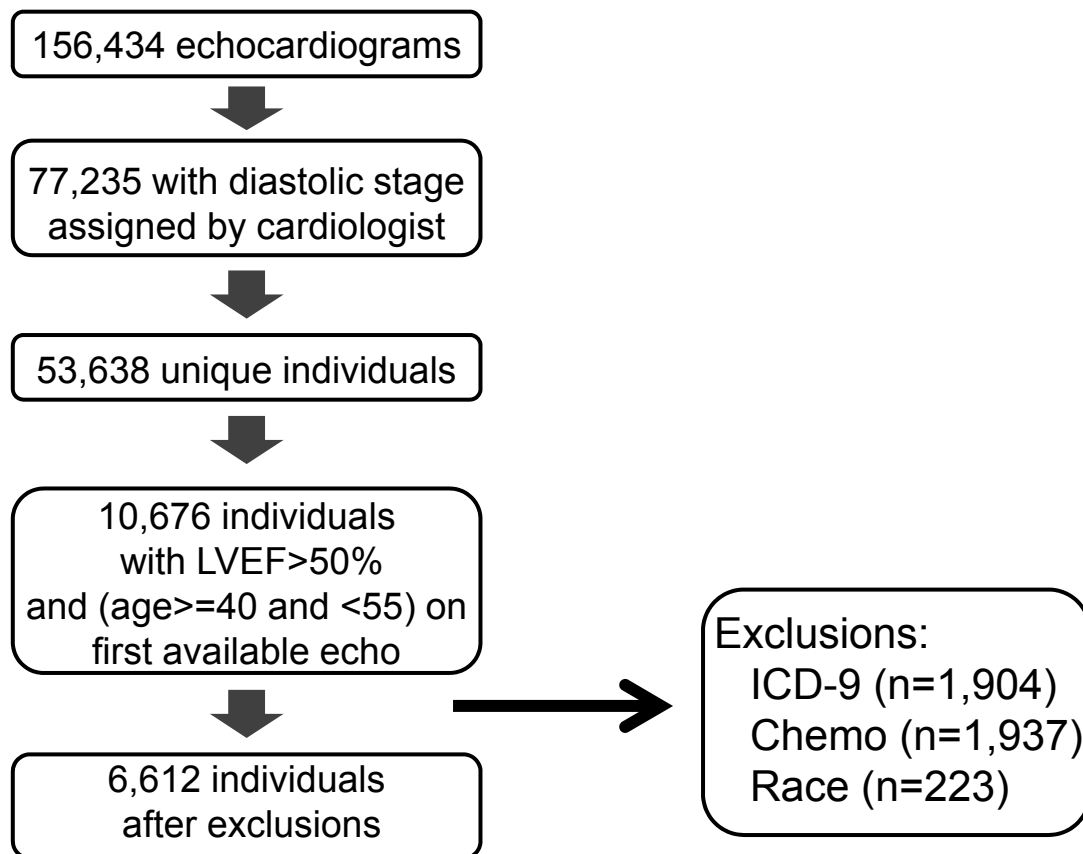
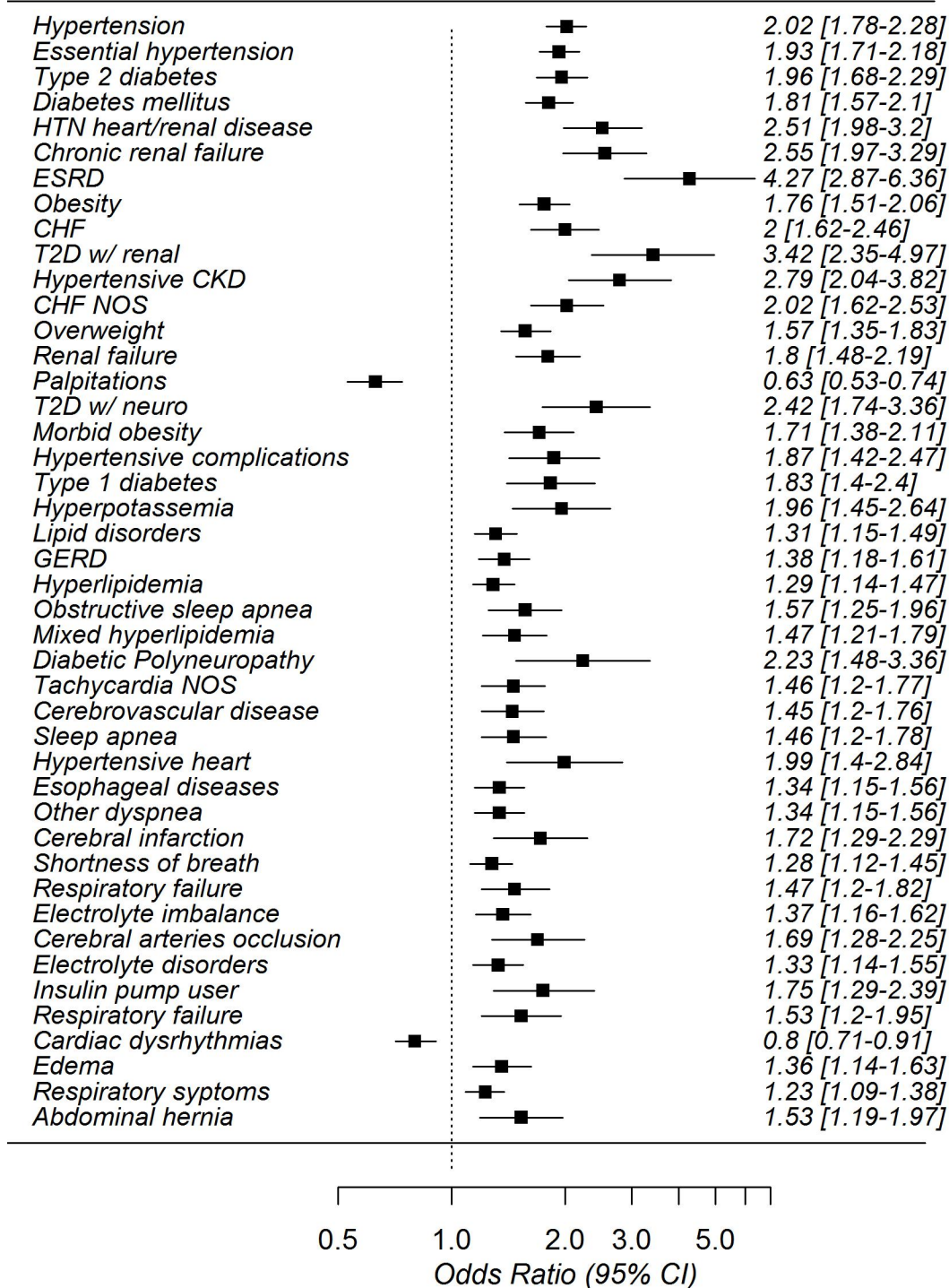


