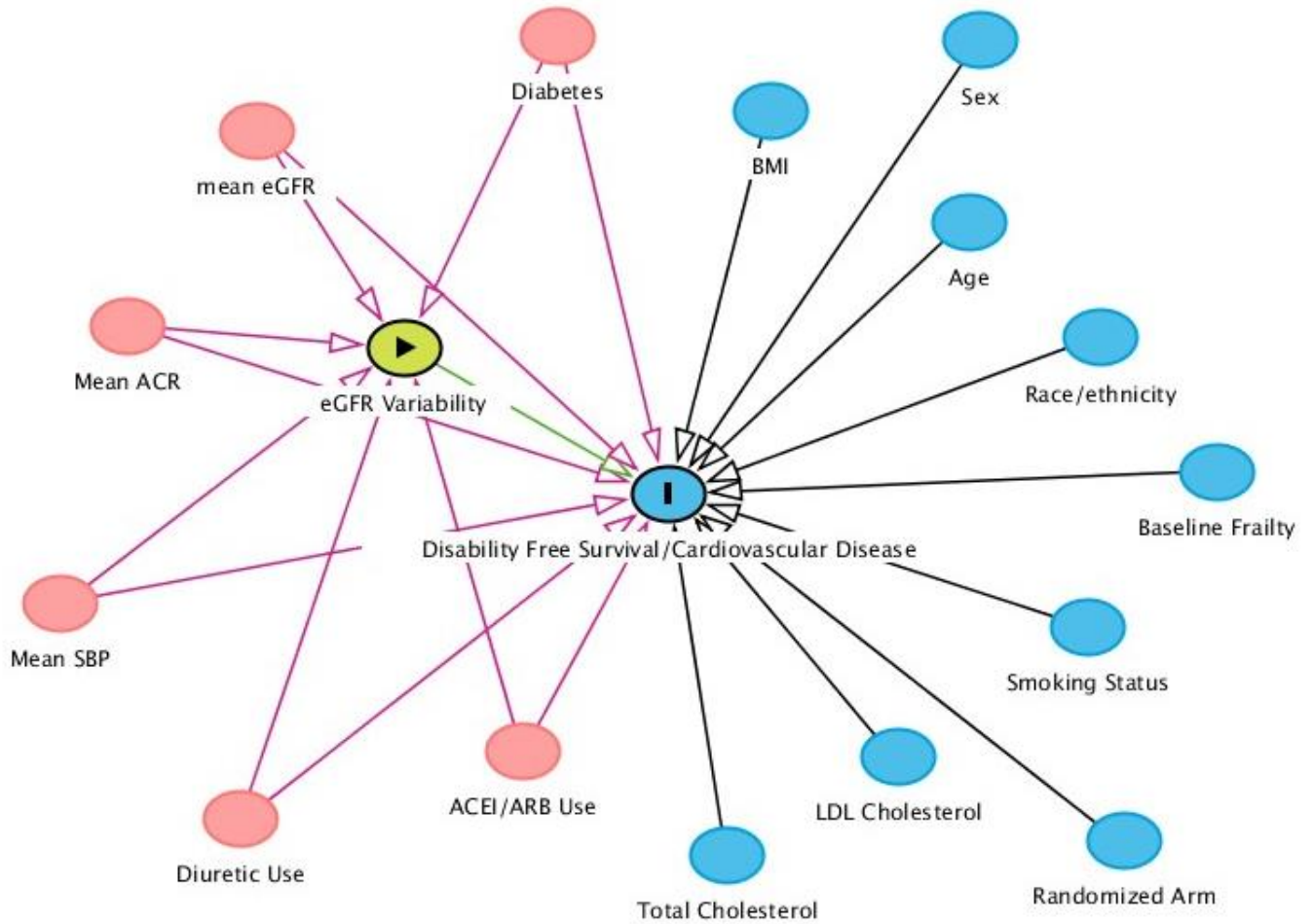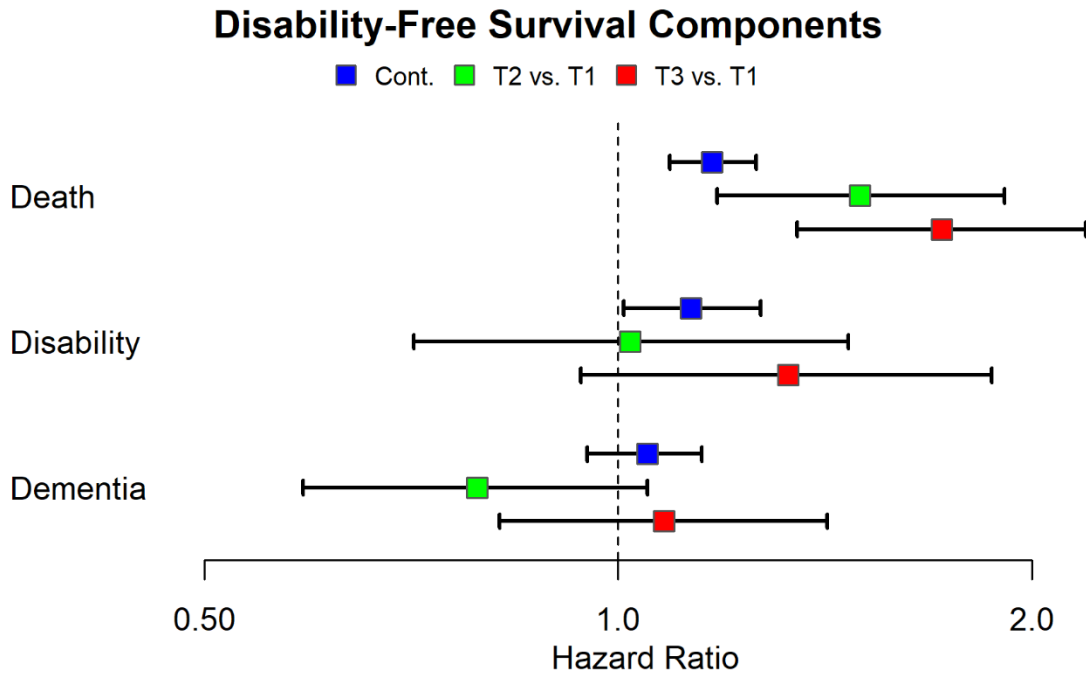**Figure S1.** Directed Acyclic Graph

