

## SUPPLEMENTARY TABLES

Supplementary Table 1. Clinical covariates.

N = 408	Baseline	Follow-up
	Mean (SD)	Mean (SD)
Age (yr)	71.3 (6.36)	77.6 (6.52)
Follow-up time (yr)	-	6.26 (3.33)
Weight (kg)	85.5 (14.1)	83.4 (14.5)
Height (cm)	173.9 (6.81)	173.3 (7.06)
BMI (kg/m <sup>2</sup> )	28.2 (4.03)	27.7 (4.17)
DNAmAge (yr)	72.1 (7.07)	75.5 (7.00)
EEAA (yr)	4.81 (5.62)	4.02 (7.78)
AAD (yr)	0.77 (5.41)	-2.02 (7.72)
EEAD (yr)	4.81 (5.62)	4.02 (7.78)
FVC (liter)	3.39 (0.66)	3.37 (0.71)
FEV1 (liter)	2.57 (0.58)	2.48 (0.59)
FEF25-75 (liter/s)	4.24 (1.83)	3.54 (1.53)
FEV1/FVC	0.76 (0.07)	0.74 (0.07)
Binary Variables	N (%)	N (%)
Female	<b>0 (0)</b>	<b>0 (0)</b>
COPD GOLD (Incidence)	-	0 (0)
COPD GLI (Incidence)	-	15 (3.68)
White	399 (97.8)	399 (97.8)
Black	5 (1.23)	5 (1.23)
Hispanic	4 (0.98)	4 (0.98)
Ex-smoker	260 (63.7)	261 (64.0)
Current-smoker	17 (4.17)	17 (4.17)

Clinical covariates for the NAS study participants. BMI = body mass index; DNAmAge = DNA methylation age; EEAA = extrinsic epigenetic age acceleration; IEAA = intrinsic epigenetic age acceleration; AAD = age acceleration difference; EEAD = extrinsic epigenetic age acceleration difference; FEV1 = forced expiratory volume in 1 s; FVC = forced vital capacity; FEF25-75 = forced expiratory flow at 25-75% of FVC; COPD = Chronic obstructive pulmonary disease; GOLD = Global Initiative for Chronic Obstructive Lung Disease; GLI = Global Lung Initiative.

**Supplementary Table 2. Associations between epigenetic aging biomarkers and COPD (a) and lung function (b) in KORA.**

<b>a. COPD</b>					
	<b>Epigenetic aging measure</b>	<b>Odds ratio</b>	<b>LCI</b>	<b>UCI</b>	<b>P</b>
COPD	AAD	1.00	0.99	1.02	0.63
COPD	EEAD	1.01	1.00	1.03	0.04
COPD	$\Delta$ AAD	1.01	0.98	1.03	0.62
COPD	$\Delta$ EEAD	1.02	1.00	1.04	0.04
<b>b. Lung function</b>					
	<b>Epigenetic aging measure</b>	<b>Effect estimate</b>	<b>LCI</b>	<b>UCI</b>	<b>P</b>
FEV1 (% difference from median)	AAD	-0.43	-1.64	0.77	0.48
FVC (% difference from median)	AAD	-0.17	-1.20	0.86	0.74
FEV1/FCV (% difference from median)	AAD	-0.22	-0.81	0.37	0.46
FEF25-75 (% difference from median)	AAD	-1.61	-4.05	0.83	0.20
FEV1 (% difference from median)	EEAD	-0.91	-1.89	0.07	0.07
FVC (% difference from median)	EEAD	-0.62	-1.45	0.22	0.15
FEV1/FCV (% difference from median)	EEAD	-0.32	-0.80	0.16	0.19
FEF25-75 (% difference from median)	EEAD	-1.34	-3.32	0.65	0.19
FEV1 (% difference from median)	$\Delta$ AAD	-0.85	-2.41	0.71	0.29
FVC (% difference from median)	$\Delta$ AAD	-0.65	-1.99	0.68	0.34
FEV1/FCV (% difference from median)	$\Delta$ AAD	-0.10	-0.86	0.66	0.80
FEF25-75 (% difference from median)	$\Delta$ AAD	-0.85	-3.98	2.27	0.59
FEV1 (% difference from median)	$\Delta$ EEAD	-0.54	-1.82	0.74	0.41
FVC (% difference from median)	$\Delta$ EEAD	-0.10	-1.19	0.99	0.86
FEV1/FCV (% difference from median)	$\Delta$ EEAD	-0.54	-1.16	0.08	0.09
FEF25-75 (% difference from median)	$\Delta$ EEAD	-1.17	-3.74	1.39	0.37

AAD = age acceleration difference;  $\Delta$ AAD = change in age acceleration difference between baseline and follow-up exams; COPD = chronic obstructive pulmonary disease; EEAD = extrinsic epigenetic age acceleration difference;  $\Delta$ EEAD = change in extrinsic epigenetic age acceleration difference between baseline and follow-up exams; FEF25-75 = forced expiratory flow at 25-75% of pulmonary volume; FEV1 = forced expiratory volume in the first second; FVC = forced vital capacity; LCI = lower 95% confidence interval; P = p-value; UCI = upper 95% confidence interval.

