

SUPPLEMENTAL MATERIAL

For the manuscript entitled

Routinely Reported Ejection Fraction and Mortality in Clinical Practice: Where Does the Nadir of Risk Lie?

Gregory J. Wehner, PhD^a; Linyuan Jing, PhD^{b,c}; Christopher M. Haggerty, PhD^{b,c}; Jonathan D. Suever, PhD^{b,c}; Joseph B. Leader, BA^c; Dustin N. Hartzel, BS^c; H. Lester Kirchner, PhD^c; Joseph N. A. Manus^c, BS; Nick James;^d Zina Ayar;^e Patrick Gladding, MD, PhD^d; Christopher W. Good, DO^f; John G.F. Cleland, MD, PhD^g; Brandon K. Fornwalt, MD, PhD^{b,c,f,h*}

^aDepartment of Biomedical Engineering, University of Kentucky, Lexington, KY, United States

^bDepartment of Imaging Science and Innovation, Geisinger, Danville, PA, United States

^cBiomedical and Translational Informatics Institute, Geisinger, Danville, PA, United States

^dDepartment of Cardiology, Waitemata District Health Board, Auckland, New Zealand

^eClinical Informatics Service, Waitemata District Health Board, Auckland, New Zealand

^fHeart Institute, Geisinger, Danville, PA, United States

^gRobertson Centre for Biostatistics and Clinical Trials, University of Glasgow and National Heart & Lung Institute, Imperial College London, London, UK

^hDepartment of Radiology, Geisinger, Danville, PA, United States

Table of Contents

LVEF Reporting Page 3

Independent New Zealand dataset Page 3

Figures Page 4

Figure S1. Unadjusted LVEF Hazard Ratios in Both the Primary (N = 403,977) and Validation (N = 45,531) datasets.

Figure S2. Confounder and LVEF Hazard Ratios Using Only the First Echocardiogram from Each Patient (N = 203,135).

Figure S3. Confounder and LVEF Hazard Ratios when Excluding Echocardiograms with Indeterminate LVEF Inequalities as well as Echocardiograms Performed on Pediatrics Patients and Patients with Congenital Heart or Great Vessel Defects (N = 384,329).

Figure S4. Confounder and LVEF Hazard Ratios in the Subgroup of Echocardiograms with at Least 90 Days of Follow-up (N = 342,220).

Figure S5. Analysis with Interactions between LVEF and Exam Setting in the Primary Dataset (Number of Echocardiograms = 403,977).

Figure S6. Confounder and LVEF Hazard Ratios from the Exploratory Echocardiographic Dataset (N = 219,278).

Figure S7. Adjusted Hazard Ratios from the Interaction between LVEF and ESVi in the Exploratory Echocardiographic Dataset (Number of Echocardiograms = 203,627).

Figure S8. Adjusted Hazard Ratios from the Interaction between LVEF and EDVi in the Exploratory Echocardiographic Dataset (Number of Echocardiograms = 215,318).

Figure S9. LVEF Adjusted Hazard Ratios Further Adjusted for NT-proBNP in Patients with Heart Failure (Number of Echocardiograms = 13,599).

Tables Page 11

Table S1. ICD-10 Codes for Each Diagnosis

Table S2. Baseline Patient Characteristics for the Primary Group and the Group without Reported LVEF

Table S3. Baseline Patient Characteristics for the Primary Group for each LVEF Interval

Table S4. Indications for Echocardiography in the Primary Group

Table S5. Baseline Characteristics for the First Echocardiogram from Each Patient in the Primary Group

Table S6. Baseline Characteristics for each LVEF Interval in Patients with Heart Failure

LVEF Reporting

LVEF was reported in any of three ways: a single number, a range (e.g. 40-45%), or an inequality (e.g. <20%). To align with the common intervals and inequalities, all LVEFs were categorized into intervals that were 5% wide and inclusive of the lower endpoint. The lowest and highest intervals were <20% and $\geq 70\%$, respectively. Reports with indeterminate inequalities were classified in the adjacent interval (e.g. <30% was categorized as 25-30%). For the small number of echocardiograms with multiple reported LVEFs, the mean was taken.

Of the 403,977 echocardiograms in the primary group, 297,287 (74%) had LVEF reported as a range. LVEF was reported as an inequality for 16,373 (4%) echocardiograms. Of those inequalities, only 3,328 (0.82% of the whole) were an indeterminate inequality (e.g. <30%). LVEF was reported as a single number for 90,317 (22%) echocardiograms.

Independent New Zealand dataset

Waitemata District Health Board is the largest regional district health provider in New Zealand, serving a population of 630,000 people. Mortality was recorded in this population using centralised government databases, from Statistics New Zealand (Tatauranga Aotearoa). Statistics New Zealand is the principal agency responsible for processing and publishing vital statistics in New Zealand, including death statistics. Under the provisions of the New Zealand Births, Deaths, Marriages, and Relationships Registration Act 1995, every death occurring in New Zealand must be registered. Mortality was censored from January 2018.

The mean age of the validation dataset was 63.1 years (SD, 17.3). The echocardiograms were acquired between 2008 – 2017 and included 45,531 echocardiograms from 35,976 patients. Death occurred in 4,781 patients (13.3%) who had 6375 echocardiograms (14.8%). The median follow-up time based on the reverse Kaplan-Meier method was 3.2 years (IQR, 1.9 – 4.7).

Figure S1 below demonstrates a similar u-shaped relationship for the unadjusted hazard ratios from the validation dataset. The confidence intervals for the validation dataset were generally wider due to its smaller sample size. Kaplan-Meier estimators demonstrated a similar ability to stratify survival based on LVEF. The validation dataset generally had better survival compared to the primary dataset for any given LVEF.