Supplementary figure 1



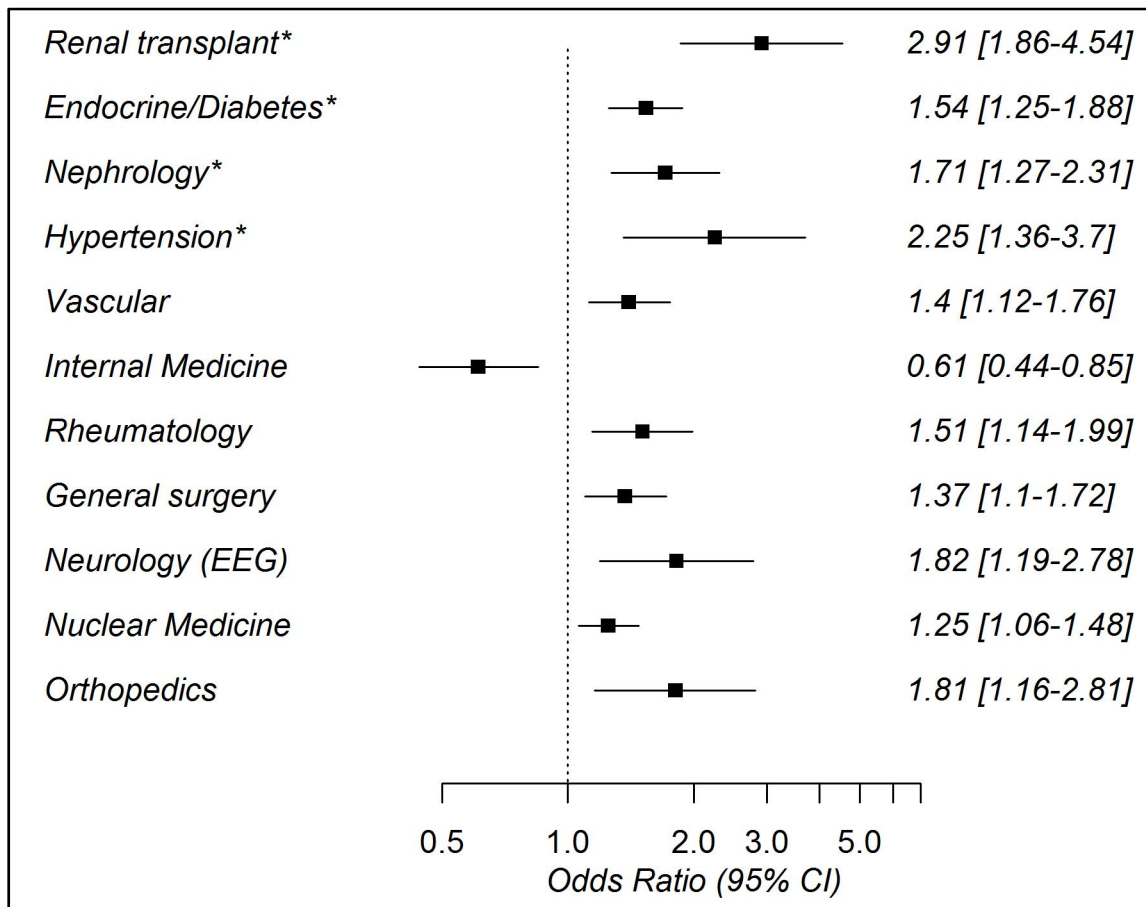
Supplementary Figure 1: Summary of the selection of the patient population.
LVEF=left ventricular ejection fraction.

