The RIACE Study Group

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Table S1. Stratification of RIACE participants by eGFR.

Criterion	Method	Groups
By absolute eGFR levels	eGFR deciles	from the highest (decile 1) to the lowest (decile 10) eGFR category
	KDIGO eGFR categories and subcategories	G1a ($\geq$105 mL·min^{-1}·1.73 m^{-2}) G1b (90-104 mL·min^{-1}·1.73 m^{-2}) G2 (60-89 mL·min^{-1}·1.73 m^{-2}) G3a (45-59 mL·min^{-1}·1.73 m^{-2}) G3b (30-44 mL·min^{-1}·1.73 m^{-2}) G4-5 (<30 mL·min^{-1}·1.73 m^{-2})
By adjusted eGFR thresholds	Corrected by age according to the formula: 130 mL·min^{-1}·1.73 m^{-2} - 1.0 per year after 40 years of age	1. hyperfiltering: above the threshold 2. hypofiltering: below 60 mL·min^{-1}·1.73 m^{-2} 3. normofiltering: in between
	Based on the 95th and 5th age- and gender specific percentiles	1. hyperfiltering: above the 95th percentile 2. hypofiltering: below the 5th percentile 3. normofiltering: in between

eGFR = estimated glomerular filtration rate; KDIGO = Kidney Disease: Improving Global Outcomes.

Table S2. Baseline clinical features in the RIACE participants with valid information on vital status on October 31 2015, stratified by eGFR KDIGO categories and subcategories.

Variable	eGFR KDIGO categories and subcategories						*P*
	1a	1b	2	3a	3b	4-5	
n (%)	1.344 (8.6)	4.432 (28.3)	7.174 (45.8)	1.667 (10.6)	760 (4.9)	279 (1.8)	
eGFR, mL/min/1.73m^2	112.7±7.8 (105.0-176.0)	96.5±4.2 (90.0-104.9)	77.1±8.5 (60.0-89.9)	53.3±4.2 (45.0-59.9)	38.4±4.3 (30.0-44.9)	22.6±6.0 (4.1-29.9)	
Deaths, n (%)	127 (9.4)	549 (12.4)	1,653 (23.0)	652 (39.1)	434 (57.1)	187 (67.0)	<0.0001
Age, years	52.2±9.3	62.2±7.7	69.3±8.6	73.5±8.4	74.4±8.7	74.3±9.0	<0.0001
Gender, n (%)							<0.0001
Females	574 (42.7)	1,838 (41.5)	2,989 (41.7)	823 (49.4)	389 (51.2)	141 (50.5)	
Males	770 (57.3)	2,594 (58.5)	4,185 (58.3)	844 (50.6)	371 (48.8)	138 (49.5)	
Smoking status, n (%)							<0.0001
Never	704 (52.4)	2,450 (55.3)	4,105 (57.2)	978 (58.7)	451 (59.3)	161 (57.7)	
Former	283 (21.1)	1,159 (26.2)	2,128 (29.7)	526 (31.6)	230 (30.3)	81 (29.0)	
Current	357 (26.6)	823 (18.6)	941 (13.1)	163 (9.8)	79 (10.4)	37 (13.3)	
Diabetes duration, years	7.7±7.1	10.9±8.7	14.1±10.3	16.9±11.2	17.0±10.7	20.0±11.4	<0.0001
Age at diagnosis, years	44.5±9.8	51.3±10.1	55.2±11.0	56.6±11.8	57.4±12.0	54.3±12.8	<0.0001
HbA_{1c}, mmol/mol	60.9±20.2	58.1±16.0	58.5±15.6	60.5±16.4	61.2±17.8	60.2±17.7	<0.0001
Anti-hyperglycaemic tx, n (%)							<0.0001
Lifestyle	229 (17.0)	619 (14.0)	1,012 (14.1)	168 (10.1)	66 (8.7)	19 (6.8)	
Non-insulin	796 (59.2)	2,885 (65.1)	4,515 (62.9)	944 (56.6)	389 (51.2)	90 (32.3)	
Insulin	319 (23.7)	928 (20.9)	1,647 (23.0)	555 (33.3)	305 (40.1)	170 (60.9)	
BMI, kg/m^2	29.9±6.4	29.0±5.2	28.7±4.9	28.9±4.9	29.2±5.1	29.8±5.8	<0.0001
Waist circumference, cm	104.4±12.9	102.6±10.5	102.0±9.9	102.3±9.9	102.8±10.2	103.9±11.4	<0.0001
Triglycerides, mmol/L	1.65±1.42	1.52±0.95	1.52±0.89	1.65±0.93	1.91±1.15	2.08±1.29	<0.0001
Total cholesterol, mmol/L	4.84±1.04	4.79±0.98	4.77±0.96	4.76±0.99	4.79±1.12	4.90±1.17	0.038
HDL cholesterol, mmol/L	1.26±0.35	1.31±0.35	1.31±0.35	1.26±0.35	1.21±0.37	1.20±0.42	<0.0001
Non-HDL cholesterol, mmol/L	3.58±1.01	3.49±0.95	3.46±0.93	3.51±0.92	3.58±1.07	3.70±1.09	<0.0001
LDL cholesterol, mmol/L	2.85±0.87	2.80±0.83	2.78±0.84	2.76±0.84	2.73±0.93	2.74±0.89	0.008
Dyslipidaemia, n (%)	1,029 (76.6)	3,631 (81.9)	5,936 (82.7)	1,402 (84.1)	623 (82.0)	235 (84.2)	<0.0001
Lipid-lowering tx, n (%)	402 (29.9)	1,945 (43.9)	3,414 (47.6)	892 (53.5)	435 (57.2)	150 (53.8)	<0.0001
Systolic BP, mmHg	131.8±16.1	136.8±17.3	139.4±18.0	139.5±18.9	139.3±19.3	141.3±20.8	<0.0001