Directed Acyclic Graph representing the hypothesized relation between eGFR variability (exposure of interest), disability free survival (DFS), or cardiovascular disease (CVD) (the two outcomes of interest), and other variables relating to the exposure and outcome. ACEI = angiotensin converting enzyme inhibitor; ACR = albumin-to-creatinine ratio; ARB = aldosterone receptor blocker; AV2 = annual visit 2; BL = baseline; BMI = body mass index; DBP = diastolic blood pressure; eGFR = estimated glomerular filtration rate; LDL = low density lipoprotein; SBP = systolic blood pressure. Pink circles mark variables associated with exposure and outcome; blue circles mark variables associated with just outcome and not exposure. Green circle black triangle marks exposure. Blue circle with vertical dash marks outcomes.

Figure S2. Hazard ratio (95% CI) for association between eGFR variability and the individual components of disability-free survival, with variability as a continuous variable (per 3 ml/min/1.73 m² difference) and according to tertiles (T) of standard deviation

Adjusted for age, sex, race/ethnicity, randomized arm (aspirin versus placebo), BMI, mean eGFR (BL-AV2), mean ACR (BL-AV2), diabetes, baseline frailty, smoking status, total cholesterol, LDL, mean SBP (BL-AV2), ACE/ARB use, diuretic use

Table S1. Pearson's correlation coefficients summarizing associations between standard deviation of eGFR and other kidney function variability estimates

Renal variability estimate	eGFR SD[1]
eGFR CV	0.941
Serum creatinine SD	0.766
Serum creatinine CV	0.882
eGFR SD[2]	0.995
eGFR SD[3]	0.915

SD = standard deviation, CV = coefficient of variation
[1]Raw estimate of SD
[2]SD estimate using linear mixed model without a correlation parameter linking within-person mean and SD
[3]SD estimate using linear mixed model, with correlation parameter

Table S2. Baseline characteristics of study participants for analysis of CVD events by eGFR variability, with variability according to tertiles of standard deviation