Supplementary figure 2



Supplementary Figure 2: Clinical diagnoses present before the TTE associated with DD stage 1 versus normal diastolic function. Association testing used a logistic regression analysis adjusting for age, gender, self-reported race and setting. Shown are all diagnoses with FDR $q < 0.01$.

Supplementary figure 3



Supplementary Figure 3: Outpatient clinics associated with individuals with stage 1 diastolic dysfunction. Clinics where each subject was evaluated prior to the echocardiogram were identified. Odds-ratios show the association between stage 1 DD versus normal diastolic function for a clinic. Multivariable logistic regression analyses were adjusted for age, gender, self-reported race and setting. Shown are all associations with FDR $q < 0.1$. An asterisk indicates FDR $q < 0.05$.

Supplementary table 1. Strings used to identify diastolic function stages within echocardiogram reports.

Diastolic function stage	Search string	Comments
Normal	normal diastolic filling pattern	
Normal	normal diastolic function	Exclude if part of any of the strings: "low normal diastolic function", "abnormal diastolic function" or "probably normal diastolic function"
Normal	normal lv diastolic filling pattern	Exclude if part of the string: "abnormal lv diastolic filling"
Normal	normal diastolic filling indices	
Normal	normal lv diastolic filling indices	
Stage 1	impaired relaxation (stage 1 diastolic dysfunction)	
Stage 1	abnormal lv relaxation (grade 1)	Exclude if part of the strings: "borderline abnormal lv relaxation (grade 1)" or "mildly abnormal lv relaxation (grade 1)"
Stage 2	pseudonormal diastolic filling (stage 2 diastolic dysfunction)	
Stage 2	pseudonormal lv relaxation (grade 2)	
Stage 2	pseudonormal lv relaxation	
Stage 3	restrictive diastolic filling (stage 3 diastolic dysfunction)	
Stage 3	restrictive lv filling pattern	
Stage 3	restrictive lv filling	
Stage 3	restrictive lv filling (grade 3)	

Supplementary table 2. ICD-9 diagnosis codes used for excluding subjects. The number of subjects with a diagnosis is shown. Some subjects may have multiple diagnoses.

ICD-9 code	ICD-9 descriptions	Number of subjects
423.9	PERICARDIAL DISEASE NOS	473
745.5	SECUNDUM ATRIAL SEPT DEF	321
746.9	CONG HEART ANOMALY NOS	200
746.4	CONG AORTA VALV INSUFFIC	177
424.9	ENDOCARDITIS NOS	167
423.8	PERICARDIAL DISEASE NEC	131
421	AC/SUBAC BACT ENDOCARD	124
37.34	OTH HEART LES EXCISION	122
35.22	REPLACE AORTIC VALVE NEC	119
425.1	HYPERTR OBSTR CARDIOMYOP	119
420.9	ACUTE PERICARDITIS NOS	117
424.3	PULMONARY VALVE DISORDER	110
V42.1	HEART TRANSPLANT STATUS	103
V42.6	LUNG TRANSPLANT STATUS	98
996.83	COMPL HEART TRANSPLANT	89
425.11	Hypertrophic obstructive cardiomyopathy	82
746.89	CONG HEART ANOMALY NEC	74
425.18	Other hypertrophic cardiomyopathy	64
996.84	COMPL LUNG TRANSPLANT	64
421.9	AC/SUBAC ENDOCARDIT NOS	52
745.8	SEPTAL CLOSURE ANOM NEC	50
394	MITRAL STENOSIS	48
745.4	VENTRICULAR SEPT DEFECT	45
746.3	CONG AORTA VALV STENOSIS	44
423.3	CARDIAC TAMPONADE	44
35.12	OPN MITRAL VALVULOPLASTY	41
33.52	BILAT LUNG TRANSPLANT	38
35.21	REPLACE AORT VALV-TISSUE	33
37.33	OP HEART LES EXCISN NEC	33
35.71	ATRIA SEPTA DEF REP NEC	31
35.24	REPLACE MITRAL VALVE NEC	31
420.99	ACUTE PERICARDITIS NEC	31
423.2	CONSTRUCTIV PERICARDITIS	31
747.3	PULMONARY ARTERY ANOM	28
747.1	COARCTATION OF AORTA	26
429	MYOCARDITIS NOS	25
746.02	CONG PULMON VALVE STENOS	25
420.91	AC IDIOPATH PERICARDITIS	23
394.2	MITRAL STENOSIS W INSUFF	23
429.83	TAKOTSUBO SYNDROME	23
37.12	PERICARDIOTOMY	22
35.52	PROS REPAIR ATRIA DEF-CL	21