Diastolic BP, mmHg	79.4±9.6	79.4±9.2	78.7±9.3	77.7±9.6	77.0±10.1	77.6±11.2	<0.0001
Pulse pressure, mmHg	52.4±12.7	57.3±14.7	60.7±15.7	61.8±16.8	62.3±17.2	63.7±18.0	<0.0001
Hypertension, n (%)	940 (69.9)	3,600 (81.2)	6,359 (88.6)	1,553 (93.2)	729 (96.9)	269 (96.4)	<0.0001
Anti-hypertensive tx, n (%)	649 (48.3)	2,762 (62.3)	5,275 (73.5)	1,425 (85.5)	699 (92.0)	262 (93.9)	<0.0001
RAS blocker tx, n (%)	553 (41.1)	2,319 (52.3)	4,437 (61.8)	1,208 (72.5)	614 (80.8)	209 (74.9)	<0.0001
Anti-platelet tx, n (%)	321 (23.9)	1,443 (32.6)	3,003 (41.9)	882 (52.9)	436 (57.4)	163 (58.4)	<0.0001
Anti-coagulant tx, n (%)	11 (0.8)	103 (2.3)	311 (4.3)	135 (8.1)	89 (11.7)	20 (7.2)	<0.0001
Albuminuria, mg/24 hours	60.0±490.1	39.6±178.8	52.4±230.0	115.4±371.4	193.1±419.2	578.4±990.6	<0.0001
Albuminuria categories, n (%)							<0.0001
Normoalbuminuria	1,027 (76.4)	3,537 (79.8)	5,420 (75.6)	1,036 (62.1)	372 (48.9)	68 (24.4)	
Microalbuminuria	281 (20.9)	791 (17.8)	1,527 (21.3)	504 (30.2)	261 (34.3)	101 (36.2)	
Macroalbuminuria	36 (2.7)	104 (2.3)	227 (3.2)	127 (7.6)	127 (16.7)	110 (39.4)	
Serum creatinine, µmol/L	51.7±11.9	63.4±10.9	80.3±13.1	104.7±15.2	137.0±22.8	233.3±112.8	<0.0001
DR, n (%)							<0.0001
No	1,144 (85.1)	3,583 (80.8)	5,618 (78.3)	1,183 (71.0)	514 (67.6)	147 (52.7)	
Non-advanced	113 (8.4)	488 (11.0)	911 (12.7)	266 (16.0)	114 (15.0)	55 (19.7)	
Advanced	87 (6.5)	361 (8.1)	645 (9.0)	218 (13.1)	132 (17.4)	77 (27.6)	
CVD, n (%)							
Any	130 (9.7)	745 (16.8)	1688 (23.5)	597 (35.8)	329 (43.3)	131 (47.0)	<0.0001
Myocardial infarction	63 (4.7)	351 (7.9)	810 (11.3)	287 (17.2)	171 (22.5)	60 (21.5)	<0.0001
Coronary revascularization	57 (4.2)	354 (8.0)	718 (10.0)	256 (15.4)	142 (18.7)	52 (18.6)	<0.0001
Any coronary event	80 (6.0)	511 (11.5)	1105 (15.4)	394 (23.6)	225 (29.6)	81 (29.0)	<0.0001
Stroke	13 (1.0)	86 (1.9)	255 (3.6)	84 (5.0)	51 (6.7)	24 (8.6)	<0.0001
Carotid revascularization	15 (1.1)	164 (3.7)	382 (5.3)	172 (10.3)	84 (11.1)	39 (14.0)	<0.0001
Any cerebro-vascular event	28 (2.1)	239 (5.4)	602 (8.4)	241 (14.5)	127 (16.7)	55 (19.7)	<0.0001
Ulcer/gangrene/amputation	24 (1.8)	89 (2.0)	248 (3.5)	103 (6.2)	62 (8.2)	30 (10.8)	<0.0001
Lower limb revascularization	4 (0.3)	72 (1.6)	204 (2.8)	106 (6.4)	46 (6.1)	18 (6.5)	<0.0001
Any peripheral event	25 (1.9)	148 (3.3)	399 (5.6)	181 (10.9)	89 (11.7)	41 (14.7)	<0.0001
Comorbidities, n (%)							
Any	215 (16.0)	718 (16.2)	1,250 (17.4)	350 (21.0)	185 (24.3)	69 (24.7)	<0.0001
COPD	56 (4.2)	143 (3.2)	276 (3.8)	115 (6.9)	54 (7.1)	30 (10.8)	<0.0001
Chronic liver disease	126 (9.4)	380 (8.6)	594 (8.3)	147 (8.8)	87 (11.4)	27 (9.7)	0.074
Cancer	59 (4.4)	241 (5.4)	510 (7.1)	129 (7.7)	66 (8.7)	26 (9.3)	<0.0001

