you ever had swelling of your feet or ankles (excluding pregnancy)?”</li> <li>• “Did it tend to come on during the day and go down overnight?”</li> </ul>	Positive response to both questions: MHXA49: Ever have swelling of the feet or ankles? MHXA50: Swelling come during day, go down overnight?

Cardiac Score	ARIC Questions	JHS Variables
Nocturnal dyspnea (1 point)	Positive response to “Have you ever been awakened at night by trouble breathing?”	Positive response to: MHXA48: Ever awakened by trouble breathing?
Pulmonary rales at physical exam	Not applicable	Not applicable
Atrial fibrillation on ECG (1 point)	Not applicable	JHS analysis variable afib=1 (Derived from ECGA15: Arrhythmia Minnesota code 8-3-1 [value=1]).
Pulmonary disease score		
History of chronic bronchitis (1 point)	Positive response “Have you ever had chronic bronchitis?”	Positive response to: PFHA9A: Doctor said you have chronic lung disease?
History of asthma (1 point)	Positive response to “Have you even had chronic asthma?”	Positive response to any series of questions: PFHA10A: Has the doctor said you have asthma? RPAA13: Have you ever had asthma? and RPAA14: Was it confirmed by a doctor?
History of coughing, phlegm, or wheezing (1 point)	Positive response to any: <ul style="list-style-type: none"> <li>• “Do you usually have a cough?”</li> <li>• “Do you usually bring up phlegm from your chest?”</li> <li>• “Does your chest ever sound wheezy or whistling apart from colds?”</li> </ul>	Positive response to any: RPAA1: Do you usually have a cough? RPAA6: Bring up phlegm, 3+ months? RPAA8: Chest ever sound wheezy w/out cold? RPAA9: Chest sound wheezy most days?
Presence of rhonchi at physical exam	Not applicable	Not applicable
Therapy score		
History of digitalis administration (1 point)	Medication codes (312xxx)	Search medications for digitalis drug code = cardiac glycosides (TC 312xxx)
History of diuretic administration (1 point)	Medication codes (37xxxx)	Search medications for drug class: Diuretics (Loop diuretics, mercurial diuretics, osmotic diuretics, potassium sparing diuretics; TC 37xxxx)

<sup>a</sup> Gothenburg is a point system that assigns heart failure grades based on cardiac, pulmonary, and drug therapy component scores. The following grades are assigned: 0 (heart failure absent) if all 3 scores are 0; 1 (latent) if cardiac score greater than 0 and pulmonary and therapy scores equal 0; 2 (manifest heart failure) if cardiac score greater than 0 and either pulmonary or therapy score greater than 0; 3 if cardiac score greater than 0 and both pulmonary and therapy scores greater than 0; and 4 if the patient died in heart failure. For the current study, we ascertained heart failure based on grade 3.