746.6	CONG MITRAL INSUFFICIENC	20
395	RHEUMAT AORTIC STENOSIS	20
747.22	AORTIC ATRESIA/STENOSIS	18
747.21	ANOMALIES OF AORTIC ARCH	18
420	AC PERICARDIT IN OTH DIS	18
212.7	BENIGN NEOPLASM HEART	17
421.1	AC ENDOCARDIT IN OTH DIS	17
745.9	SEPTAL CLOSURE ANOM NOS	17
37.51	HEART TRANSPLANTATION	15
747.49	GREAT VEIN ANOMALY NEC	15
35	HEART VALVES & SEPTA OPS	13
745.2	TETRALOGY OF FALLOT	13
747.42	PART ANOM PULM VEN CONN	13
391.1	ACUTE RHEUMATIC ENDOCARD	12
746.81	CONG SUBAORTIC STENOSIS	11
746.2	EBSTEIN'S ANOMALY	11
37.5	HEART TRANSPLANTATION	11
747	PATENT DUCTUS ARTERIOSUS	11
35.61	GRAFT REPAIR ATRIAL DEF	10
745.61	OSTIUM PRIMUM DEFECT	10
35.23	REPLACE MITR VALV-TISSUE	9
746.09	PULMONARY VALVE ANOM NEC	9
420	ACUTE PERICARDITIS	9
35.96	PERCUTAN VALVULOPLASTY	9
397.9	RHEUM ENDOCARDITIS NOS	8
35.11	OPN AORTIC VALVULOPLASTY	8
424.91	ENDOCARDITIS IN OTH DIS	8
747.29	CONG ANOM OF AORTA NEC	7
422.91	IDIOPATHIC MYOCARDITIS	7
745.69	ENDOCARD CUSHION DEF NEC	7
674.54	CARDIOMYOPATH POSTPARTUM	7
424.9	ENDOCARDITIS NOS	7
35.25	REPLACE PULM VALV-TISSUE	7
747	OTH CONG CIRC SYST ANOM	6
422.9	ACUTE MYOCARDITIS NOS	6
746.1	CONG TRICUSP ATRES/STEN	6
745.6	ENDOCARD CUSHION DEF NOS	6
424.99	ENDOCARDITIS NEC	6
35.26	REPLACE PULMON VALVE NEC	6
746.01	CONG PULMON VALV ATRESIA	5
390	RHEUM FEV W/O HRT INVOLV	5
35.28	REPLACE TRICUSP VALV NEC	5
425.3	ENDOCARD FIBROELASTOSIS	5
35.91	INTERAT VEN RETRN TRANSP	4
746.87	MALPOSITION OF HEART	4
746.5	CONGEN MITRAL STENOSIS	4
33.51	UNILAT LUNG TRANSPLANT	4
745.11	DOUBLE OUTLET RT VENTRIC	4
35.32	CHORDAE TENDINEAE OPS	4
423.1	ADHESIVE PERICARDITIS	4

747.4	GREAT VEIN ANOMALY NOS	4
747.39	Other anomalies of pulmonary artery and pulmonary	4
747.2	CONG ANOM OF AORTA NOS	3
747.1	COARCTATION OF AORTA	3
746	PULMONARY VALVE ANOM NOS	3
745.3	COMMON VENTRICLE	3
745.12	CORRECT TRANSPOS GRT VES	3
745.1	COMPL TRANSPOS GREAT VES	3
745	COMMON TRUNCUS	3
35.27	REPLACE TRIC VALV-TISSUE	3
V43.2	HEART REPLACEMENT NEC	3
35.94	CONDUIT ATRIUM-PULM ART	3
747.31	Pulmonary artery coarctation and atresia	2
35.92	CONDUIT RT VENT-PUL ART	2
422	ACUTE MYOCARDITIS	2
747.32	Pulmonary arteriovenous malformation	2
35.72	VENTR SEPTA DEF REP NEC	2
746.82	COR TRIARIATUM	2
746.8	CONG HEART ANOMALY NEC	2
35.7	HEART SEPTA REPAIR NOS	2
746	OTHER CONGEN HEART ANOM	2
745.6	ENDOCARD CUSHION DEFECTS	2
35.42	CREATE SEPTAL DEFECT	2
425.2	OBSC AFRIC CARDIOMYOPATH	2
115.94	HISTOPLASMOSIS ENDOCARD	2
112.81	CANDIDAL ENDOCARDITIS	2
747.41	TOT ANOM PULM VEN CONNEC	2
422.99	ACUTE MYOCARDITIS NEC	1
35.82	TOTAL REPAIR OF TAPVC	1
422	AC MYOCARDIT IN OTH DIS	1
33.6	HEART-LUNG TRANSPLANT	1
746.86	CONGENITAL HEART BLOCK	1
746.84	OBSTRUCT HEART ANOM NEC	1
746.83	INFUNDIB PULMON STENOSIS	1
421	AC/SUBAC ENDOCARDITIS	1
746	PULMONARY VALVE ANOMALY	1
35.51	PROS REP ATRIAL DEF-OPN	1
391.2	AC RHEUMATIC MYOCARDITIS	1
35.34	INFUNDIBULECTOMY	1
391	ACUTE RHEUMATIC PERICARD	1
674.5	PERIPARTUM CM, UNSPEC	1
35.06	Transapical replacement of aortic valve	1
33.49	LUNG REPAIR NEC	1
35.98	OTHER HEART SEPTA OPS	1
35.95	HEART REPAIR REVISION	1

Supplementary table 3. Percentage of measurements available prior to the TTE for each continuous variable. Shown are the counts and percentages of individuals with a risk factor measured any time before the TTE (top) and within 14 or 30 days prior to the TTE (as described in the Methods).

