Table S1. Details of included diseases; International Classification of Diseases 10th revision (ICD-10) codes included from inpatient hospital records

	ICD-10 Codes
Coronary artery disease	I20–I25
Atrial fibrillation	I48
Stroke	G45-G46; I61; I63
Hypertension	I10-I15
Diabetes (Type 2)	E11
Chronic kidney disease	N18; N183; N184; N185; Y841
Depression	F32; F33; F34.1
Dementia	F00; F01; F02; F03; G30
Asthma	J45-J46
Chronic obstructive pulmonary disease	J42-J44
Osteoporosis	M80; M81; M811; M812; M813; M814; M815; M816; M818; M819
Osteoarthritis	M15.0; M15.1; M15.2; M15.9; M16.0; M16.1; M17.0; M17.1; M18.0; M18.1; M19.0
Liver disease	K70-K77
Delirium	F05
Pneumonia	J13; J14; J15; J16; J17; J18
Falls/Fragility fractures	W00; W01; W04; W05; W06; W07; W08; W10; W17; W18; W19; R296 S220; S32; S325; S328; S422-S424; S524; S525; S720-S722; S582; S5823; T08

Table S2. Models for COVID-19 inpatient test positivity and COVID-19 related mortality with inpatient test-confirmed COVID-19: M6 and M7

	M6: age at the pandemic (3/16/2020) + pre-existing diseases or conditions to March 2020 + PhenoAgeAccel at baseline		M7: age at the pandemic (3/16/2020) + pre-existing diseases or conditions to March 2020 + PhenoAge biomarkers	
	Positive (n=613) vs. untested or negative (n=338,672)	Positive dead vs. positive alive, untested or negative (n=338,108)	Positive (n=613) vs. untested or negative (n=338,672)	Positive dead vs. positive alive, untested or negative (n=338,108)
Sex[1] (=Male)	**1.37 (1.16, 1.62)** p=2.0e-04	**1.66 (1.17, 2.37)** p=4.6e-03	**1.46 (1.20, 1.79)** p=2.2e-04	**2.12 (1.41, 3.2)** p=3.2e-04
Ethnicity[2] Black	**2.56 (1.69, 3.86)** p=8.1e-06	2.34 (0.98, 5.59) p=0.055	**2.23 (1.44, 3.44)** p=3e-04	**2.65 (1.08, 6.54)** p=0.034
Other (incl. Asian, Chinese, and Mixed)	**1.82 (1.31, 2.52)** p=3.3e-04	1.42 (0.67, 3.02) p=0.37	**1.67 (1.2, 2.34)** p=2.6e-03	1.45 (0.67, 3.13) p=0.34
Age at the pandemic (per 5 years)	0.95 (0.90, 1.01) p=0.09	**1.48 (1.28, 1.71)** p=1.7e-07	**0.94 (0.88, 0.99)** p=2.2e-02	**1.45 (1.25, 1.68)** p=1e-06
PhenoAgeAccel (per 5 years)	**1.10 (1.02, 1.19)** p=0.016	**1.21 (1.04, 1.40)** p=0.011		
Albumin			**0.87 (0.80, 0.94)** p=5.9e-4	0.88 (0.75, 1.04) p=0.12
Creatinine			1.04 (0.95, 1.14) p=0.43	0.87 (0.73, 1.04) p=0.12
Glucose			0.98 (0.91, 1.05) p=0.55	1.03 (0.92, 1.16) p=0.61
log(CRP)			**1.10 (1.01, 1.20)** p=0.037	1.12 (0.94, 1.34) p=0.21
Lymphocyte percent			1.05 (0.97, 1.14) p=0.26	0.96 (0.82, 1.14) p=0.66
Mean corpuscular volume			0.97 (0.89, 1.05) p=0.40	1.12 (0.95, 1.31) p=0.17
RDW			1.01 (0.93, 1.09) p=0.83	1.13 (0.97, 1.31) p=0.11
Alkaline phosphatase			1.04 (0.96, 1.13) p=0.31	1.07 (0.91, 1.26) p=0.39
White blood cell count			1.02 (0.97, 1.07) p=0.46	1.02 (0.93, 1.12) p=0.65
Dementia (n_1=60; n_2=31)	**5.62 (4.04, 7.82)** p=1.2e-24	**7.35 (4.46, 12.11)** p=4.7e-15	**5.80 (4.17, 8.06)** p=1.9e-25	**7.46 (4.53, 12.29)** p=2.7e-15
Type II diabetes (n_1=131; n_2=52)	**1.54 (1.23, 1.93)** p=2.1e-04	**1.80 (1.21, 2.67)** p=3.7e-03	**1.61 (1.27, 2.06)** p=1.1e-04	**1.88 (1.23, 2.88)** p=3.8e-03
History of pneumonia (n_1=112; n_2=41)	**2.24 (1.76, 2.84)** p=3.9e-11	**2.20 (1.43, 3.39)** p=3.3e-04	**2.19 (1.73, 2.79)** p=1.3e-10	**2.11 (1.37, 3.25)** p=7.3e-04
Depression (n_1=104; n_2=31)	**1.37 (1.09, 1.72)** p=6.1e-03	1.50 (0.97, 2.32) p=0.068	**1.35 (1.07, 1.69)** p=9.8e-03	1.46 (0.95, 2.26) p=0.086
Atrial fibrillation (n_1=99; n_2=36)	**1.46 (1.14, 1.87)** p=2.7e-03	1.27 (0.83, 1.95) p=0.26	**1.46 (1.14, 1.87)** p=2.8e-03	1.26 (0.82, 1.92) p=0.29
Hypertension (n_1=352; n_2=118)	**1.44 (1.19, 1.74)** p=1.3e-04	**2.15 (1.41, 3.28)** p=3.5e-04	**1.43 (1.19, 1.73)** p=1.9e-04	**2.16 (1.42, 3.29)** p=3.4e-04
COPD (n_1=71; n_2=29)	1.18 (0.89, 1.57) p=0.24	**1.61 (1.01, 2.57)** p=0.047	1.17 (0.88, 1.55) p=0.29	**1.54 (0.97, 2.47)** p=0.069
Chronic kidney disease (n_1=72; n_2=29)	**1.57 (1.18, 2.08)** p=1.7e-03	1.48 (0.93, 2.36) p=0.10	**1.56 (1.16, 2.10)** p=3.5e-03	**1.84 (1.12, 3.03)** p=0.016
Liver disease (n_1=36; n_2=6)	1.25 (0.87, 1.78) p=0.23	0.58 (0.24, 1.37) p=0.21	1.24 (0.87, 1.77) p=0.24	0.57 (0.24, 1.33) p=0.19