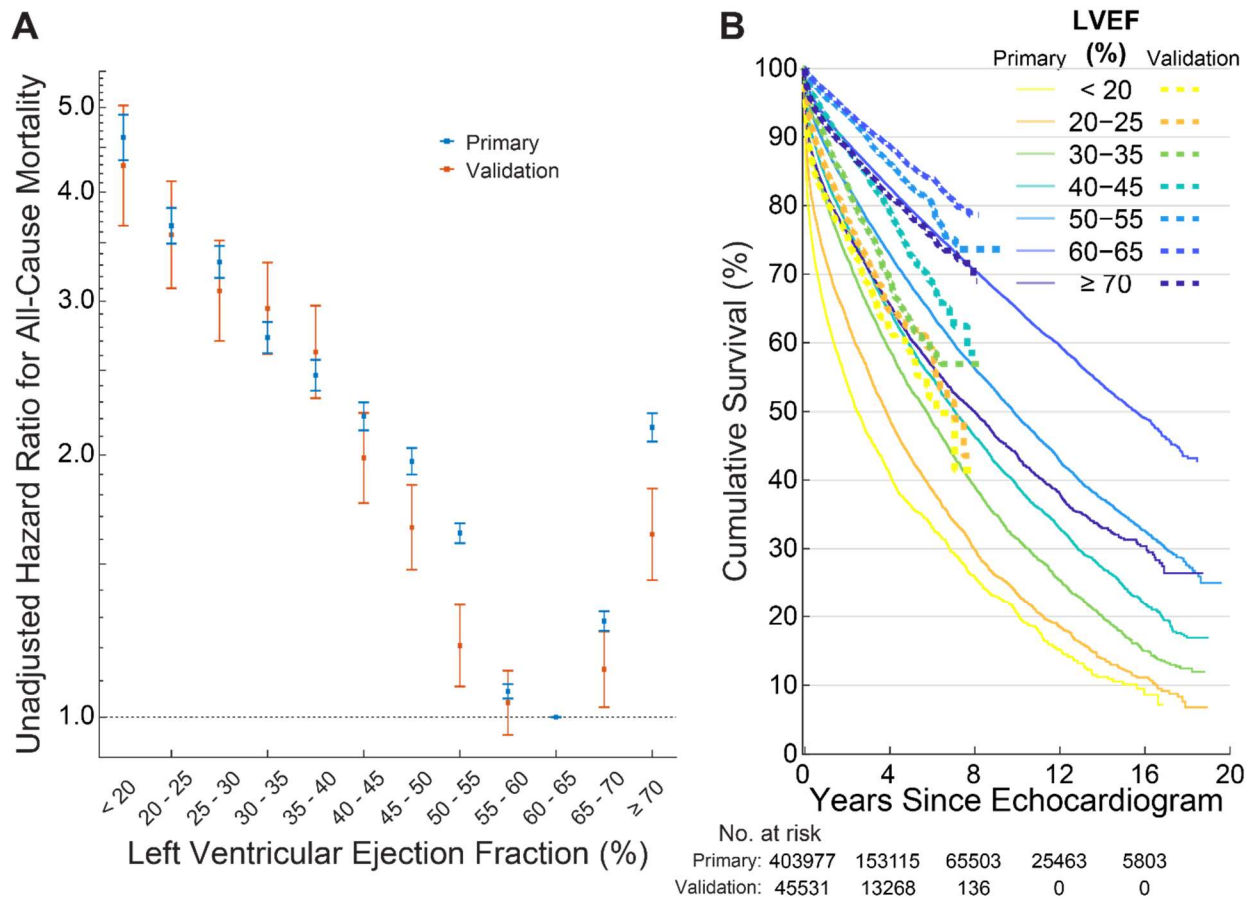


Figure S1. Unadjusted LVEF Hazard Ratios in Both the Primary (N = 403,977) and Validation (N = 45,531) datasets. LVEF, left ventricular ejection fraction. LVEF intervals are inclusive of the lower endpoint. **A)** The unadjusted hazard ratios for both the primary and validation datasets had u-shaped relationships. **B)** Unadjusted Kaplan Meier estimators illustrate the ability of LVEF to stratify survival in both datasets.

Characteristic	Adjusted Hazard Ratio (95% CI)
Age, y	
<18	0.04 (0.01-0.13)
18 - 30	0.33 (0.30-0.37)
30 - 40	0.37 (0.34-0.41)
40 - 50	0.54 (0.51-0.57)
50 - 60	1.00 (referent)
60 - 70	1.74 (1.69-1.81)
70 - 80	3.08 (2.98-3.18)
≥80	6.00 (5.79-6.22)
BMI, kg/m²	
<18.5	1.95 (1.84-2.07)
18.5 - 25	1.00 (referent)
25 - 30	0.71 (0.70-0.73)
30 - 35	0.67 (0.65-0.69)
35 - 40	0.73 (0.70-0.75)
≥40	0.91 (0.87-0.94)
Date of Echocardiogram	
<2002	0.58 (0.56-0.61)
2002 - 2005	0.70 (0.67-0.72)
2005 - 2008	0.81 (0.78-0.83)
2008 - 2011	0.89 (0.86-0.92)
2011 - 2014	0.91 (0.89-0.94)
≥2014	1.00 (referent)
Height (per 10 cm)	0.93 (0.92-0.94)
Male sex	1.36 (1.32-1.39)
Previous Myocardial Infarction	0.96 (0.92-1.00)
Hypertension	1.00 (0.98-1.02)
Diabetes	1.56 (1.53-1.60)
Atrial Fibrillation	1.18 (1.15-1.22)
Congenital Defect	0.81 (0.76-0.86)
Dyslipidemia	0.68 (0.66-0.69)
Chronic Kidney Disease	1.42 (1.37-1.46)
Heart Failure	1.47 (1.42-1.52)
Positive Smoking History	1.20 (1.18-1.22)
LVEF, %	
<20	3.04 (2.80-3.29)
20 - 25	2.59 (2.42-2.76)
25 - 30	2.31 (2.18-2.46)
30 - 35	2.00 (1.89-2.12)
35 - 40	1.90 (1.80-2.00)
40 - 45	1.79 (1.71-1.88)
45 - 50	1.59 (1.51-1.66)
50 - 55	1.39 (1.34-1.44)
55 - 60	1.06 (1.03-1.08)
60 - 65	1.00 (referent)
65 - 70	1.19 (1.15-1.24)
≥70	1.69 (1.61-1.78)

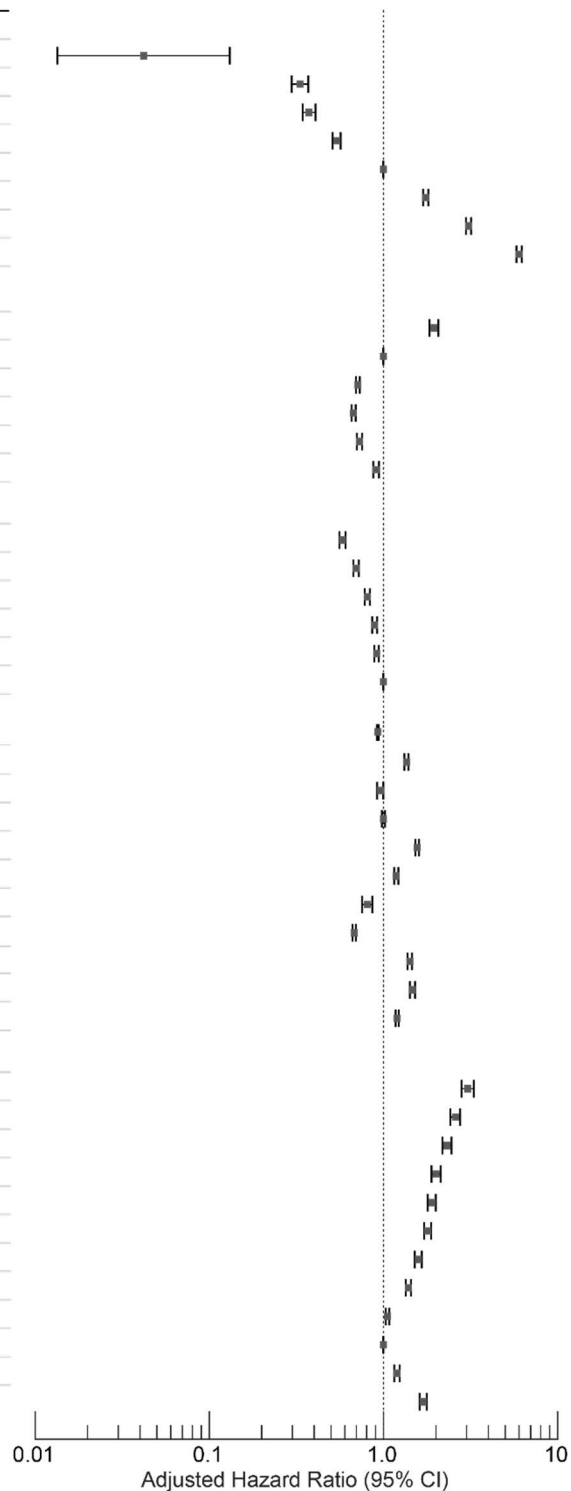


Figure S2. Confounder and LVEF Hazard Ratios Using Only the First Echocardiogram from Each Patient (N = 203,135). LVEF, left ventricular ejection fraction. LVEF intervals are inclusive of the lower endpoint.