Characteristic	Grade 0 n (%)	Grade 1 n (%)
All available measurements prior to TTE		
Blood pressures	4283 (93.4)	1601 (95.5)
Heart rate	4087 (89.1)	1521 (90.8)
BMI	3758 (81.9)	1391 (83.0)
Creatine level	3345 (72.9)	1337 (79.8)
Serum glucose	3418 (74.5)	1349 (80.5)
Measures near time of TTE (as described in methods)		
Blood pressures	3534 (77.0)	1347 (80.4)
Heart rate	3202 (69.8)	1213 (72.4)
BMI	3225 (70.3)	1200 (71.6)
Creatine level	2328 (50.8)	1015 (60.6)
Serum glucose	2453 (53.5)	1055 (62.9)

Supplementary table 4. Prevalence of grade 1 DD by year of TTE and age groups.
The values in the cells are the percentage of individuals with grade 1 DD.

	Number of stage 1 DD cases	40-45 years	45-50 years	50-55 years
1997-2004	85	7	13.4	28.1
2005-2009	754	16.7	22.9	40.8
2010-2015	888	14.6	23.8	37.5

Supplementary table 5. Clinical diagnosis present before the TTE associated with DD stage 1 versus normal diastolic function. Association testing used a logistic regression analysis adjusting for age, gender, self-reported race and setting. Shown are all diagnoses with FDR $q < 0.01$.

PheWAS code	Diagnosis	Cases	Controls	Odds-ratio	95% CI	p-value	FDR q-value
401	Hypertension	2795	3142	2.02	(1.78-2.28)	5.3E-29	2.2E-26
401.1	Essential hypertension	2732	3205	1.93	(1.71-2.18)	6.3E-26	1.3E-23
250.2	Type 2 diabetes	882	5055	1.96	(1.68-2.29)	2.1E-17	2.8E-15
250	Diabetes mellitus	1096	4841	1.81	(1.57-2.10)	8.2E-16	8.3E-14
401.2	Hypertensive heart and/or renal disease	309	5628	2.51	(1.98-3.20)	6.2E-14	5.0E-12
585.3	Chronic renal failure [CKD]	272	5665	2.55	(1.97-3.29)	8.2E-13	4.8E-11
585.32	End stage renal disease	114	5823	4.27	(2.87-6.36)	8.2E-13	4.8E-11
278.1	Obesity	879	5058	1.76	(1.51-2.06)	1.7E-12	8.4E-11
428	Congestive heart failure; nonhypertensive	420	5517	2.00	(1.62-2.46)	1.1E-10	5.2E-09
250.22	Type 2 diabetes with renal manifestations	125	5812	3.42	(2.35-4.97)	1.3E-10	5.2E-09
401.22	Hypertensive chronic kidney disease	178	5759	2.79	(2.04-3.82)	1.5E-10	5.6E-09
428.1	Congestive heart failure (CHF) NOS	361	5576	2.02	(1.62-2.53)	7.7E-10	2.6E-08
278	Overweight, obesity and other hyperalimentation	1050	4887	1.57	(1.35-1.83)	2.6E-09	8.2E-08
585	Renal failure	537	5400	1.80	(1.48-2.19)	3.0E-09	8.8E-08
427.9	Palpitations	1254	4683	0.63	(0.53-0.74)	2.9E-08	7.8E-07
250.24	Type 2 diabetes with neurological manifestations	159	5778	2.42	(1.74-3.36)	1.3E-07	3.3E-06
278.11	Morbid obesity	428	5509	1.71	(1.38-2.11)	9.1E-07	2.2E-05
401.3	Other hypertensive complications	231	5706	1.87	(1.42-2.47)	9.7E-06	2.2E-04
250.1	Type 1 diabetes	246	5691	1.83	(1.40-2.40)	1.1E-05	2.3E-04
276.13	Hyperpotassemia	197	5740	1.96	(1.45-2.64)	1.1E-05	2.3E-04
272	Disorders of lipid metabolism	1822	4115	1.31	(1.15-1.49)	2.9E-05	5.6E-04
530.11	GERD	965	4972	1.38	(1.18-1.61)	4.1E-05	7.6E-04
272.1	Hyperlipidemia	1816	4121	1.29	(1.14-1.47)	6.3E-05	0.001
327.32	Obstructive sleep apnea	379	5558	1.57	(1.25-1.96)	8.0E-05	0.001
272.13	Mixed hyperlipidemia	517	5420	1.47	(1.21-1.79)	1.1E-04	0.002
250.6	Polyneuropathy in diabetes	101	5836	2.23	(1.48-3.36)	1.2E-04	0.002
427.7	Tachycardia NOS	564	5373	1.46	(1.20-1.77)	1.2E-04	0.002
433	Cerebrovascular disease	566	5371	1.45	(1.20-1.76)	1.2E-04	0.002
327.3	Sleep apnea	531	5406	1.46	(1.20-1.78)	1.3E-04	0.002
401.21	Hypertensive heart disease	136	5801	1.99	(1.40-2.84)	1.4E-04	0.002
530.1	Esophagitis, GERD and related diseases	1013	4924	1.34	(1.15-1.56)	1.5E-04	0.002
512.9	Other dyspnea	1011	4926	1.34	(1.15-1.56)	1.6E-04	0.002
433.21	Cerebral artery occlusion, with cerebral infarction	216	5721	1.72	(1.29-2.29)	2.4E-04	0.003
512.7	Shortness of breath	1622	4315	1.28	(1.12-1.45)	2.5E-04	0.003
509	Respiratory failure, insufficiency, arrest	489	5448	1.47	(1.20-1.82)	2.6E-04	0.003
276.1	Electrolyte imbalance	819	5118	1.37	(1.16-1.62)	2.7E-04	0.003
433.2	Occlusion of cerebral arteries	225	5712	1.69	(1.28-2.25)	2.7E-04	0.003
276	Disorders of fluid, electrolyte, and acid-base balance	1100	4837	1.33	(1.14-1.55)	3.4E-04	0.004
250.3	Insulin pump user	187	5750	1.75	(1.29-2.39)	3.4E-04	0.004
509.1	Respiratory failure	339	5598	1.53	(1.20-1.95)	5.2E-04	0.005
427	Cardiac dysrhythmias	2096	3841	0.80	(0.71-0.91)	5.9E-04	0.006
782.3	Edema	677	5260	1.36	(1.14-1.63)	6.1E-04	0.006
512	Other symptoms of respiratory system	2597	3340	1.23	(1.09-1.38)	8.1E-04	0.008
550	Abdominal hernia	293	5644	1.53	(1.19-1.97)	9.3E-04	0.009