Rheumatoid Arthritis (n_1=26; n_2=12)	1.12 (0.74, 1.68) p=0.60	**1.46 (0.76, 2.82)** p=0.26	1.10 (0.73, 1.66) p=0.66	**1.39 (0.72, 2.67)** p=0.32
Coronary artery disease (n_1=133; n_2=47)	1.03 (0.82, 1.28) p=0.83	0.96 (0.65, 1.43) p=0.85	1.02 (0.81, 1.27) p=0.89	0.97 (0.65, 1.44) p=0.88
Delirium (n_1=40; n_2=19)	**1.79 (1.21, 2.66)** p=3.9e-03	**1.85 (1.01, 3.39)** p=0.045	**1.81 (1.22, 2.69)** p=3.2e-03	**1.89 (1.04, 3.44)** p=0.038
Stroke (n_1=30; n_2=11)	**1.39 (0.94, 2.06)** p=0.10	1.26 (0.66, 2.43) p=0.48	1.37 (0.93, 2.03) p=0.12	1.24 (0.64, 2.38) p=0.52
Asthma (n_1=117; n_2=24)	1.09 (0.88, 1.35) p=0.45	0.70 (0.44, 1.13) p=0.14	1.07 (0.87, 1.33) p=0.52	0.69 (0.43, 1.1) p=0.12
Previous falls/fragile fractures (n_1=140; n_2=48)	**1.85 (1.49, 2.31)** p=3.5e-08	**1.65 (1.09, 2.50)** p=0.018	**1.86 (1.49, 2.31)** p=3.2e-08	**1.6 (1.05, 2.42)** p=0.027
Osteoarthritis (n_1=80; n_2=28)	0.83 (0.65, 1.07) p=0.15	0.89 (0.58, 1.37) p=0.60	0.81 (0.64, 1.04) p=0.10	0.87 (0.56, 1.34) p=0.51