Values are mean±SD or median (interquartile range) for continuous variables, and number of cases (percentage) for categorical variables. eGFR = estimated glomerular filtration rate; KDIGO = Kidney Disease: Improving Global Outcomes; HbA_{1c} = haemoglobin A_{1c}; BMI = body mass index; BP = blood pressure; RAS = renin angiotensin system; DR = diabetic retinopathy; CVD = cardiovascular disease; COPD = chronic obstructive pulmonary disease.

Table S3. Baseline clinical features in the RIACE participants with valid information on vital status on October 31 2015, stratified by filtration status according to age- and gender-specific 95th and 5th percentiles.

Variable	Normofiltering	Hyperfiltering	Hypofiltering	*P*
n (%)	14,108 (90.1)	774 (4.9)	774 (4.9)	
eGFR, mL/min/1.73m^2	81.1±17.7 (27.8-127.2)	108.8±12.5 (86.4-176.0)	35.5±13.0 (4.1-75.2)	
Deaths, n (%)	3,047 (21.6)	176 (22.7)	379 (49.0)	<0.0001
Age, years	66.6±10.3	64.8±11.0	67.4±10.3	<0.0001
Gender, n (%)				0.995
Females	6,088 (43.2)	333 (43.0)	333 (43.0)	
Males	8,020 (56.8)	441 (57.0)	441 (57.0)	
Smoking status, n (%)				0.013
Never	7,998 (56.7)	427 (55.2)	424 (54.8)	
Former	3,965 (28.1)	200 (25.8)	242 (31.3)	
Current	2,145 (15.2)	147 (19.0)	108 (14.0)	
Diabetes duration, years	13.2±10.2	11.2±9.4	15.6±10.7	<0.0001
Age at diagnosis, years	53.5±11.3	53.6±11.8	51.8±12.0	<0.0001
HbA_{1c}, mmol/mol	58.8±16.2	59.9±18.7	60.3±18.0	0.009
Anti-hyperglycaemic tx, n (%)				<0.0001
Lifestyle	1,934 (13.7)	106 (13.7)	73 (9.4)	
Non-insulin	8,840 (62.7)	482 (62.3)	297 (38.4)	
Insulin	3,334 (23.6)	186 (24.0)	404 (52.2)	
BMI, kg/m^2	28.9±5.1	29.0±5.8	30.1±5.5	<0.0001
Waist circumference, cm	102.4±10.3	102.5±11.9	104.9±11.1	<0.0001
Triglycerides, mmol/L	1.55±0.95	1.55±1.33	2.10±1.31	<0.0001
Total cholesterol, mmol/L	4.78±0.98	4.80±1.06	4.80±1.16	0.754
HDL cholesterol, mmol/L	1.29±0.35	1.34±0.37	1.17±0.38	<0.0001
Non-HDL cholesterol, mmol/L	3.49±0.94	3.47±1.04	3.63±1.10	<0.0001
LDL cholesterol, mmol/L	2.79±0.84	2.78±0.86	2.69±0.92	0.004
Dyslipidaemia, n (%)	10,120 (82.2)	476 (73.9)	2,260 (83.5)	<0.0001
Lipid-lowering tx, n (%)	5,524 (44.9)	237 (36.8)	1,477 (54.6)	<0.0001
Systolic BP, mmHg	138.1±17.9	136.0±17.3	138.6±20.2	0.004
Diastolic BP, mmHg	78.8±9.4	78.3±9.5	77.9±10.3	0.006
Pulse pressure, mmHg	59.3±15.7	57.7±14.3	60.8±17.6	0.001
Hypertension, n (%)	12,096 (85.7)	621 (80.2)	733 (94.7)	<0.0001
Anti-hypertensive tx, n (%)	9,881 (70.0)	491 (63.4)	700 (90.4)	<0.0001
RAS blocker tx, n (%)	8,356 (59.2)	403 (52.1)	581 (75.1)	<0.0001
Anti-platelet tx, n (%)	5,545 (39.3)	291 (37.6)	412 (53.2)	<0.0001
Anti-coagulant tx, n (%)	583 (4.1)	14 (1.8)	72 (9.3)	<0.0001
Albuminuria, mg/24 hours	57.5±243.7	70.2±603.1	345.6±713.2	<0.0001
Albuminuria categories, n (%)				<0.0001
Normoalbuminuria	10,600 (75.1)	557 (72.0)	303 (39.1)	
Microalbuminuria	3,008 (21.3)	190 (24.5)	267 (34.5)	
Macroalbuminuria	500 (3.5)	27 (3.5)	204 (26.4)	
Serum creatinine, µmol/L	78.0±19.6	45.1±9.0	173.2±83.6	<0.0001
DR, n (%)				<0.0001
No	11,077 (78.5)	638 (82.4)	474 (61.2)	
Non-advanced	1,750 (12.4)	74 (9.6)	123 (15.9)	
Advanced	1,281 (9.1)	62 (8.0)	177 (22.9)	
CVD, n (%)				