Supplementary table 6. Clinical diagnosis associated with DD stage 1 versus normal diastolic function. This reduced subset comprises those diagnoses selected using a multivariable selection model incorporating diagnoses associated with DD at FDR $q < 0.01$.

Diagnosis	Odds-ratio	95% CI	p-value
Hypertension	1.66	(1.45 - 1.89)	6.7E-14
Cardiac dysrhythmias	0.62	(0.53 - 0.72)	1.1E-09
End stage renal disease	3.29	(2.19 - 4.96)	1.2E-08
Tachycardia NOS	1.74	(1.38 - 2.19)	2.9E-06
Congestive heart failure; nonhypertensive	1.54	(1.24 - 1.93)	1.2E-04
Type 2 diabetes	1.37	(1.16 - 1.62)	2.2E-04
Obesity	1.28	(1.08 - 1.52)	4.1E-03
Cerebral artery occlusion, with cerebral infarction	1.5	(1.12 - 2.02)	6.9E-03
GERD	1.18	(1 - 1.38)	0.048

Supplementary table 7. Risk factor levels, by DD status, using all available data prior to the TTE for each risk factor.

Values are mean (standard deviation) except for creatinine and glucose which are median (interquartile range). P-values are from a linear regression model adjusting for age, gender, self-reported race and setting. Log-transformed values were analyzed for creatinine and glucose.

Characteristic	Stage 0	Stage 1	p-value
Systolic blood pressure (mmHg)	123 (17)	130 (19)	<.0001
Diastolic blood pressure (mmHg)	75 (11)	79 (12)	<.0001
Heart rate (bpm)	78 (16)	85 (16)	<.0001
BMI (kg/m ²)	30.3 (7.8)	33.3 (8.5)	<.0001
Creatinine level (mg/dl) (median [IQR])	0.85 (0.7 - 1.00)	0.90 (0.75 - 1.13)	<.0001
Serum glucose (mg/dl) (median [IQR])	96 (87 - 111)	103 (92 - 130)	<.0001

Supplementary table 8. Incident clinical diagnosis associated with DD stage 1 versus normal diastolic function. Subjects assigned a diagnosis prior to the echocardiogram were excluded from the analysis of that diagnosis. Association testing used a logistic regression analysis adjusting for age, gender, self-reported race and setting. Shown are all diagnoses with a FDR $q < 0.01$.