[1]reference: female; [2]reference: White; in bold if p<0.05; assessment center results skipped; n_1: number of inpatient positives between March 16 and April 27, 2020; n_2: number of COVID-19 related deaths following an inpatient positive result between March 16 and April 27, 2020

Table S3. Diagnostic values when the sensitivity is controlled at 0.6, or 0.8 for inpatient test positivity or COVID-19 mortality with inpatient test-confirmed COVID-19

Model	AUC	Threshold	SEN	SPEC	PPV	NPV
Inpatient test positivity						
M1	0.626	0.00179	0.602	0.587	0.00263	0.99877
M1	0.626	0.00128	0.809	0.333	0.00219	0.99896
M2	0.653	0.00180	0.613	0.622	0.00293	0.99888
M2	0.653	0.00128	0.806	0.389	0.00238	0.99910
M3	0.657	0.00172	0.615	0.622	0.00294	0.99888
M3	0.657	0.00125	0.806	0.395	0.00241	0.99911
M4	0.670	0.00178	0.612	0.652	0.00317	0.99892
M4	0.670	0.00122	0.808	0.399	0.00243	0.99913
M5	0.734	0.00183	0.607	0.753	0.00442	0.99906
M5	0.734	0.00116	0.801	0.480	0.00278	0.99925
M6	0.736	0.00183	0.600	0.753	0.00438	0.99904
M6	0.736	0.00115	0.806	0.480	0.00280	0.99927
M7	0.738	0.00185	0.600	0.753	0.00438	0.99904
M7	0.738	0.00111	0.804	0.470	0.00274	0.99925
COVID-19 related mortality with inpatient test-confirmed COVID-19						
M1	0.762	0.00066	0.603	0.786	0.00125	0.99977
M1	0.762	0.00033	0.808	0.594	0.00089	0.99986
M2	0.793	0.00065	0.603	0.803	0.00136	0.99978
M2	0.793	0.00035	0.815	0.652	0.00104	0.99987
M3	0.773	0.00055	0.609	0.769	0.00117	0.99977
M3	0.773	0.00030	0.808	0.608	0.00092	0.99986
M4	0.791	0.00063	0.603	0.813	0.00144	0.99978
M4	0.791	0.00032	0.801	0.652	0.00102	0.99986
M5	0.851	0.00090	0.609	0.914	0.00314	0.99981
M5	0.851	0.00035	0.808	0.745	0.00141	0.99989
M6	0.854	0.00083	0.623	0.904	0.00289	0.99981
M6	0.854	0.00036	0.808	0.753	0.00145	0.99989
M7	0.853	0.00084	0.616	0.905	0.00287	0.99981
M7	0.853	0.00034	0.808	0.743	0.00140	0.99988

M1: age at the pandemic; M2: age at the pandemic + PhenoAgeAccel at baseline; M3: age at the pandemic + pre-existing diseases or conditions at baseline; M4: age at the pandemic + pre-existing diseases or conditions at baseline + PhenoAgeAccel at baseline; M5: age at the pandemic + pre-existing diseases or conditions to March 2020; M6: age at the pandemic + pre-existing diseases or conditions to March 2020 + PhenoAgeAccel at baseline; M7: age at the pandemic + biomarkers in PhenoAge at baseline + pre-existing diseases or conditions to March 2020; Threshold: predicted probability threshold; SEN: sensitivity; SPEC: specificity; PPV: Positive Predictive Value; NPV: Negative Predictive Value

Table S4. Mediation analysis results for the mediation effects of incident diseases and comorbidities on the effect of accelerated aging (PhenoAgeAccel > 0) on test positivity restricted to inpatient positives