Any	3,172 (22.5)	124 (16.0)	324 (41.9)	<0.0001
Myocardial infarction	1,514 (10.7)	66 (8.5)	162 (20.9)	<0.0001
Coronary revascularization	1,369 (9.7)	51 (6.6)	159 (20.5)	<0.0001
Any coronary event	2,088 (14.8)	84 (10.9)	224 (28.9)	<0.0001
Stroke	443 (3.1)	17 (2.2)	53 (6.8)	<0.0001
Carotid revascularization	758 (5.4)	16 (2.1)	82 (10.6)	<0.0001
Any cerebro-vascular event	1,136 (8.1)	30 (3.9)	126 (16.3)	<0.0001
Ulcer/gangrene/amputation	465 (3.3)	22 (2.8)	69 (8.9)	<0.0001
Lower limb revascularization	393 (2.8)	6 (0.8)	51 (6.6)	<0.0001
Any peripheral event	758 (5.4)	25 (3.2)	100 (12.9)	<0.0001
Comorbidities, n (%)				
Any	2,439 (17.3)	165 (21.3)	183 (23.6)	<0.0001
COPD	572 (4.1)	50 (6.5)	52 (6.7)	<0.0001
Chronic liver disease	1,188 (8.4)	78 (10.1)	95 (12.3)	<0.0001
Cancer	908 (6.4)	59 (7.6)	64 (8.3)	0.066

Values are mean±SD or median (interquartile range) for continuous variables, and number of cases (percentage) for categorical variables. eGFR = estimated glomerular filtration rate; HbA_{1c} = haemoglobin A_{1c}; BMI = body mass index; BP = blood pressure; RAS = renin angiotensin system; DR = diabetic retinopathy; CVD = cardiovascular disease; COPD = chronic obstructive pulmonary disease.

