Web appendix for "Association of estimated glomerular filtration rate and albuminuria with kidney outcomes: a collaborative meta-analysis of general population and high risk cohorts" Kidney Int (submitted)

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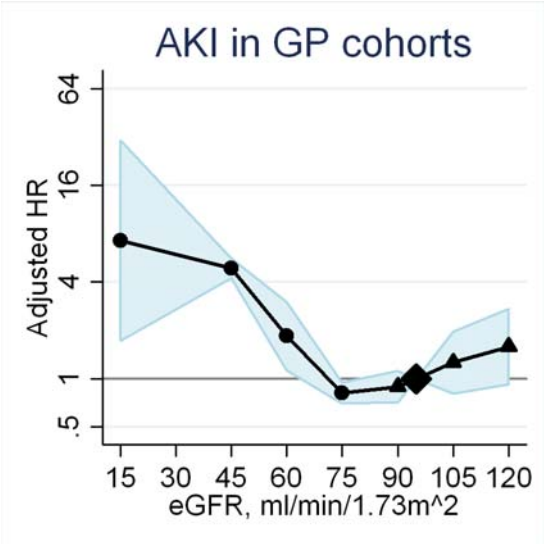
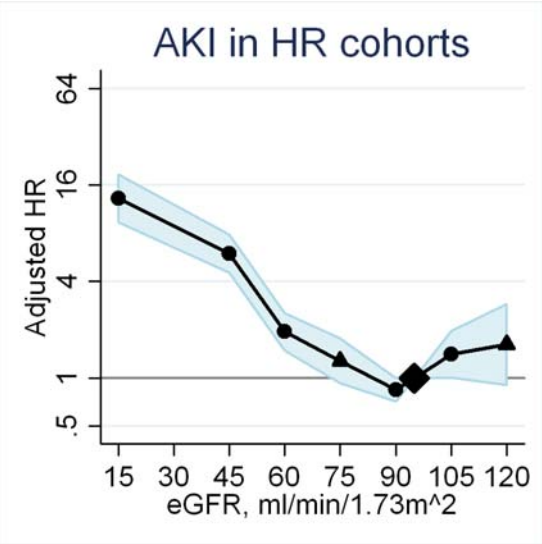
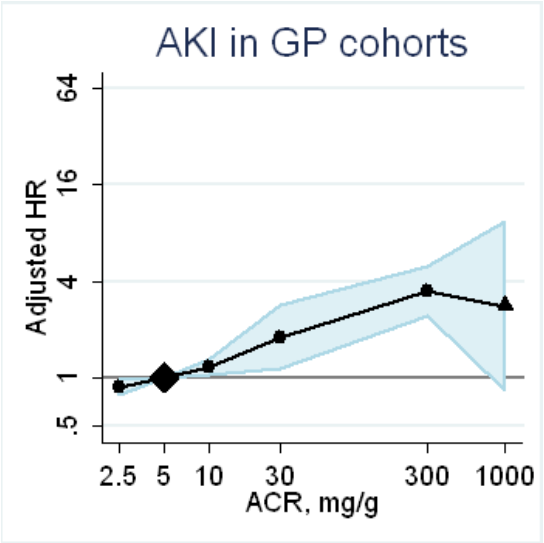
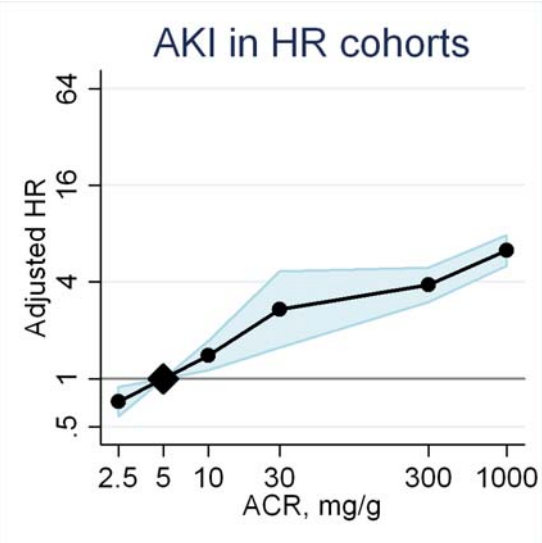
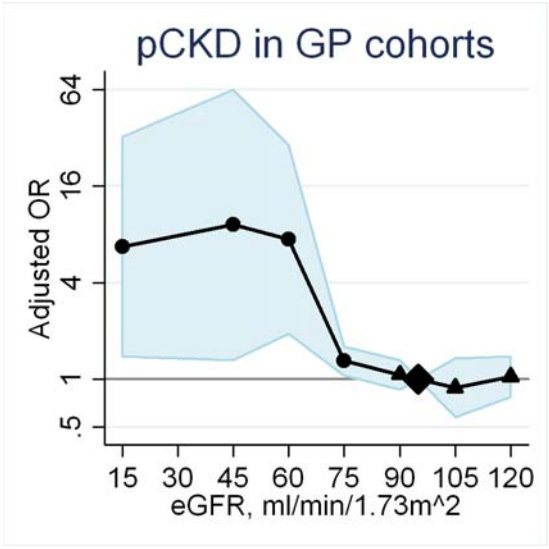