Variable	Standard deviation of eGFR (eGFR variability)			
	T1 (0.01-3.07)	T2 (3.07-5.85)	T3 (>5.85)	Overall
Number of participants	4151	4150	4151	12452
Age (years), mean (SD)	75.1 (4.2)	75.2 (4.3)	75.0 (4.3)	75.1 (4.3)
Female, n (%)	2193 (52.8)	2198 (53.0)	2448 (59.0)	6839 (54.9)
Race/Ethnicity, n (%)				
White	4017 (96.8)	4012 (96.7)	3915 (94.3)	11944 (95.9)
Black	36 (0.9)	38 (0.9)	138 (3.3)	212 (1.7)
Hispanic	45 (1.1)	39 (0.9)	42 (1.0)	126 (1.0)
Asian	28 (0.7)	47 (1.1)	31 (0.7)	106 (0.9)
Other	25 (0.6)	14 (0.3)	25 (0.6)	64 (0.5)
Aspirin treatment assignment, n (%)	2045 (49.3)	2047 (49.3)	2101 (50.6)	6193 (49.7)
Kidney function (BL-AV2)				
eGFR (ml/min/1.73 m²), mean (SD)	74.4 (14.6)	70.9 (12.9)	70.35 (10.8)	71.9 (13.0)
ACR (mg/g), median (IQR)	8.0 (5.0, 14.2)	8.0 (5.0, 13.9)	8.4 (5.3, 15.3)	8.0 (5.0, 14.5)
Serum creatinine (mg/dL), mean (SD)	0.9 (0.2)	0.9 (0.2)	0.9 (0.2)	0.9 (0.2)
Mean (BL-AV2) SBP, mmHg, mean (SD)	138.4 (13.4)	138.3 (13.6)	138.0 (13.8)	138.2 (13.6)
Mean (BL-AV2) DBP, mmHg, mean (SD)	76.3 (8.0)	75.9 (8.1)	75.5 (8.1)	75.9 (8.1)
BMI, n (%)				
< 18.5 kg/m²	20 (0.5)	22 (0.5)	19 (0.5)	61 (0.5)
18.5-25 kg/m²	1119 (27.0)	1021 (24.6)	1024 (24.7)	3164 (25.4)
25-30 kg/m²	1884 (45.4)	1903 (45.9)	1846 (44.5)	5633 (45.2)
≥ 30 kg/m²	1128 (27.2)	1204 (29.0)	1262 (30.4)	3594 (28.9)
Total cholesterol (mg/dL), mean (SD)	203.1 (37.3)	202.9 (37.3)	203.3 (38.4)	203.1 (37.7)
LDL (mg/dL), mean (SD)	118.7 (33.3)	118.5 (33.6)	118.0 (34.3)	118.4 (33.8)
Diabetes, n (%)	383 (9.2)	405 (9.8)	468 (11.3)	1256 (10.1)
Baseline frailty, n (%)[1]				
Not frail	2613 (62.9)	2623 (63.2)	2506 (60.4)	7742 (62.2)
Prefrail	1468 (35.4)	1465 (35.3)	1566 (37.7)	4499 (36.1)
Frail	70 (1.7)	62 (1.5)	79 (1.9)	211 (1.7)
Anti-hypertension drug use				
ACEI/ARBs, n (%)				
No use at BL or AV1	2320 (55.9)	2244 (54.1)	2047 (49.3)	6611 (53.1)
BL or AV1	102 (2.5)	131 (3.2)	149 (3.6)	382 (3.1)
Both BL and AV1	1729 (41.7)	1775 (42.8)	1955 (47.1)	5459 (43.8)
Diuretics, n (%)				
No use at BL or AV1	3363 (81.0)	3342 (80.5)	3176 (76.5)	9881 (79.4)
BL or AV1	70 (1.7)	72 (1.7)	108 (2.6)	250 (2.0)
Both BL and AV1	718 (17.3)	736 (17.7)	867 (20.9)	2321 (18.6)

Abbreviations: SD, standard deviation; IQR, interquartile range; BL, baseline; AV1, first annual visit; AV2, second annual visit; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; eGFR, estimated glomerular filtration rate

[1] Frailty/pre-frailty : participants were classified as frail if they met at least three of the following criteria and pre-frail if they met one or two of the criteria: (1) BMI < 20 kg/m^2; (2) lowest 20% of grip strength taking into account gender and BMI; (3) the participant endorsed "I felt that everything I did was an effort" and/or "I could not get going" for three or more days during the last week, according to the Center for Epidemiological Studies-Depression 10 (CES-D10) scale; (4) time to walk 3 meters (10 feet) was in the lowest 20% taking into account gender and height, and (5) no walking outside the home in the last two weeks, or the longest amount of time walking outside without sitting down to rest was less than 10 minutes, according to LIFE Disability questionnaire responses

Table S3. Hazard ratio (95% CI) for association between eGFR variability and (A, B) death/dementia/persistent physical disability (DFS) and (C, D) CVD, stratified by baseline CKD status with variability as a continuous variable and according to tertiles (T) of standard deviation.