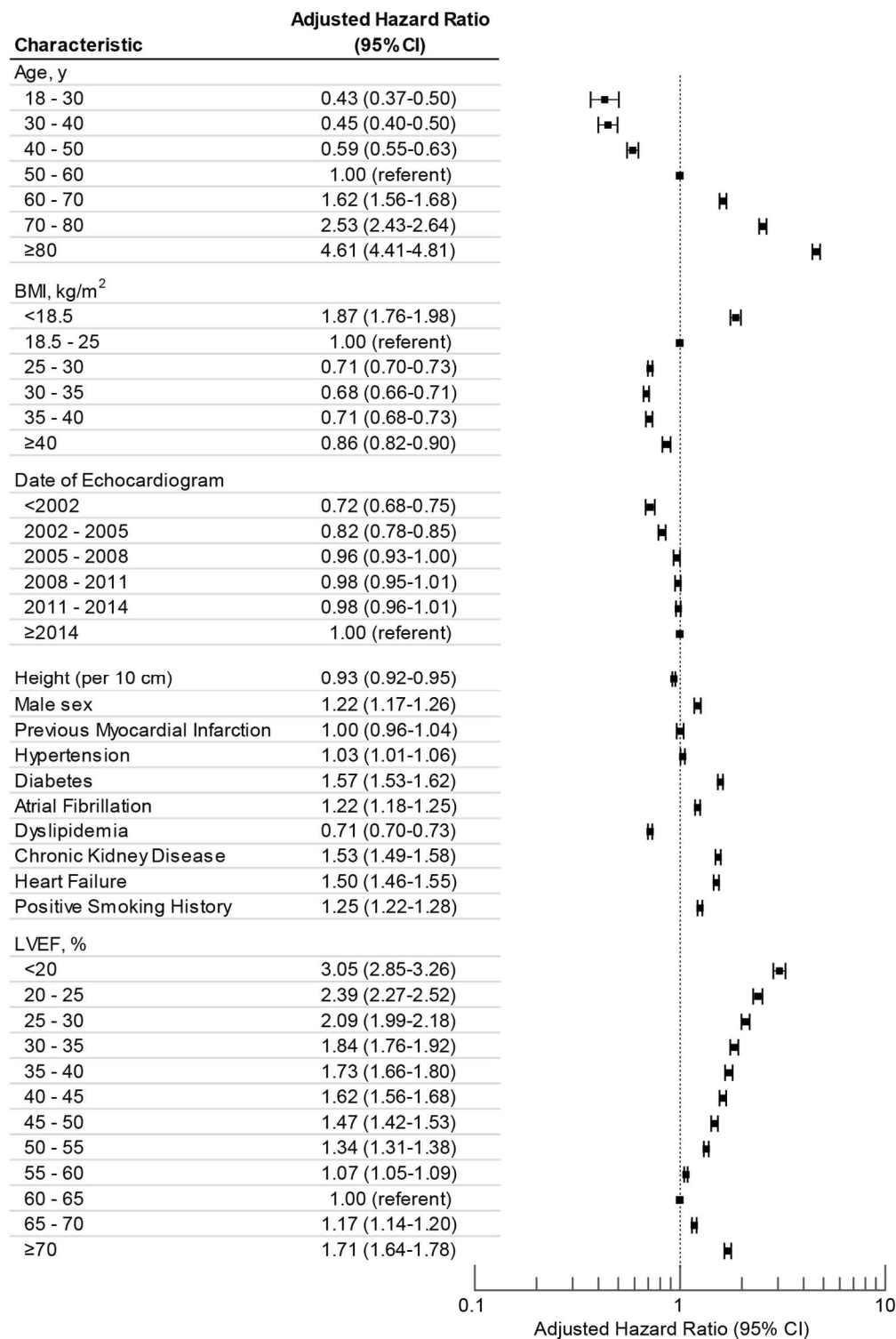


Figure S3. Confounder and LVEF Hazard Ratios when Excluding Echocardiograms with Indeterminate LVEF Inequalities as well as Echocardiograms Performed on Pediatrics Patients and Patients with Congenital Heart or Great Vessel Defects (N = 384,329). LVEF, left ventricular ejection fraction. LVEF intervals are inclusive of the lower endpoint.