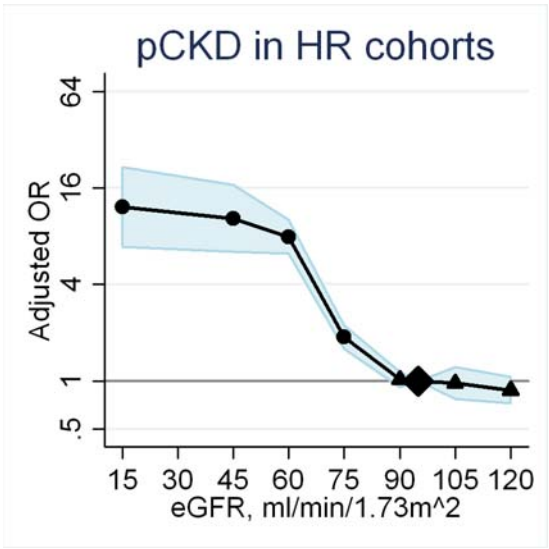


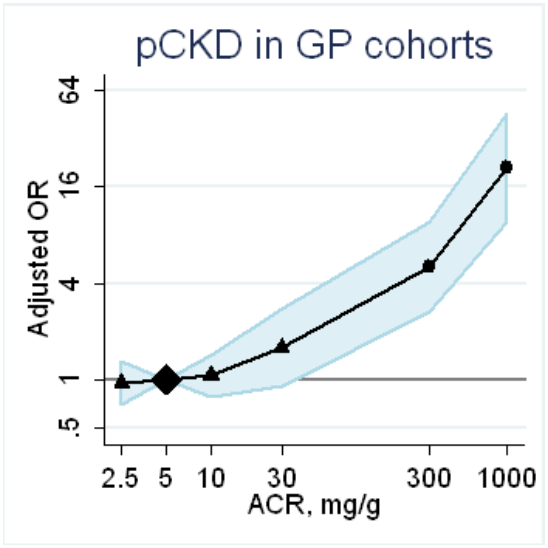


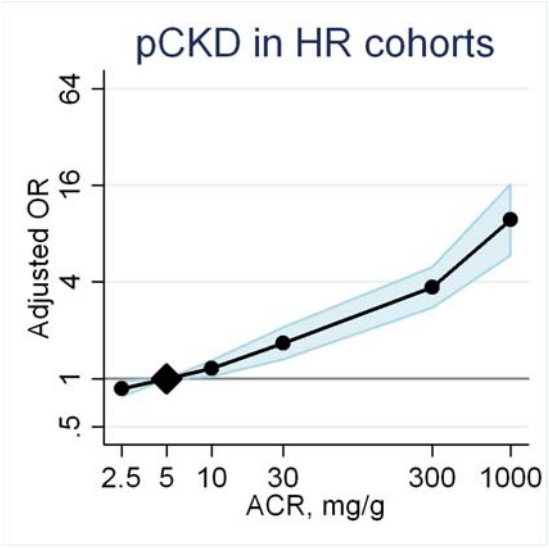


Web appendix Figure 2: Pooled adjusted hazard ratios (95% confidence intervals) for progressive chronic kidney disease (pCKD) according to spline eGFR and albumin-to-creatinine ratio adjusted for each other and for age, sex and cardiovascular risk factors. Reference category is eGFR 95 mL/min/1.73 m2 plus albumin-to-creatinine ratio 5 mg/g or dipstick -/±. Left panels show results for General Population cohorts, and right panels for high risk cohorts. Dots represent statistical significance and triangles represent non significance.