Mediator	Effect Decomposition	Estimate	2.5%	97.5%	P-Value
Comorbidities	ACME	1.1E-04	8.4E-05	0.0E+00	<2e-16
Comorbidities	ADE	4.0E-04	8.4E-05	0.0E+00	0.016
Comorbidities	Prop. Mediated	0.22	0.13	0.54	<2e-16
Asthma	ACME	1.3E-05	3.2E-06	0.0E+00	<2e-16
Asthma	ADE	5.9E-04	2.7E-04	0.0E+00	<2e-16
Asthma	Prop. Mediated	0.02	0.01	0.06	<2e-16
Atrial Fibrillation	ACME	1.2E-05	3.4E-06	0.0E+00	<2e-16
Atrial Fibrillation	ADE	5.9E-04	2.1E-04	0.0E+00	<2e-16
Atrial Fibrillation	Prop. Mediated	0.02	0.01	0.06	<2e-16
Chronic Kidney Disease	ACME	3.3E-05	8.8E-06	0.0E+00	<2e-16
Chronic Kidney Disease	ADE	5.8E-04	2.6E-04	0.0E+00	<2e-16
Chronic Kidney Disease	Prop. Mediated	0.05	0.01	0.13	<2e-16
COPD	ACME	2.3E-05	4.0E-06	0.0E+00	0.012
COPD	ADE	5.8E-04	2.5E-04	0.0E+00	0.004
COPD	Prop. Mediated	0.04	0.01	0.10	0.016
Coronary Artery Disease	ACME	1.0E-06	-6.1E-06	0.0E+00	0.92
Coronary Artery Disease	ADE	5.8E-04	2.2E-04	0.0E+00	<2e-16
Coronary Artery Disease	Prop. Mediated	7.2E-04	-1.6E-02	2.0E-02	0.92
Delirium	ACME	1.5E-05	3.5E-06	0.0E+00	<2e-16
Delirium	ADE	5.8E-04	2.2E-04	0.0E+00	<2e-16
Delirium	Prop. Mediated	0.02	0.01	0.08	<2e-16
Dementia	ACME	8.6E-07	-2.5E-05	0.0E+00	0.95
Dementia	ADE	5.9E-04	2.2E-04	0.0E+00	<2e-16
Dementia	Prop. Mediated	1.5E-03	-5.7E-02	5.0E-02	0.95
Depression	ACME	3.1E-06	-4.4E-06	0.0E+00	0.66
Depression	ADE	5.9E-04	2.3E-04	0.0E+00	<2e-16
Depression	Prop. Mediated	3.2E-03	-8.0E-03	4.0E-02	0.66
Falls or Fragility Fracture	ACME	1.3E-05	4.9E-06	0.0E+00	0.004
Falls or Fragility Fracture	ADE	5.7E-04	2.0E-04	0.0E+00	<2e-16
Falls or Fragility Fracture	Prop. Mediated	0.02	0.01	0.06	0.004
Hypertension	ACME	5.1E-05	2.8E-05	0.0E+00	<2e-16
Hypertension	ADE	5.3E-04	1.9E-04	0.0E+00	0.004
Hypertension	Prop. Mediated	0.09	0.04	0.22	<2e-16
Liver Disease	ACME	1.8E-05	3.6E-06	0.0E+00	<2e-16
Liver Disease	ADE	5.8E-04	2.4E-04	0.0E+00	<2e-16
Liver Disease	Prop. Mediated	0.03	0.01	0.08	<2e-16

Osteoarthritis	ACME	4.4E-06	-7.0E-06	0.0E+00	0.55
Osteoarthritis	ADE	8.4E-04	5.3E-04	0.0E+00	<2e-16
Osteoarthritis	Prop. Mediated	5.2E-03	-8.5E-03	2.0E-02	0.55
Pneumonia	ACME	4.6E-05	2.5E-05	0.0E+00	<2e-16
Pneumonia	ADE	5.5E-04	2.1E-04	0.0E+00	<2e-16
Pneumonia	Prop. Mediated	0.08	0.04	0.19	<2e-16
Rheumatoid Arthritis	ACME	8.3E-07	-2.7E-06	0.0E+00	0.8
Rheumatoid Arthritis	ADE	6.0E-04	2.6E-04	0.0E+00	<2e-16
Rheumatoid Arthritis	Prop. Mediated	-7.4E-04	-5.6E-03	2.0E-02	0.8
Stroke	ACME	9.3E-06	1.8E-06	0.0E+00	<2e-16
Stroke	ADE	5.7E-04	2.4E-04	0.0E+00	<2e-16
Stroke	Prop. Mediated	0.01	0.00	0.05	<2e-16
Type II Diabetes	ACME	7.5E-05	3.3E-05	0.0E+00	<2e-16
Type II Diabetes	ADE	5.0E-04	1.4E-04	0.0E+00	0.008
Type II Diabetes	Prop. Mediated	0.13	0.05	0.36	0.004