Variability Measure	Variability (continuous, per 3 ml/min/1.73 m² difference in SD)	Variability (Tertiles)		
		T1	T2	T3
A. DFS (No BL CKD), N	9338	3113	3112	3113
Variability Range, ml/min/1.73 m²	--	0.04-3.04	3.04-5.80	5.80-52.00
Number of events	535	170	173	192
Event rate per 1000 person years	21.7	20.1	21.4	23.8
HR (95% CI)				
Model 1	1.06 (0.99, 1.14)	REF	1.08 (0.87, 1.33)	1.21 (0.98, 1.49)
Model 2	1.09 (1.01, 1.17)	REF	1.08 (0.87, 1.33)	1.26 (1.02, 1.55)
Model 3	1.12 (1.04, 1.21)	REF	1.20 (0.97, 1.49)	1.40 (1.12, 1.76)
B. DFS (Yes BL CKD), N	2540	847	846	847
Variability Range, ml/min/1.73 m²	--	0.17-3.07	3.07-5.79	5.80-32.94
Number of events	219	56	79	84
Event rate per 1000 person years	32.3	24.2	35.3	37.6
HR (95% CI)				
Model 1	1.13 (1.02, 1.25)	REF	1.49 (1.06, 2.10)	1.58 (1.13, 2.21)
Model 2	1.15 (1.04, 1.27)	REF	1.41 (1.00, 1.99)	1.65 (1.18, 2.32)
Model 3	1.15 (1.03, 1.28)	REF	1.44 (1.02, 2.04)	1.61 (1.14, 2.28)
Variability Measure	Variability (continuous, per 3 ml/min/1.73 m² difference in SD)	Variability (Tertiles)		
		T1	T2	T3
C. CVD (No BL CKD), N	9268	3090	3089	3089
Variability Range, ml/min/1.73 m²	--	0.04-3.03	3.03-5.80	5.80-52.00
Number of events	216	68	64	84
Event rate per 1000 person years	8.9	8.2	8.0	10.6
HR (95% CI)				
Model 1	1.10 (0.99, 1.22)	REF	0.99 (0.70, 1.39)	1.31 (0.95, 1.81)
Model 2	1.13 (1.02, 1.26)	REF	1.00 (0.71, 1.41)	1.40 (1.01, 1.93)
Model 3	1.14 (1.03, 1.26)	REF	1.05 (0.74, 1.49)	1.51 (1.07, 2.12)
D. CVD (Yes BL CKD), N	2525	842	841	842
Variability Range, ml/min/1.73 m²	--	0.17-3.06	3.06-5.76	5.76-32.94
Number of events	123	30	50	43
Event rate per 1000 person years	18.5	13.2	22.9	19.8
HR (95% CI)				
Model 1	1.08 (0.94, 1.24)	REF	1.76 (1.12, 2.77)	1.52 (0.95, 2.42)
Model 2	1.11 (0.96, 1.27)	REF	1.69 (1.07, 2.66)	1.61 (1.01, 2.57)
Model 3	1.09 (0.94, 1.25)	REF	1.72 (1.09, 2.71)	1.54 (0.96, 2.47)

REF = reference
Model 1: unadjusted
Model 2: adjusted for age, sex, race/ethnicity
Model 3: includes Model 2 adjustments and randomized arm (aspirin versus placebo), BMI, mean eGFR (BL-AV2), mean ACR (BL-AV2), diabetes, baseline frailty, smoking status, total cholesterol, LDL, mean SBP (BL-AV2), ACE/ARB use, diuretic use
Baseline (BL) CKD status determined by eGFR < 60 ml/min/1.73 m^2 or ACR ≥ 3 mg/mmol at year 2 visit *and* baseline or year 1 visit. CKD was defined as "Yes CKD" at AV2, and "Yes CKD" at BL or AV1. Both ACR and eGFR were required to determine CKD, and ACR has higher missingness than eGFR (so the eGFR values used to compute variability were not sufficient to determine CKD status in the same period). Therefore, some participants were excluded on the basis that CKD status could not be determined.