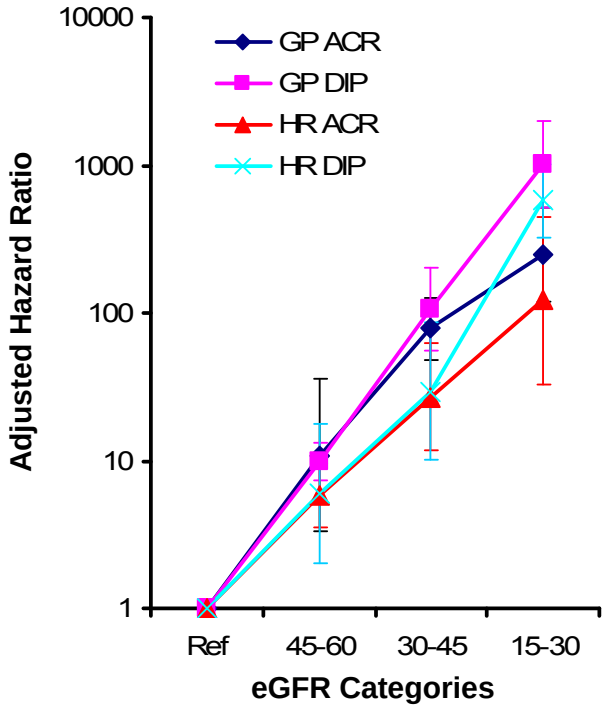


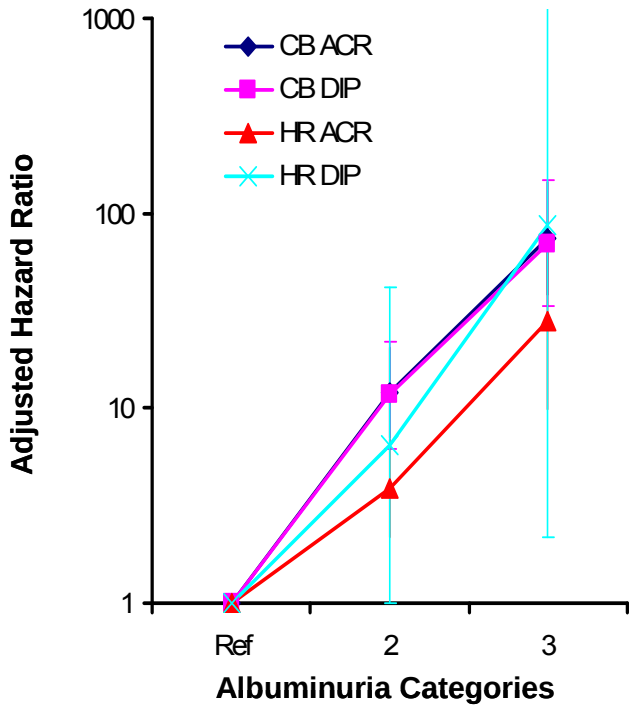






Web appendix Figure 3: Pooled hazard ratios for end-stage renal disease according to eGFR and albuminuria, adjusted for each other and for age, sex and cardiovascular risk factors (categorical analyses). Four groups are shown (general population cohorts with albumin-to-creatinine ratio data (GP ACR), general population cohorts with dipstick data (GP DIP), high risk cohorts with albumin-to-creatinine ratio data (HR ACR) and high risk cohorts with dipstick data (HR DIP)). Upper panel shows results for eGFR (reference category is eGFR >60 ml/min/1.73m^2), and lower panel for albuminuria (reference category is albumin-to-creatinine ratio <30 mg/g or dipstick -/±. Category 2 represents an albumin-to-creatinine ratio 30-299 mg/g or dipstick 1+, and category 3 represents albumin-to-creatinine ratio ≥300 mg/g or dipstick ≥2+).





Web Appendix Table 1. Acronyms or abbreviations for studies included in the current report and their key references.

General population cohorts:

AKDN UDIP:	Alberta Kidney Disease Network[1]
ARIC:	Atherosclerosis Risk in Communities Study[2]
AusDiab:	Australian Diabetes, Obesity, and Lifestyle Study[3]
Beaver Dam:	Beaver Dam CKD Study[4]
CHS:	Cardiovascular Health Study[5]
HUNT:	Nord Trøndelag Health Study[6]
MESA:	Multi-Ethnic Study of Atherosclerosis Study[7]
Okinawa 83:	Okinawa Study (1983)[8]
Okinawa 93	Okinawa Study (1993)[9]

High Risk cohorts:

ADVANCE:	The Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation (ADVANCE) trial[10]
AKDN ACR:	Alberta Kidney Disease Network[1]
CARE:	the Cholesterol and Recurrent Events (CARE) Trial[11]
ONTARGET:	Ongoing Telmisartan Alone and in combination with Ramipril Global Endpoint Trial (ONTARGET) study[12]
Pima:	PIMA Indian Study[13]
TRANSCEND:	Telmisartan Randomised Assessment Study in ACE Intolerant Subjects with Cardiovascular Disease Trial[14]
KP Hawaii:	Kaiser Permanente Hawaii Region[15]
MRFIT:	Multiple Risk Factor Intervention Trial[16]

Key references:

1. Hemmelgarn BR, Manns BJ, Lloyd A, James MT, Klarenbach S, Quinn RR, et al. Relation between kidney function, proteinuria, and adverse outcomes. JAMA 2010; 303:423-9.