**Supplemental Table 2.** Baseline Characteristics of the Study Population Stratified by Severity of Conduction Delay

Characteristic	Severity of Conduction Delay			P Value
	Mild (QRS 100-119 msec)	Moderate (QRS 120-149 msec)	Severe (QRS ≥ 150 msec)	
No. of participants	1360	88	80	
Age, median (IQR), y	58.1 (47.6-66.3)	66.5 (59.6-73.0)	68.9 (63.0-73.4)	< .001
Male sex, No. (%)	669 (49.2)	42 (47.7)	41 (51.3)	< .001
Medical history, No. (%)				
Atrial fibrillation	10 (0.7)	1 (1.1)	0 (0.0)	.02
Chronic lung disease	102 (7.5)	11 (12.5)	8 (10.0)	.15
Diabetes mellitus	312 (22.9)	33 (37.5)	30 (37.5)	< .001
Heart failure	126 (9.3)	11 (12.5)	16 (20.0)	< .001
Hypertension	919 (67.6)	69 (78.4)	66 (82.5)	< .001
Myocardial infarction	88 (6.5)	12 (13.6)	17 (21.3)	< .001
Smoker currently	185 (13.6)	9 (10.2)	11 (13.8)	.73
Smoker previously	312 (22.9)	22 (25.0)	19 (23.8)	< .001
Stroke	56 (4.1)	6 (6.8)	9 (11.3)	.01
Physical examination, median (IQR)				
Body mass index, kg/m <sup>2</sup>	31.4 (27.7-36.5)	30.6 (27.6-34.7)	31.1 (27.8-35.4)	< .001
Pulse, beats/min	62.0 (56.0-70.0)	64.0 (56.5-71.0)	64.5 (55.0-70.5)	< .001
Systolic blood pressure, mm Hg	125.0 (115.0-138.0)	132.0 (123.0-141.5)	135.0 (123.5-148.5)	< .001
Laboratory test results, median (IQR)				
eGFR, mL/min/1.73 m <sup>2</sup>	85.9 (76.0-96.0)	82.5 (69.5-91.5)	76.4 (59.6-85.9)	< .001
Glucose, mg/dL	93.0 (87.0-104.0)	94.5 (88.0-104.0)	98.0 (90.0-115.5)	< .001
Hemoglobin, g/dL	13.2 (12.4-14.3)	13.0 (12.0-14.4)	12.8 (11.9-13.5)	< .001
Low-density lipoprotein, mg/dL	124.0 (102.0-147.0)	121.0 (94.5-143.5)	123.5 (103.0-147.0)	.67
Serum potassium, mEq/L	4.3 (4.0-4.5)	4.3 (4.0-4.6)	4.3 (4.0-4.5)	.32
Serum sodium, mEq/L	141.0 (139.0-142.0)	141.0 (140.0-142.5)	141.0 (139.0-143.0)	.001
Cardiac test results				
Complete LBBB, No. (%)	0	19 (21.6)	33 (41.3)	< .001
Complete RBBB, No. (%)	1 (0.1)	30 (34.1)	33 (41.3)	< .001
Other IV conduction Defect, No. (%)	79 (5.8)	39 (44.3)	14 (17.5)	< .001
Ejection fraction, mean (SD), %	61.0 (8.3)	59.8 (11.1)	57.7 (13.5)	< .001
Ejection fraction < 40%, No. (%)	24 (1.8)	3 (3.4)	8 (10.0)	< .001
Left ventricular dimension, median (IQR), cm	49.3 (46.9-52.3)	50.6 (46.5-53.7)	49.0 (47.9-53.4)	< .001
Left ventricular hypertrophy, No. (%)	141 (10.4)	14 (15.9)	11 (13.8)	< .001
Medications, No. (%)				

Characteristic	Severity of Conduction Delay			<i>P</i> Value
	Mild (QRS 100-119 msec)	Moderate (QRS 120-149 msec)	Severe (QRS ≥ 150 msec)	
ACE inhibitor/ARB	251 (18.5)	21 (23.9)	30 (37.5)	< .001
Anti-arrhythmic agent	8 (0.6)	3 (3.4)	1 (1.3)	< .001
Antiplatelet agent	30 (2.2)	2 (2.3)	2 (2.5)	.06
β-Blocker	160 (11.8)	13 (14.8)	16 (20.0)	< .001
Calcium channel blocker	313 (23.0)	21 (23.9)	23 (28.8)	< .001
Digoxin	32 (2.4)	7 (8.0)	7 (8.8)	< .001
Diuretic	358 (26.3)	37 (42.0)	35 (43.8)	< .001
Insulin	95 (7.0)	11 (12.5)	15 (18.8)	< .001
Oral diabetic agent	138 (10.1)	22 (25.0)	12 (15.0)	< .001
Statin	169 (12.4)	19 (21.6)	19 (23.8)	< .001

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; eGFR, estimated glomerular filtration rate.