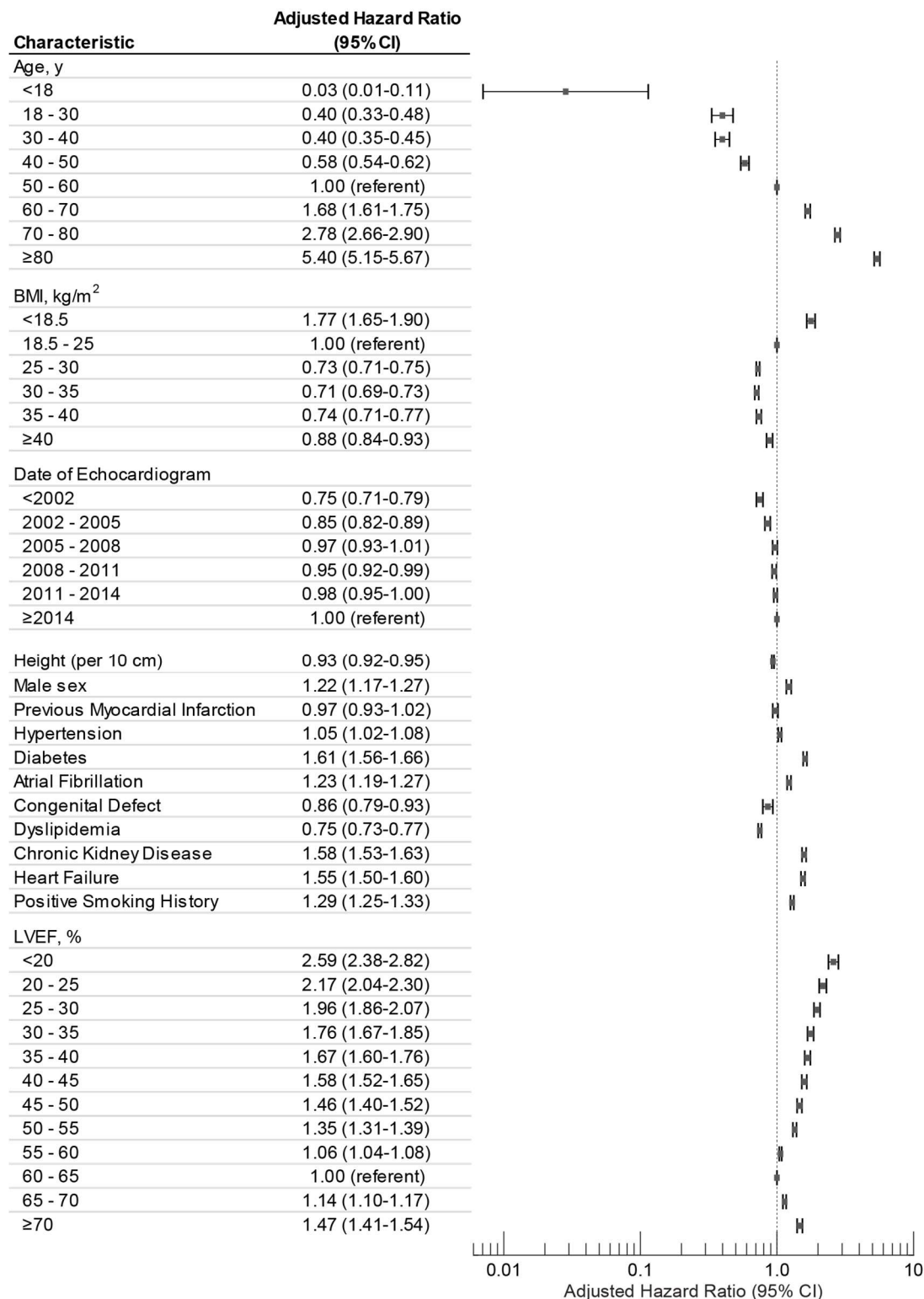


Figure S4. Confounder and LVEF Hazard Ratios in the Subgroup of Echocardiograms with at Least 90 Days of Follow-up (N = 342,220). LVEF, left ventricular ejection fraction. LVEF intervals are inclusive of the lower endpoint.

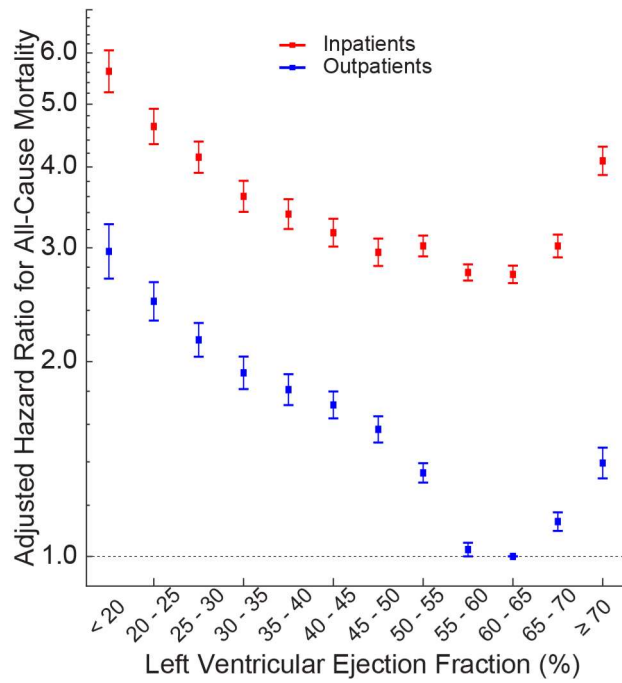


Figure S5. Analysis with Interactions between LVEF and Exam Setting in the Primary Dataset (Number of Echocardiograms = 403,977). LVEF, left ventricular ejection fraction. LVEF intervals are inclusive of the lower threshold. The referent group was “Outpatients with LVEF of 60-65%”.

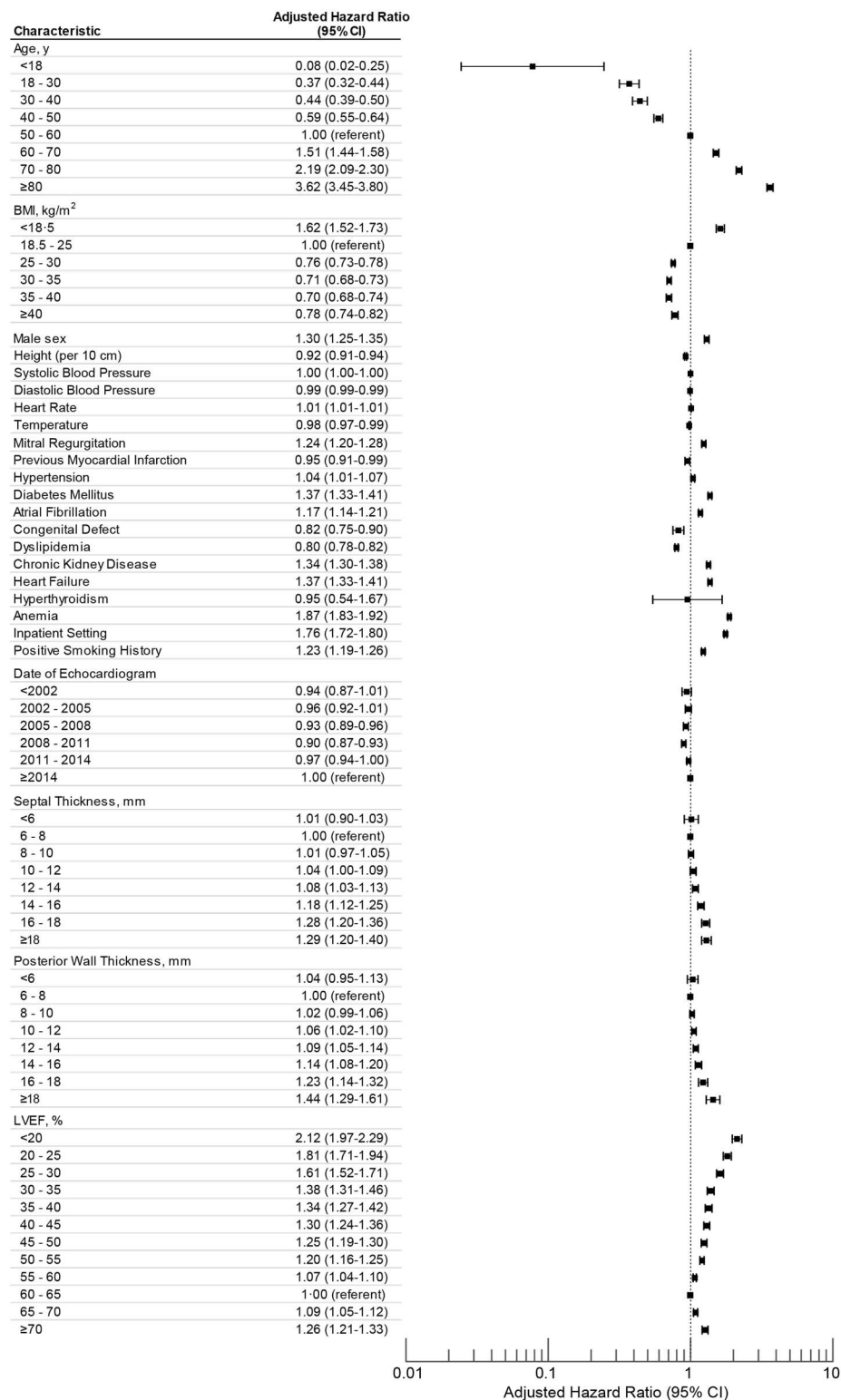
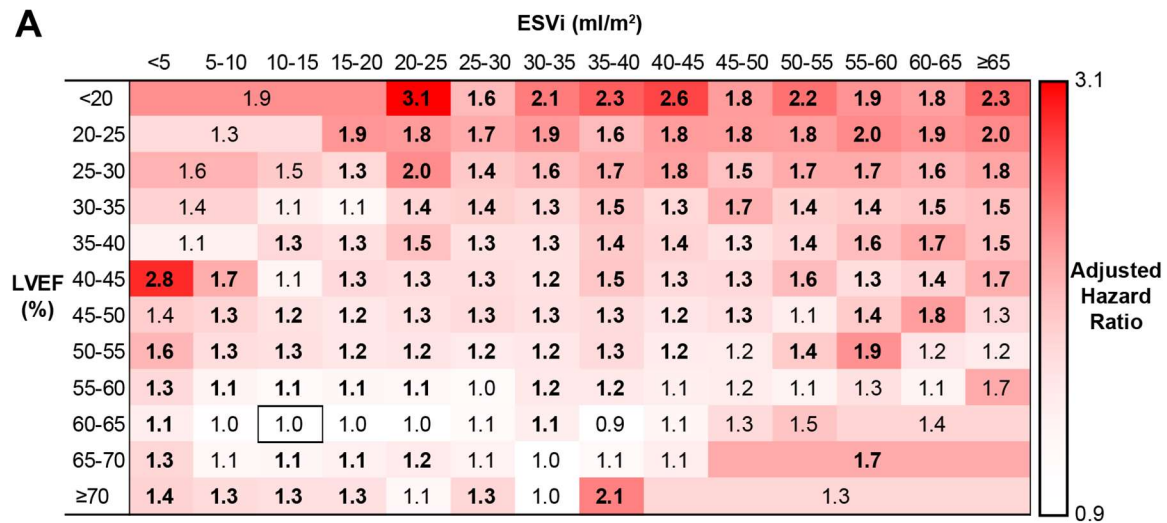