Table S4. Hazard ratio (95% CI) for association between eGFR variability and (A,B,C) the individual components of disability-free survival and (D, E, F, G) the individual components of CVD with variability as a continuous variable and according to tertiles (T) of standard deviation

Variability Measure	Variability (continuous, per 3 ml/min/1.73 m² difference in SD)	Variability (Tertiles)		
		T1	T2	T3
DFS Components				
A. Death, N	12701	4234	4233	4234
Variability Range	--	0.01-3.07	3.07-5.86	5.86-52.00
Number of events	448	113	162	173
Event rate per 1000 person years	13.1	9.6	14.4	15.5
HR (95% CI)				
Model 1	1.14 (1.06, 1.22)	REF	1.53 (1.20, 1.94)	1.66 (1.31, 2.10)
Model 2	1.18 (1.10, 1.27)	REF	1.49 (1.17, 1.90)	1.76 (1.38, 2.23)
Model 3	1.17 (1.09, 1.26)	REF	1.50 (1.18, 1.91)	1.72 (1.35, 2.19)
B. Physical Disability, N	12521	4174	4173	4174
Variability Range	--	0.01-3.07	3.07-5.85	5.85-52.00
Number of events	197	61	59	77
Event rate per 1000 person years	6.0	5.4	5.4	7.2
HR (95% CI)				
Model 1	1.13 (1.01, 1.26)	REF	1.02 (0.72, 1.47)	1.36 (0.97, 1.90)
Model 2	1.15 (1.03, 1.29)	REF	1.00 (0.70, 1.43)	1.38 (0.99, 1.94)
Model 3	1.13 (1.01, 1.27)	REF	1.02 (0.71, 1.47)	1.33 (0.94, 1.87)
C. Dementia, N	12556	4186	4185	4185
Variability Range	--	0.01-3.07	3.07-5.86	5.86-52.00
Number of events	297	110	81	106
Event rate per 1000 person years	9.0	9.7	7.5	9.9
HR (95% CI)				
Model 1	1.03 (0.93, 1.13)	REF	0.77 (0.58, 1.03)	1.03 (0.79, 1.35)
Model 2	1.04 (0.94, 1.14)	REF	0.76 (0.57, 1.01)	1.06 (0.81, 1.38)
Model 3	1.05 (0.95, 1.15)	REF	0.79 (0.59, 1.05)	1.08 (0.82, 1.42)
CVD Components				
D. CHD Death, N	12701	4234	4233	4234
Variability Range	--	0.01-3.07	3.07-5.86	5.86-52.00
Number of events	90	32	29	29
Event rate per 1000 person years	2.6	2.7	2.6	2.6
HR (95% CI)				
Model 1	0.95 (0.78, 1.14)	REF	0.97 (0.58, 1.60)	0.98 (0.59, 1.62)
Model 2	0.99 (0.81, 1.20)	REF	0.92 (0.56, 1.53)	1.08 (0.65, 1.80)
Model 3	0.98 (0.81, 1.19)	REF	0.96 (0.57, 1.59)	1.08 (0.64, 1.80)
E. Non-fatal MI, N	12533	4178	4177	4178
Variability Range	--	0.01-3.07	3.07-5.85	5.85-52.00
Number of events	125	31	47	47
Event rate per 1000 person years	3.8	2.7	4.3	4.4
HR (95% CI)				

Model 1	1.09 (0.95, 1.26)	REF	1.60 (1.01, 2.51)	1.62 (1.03, 2.55)
Model 2	1.14 (0.99, 1.31)	REF	1.59 (1.01, 2.50)	1.75 (1.11, 2.77)
Model 3	1.10 (0.95, 1.27)	REF	1.47 (0.93, 2.32)	1.59 (1.01, 2.52)
F. Stroke (fatal/non), N	12554	4185	4184	4185
Variability Range	--	0.01-3.07	3.07-5.86	5.86-52.00
Number of events	163	59	50	54
Event rate per 1000 person years	4.9	5.2	4.6	5.0
HR (95% CI)				
Model 1	1.00 (0.88, 1.14)	REF	0.89 (0.61, 1.29)	0.97 (0.67, 1.40)
Model 2	1.00 (0.88, 1.15)	REF	0.87 (0.60, 1.27)	0.98 (0.67, 1.42)
Model 3	1.01 (0.89, 1.15)	REF	0.89 (0.61, 1.31)	1.01 (0.69, 1.47)
G. Hosp. for HF, N	12587	4196	4195	4196
Variability Range	--	0.01-3.07	3.07-5.85	5.85-52.00
Number of events	83	18	26	39
Event rate per 1000 person years	2.5	1.6	2.4	3.6
HR (95% CI)				
Model 1	1.23 (1.07, 1.40)	REF	1.51 (0.83, 2.76)	2.31 (1.32, 4.04)
Model 2	1.33 (1.14, 1.56)	REF	1.46 (0.80, 2.67)	2.51 (1.43, 4.39)
Model 3	1.28 (1.10, 1.50)	REF	1.52 (0.83, 2.77)	2.51 (1.43, 4.43)