PheWAS code	Diagnosis	Cases	Controls	Odds-ratio	95% CI	p-value	FDR q-value
428	Congestive heart failure; nonhypertensive	424	5278	2.85	(2.32-3.51)	6.8E-23	3.1E-20
428.4	Heart failure with preserved EF [Diastolic heart failure]	199	5859	4.63	(3.39-6.32)	6.3E-22	1.4E-19
401.1	Essential hypertension	1054	2344	2.17	(1.83-2.57)	4.9E-19	7.4E-17
401	Hypertension	1044	2285	2.09	(1.76-2.48)	6.0E-17	6.8E-15
428.1	Congestive heart failure (CHF) NOS	345	5418	2.57	(2.04-3.23)	6.3E-16	5.7E-14
401.2	Hypertensive heart and/or renal disease	355	5435	2.24	(1.79-2.80)	2.1E-12	1.4E-10
416	Cardiomegaly	532	5335	1.96	(1.62-2.36)	2.1E-12	1.4E-10
278.1	Obesity	556	4686	1.89	(1.56-2.29)	4.5E-11	2.6E-09
401.21	Hypertensive heart disease	201	5801	2.40	(1.79-3.22)	4.8E-09	2.3E-07
428.2	Heart failure NOS	128	5951	3.02	(2.08-4.37)	5.1E-09	2.3E-07
411.4	Coronary atherosclerosis	511	4822	1.78	(1.46-2.16)	5.8E-09	2.4E-07
278	Overweight, obesity and other hyperalimentation	647	4420	1.70	(1.42-2.03)	1.0E-08	3.8E-07
411	Ischemic Heart Disease	665	4388	1.64	(1.38-1.96)	3.6E-08	1.2E-06
250.2	Type 2 diabetes	474	4741	1.76	(1.44-2.15)	4.3E-08	1.4E-06
250	Diabetes mellitus	765	4228	1.56	(1.32-1.84)	2.2E-07	6.7E-06
425	Cardiomyopathy	154	5857	2.41	(1.73-3.37)	2.4E-07	6.8E-06
250.24	Type 2 diabetes with neurological manifestations	227	5758	2.00	(1.52-2.64)	8.4E-07	2.2E-05
327.3	Sleep apnea	558	5037	1.58	(1.31-1.91)	2.3E-06	5.8E-05
401.22	Hypertensive chronic kidney disease	210	5732	1.99	(1.49-2.65)	2.8E-06	6.8E-05
411.8	Other chronic ischemic heart disease, unspecified	226	5785	1.93	(1.46-2.54)	3.7E-06	8.2E-05
272.1	Hyperlipidemia	1066	3250	1.44	(1.24-1.69)	3.8E-06	8.2E-05
414	Other forms of chronic heart disease	313	5640	1.76	(1.38-2.23)	4.2E-06	8.6E-05
292	Neurological disorders	444	5309	1.61	(1.31-1.98)	5.7E-06	1.1E-04
327.32	Obstructive sleep apnea	554	5207	1.55	(1.28-1.87)	6.0E-06	1.1E-04
272	Disorders of lipid metabolism	1064	3246	1.43	(1.22-1.67)	7.3E-06	1.3E-04
276	Disorders of fluid, electrolyte, and acid-base balance	773	4222	1.46	(1.24-1.73)	8.4E-06	1.4E-04
580	Nephritis; nephrosis; renal sclerosis	116	5892	2.40	(1.63-3.53)	8.5E-06	1.4E-04
276.14	Hypopotassemia	426	5193	1.60	(1.30-1.98)	1.0E-05	1.7E-04
250.6	Polyneuropathy in diabetes	183	5860	1.99	(1.46-2.70)	1.1E-05	1.7E-04
428.3	Heart failure with reduced EF [Systolic or combined heart failure]	116	5972	2.35	(1.60-3.45)	1.2E-05	1.8E-04
272.13	Mixed hyperlipidemia	691	4913	1.46	(1.23-1.73)	2.0E-05	2.9E-04
327	Sleep disorders	843	4563	1.42	(1.20-1.66)	2.5E-05	3.5E-04
278.11	Morbid obesity	350	5355	1.63	(1.29-2.06)	3.5E-05	4.8E-04
585	Renal failure	455	5106	1.53	(1.25-1.88)	3.9E-05	5.1E-04
627	Menopausal and postmenopausal disorders	418	5365	0.57	(0.44-0.75)	4.1E-05	5.3E-04
401.3	Other hypertensive complications	178	5712	1.91	(1.40-2.62)	4.7E-05	6.0E-04
250.22	Type 2 diabetes with renal manifestations	123	5893	2.15	(1.48-3.12)	5.4E-05	6.5E-04
395.2	Nonrheumatic aortic valve disorders	173	5846	1.90	(1.38-2.60)	7.0E-05	8.3E-04
512.7	Shortness of breath	1092	3474	1.36	(1.17-1.58)	7.2E-05	8.4E-04
425.1	Primary/intrinsic cardiomyopathies	127	5914	2.10	(1.45-3.03)	7.7E-05	8.5E-04
356	Hereditary and idiopathic peripheral neuropathy	205	5769	1.81	(1.35-2.42)	7.7E-05	8.5E-04
411.2	Myocardial infarction	260	5473	1.69	(1.30-2.19)	9.4E-05	0.001
585.3	Chronic renal failure [CKD]	273	5571	1.65	(1.28-2.13)	1.2E-04	0.001
585.1	Acute renal failure	382	5366	1.51	(1.21-1.88)	2.3E-04	0.002
276.6	Fluid overload	276	5694	1.61	(1.25-2.08)	2.4E-04	0.002
415.21	Primary pulmonary hypertension	116	5974	2.06	(1.40-3.03)	2.5E-04	0.002
573.2	Liver replaced by transplant	136	5990	0.45	(0.29-0.70)	3.4E-04	0.003
288.2	Elevated white blood cell count	315	5597	1.55	(1.22-1.97)	3.6E-04	0.003
433.8	Late effects of cerebrovascular disease	158	5888	1.81	(1.30-2.52)	4.0E-04	0.004
250.3	Insulin pump user	243	5707	1.62	(1.24-2.13)	4.4E-04	0.004
458	Hypotension	476	5281	1.43	(1.17-1.75)	5.1E-04	0.005
452	Other venous embolism and thrombosis	220	5661	1.65	(1.24-2.19)	5.5E-04	0.005
300.4	Dysthymic disorder	163	5821	1.79	(1.29-2.50)	5.7E-04	0.005
743.11	Osteoporosis NOS	201	5818	0.55	(0.39-0.78)	8.6E-04	0.007
276.1	Electrolyte imbalance	632	4657	1.36	(1.13-1.62)	9.3E-04	0.008
292.1	Aphasia/speech disturbance	106	5907	1.97	(1.32-2.94)	9.3E-04	0.008
512	Other symptoms of respiratory system	1349	2226	1.29	(1.11-1.51)	9.6E-04	0.008
250.1	Type 1 diabetes	155	5729	1.75	(1.26-2.44)	9.7E-04	0.008
338.2	Chronic pain	303	5708	1.51	(1.18-1.94)	1.0E-03	0.008
586	Other disorders of the kidney and ureters	363	5444	1.45	(1.16-1.82)	1.2E-03	0.009

Supplementary table 9. Characteristics of subjects with second a echocardiogram.
 Characteristics are grouped by the diastolic function staging at the first and second echo.