Figure S6. Confounder and LVEF Hazard Ratios from the Exploratory Echocardiographic Dataset (N = 219,278). LVEF, left ventricular ejection fraction. LVEF intervals are inclusive of the lower endpoint. Additional confounders include systolic and diastolic blood pressure, heart rate, temperature, mitral regurgitation, anemia (hemoglobin < 10 g/dL), hyperthyroidism (TSH < 0.10 mIU/L), and septal and posterior wall thicknesses.

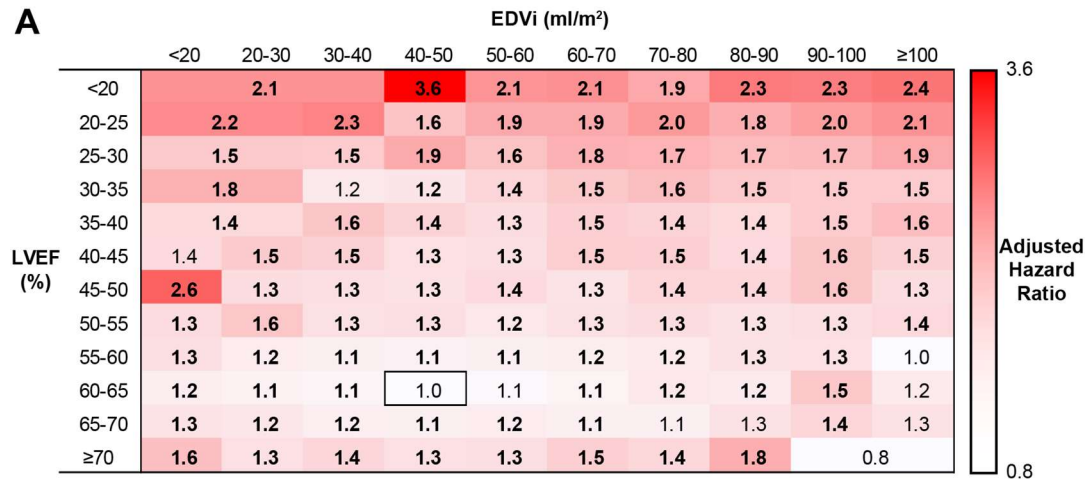


B

ESVi (ml/m²)

	<5	5-10	10-15	15-20	20-25	25-30	30-35	35-40	40-45	45-50	50-55	55-60	60-65	≥65	
<20		20			20	49	51	85	101	125	137	143	158	1695	
20-25		29		41	57	119	166	199	237	282	288	289	278	1524	
25-30		29	50	116	175	258	323	368	419	437	396	376	332	1072	
30-35		44	105	178	284	419	515	570	548	522	461	335	305	603	
35-40		62	204	388	488	633	720	654	634	472	360	236	148	323	
LVEF (%)															
40-45		16	132	349	666	956	1175	1051	914	734	518	321	191	123	176
45-50		27	187	623	1108	1449	1390	1240	850	575	302	193	127	59	75
50-55		99	1024	3001	4504	4574	3331	2055	1157	635	314	137	74	43	42
55-60		601	6883	16298	17655	12320	6657	3060	1388	604	247	111	71	34	41
60-65		829	8038	16439	14573	8052	3664	1416	597	237	117	51		40	
65-70		591	4233	6572	4391	1995	881	341	130	58			44		
≥70		604	2564	2241	1106	379	176	67	27			32			

Figure S7. Adjusted Hazard Ratios from the Interaction between LVEF and ESVi in the Exploratory Echocardiographic Dataset (Number of Echocardiograms = 203,627). LVEF, left ventricular ejection fraction. ESVi, left ventricular end systolic volume index. LVEF intervals are inclusive of the lower endpoint. Additional confounders include systolic and diastolic blood pressure, heart rate, temperature, mitral regurgitation, anemia (hemoglobin < 10 g/dL), hyperthyroidism (TSH < 0.10 mIU/L), and septal and posterior wall thicknesses. **(A)** Bold values are significantly different from the boxed “1.0” reference interval (P < 0.05). Adjacent intervals were merged as needed to encompass at least 10 instances of mortality. **(B)** The number of echocardiograms in each group.