ACME: average causal mediation effects; ADE: average direct effects; Prop. Mediated: proportion mediated: ACME/total effect = ACME/(ACME + ADE)

Table S5. Mediation analysis results for the mediation effects of incident diseases and comorbidities on the effect of accelerated aging (PhenoAgeAccel > 0) on mortality with inpatient test-confirmed COVID-19

Mediator	Effect Decomposition	Estimate	2.5%	97.5%	P-Value
Comorbidities	ACME	3.6E-05	2.2E-05	0.0E+00	<2e-16
Comorbidities	ADE	1.6E-04	-1.8E-05	0.0E+00	0.08
Comorbidities	Prop. Mediated	0.18	0.07	1.03	0.028
Asthma	ACME	3.6E-06	-4.6E-07	0.0E+00	0.188
Asthma	ADE	2.3E-04	5.7E-05	0.0E+00	0.028
Asthma	Prop. Mediated	0.01	0.00	0.09	0.204
Atrial Fibrillation	ACME	2.5E-06	-1.2E-06	0.0E+00	0.284
Atrial Fibrillation	ADE	2.2E-04	3.6E-05	0.0E+00	0.028
Atrial Fibrillation	Prop. Mediated	7.3E-03	-5.9E-03	7.0E-02	0.312
Chronic Kidney Disease	ACME	7.9E-06	-2.4E-06	0.0E+00	0.272
Chronic Kidney Disease	ADE	2.3E-04	4.1E-05	0.0E+00	0.016
Chronic Kidney Disease	Prop. Mediated	0.02	-0.01	0.18	0.28
COPD	ACME	1.5E-05	1.8E-06	0.0E+00	0.016
COPD	ADE	2.2E-04	2.8E-05	0.0E+00	0.02
COPD	Prop. Mediated	0.06	0.01	0.38	0.024
Coronary Artery Disease	ACME	4.0E-07	-4.1E-06	0.0E+00	0.9
Coronary Artery Disease	ADE	2.2E-04	3.3E-05	0.0E+00	0.02
Coronary Artery Disease	Prop. Mediated	-1.0E-03	-4.6E-02	4.0E-02	0.92
Delirium	ACME	8.8E-06	6.3E-07	0.0E+00	0.028
Delirium	ADE	2.2E-04	2.0E-05	0.0E+00	0.04
Delirium	Prop. Mediated	0.03	0.00	0.16	0.056
Dementia	ACME	7.4E-07	-2.1E-05	0.0E+00	0.96
Dementia	ADE	2.4E-04	5.6E-05	0.0E+00	0.016
Dementia	Prop. Mediated	2.2E-03	-1.6E-01	1.2E-01	0.96
Depression	ACME	1.9E-06	-2.0E-06	0.0E+00	0.852
Depression	ADE	2.2E-04	1.9E-05	0.0E+00	0.024
Depression	Prop. Mediated	1.1E-03	-8.6E-03	1.4E-01	0.868
Falls or Fragility Fracture	ACME	7.1E-06	7.9E-07	0.0E+00	0.028
Falls or Fragility Fracture	ADE	2.1E-04	2.2E-05	0.0E+00	0.02
Falls or Fragility Fracture	Prop. Mediated	0.03	0.00	0.19	0.048
Hypertension	ACME	1.9E-05	5.7E-06	0.0E+00	<2e-16
Hypertension	ADE	2.0E-04	7.5E-06	0.0E+00	0.032
Hypertension	Prop. Mediated	0.08	0.02	0.46	0.024
Liver Disease	ACME	-2.0E-06	-3.1E-06	0.0E+00	<2e-16
Liver Disease	ADE	2.3E-04	5.4E-05	0.0E+00	0.008
Liver Disease	Prop. Mediated	-8.5E-03	-3.9E-02	0.0E+00	0.008