Characteristic	No change (stage 0 for both)	Progression (Normal to stage 1)	No change (stage 1 for both)	Regression (Stage 1 to stage 0)
n	291	101	119	61
Gender				
Male	129 (44.3%)	51 (50.5%)	54 (45.4%)	27 (44.3%)
Female	162 (55.7%)	50 (49.5%)	65 (54.6%)	34 (55.7%)
Age				
mean (s.d.)				
40-45	90 (30.9%)	22 (21.8%)	19 (16.0%)	16 (26.2%)
45-50	109 (37.5%)	30 (29.7%)	38 (31.9%)	22 (36.1%)
50-55	92 (31.6%)	49 (48.5%)	62 (52.1%)	23 (37.7%)
Race				
W	238 (81.8%)	79 (78.2%)	98 (82.4%)	50 (82%)
B	44 (15.1%)	21 (20.8%)	17 (14.3%)	11 (18.0%)
U	9 (3.1%)	1 (1.0%)	4 (3.4%)	0 (0%)
Years between echoes [Mean (s.d.)]				
	2.1 (1.7)	3.4 (2.6)	2.5 (2.0)	1.9 (1.8)
Years between echoes Median (IQR)]				
	1.6 (1.0 - 2.9)	3.0 (1.2 - 4.9)	1.8 (1.0 - 3.7)	1.5 (0.8 - 2.6)

Supplementary table 10. Association of continuous variables with progression and regression of DD stage between the first and second echocardiogram. The average change is the beta coefficient from a multivariable regression model where the difference in the continuous variable between the second and first echocardiogram was the dependent variable and either progressor (Yes vs. no) or regressor (Yes vs. no) was the independent variable. All models were adjusted for age, gender, self-reported race and time duration between echocardiograms.

Creatine and glucose levels were log-transformed.

Characteristic	Number subjects with measurements	Average change	95% CI	p-value
Comparison of progressors (stage 0 to stage 1) versus no change from normal (stage 0 in both)				
Systolic blood pressure (mmHg)	328	4.2	(0.4 - 8.0)	0.03
Diastolic blood pressure (mmHg)	328	2.4	(-0.3 - 5.2)	0.08
Heart rate (bpm)	298	8.3	(4.2 - 12.4)	0.0001
BMI (kg/m ²)	315	1.4	(-0.7 - 3.4)	0.19
Creatinine level (mg/dl) (median [IQR])	202	0.04	(0.00 - 0.09)	0.06
Serum glucose (mg/dl) (median [IQR])	218	0.04	(-0.02 - 0.10)	0.21
Comparison of regressors (stage 1 to stage 0) versus no change from stage 1 (stage 1 in both)				
Systolic blood pressure (mmHg)	157	-8.4	(-14.7 - -2.0)	0.01
Diastolic blood pressure (mmHg)	157	-6.5	(-10.5 - -2.5)	0.002
Heart rate (bpm)	145	-0.1	(-5.8 - 5.6)	0.97
BMI (kg/m ²)	145	-2.0	(-4.8 - 0.8)	0.15
Creatinine level (mg/dl) (median [IQR])	98	-0.05	(-0.12 - 0.02)	0.19
Serum glucose (mg/dl) (median [IQR])	106	-0.05	(-0.16 - 0.05)	0.33

Supplementary table 11. Repeat of association analyses for continuous variables with progression and regression of DD stage between the first and second echocardiogram, restricting the analyses to individuals with >1.5 years between TTEs.

Creatine and glucose levels were log-transformed.

Characteristic	Number subjects with measurements	Average change	95% CI	p-value
Comparison of progressors (stage 0 to stage 1) versus no change from normal (stage 0 in both)				
Systolic blood pressure (mmHg)	179	2.8	(-2.4 - 7.9)	0.30
Diastolic blood pressure (mmHg)	179	1.8	(-1.9 - 5.5)	0.34
Heart rate (bpm)	171	6.0	(0.6 - 11.3)	0.03
BMI (kg/m ²)	177	0.6	(-2.0 - 3.3)	0.63
Creatinine level (mg/dl) (median [IQR])	105	0.02	(-0.05 - 0.08)	0.67
Serum glucose (mg/dl) (median [IQR])	117	-0.02	(-0.08 - 0.05)	0.62
Comparison of regressors (stage 1 to stage 0) versus no change from stage 1 (stage 1 in both)				
Systolic blood pressure (mmHg)	84	-12.1	(-20.8 - -3.5)	0.0075
Diastolic blood pressure (mmHg)	84	-11.0	(-16.2 - -5.7)	0.0001
Heart rate (bpm)	79	1.0	(-6.9 - 9.0)	0.80
BMI (kg/m ²)	80	-3.9	(-7.9 - 0.0)	0.06
Creatinine level (mg/dl) (median [IQR])	59	-0.09	(-0.19 - 0.02)	0.13
Serum glucose (mg/dl) (median [IQR])	51	0.05	(-0.07 - 0.16)	0.43