*A difference of 3 ml/min/1.73 m² is approximately the difference between tertile cut-offs, and allows for easier comparison between hazard ratios

REF = reference
Model 1: unadjusted
Model 2: adjusted for age, sex, race/ethnicity
Model 3: includes Model 2 adjustments and randomized arm (aspirin versus placebo), BMI, mean eGFR (BL-AV2), mean ACR (BL-AV2), diabetes, baseline frailty, smoking status, total cholesterol, LDL, mean SBP (BL-AV2), ACE/ARB use, diuretic use

Table S5. Hazard ratio (95% CI) for association between eGFR variability and (A) death/dementia/persistent physical disability (DFS) and (B) CVD events, with variability as continuous variable and according to tertiles (T) of standard deviation with inclusion of participants with two or more baseline eGFR values

Variability Measure	Variability (continuous, per 3 ml/min/1.73 m² difference in SD*)	Variability (Tertiles)		
		T1	T2	T3
A. DFS, N	15199	5066	5066	5066
Variability Range	--	0.00-2.99	2.99-5.83	5.83-52.00
Number of events	1039	314	344	381
Event rate per 1000 person years	26.3	23.3	26.3	29.4
HR (95% CI)				
Model 1	1.08 (1.03, 1.14)	REF	1.14 (0.98, 1.32)	1.28 (1.10, 1.48)
Model 2	1.10 (1.05, 1.16)	REF	1.13 (0.97, 1.32)	1.32 (1.14, 1.53)
Model 3	1.08 (1.03, 1.14)	REF	1.14 (0.98, 1.34)	1.28 (1.10, 1.49)
B. CVD, N	15038	5013	5012	5012
Variability Range	--	0.00-2.98	2.98-5.81	5.81-52.00
Number of events	463	136	156	171
Event rate per 1000 person years	12.0	10.3	12.2	13.5
HR (95% CI)				
Model 1	1.06 (0.99, 1.14)	REF	1.19 (0.95, 1.50)	1.32 (1.06, 1.66)
Model 2	1.09 (1.01, 1.17)	REF	1.19 (0.94, 1.49)	1.39 (1.11, 1.74)
Model 3	1.07 (0.99, 1.15)	REF	1.14 (0.91, 1.44)	1.33 (1.06, 1.67)

*A difference of 3 ml/min/1.73 m² is approximately the difference between tertile cut-offs, and allows for easier comparison between hazard ratios

REF = reference

Model 1: unadjusted

Model 2: adjusted for age, sex, race/ethnicity

Model 3: includes Model 2 adjustments and randomized arm (aspirin versus placebo), BMI, mean eGFR (BL-AV2), mean ACR (BL-AV2), diabetes, baseline frailty, smoking status, total cholesterol, LDL, mean SBP (BL-AV2), ACE/ARB use, diuretic use

Table S6. Hazard ratio (95% CI) for the association between eGFR variability and (A) death/dementia/persistent physical disability (DFS) and (B) CVD events, with variability as a continuous variable and according to tertiles (T) of coefficient of variation