Osteoarthritis	ACME	1.9E-06	-7.5E-07	0.0E+00	0.408
Osteoarthritis	ADE	2.2E-04	2.2E-05	0.0E+00	0.036
Osteoarthritis	Prop. Mediated	4.9E-03	-4.8E-03	7.0E-02	0.428
Pneumonia	ACME	1.9E-05	6.4E-06	0.0E+00	<2e-16
Pneumonia	ADE	2.1E-04	3.0E-05	0.0E+00	0.008
Pneumonia	Prop. Mediated	0.08	0.03	0.41	0.008
Rheumatoid Arthritis	ACME	-6.3E-07	-1.3E-06	0.0E+00	0.008
Rheumatoid Arthritis	ADE	2.3E-04	5.0E-05	0.0E+00	0.004
Rheumatoid Arthritis	Prop. Mediated	-2.7E-03	-1.3E-02	0.0E+00	0.012
Stroke	ACME	4.3E-06	-1.8E-07	0.0E+00	0.08
Stroke	ADE	2.2E-04	4.7E-05	0.0E+00	0.02
Stroke	Prop. Mediated	0.01	0.00	0.12	0.1
Type II Diabetes	ACME	2.0E-05	1.3E-06	0.0E+00	0.02
Type II Diabetes	ADE	2.1E-04	-1.0E-05	0.0E+00	0.056
Type II Diabetes	Prop. Mediated	0.08	0.00	0.49	0.048

ACME: average causal mediation effects; ADE: average direct effects; Prop. Mediated: proportion mediated: ACME/total effect = ACME/(ACME + ADE)