B

		EDVi (ml/m ²)									
		<20	20-30	30-40	40-50	50-60	60-70	70-80	80-90	90-100	≥100
LVEF (%)	<20		41		81	173	212	325	318	306	1425
	20-25		23	81	221	282	424	542	519	492	1224
	25-30		46	168	337	521	743	737	689	519	903
	30-35		97	230	496	736	954	908	658	487	623
	35-40		144	364	704	1023	1088	884	628	347	424
	40-45	34	189	640	1273	1595	1531	1111	665	383	321
	45-50	38	340	966	1605	1927	1662	1067	579	243	220
	50-55	290	1629	3689	5175	4981	3531	1860	755	317	204
	55-60	973	6216	14072	18447	15405	8966	3667	1280	419	217
	60-65	911	5447	12087	15885	12416	6497	2422	731	238	150
	65-70	477	2458	5069	5415	3885	1815	651	196	74	51
	≥70	387	1515	2185	1901	1053	469	188	77	39	

Figure S8. Adjusted Hazard Ratios from the Interaction between LVEF and EDVi in the Exploratory Echocardiographic Dataset (Number of Echocardiograms = 215,318). LVEF, left ventricular ejection fraction. EDVi, left ventricular end diastolic volume index. LVEF intervals are inclusive of the lower endpoint. Additional confounders include systolic and diastolic blood pressure, heart rate, temperature, mitral regurgitation, anemia (hemoglobin < 10 g/dL), hyperthyroidism (TSH < 0.10 mIU/L), and septal and posterior wall thicknesses. **(A)** Bold values are significantly different from the boxed “1.0” reference interval (P < 0.05). Adjacent intervals were merged as needed to encompass at least 10 instances of mortality. **(B)** The number of echocardiograms in each group.

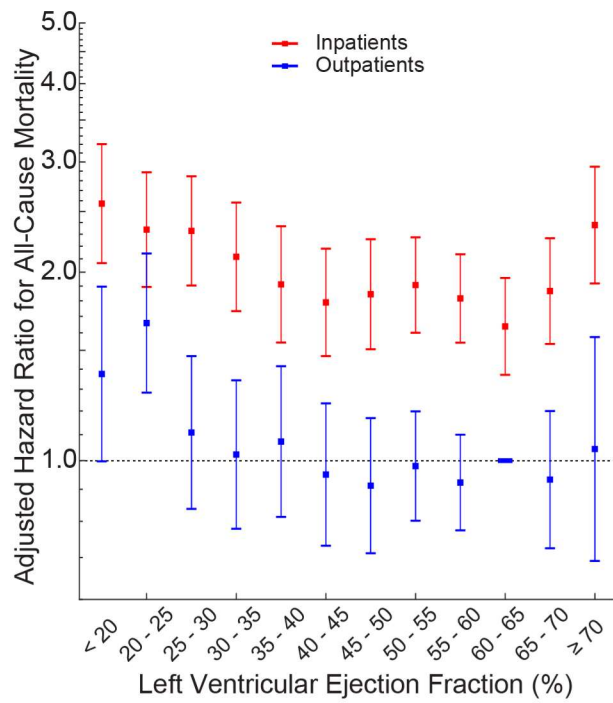


Figure S9. LVEF Adjusted Hazard Ratios Further Adjusted for NT-proBNP in Patients with Heart Failure (Number of Echocardiograms = 13,599). LVEF, left ventricular ejection fraction. LVEF intervals are inclusive of the lower threshold. Error bars represent the 95% confidence interval. The referent group was “Outpatients with LVEF of 60-65%”.

Table S1. ICD-10 Codes for Each Diagnosis

Diagnosis	ICD-10 Codes
Previous Myocardial Infarction	I21, I22, I23, I25.2
Hypertension	I10, I11, I12, I13, I14, I15
Diabetes Mellitus	E08, E09, E10, E11, E12, E13
Atrial Fibrillation	I48
Congenital Defect	Q20, Q21, Q22, Q23, Q24, Q25, Q26
Dyslipidemia	E78.0, E78.2, E78.4, E78.5
Chronic Kidney Disease	N18
Heart Failure	I50

Abbreviations: ICD-10, *International Classification of Disease, Tenth Edition*

Table S2. Baseline Patient Characteristics for the Primary Group and the Group without Reported LVEF

Characteristic	Primary Group, No. (%) (N = 403977)	Missing LVEF Group, No. (%) (N = 178371)	Standardized Difference
Age, mean (SD), y	63.8 (15.9)	61.6 (17.1)	0.14
Male	208408 (52)	90720 (51)	0.02
BMI, mean (SD), kg/m ²	30.5 (7.8)	30.5 (8.5)	0.01
Date of Echocardiogram			
Q1	16-Sep-2009	12-July-2006	
Median	29-Nov-2013	13-Dec-2010	
Q3	7-Sep-2016	24-Feb-2014	
Previous Myocardial Infarction	38085 (9)	8854 (5)	0.18
Hypertension	196742 (49)	55355 (31)	0.37
Diabetes Mellitus	91464 (23)	25612 (14)	0.22
Atrial Fibrillation	65866 (16)	17250 (10)	0.20
Congenital Heart Defect	16110 (4)	7256 (4)	0.00
Dyslipidemia	176109 (44)	49793 (28)	0.33
Chronic Kidney Disease	55092 (14)	10305 (6)	0.27
Heart Failure	52192 (13)	12754 (7)	0.19
Positive Smoking History	232951 (58)	99397 (56)	0.04
Hazard Ratio for Mortality (95% CI) ^a	1.24 (1.22-1.26)	1.00 (referent)	

Abbreviations: BMI, body mass index calculated as weight in kilograms divided by height in meters squared; LVEF, left ventricular ejection fraction; CI, confidence interval

^aUnadjusted hazard ratio for the primary group vs. the missing LVEF group.

Table S3. Baseline Patient Characteristics for the Primary Group for each LVEF Interval