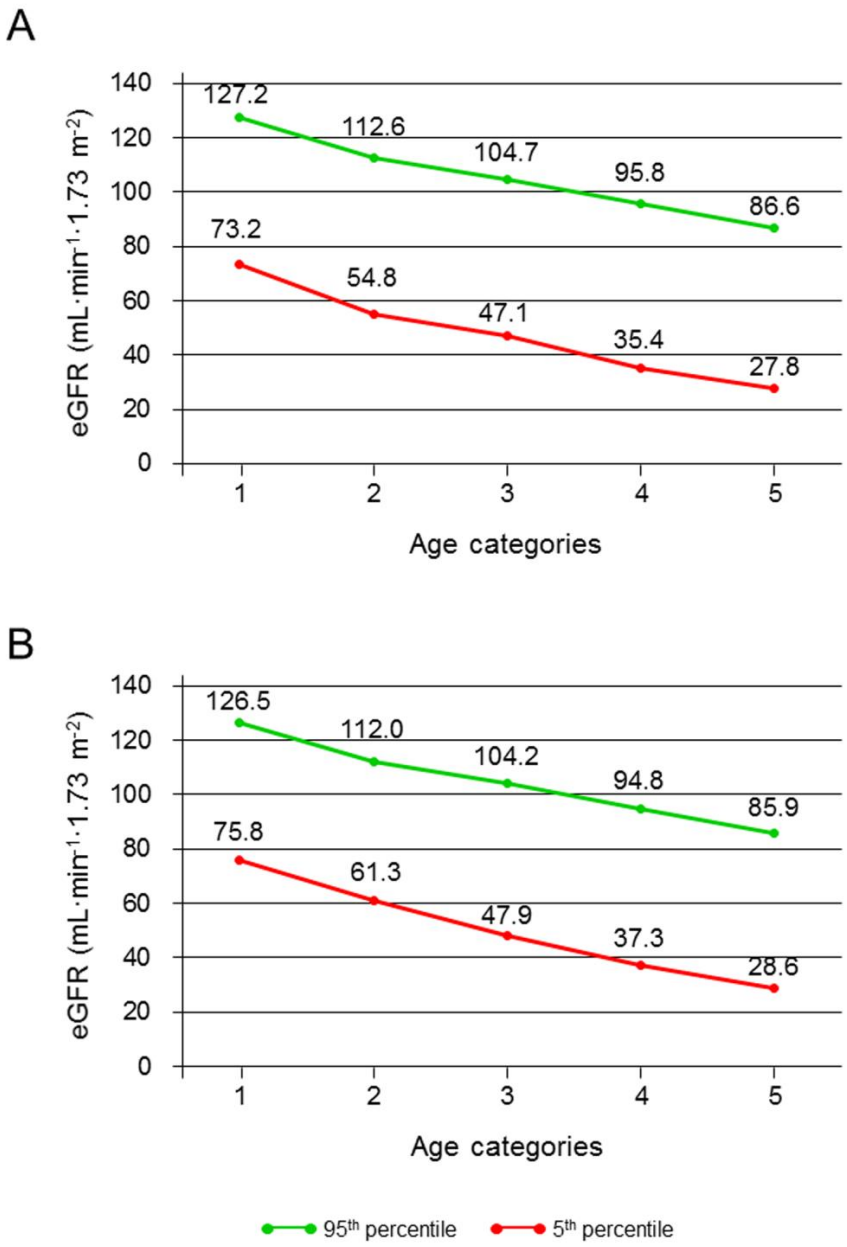

Figure S1. Hyperfiltration (95th percentile) and hypofiltration (5th percentile) eGFR thresholds by age categories in females (A) and males (B). Age categories: 1 = <50 years; 2 = 50-59 years; 3 = 60-69 years; 4 = 70-79 years; 5 = ≥80 years. eGFR = estimated glomerular filtration rate.