**Supplemental Table 3. Outcomes Stratified by Severity of Conduction Delay**

Outcome	Severity of Conduction Delay			<i>P</i> Value
	Mild (100-119 msec)	Moderate (120-149 msec)	Severe (≥ 150 msec)	
Mortality, No. (cumulative incidence <sup>a</sup> )	147 (11.2)	13 (14.9)	26 (33.7)	< .001
95% CI	9.6-13.1	9.0-24.6	24.5-46.3	
Mode of death, No. (%)				
Cardiac mortality	75 (51.0)	6 (46.2)	16 (61.5)	.13
95% CI	42.7-59.3	19.2-74.9	40.6-79.8	
Sudden cardiac death	12 (8.2)	0 (0.0)	3 (11.5)	.07
95% CI	4.3-13.8	—	6.6-39.4	
Heart failure or cardiomyopathy	4 (2.7)	1 (7.7)	5 (19.2)	.004
95% CI	0.7-6.8	0.2-36.0	6.6-39.4	
Noncardiovascular mortality	72 (49.0)	7 (53.8)	10 (38.5)	.13
95% CI	40.7-57.3	25.1-80.8	20.2-59.4	
Heart failure hospitalization, No. (cumulative incidence) <sup>b</sup>	86 (6.7)	9 (11.2)	23 (33.4)	< .001
95% CI	5.4-8.2	6.0-20.8	23.8-47.0	

a Cumulative incidence of death within 8 years after exam 1.

b Calculated among the 5065 participants who survived to January 1, 2005, when heart failure hospitalization surveillance began.

**Supplemental Table 4.** Baseline Characteristics of Participants Who Completed Exam 3 and Had Normal Conduction at Baseline

Characteristic	Participants (n = 2599)
Age, median (IQR), y	53.0 (44.2-62.2)
Male sex, No. (%)	799 (30.7)
Medical history, No. (%)	
Atrial fibrillation	4 (0.2)
Chronic lung disease	168 (6.5)
Diabetes mellitus	452 (17.4)
Heart failure	130 (5.0)
Hypertension	1,432 (55.1)
Myocardial infarction	86 (3.3)
Smoking status	
Current smoker	287 (11.0)
Prior smoker	429 (16.5)
Stroke	74 (2.8)
Physical examination results, median (IQR)	
Body mass index, kg/m <sup>2</sup>	30.2 (26.6-35.1)
Pulse, beats/min	63.0 (57.0-71.0)
Systolic blood pressure, mm Hg	123.0 (113.0-134.0)
Laboratory test results, median (IQR)	
eGFR, mL/min/1.73 m <sup>2</sup>	86.7 (76.8-97.3)
Glucose, mg/dL	91.0 (85.0-99.0)
Hemoglobin, g/dL	13.0 (12.1-13.8)
Low-density lipoprotein, mg/dL	124.0 (102.0-147.0)
Potassium, mEq/L	4.3 (4.0-4.5)
Sodium, mEq/L	140.0 (139.0-142.0)
Uric acid, mg/dL	5.2 (4.2-6.2)
Cardiac test results	
Ejection fraction, %	
Mean (SD)	62.5 (6.5)
Median (IQR)	65.0 (55.0-65.0)

Characteristic	Participants (n = 2599)
Ejection fraction < 40%, No. (%)	3 (0.1)
Left ventricular dimension, median (IQR), cm	48.1 (45.3-50.3)
Left ventricular hypertrophy, No. (%)	138 (5.3)
Medications, No. (%)	
ACE inhibitor/ARB	349 (13.4)
Anti-arrhythmic agent	2 (0.1)
Antiplatelet agent	24 (0.9)
$\beta$ -Blocker	211 (8.1)
Calcium channel blocker	405 (15.6)
Digoxin	11 (0.4)
Diuretic	492 (18.9)
Insulin	99 (3.8)
Oral diabetic agent	242 (9.3)
Statin	257 (9.9)

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; eGFR, estimated glomerular filtration rate; IQR, interquartile range.