Characteristic	LVEF < 20 No. (%) (N = 5205)	LVEF 20 - 25 No. (%) (N = 7202)	LVEF 25 - 30 No. (%) (N = 8814)	LVEF 30 - 35 No. (%) (N = 9726)	LVEF 35 - 40 No. (%) (N = 10595)	LVEF 40 - 45 No. (%) (N = 14478)	LVEF 45 - 50 No. (%) (N = 15889)	LVEF 50 - 55 No. (%) (N = 41859)	LVEF 55 - 60 No. (%) (N = 138705)	LVEF 60 - 65 No. (%) (N = 103433)	LVEF 65 - 70 No. (%) (N = 34508)	LVEF ≥ 70 No. (%) (N = 13563)
No. of Unique Patients ^a	3515	5138	6470	7360	8206	11064	12574	32882	99140	76856	28983	11509
Age, mean (SD), y	66.2 (14.1)	68.0 (13.4)	69.0 (13.1)	68.4 (13.4)	68.5 (13.6)	67.9 (14.0)	67.1 (14.3)	65.0 (15.8)	61.9 (16.2)	62.3 (16.2)	64.9 (16.1)	67.6 (15.5)
Male Sex	3806 (73)	5029 (70)	6088 (69)	6498 (67)	7152 (68)	9634 (67)	10427 (66)	25179 (60)	69145 (50)	46351 (45)	14082 (41)	5017 (37)
BMI, mean (SD), kg/m ²	29.0 (7.7)	29.2 (7.1)	29.7 (7.7)	29.8 (8.1)	29.9 (8.0)	29.9 (7.5)	30.2 (7.7)	30.7 (8.0)	30.8 (7.8)	30.5 (7.7)	30.6 (8.0)	30.4 (8.2)
Previous Myocardial Infarction	1154 (22)	1794 (25)	2269 (26)	2492 (26)	2632 (25)	3410 (24)	3305 (21)	5281 (13)	8970 (6)	4669 (5)	1444 (4)	665 (5)
Hypertension	2447 (47)	3578 (50)	4626 (52)	5138 (53)	5664 (53)	7607 (53)	8365 (53)	21166 (51)	64793 (47)	48165 (47)	17649 (51)	7544 (56)
Diabetes Mellitus	1689 (32)	2520 (35)	2995 (34)	3193 (33)	3324 (31)	4138 (29)	4434 (28)	10290 (25)	28044 (20)	19992 (19)	7501 (22)	3344 (25)
Atrial Fibrillation	1486 (29)	1952 (27)	2357 (27)	2524 (26)	2641 (25)	3675 (25)	3908 (25)	9180 (22)	19466 (14)	12358 (12)	4364 (13)	1955 (14)
Congenital Heart Defect	109 (2)	201 (3)	223 (3)	263 (3)	326 (3)	491 (3)	534 (3)	1664 (4)	5775 (4)	4592 (4)	1389 (4)	543 (4)
Dyslipidemia	2246 (43)	3290 (46)	4202 (48)	4728 (49)	5062 (48)	6868 (47)	7695 (48)	19014 (45)	58535 (42)	43016 (42)	15230 (44)	6223 (46)
Chronic Kidney Disease	1248 (24)	1645 (23)	2010 (23)	2105 (22)	2100 (20)	2722 (19)	2890 (18)	6528 (16)	16042 (12)	10960 (11)	4640 (13)	2202 (16)
Heart Failure	2907 (56)	3508 (49)	3845 (44)	3707 (38)	3422 (32)	3822 (26)	3583 (23)	6201 (15)	10493 (8)	6436 (6)	2834 (8)	1434 (11)
Positive Smoking History	3537 (68)	4832 (67)	5839 (66)	6488 (67)	6803 (64)	9344 (65)	10262 (65)	25539 (61)	78730 (57)	55688 (54)	18353 (53)	7536 (56)

^aThe sum of the number of unique patients across the LVEF intervals is larger than the overall number of unique patients because patients with multiple echocardiograms can appear in multiple LVEF intervals
Abbreviations: BMI, body mass index calculated as weight in kilograms divided by height in meters squared; LVEF, left ventricular ejection fraction

Table S4. Indications for Echocardiography in the Primary Group

Indication/Diagnosis^a	No. of Echocardiograms^b	%
Chest Pain	62370	15.4
Dyspnea / Fatigue	51111	12.7
Coronary Artery Disease	41487	10.3
Aortic Valve Disease	37147	9.2
Congestive Heart Failure	31786	7.9
Atrial Fibrillation	28835	7.1
Stroke / Transient Ischemic Attack	20300	5.0
Syncope / Orthostatic hypotension / Dizziness	17097	4.2
Hypertension	15323	3.8
Mitral Valve Disease	15011	3.7
Murmur	13186	3.3
Acute Coronary Syndrome	12964	3.2
ECG Abnormal	12040	3.0
Cardiomyopathy	9622	2.4
Sepsis / Bacteremia / Endocarditis	8918	2.2
Palpitations	8700	2.2
Other Arrhythmia	8422	2.1
Edema	7459	1.9
Other Valvular Disease	7072	1.8
Pericardial Disease	6501	1.6
Pre-op Exam	5583	1.4
Aortic Disease	3612	0.9
Pulmonary Embolism	3289	0.8
Pulmonary Hypertension	3242	0.8
Dyslipidemia	2972	0.7
Congenital Heart Disease	2419	0.6
Atrial Flutter	2380	0.6
Chemotherapy	2174	0.5
Tricuspid Valve Disease	1936	0.5

Cardiac Arrest	1809	0.5
Family History of Cardiovascular Disease	1793	0.4
Fever	1638	0.4
Ventricular Tachycardia	1373	0.3
Shock	1344	0.3
Chronic Obstructive Pulmonary Disease	1268	0.3
Hypotension	1256	0.3
Tachycardia	1226	0.3
Pulmonary Edema	863	0.2
Cardiac Contusion	470	0.1
Other	30618	7.6
Unknown	35389	8.8

^aCategories were defined by reviewing diagnoses which occurred in more than 0.1% of all the echocardiograms.

^bThe sum of the number of studies (or percentage) is larger than the total number of echocardiograms (or 100%) as an echocardiogram could have more than one indication.

Table S5. Baseline Characteristics for the First Echocardiogram from Each Patient in the Primary Group

Characteristic	All Echoes^a No. (%) (N = 403977)	First Echo Only No. (%) (N = 203135)
Age, mean (SD), y	63.8 (15.9)	61.0 (16.9)
Men	208408 (52)	99981 (49)
BMI, mean (SD), kg/m ²	30.5 (7.8)	30.4 (8.0)
Previous Myocardial Infarction	38085 (9)	10010 (5)
Hypertension	196742 (49)	79852 (39)
Diabetes Mellitus	91464 (23)	34541 (17)
Atrial Fibrillation	65866 (16)	18297 (9)
Congenital Heart Defect	16110 (4)	4700 (2)
Dyslipidemia	176109 (44)	68579 (34)
Chronic Kidney Disease	55092 (14)	14871 (7)
Heart Failure	52192 (13)	10698 (5)
Positive Smoking History	232951 (58)	112579 (55)
LVEF, mean (SD), %	55.2 (11.1)	56.6 (9.8)
Under 20	5205 (1)	1838 (1)
20 - 25	7202 (2)	2409 (1)
25 - 30	8814 (2)	2926 (1)
30 - 35	9726 (2)	3216 (2)
35 - 40	10595 (3)	3854 (2)
40 - 45	14478 (4)	5273 (3)
45 - 50	15889 (4)	6106 (3)
50 - 55	41895 (10)	19577 (10)
55 - 60	138705 (34)	74839 (37)
60 - 65	103433 (26)	57920 (29)
65 - 70	34508 (9)	18279 (9)
Over 70	13563 (3)	6898 (3)

Abbreviations: BMI, body mass index; LVEF, left ventricular ejection fraction

^a121,613 patients had exactly one echo; 38,406 had exactly two echoes; 43,116 had three or more echoes

Table S6. Baseline Characteristics for each LVEF Interval in Patients with Heart Failure