Variability Measure	Variability (continuous, per difference of 3 in CV*)	Variability (Tertiles)		
		T1	T2	T3
A. DFS, N	12549	4183	4183	4183
Variability Range	--	0.01-4.26	4.26-8.52	8.52-94.73
Number of events	838	250	263	325
Event rate per 1000 person years	25.3	22.1	24.0	29.8
HR (95% CI)				
Model 1	1.08 (1.04, 1.11)	REF	1.09 (0.92, 1.30)	1.37 (1.16, 1.61)
Model 2	1.06 (1.03, 1.10)	REF	1.04 (0.88, 1.24)	1.25 (1.06, 1.47)
Model 3	1.06 (1.03, 1.10)	REF	1.09 (0.91, 1.30)	1.31 (1.09, 1.56)
B. CVD, N	12452	4151	4150	4151
Variability Range	--	0.01-4.24	4.25-8.50	8.50-94.73
Number of events	379	99	132	148
Event rate per 1000 person years	11.7	8.9	12.3	13.9
HR (95% CI)				
Model 1	1.08 (1.03, 1.13)	REF	1.38 (1.07, 1.80)	1.57 (1.21, 2.02)
Model 2	1.07 (1.02, 1.12)	REF	1.34 (1.03, 1.74)	1.48 (1.15, 1.92)
Model 3	1.05 (1.00, 1.11)	REF	1.29 (0.99, 1.69)	1.40 (1.07, 1.85)

*CV is the ratio of SD/mean and therefore is unitless
REF = reference
Model 1: unadjusted
Model 2: adjusted for age, sex, race/ethnicity
Model 3: includes Model 2 adjustments and randomized arm (aspirin versus placebo), BMI, mean eGFR (BL-AV2), mean ACR (BL-AV2), diabetes, baseline frailty, smoking status, total cholesterol, LDL, mean SBP (BL-AV2), ACE/ARB use, diuretic use

Table S7. Hazard ratio (95% CI) for the association between serum creatinine variability (standard deviation (A, B) and coefficient of variation (C, D)) and death/dementia/persistent physical disability (DFS) and CVD events, with variability as a continuous variable and according to tertiles (T)

Variability Measure	Variability (continuous, per .03 mg/dL difference in SD)	Variability (Tertiles)		
		T1	T2	T3
A. DFS (SCr SD), N	12549	4276	4093	4180
Variability Range	--	0-0.04	0.04-0.08	0.08-1.66
Number of events	838	241	249	348
Event rate per 1000 person years	25.3	20.7	23.3	32.2
HR (95% CI)				
Model 1	1.06 (1.04, 1.07)	REF	1.14 (0.95, 1.36)	1.59 (1.35, 1.87)
Model 2	1.04 (1.02, 1.07)	REF	1.11 (0.93, 1.32)	1.39 (1.18, 1.64)
Model 3	1.05 (1.02, 1.08)	REF	1.09 (0.91, 1.30)	1.38 (1.16, 1.64)
B. CVD (SCr SD), N	12452	4254	4051	4147
Variability Range	--	0-0.04	0.04-0.07	0.07-1.66
Number of events	379	96	122	161
Event rate per 1000 person years	11.7	8.4	11.6	15.2
HR (95% CI)				
Model 1	1.06 (1.03, 1.09)	REF	1.40 (1.07, 1.83)	1.85 (1.43, 2.38)
Model 2	1.05 (1.01, 1.09)	REF	1.37 (1.04, 1.78)	1.61 (1.25, 2.08)
Model 3	1.03 (0.98, 1.07)	REF	1.35 (1.03, 1.76)	1.52 (1.17, 1.98)
Variability Measure	**Variability (continuous, per difference of 3 in CV*)**	**Variability (Tertiles)**		
		T1	T2	T3
C. DFS (SCr CV), N	12549	4183	4184	4182
Variability Range	--	0-4.86	4.87-8.53	8.53-72.1
Number of events	838	232	282	324
Event rate per 1000 person years	25.3	20.4	25.6	30.0
HR (95% CI)				
Model 1	1.10 (1.06, 1.13)	REF	1.27 (1.07, 1.51)	1.50 (1.27, 1.78)
Model 2	1.09 (1.05, 1.12)	REF	1.27 (1.06, 1.51)	1.45 (1.23, 1.72)
Model 3	1.07 (1.04, 1.11)	REF	1.25 (1.05, 1.48)	1.38 (1.16, 1.64)
D. CVD (SCr CV), N	12452	4152	4149	4151
Variability Range	--	0-4.85	4.86-8.52	8.53-72.1
Number of events	379	106	130	143
Event rate per 1000 person years	11.7	9.5	12.0	13.6
HR (95% CI)				
Model 1	1.07 (1.02, 1.13)	REF	1.28 (0.99, 1.65)	1.45 (1.13, 1.86)
Model 2	1.07 (1.02, 1.13)	REF	1.28 (0.99, 1.66)	1.45 (1.13, 1.87)
Model 3	1.06 (1.00, 1.12)	REF	1.27 (0.98, 1.65)	1.39 (1.08, 1.80)