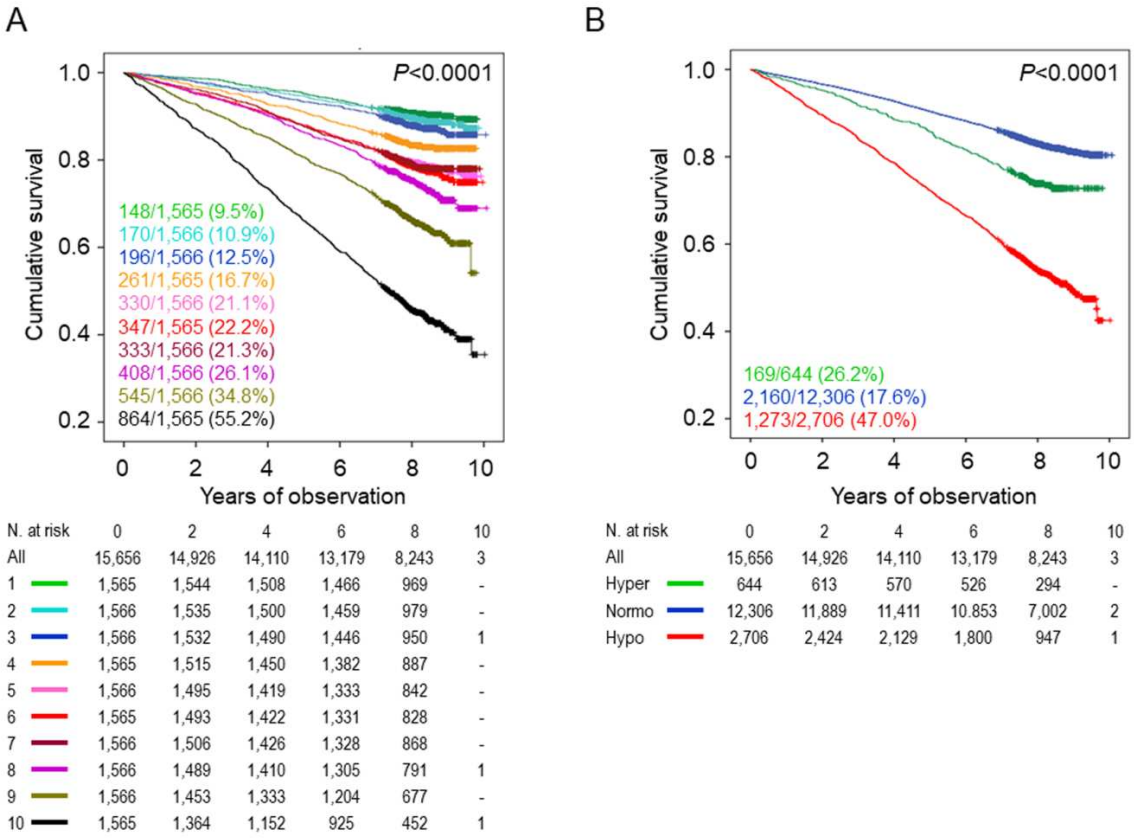

Figure S2. Cumulative survival by Kaplan-Meier analysis according to eGFR deciles (A) and age-adjusted filtration status (B). Numbers (percentages) of death are shown for each group. eGFR = estimated glomerular filtration rate.

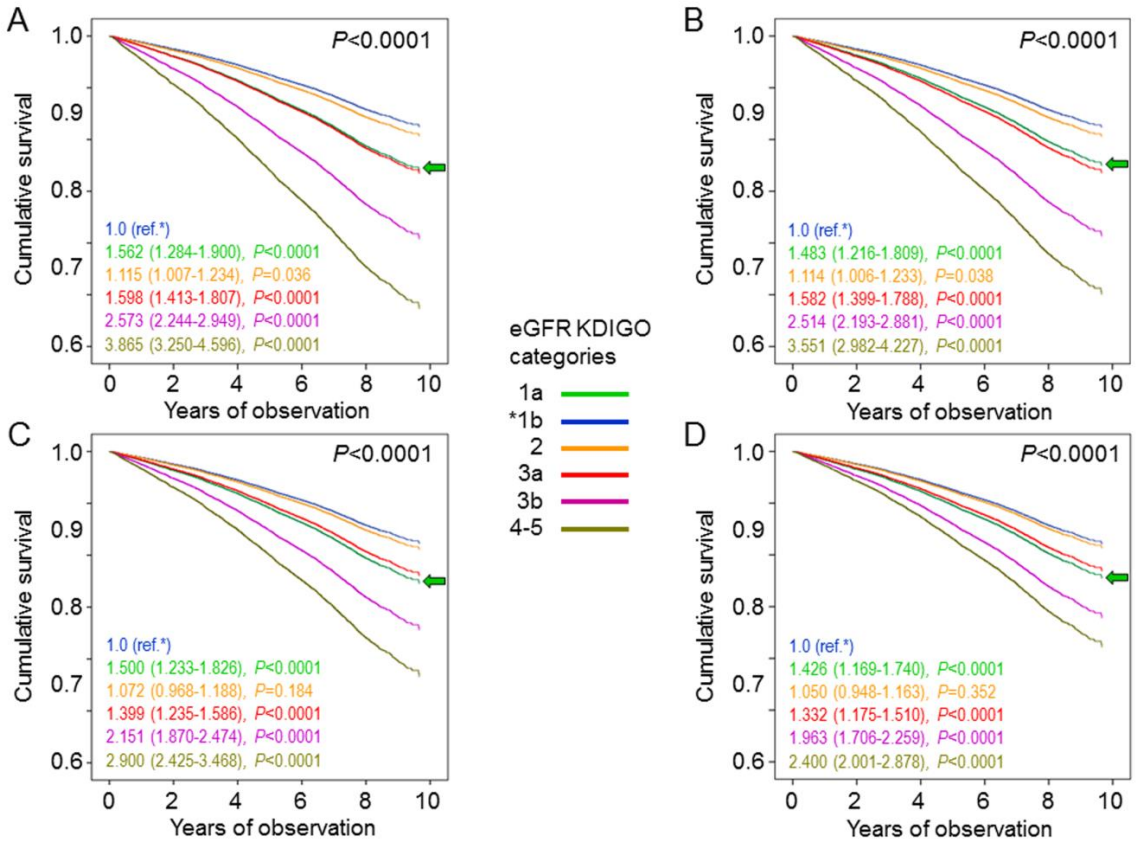

Figure S3. Cox proportional hazards regression, adjusted for age and gender (A), plus albuminuria (B), plus CVD risk factors (C) plus complications/comorbidities (D), according to eGFR KDIGO categories and subcategories. HRs (95% CI) for mortality are shown for each group; the green arrow indicates the G1a category. CVD = cardiovascular disease; eGFR = estimated glomerular filtration rate; KDIGO = Kidney Disease: Improving Global Outcomes; HR = hazard ratio; CI = confidence interval.