Characteristic	LVEF	LVEF	LVEF	LVEF	LVEF	LVEF	LVEF	LVEF	LVEF	LVEF	LVEF	LVEF
	< 20 No. (%) (N = 2111)	20 - 25 No. (%) (N = 2579)	25 - 30 No. (%) (N = 2830)	30 - 35 No. (%) (N = 2775)	35 - 40 No. (%) (N = 2570)	40 - 45 No. (%) (N = 2953)	45 - 50 No. (%) (N = 2836)	50 - 55 No. (%) (N = 4882)	55 - 60 No. (%) (N = 8362)	60 - 65 No. (%) (N = 5273)	65 - 70 No. (%) (N = 2317)	≥ 70 No. (%) (N = 1128)
No. of Unique Patients ^a	1551	2029	2268	2272	2136	2438	2343	3938	6205	4113	1982	947
Age, mean (SD), y	67.5 (13.7)	70.0 (13.0)	70.7 (12.6)	70.4 (13.0)	71.3 (13.0)	71.8 (12.7)	71.7 (12.9)	72.5 (12.9)	73.1 (12.8)	73.9 (12.4)	75.0 (11.9)	75.4 (12.4)
Male Sex	1534 (73)	1801 (70)	1933 (68)	1815 (65)	1672 (65)	1832 (62)	1699 (60)	2510 (51)	3752 (45)	2039 (39)	748 (32)	319 (28)
BMI, mean (SD), kg/m ²	29.0 (7.4)	29.3 (6.7)	29.6 (7.2)	30.0 (7.8)	30.1 (7.2)	30.2 (7.2)	30.7 (7.7)	31.5 (8.4)	32.2 (8.7)	32.3 (9.0)	32.3 (9.3)	31.4 (9.7)
Previous Myocardial Infarction	589 (28)	840 (33)	926 (33)	874 (31)	820 (32)	878 (30)	722 (25)	958 (20)	1202 (14)	608 (12)	263 (11)	156 (14)
Hypertension	1164 (55)	1563 (61)	1786 (63)	1818 (66)	1755 (68)	2031 (69)	2009 (71)	3537 (72)	6233 (75)	4020 (76)	1816 (78)	890 (79)
Diabetes Mellitus	817 (39)	1112 (43)	1286 (45)	1217 (44)	1130 (44)	1228 (42)	1236 (44)	2109 (43)	3570 (43)	2259 (43)	1013 (44)	464 (41)
Atrial Fibrillation	732 (35)	916 (36)	1056 (37)	1087 (39)	995 (39)	1270 (43)	1249 (44)	2227 (46)	3805 (46)	2274 (43)	968 (42)	484 (43)
Congenital Heart Defect	40 (2)	58 (2)	68 (2)	67 (2)	66 (3)	93 (3)	82 (3)	179 (4)	322 (4)	203 (4)	84 (4)	38 (3)
Dyslipidemia	1142 (54)	1490 (58)	1684 (60)	1644 (59)	1552 (60)	1796 (61)	1781 (63)	3010 (62)	4958 (59)	3137 (59)	1403 (61)	697 (62)
Chronic Kidney Disease	714 (34)	906 (35)	1050 (37)	1002 (36)	940 (37)	1091 (37)	1094 (39)	1094 (39)	3222 (39)	2025 (38)	948 (41)	458 (41)
Positive Smoking History	1478 (70)	1806 (70)	1936 (68)	1874 (68)	1707 (66)	1932 (65)	1853 (65)	3011 (62)	5078 (61)	3005 (57)	1267 (55)	648 (57)
ACEi or ARB	1174 (56)	1423 (55)	1458 (52)	1440 (52)	1265 (49)	1362 (46)	1253 (44)	1888 (39)	2871 (34)	1772 (34)	773 (33)	349 (31)
β-blocker	1276 (60)	1484 (58)	1507 (53)	1407 (51)	1277 (50)	1305 (44)	1159 (41)	1631 (33)	2371 (28)	1374 (26)	581 (25)	319 (28)
Loop Diuretics	1551 (73)	1801 (70)	1869 (66)	1761 (63)	1564 (61)	1806 (61)	1677 (59)	2896 (59)	4803 (57)	2989 (57)	1372 (59)	679 (60)
MCRA	617 (29)	569 (22)	538 (19)	423 (15)	385 (15)	357 (12)	269 (9)	485 (10)	643 (8)	433 (8)	177 (7)	88 (8)
Digoxin	654 (31)	638 (25)	517 (18)	389 (14)	364 (14)	347 (12)	318 (11)	532 (11)	746 (9)	437 (8)	208 (9)	110 (10)
Dobutamine	24 (1)	11 (0)	8 (0)	8 (0)	2 (0)	2 (0)	6 (0)	5 (0)	14 (0)	15 (0)	11 (0)	5 (0)
Dopamine	64 (3)	56 (2)	53 (2)	41 (1)	35 (1)	30 (1)	25 (1)	44 (1)	56 (1)	37 (1)	14 (1)	18 (2)
Ephedrine	9 (0)	7 (0)	9 (0)	11 (0)	12 (0)	17 (1)	12 (0)	27 (1)	41 (0)	30 (1)	15 (1)	21 (2)
Epinephrine	25 (1)	17 (1)	21 (1)	14 (1)	12 (0)	7 (0)	13 (0)	32 (1)	32 (0)	12 (0)	9 (0)	9 (1)
Isoproterenol	1 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0)	2 (0)	0 (0)	2 (0)	0 (0)	0 (0)
Milrinone	94 (4)	58 (2)	43 (2)	23 (1)	17 (1)	12 (0)	9 (0)	10 (0)	17 (0)	4 (0)	1 (0)	10 (1)
Norepinephrine	81 (4)	66 (3)	70 (2)	56 (2)	29 (1)	31 (1)	41 (1)	49 (1)	85 (1)	38 (1)	23 (1)	36 (3)
Phenylephrine	74 (4)	71 (3)	64 (2)	59 (2)	53 (2)	58 (2)	43 (2)	87 (2)	136 (2)	95 (2)	49 (2)	68 (6)
Vasopressin	9 (0)	3 (0)	3 (0)	4 (0)	2 (0)	2 (0)	2 (0)	3 (0)	6 (0)	1 (0)	1 (0)	2 (0)
Septal Thickness, mean (SD), mm	10.4 (2.6)	10.9 (2.8)	11.2 (2.7)	11.6 (2.7)	11.9 (2.7)	12.0 (2.8)	12.0 (2.7)	12.0 (2.6)	12.0 (2.6)	12.2 (2.7)	12.6 (2.8)	13.4 (3.4)
Posterior Wall Thickness, mean (SD), mm	10.3 (2.4)	10.5 (2.5)	10.7 (2.4)	11.0 (2.4)	11.1 (2.4)	11.2 (2.4)	11.3 (2.3)	11.4 (2.3)	11.4 (2.3)	11.5 (2.3)	11.8 (2.4)	12.3 (2.7)
End Diastolic Volume Index, mean (SD), mL/m ²	109.4 (40.2)	93.3 (31.3)	83.4 (26.7)	75.7 (24.8)	70.1 (22.3)	64.9 (20.4)	60.7 (19.3)	53.7 (17.8)	49.3 (16.7)	47.2 (16.4)	43.6 (15.6)	39.7 (15.1)

^aThe sum of the number of unique patients across the LVEF intervals is larger than the overall number of unique patients because patients with multiple echocardiograms can appear in multiple LVEF intervals
Abbreviations: BMI, body mass index calculated as weight in kilograms divided by height in meters squared; LVEF, left ventricular ejection fraction; ACEi, angiotensin converting enzyme inhibitors; ARB, angiotensin II receptor blockers, MCRA, mineralocorticoid receptor antagonists