Figure S1. Boxplots and violin plots of PhenoAge acceleration by sex, ethnicity, inpatient test positivity status, or status of COVID-19 related mortality with inpatient test-confirmed COVID-19
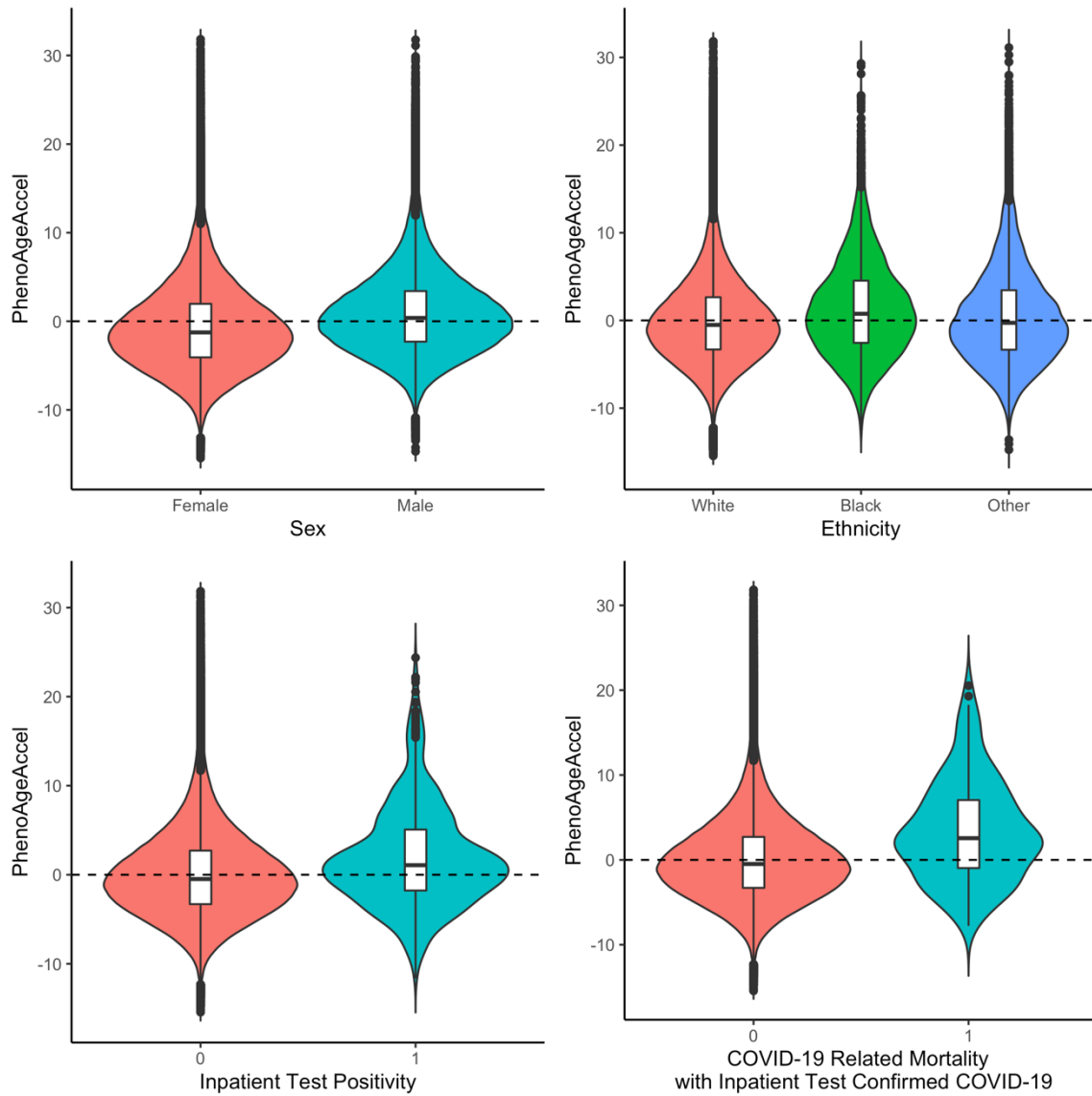
Figure S2. Boxplots and violin plots of PhenoAge acceleration by disease status updated to March 2020: delirium, dementia, depression, atrial fibrillation, delirium, hypertension