*CV is the ratio of SD/mean and therefore is unitless

REF = reference

Model 1: unadjusted

Model 2: adjusted for age, sex, race/ethnicity

Model 3: includes Model 2 adjustments and randomized arm (aspirin versus placebo), BMI, mean eGFR (BL-AV2),

mean ACR (BL-AV2), diabetes, baseline frailty, smoking status, total cholesterol, LDL, mean SBP (BL-AV2), ACE/ARB use, diuretic use

Table S8. Hazard ratio (95% CI) for association between eGFR variability (mixed model two-stage approach) and (A,C) death/dementia/persistent physical disability (DFS) and (C,D) CVD events, with variability as a continuous variable and according to tertiles (T)

Variability Measure	Variability (continuous, per 1 ml/min/1.73 m² difference in SD)	Variability (Tertiles)		
		T1	T2	T3
A. DFS (M1), N	12549	4183	4183	4183
Variability Range	--	4.08-4.92	4.92-5.97	5.97-25.50
Number of events	838	246	282	310
Event rate per 1000 person years	25.3	21.6	25.7	28.7
HR (95% CI)				
Model 1	1.09 (1.04, 1.14)	REF	1.20 (1.01, 1.42)	1.35 (1.14, 1.60)
Model 2	1.10 (1.05, 1.16)	REF	1.16 (0.98, 1.37)	1.38 (1.16, 1.63)
Model 3	1.09 (1.04, 1.15)	REF	1.18 (0.99, 1.40)	1.37 (1.15, 1.62)
B. CVD (M1), N	12452	4151	4150	4151
Variability Range	--	4.08-4.92	4.92-5.96	5.96-25.50
Number of events	379	107	130	142
Event rate per 1000 person years	11.7	9.6	12.1	13.4
HR (95% CI)				
Model 1	1.07 (1.00, 1.15)	REF	1.27 (0.98, 1.64)	1.42 (1.10, 1.82)
Model 2	1.09 (1.02, 1.17)	REF	1.23 (0.95, 1.59)	1.48 (1.15, 1.91)
Model 3	1.08 (1.00, 1.16)	REF	1.18 (0.91, 1.53)	1.42 (1.10, 1.83)
Variability Measure	**Variability (continuous, per 1 ml/min/1.73 m² difference in SD)**	**Variability (Tertiles)**		
		T1	T2	T3
C. DFS (M2), N	12549	4183	4183	4183
Variability Range	--	3.08-4.98	4.98-6.17	6.17-29.10
Number of events	838	250	253	335
Event rate per 1000 person years	25.3	22.4	23.0	30.6
HR (95% CI)				
Model 1	1.11 (1.07, 1.16)	REF	1.03 (0.86, 1.23)	1.38 (1.17, 1.63)
Model 2	1.07 (1.03, 1.12)	REF	0.94 (0.79, 1.12)	1.17 (0.99, 1.38)
Model 3	1.10 (1.05, 1.16)	REF	1.05 (0.87, 1.28)	1.30 (1.06, 1.59)
D. CVD (M2), N	12452	4151	4150	4151
Variability Range	--	3.08-4.98	4.98-6.16	6.17-29.10
Number of events	379	91	130	158
Event rate per 1000 person years	11.7	8.3	12.0	14.8
HR (95% CI)				
Model 1	1.12 (1.06, 1.18)	REF	1.45 (1.11, 1.90)	1.80 (1.39, 2.32)
Model 2	1.10 (1.04, 1.17)	REF	1.34 (1.02, 1.75)	1.61 (1.24, 2.09)
Model 3	1.08 (1.01, 1.16)	REF	1.37 (1.02, 1.84)	1.61 (1.18, 2.19)

M1: Mixed model without a correlation parameter linking within-person mean and SD
M2: Mixed model with a correlation parameter linking within-person mean and SD
REF = reference
Model 1: unadjusted
Model 2: adjusted for age, sex, race/ethnicity

Model 3: includes Model 2 adjustments and randomized arm (aspirin versus placebo), BMI, mean eGFR (BL-AV2), mean ACR (BL-AV2), diabetes, baseline frailty, smoking status, total cholesterol, LDL, mean SBP (BL-AV2), ACE/ARB use, diuretic use