**Supplementary Table 3. Associations between epigenetic aging measures and COPD (a) and lung function (b) in NAS.**

<b>a. COPD</b>					
	<b>Epigenetic aging measure</b>	<b>Odds ratio</b>	<b>LCI</b>	<b>UCI</b>	<b>P</b>
COPD	$\Delta$ EEAD	1.02	1.00	1.03	0.008044
COPD	$\Delta$ AAD	1.02	1.00	1.03	0.02502
COPD	AAD	1.02	1.00	1.04	0.03089
COPD	EEAD	1.01	0.99	1.02	0.485577
<b>b. Lung function</b>					
	<b>Epigenetic aging measure</b>	<b>Effect estimate</b>	<b>LCI</b>	<b>UCI</b>	<b>P</b>
FEF25-75	$\Delta$ EEAD	-2.55	-5.21	0.10	0.06042
FEF25-75	$\Delta$ AAD	-2.33	-5.19	0.53	0.111603
FEF25-75	EEAD	-2.23	-5.50	1.04	0.182474
FEF25-75	AAD	-0.65	-4.20	2.89	0.717814
FEV1	$\Delta$ AAD	-1.32	-2.79	0.15	0.07916
FEV1	EEAD	-1.10	-2.75	0.56	0.194244
FEV1	$\Delta$ EEAD	-0.73	-2.10	0.64	0.297151
FEV1	AAD	0.28	-1.51	2.07	0.761846
FEV1/FVC	$\Delta$ EEAD	-0.79	-1.38	-0.20	0.008856
FEV1/FVC	$\Delta$ AAD	-0.79	-1.42	-0.15	0.015798
FEV1/FVC	EEAD	-0.59	-1.31	0.13	0.108924
FEV1/FVC	AAD	-0.49	-1.27	0.30	0.223369
FVC	AAD	0.96	-0.66	2.58	0.244423
FVC	$\Delta$ AAD	-0.49	-1.83	0.85	0.47577
FVC	EEAD	-0.31	-1.81	1.19	0.683633
FVC	$\Delta$ EEAD	0.10	-1.15	1.35	0.877678

AAD = age acceleration difference;  $\Delta$ AAD = change in age acceleration difference between baseline and follow-up exams; COPD = chronic obstructive pulmonary disease; EEAD = extrinsic epigenetic age acceleration difference;  $\Delta$ EEAD = change in extrinsic epigenetic age acceleration difference between baseline and follow-up exams; FEF25-75 = forced expiratory flow at 25-75% of pulmonary volume; FEV1 = forced expiratory volume in the first second; FVC = forced vital capacity; LCI = lower 95% confidence interval; P = p-value; UCI = upper 95% confidence interval.

**Supplementary Table 4. Meta-analysis of KORA and NAS for COPD (a) and lung function (b) outcomes.**

<b>a. COPD</b>					
<b>Outcome</b>	<b>Epigenetic aging measure</b>	<b>OR</b>	<b>OR LCI</b>	<b>OR UCI</b>	<b>P</b>
COPD	EEAD	1.01	1.00	1.02	0.043004
COPD	AAD	1.01	1.00	1.02	0.06543
COPD	$\Delta$ AAD	1.01	1.00	1.03	0.031643
COPD	$\Delta$ EEAD	1.02	1.01	1.03	0.000706
<b>b. Lung function</b>					
	<b>Epigenetic aging measure</b>	<b>Effect estimate</b>	<b>LCI</b>	<b>UCI</b>	<b>P</b>
FEV1	AAD	-0.21	-1.21	0.79	0.677415
FEV1	EEAD	-0.96	-1.80	-0.12	0.025818
FEV1	$\Delta$ AAD	-1.10	-2.17	-0.03	0.044241
FEV1	$\Delta$ EEAD	-0.63	-1.56	0.31	0.1883
FVC	AAD	0.16	-0.71	1.02	0.72534
FVC	EEAD	-0.54	-1.27	0.19	0.145254
FVC	$\Delta$ AAD	-0.57	-1.52	0.37	0.236804
FVC	$\Delta$ EEAD	-0.01	-0.84	0.81	0.973866
FEV1/FVC	AAD	-0.32	-0.79	0.15	0.185455
FEV1/FVC	EEAD	-0.40	-0.80	-0.01	0.046866
FEV1/FVC	$\Delta$ AAD	-0.50	-0.99	-0.02	0.04325
FEV1/FVC	$\Delta$ EEAD	-0.67	-1.10	-0.25	0.001988
FEF25-75	AAD	-1.30	-3.31	0.71	0.204109
FEF25-75	EEAD	-1.58	-3.27	0.12	0.068706
FEF25-75	$\Delta$ AAD	-1.65	-3.76	0.46	0.124265
FEF25-75	$\Delta$ EEAD	-1.84	-3.68	0.01	0.050812

AAD = age acceleration difference;  $\Delta$ AAD = change in age acceleration difference between baseline and follow-up exams; COPD = chronic obstructive pulmonary disease; EEAD = extrinsic epigenetic age acceleration difference;  $\Delta$ EEAD = change in extrinsic epigenetic age acceleration difference between baseline and follow-up exams; FEF25-75 = forced expiratory flow at 25-75% of pulmonary volume; FEV1 = forced expiratory volume in the first second; FVC = forced vital capacity; LCI = lower 95% confidence interval; P = p-value; UCI = upper 95% confidence interval.