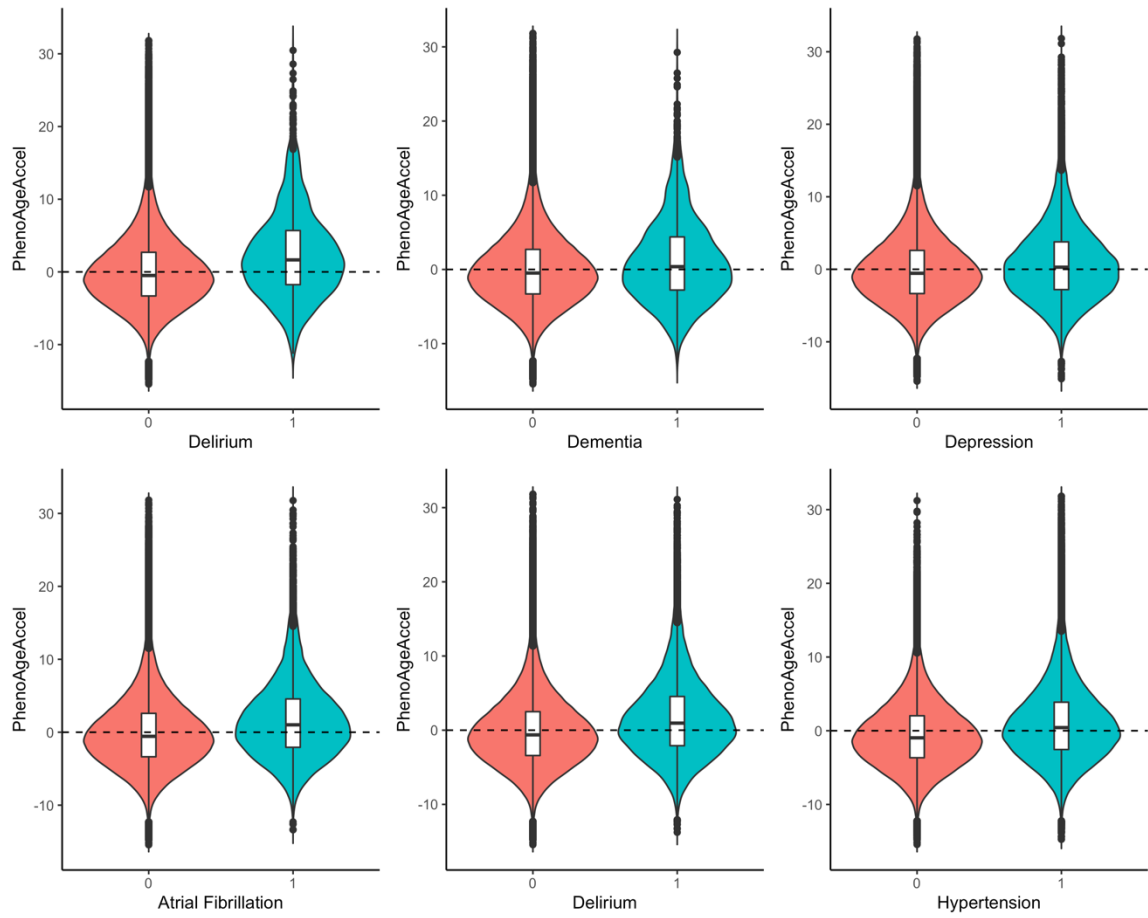
Figure S3. Boxplots and violin plots of PhenoAge acceleration by disease status updated to March 2020: stroke, type II diabetes, liver disease, osteoarthritis, rheumatoid Arthritis, chronic kidney disease
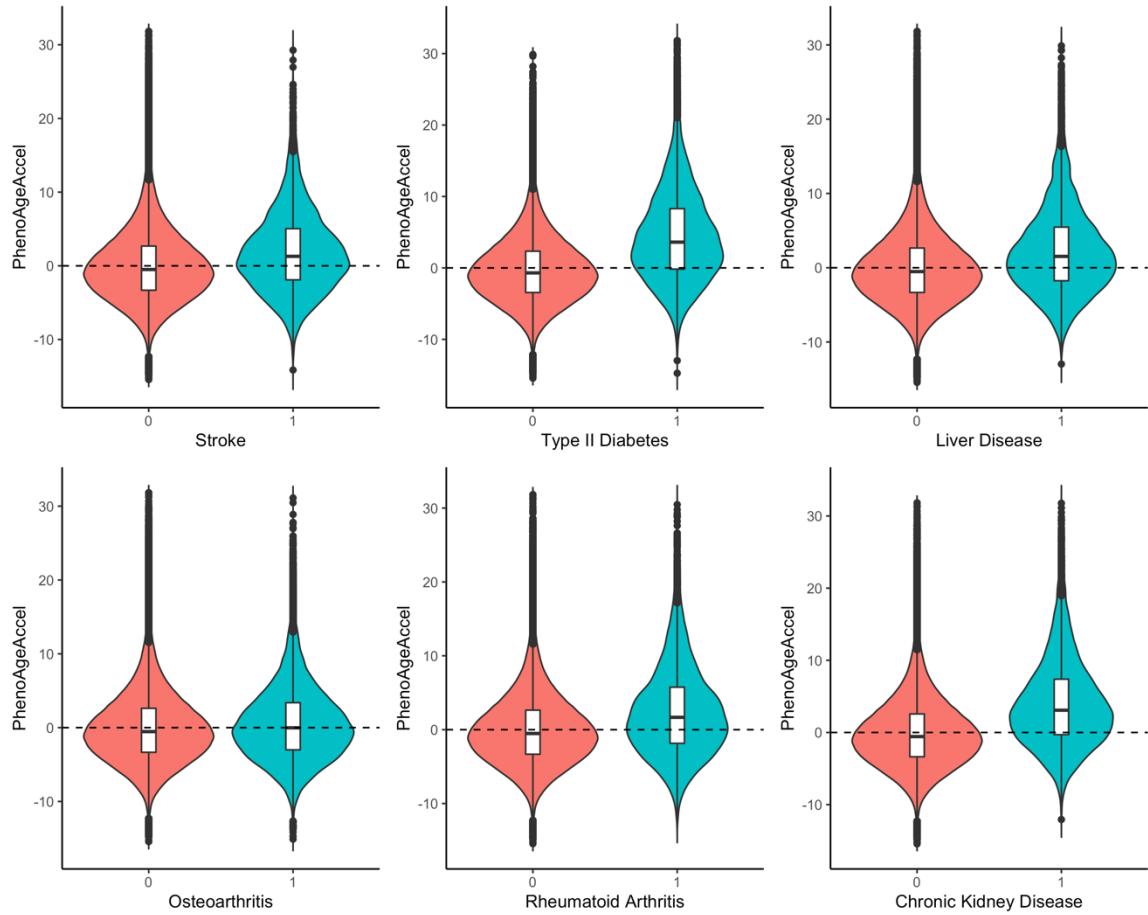
Figure S4. Boxplots and violin plots of PhenoAge acceleration by disease status updated to March 2020: asthma, COPD, pneumonia, falls/fragility fracture