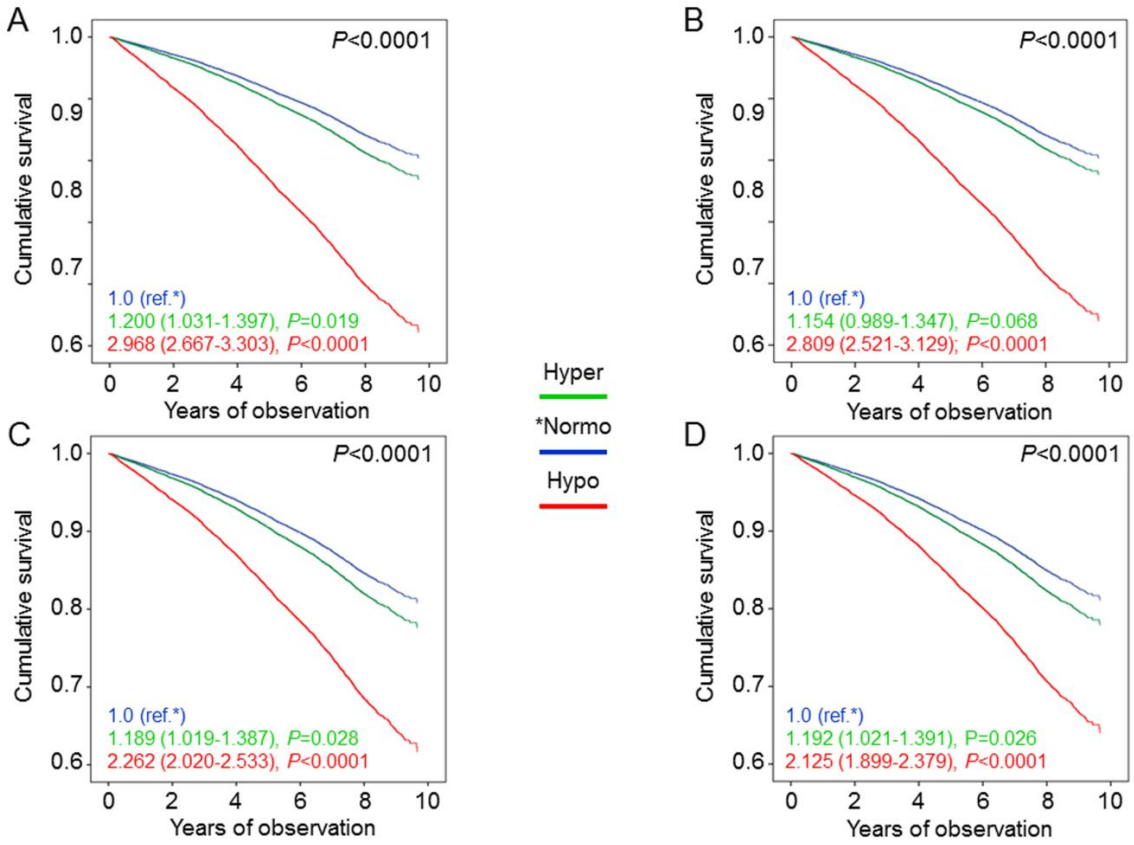

Figure S4. Cox proportional hazards regression, adjusted for age and gender (A), plus albuminuria (B), plus CVD risk factors (C) plus complications/comorbidities (D), according to age- and gender-adjusted filtration status. HRs (95% CI) for mortality are shown for each group. CVD = cardiovascular disease; HR = hazard ratio; CI = confidence interval; hyper = hyperfiltering; normo = normofiltering; hypo = hypofiltering.