2. Matsushita K, Selvin E, Bash LD, Franceschini N, Astor BC, Coresh J. Change in estimated GFR associates with coronary heart disease and mortality. J Am Soc Nephrol 2009; 20:2617-24.

3. White SL, Polkinghorne KR, Atkins RC, Chadban SJ. Comparison of the Prevalence and Mortality Risk of CKD in Australia Using the CKD Epidemiology Collaboration (CKD-EPI) and Modification of Diet in Renal Disease (MDRD) Study GFR Estimating Equations: The AusDiab (Australian Diabetes, Obesity and Lifestyle) Study. Am J Kidney Dis 2010;55:660-7

4. Shankar A, Klein R, Klein BEK. The association among smoking, heavy drinking and chronic kidney disease. American Journal of Epidemiology. 2006;164:263-71

5. Shlipak MG, Katz R, Kestenbaum B, Fried LF, Newman AB, Siscovick DS, et al. Rate of kidney function decline in older adults: a comparison using creatinine and cystatin C. Am J Nephrol 2009; 30:171-8.

6. Hallan SI, Ritz E, Lydersen S, Romundstad S, Kvenild K, Orth SR. Combining GFR and albuminuria to classify CKD improves prediction of ESRD. J Am Soc Nephrol 2009;20:1069-77

7. Bui AL, Katz R, Kestenbaum B, de Boer IH, Fried LF, Polak JF, et al. Cystatin C and carotid intima-media thickness in asymptomatic adults: the Multi-Ethnic Study of Atherosclerosis (MESA). Am J Kidney Dis 2009; 53:389-98.

8. Iseki K, Ikemiya Y, Iseki C, Takishita S. Proteinuria and the risk of developing end-stage renal disease. Kidney Int 2003;63:1468-74.

9. Iseki K, Kinjo K, Iseki C, Takishita S. Relationship between predicted creatinine clearance and proteinuria and the risk of developing ESRD in Okinawa, Japan. Am J Kidney Dis 2004;44:806-14

10. ADVANCE Collaborative Group, Patel A, MacMahon S, Chalmers J, Neal B, Billot L, Woodward M, Marre M, Cooper M, Glasziou P, Grobbee D, Hamet P, Harrap S, Heller S, Liu L, Mancia G, Mogensen CE, Pan C, Poulter N, Rodgers A, Williams B, Bompoint S, de Galan BE, Joshi R, Travert F. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. N Engl J Med 2008;358:2560-72

11. Tonelli M, Jose P, Curhan G, Sacks F, Braunwald E, Pfeffer M and Cholesterol and Recurrent Events (CARE) Trial Investigators: Proteinuria, impaired kidney function, and adverse outcomes in people with coronary disease: analysis of a previously conducted randomised trial. BMJ 2006;332;1426-31

12. Mann JF, Schmieder RE, McQueen M, Dyal L, Schumacher H, Pogue J, et al; ONTARGET investigators. Renal outcomes with telmisartan, ramipril, or both, in people at high vascular risk (the ONTARGET study): a multicentre, randomised, double-blind, controlled trial. Lancet 2008;372:547-53

13. Pavkov ME, Knowler WC, Hanson RL, Bennett PH, Nelson RG. Predictive power of sequential measures of albuminuria for progression to ESRD or death in Pima Indians with type 2 diabetes. Am J Kidney Dis 2008;51:759-66

14. Mann JFE, Schmieder RE, Dyal L, McQueen M, Schumacher H, Pogue J, Wang X, Probstfield JL, Avezum A, Carduna-Munoz E, Dagenais GR, Diaz R, Fodor G, Maillon JM, Ryden LR, Yu CM, Teo KK, Yusuf S. Effects of telmisartan on renal outcomes. Ann Int Med 2009;151:1-10

15. Lee BJ, Forbes K. The role of specialists in managing the health of populations with chronic illness: the example of chronic kidney disease. BMJ. 2009;339:800-2

16. Ishani A, Grandits GA, Grimm RH, Svendsen KH, Collins AJ, Prineas RJ, Neaton JD. Association of single measurements of dipstick proteinuria, estimated glomerular filtration rate, and hematocrit with 25-year incidence of end-stage renal disease in the multiple risk factor intervention trial. J Am Soc Nephrol 2006;17:1444-52

Web appendix Table 2: Incidence rate for end-stage renal disease (expressed per 1000 patient years). Shaded areas make up the combined reference groups.

Pooled analysis of general population cohorts with albumin-to-creatinine ratio or dipstick data

		Overall					Subdivision according to age									
							<65 year					>65 year				
		Albuminuria					Albuminuria					Albuminuria				
		1	2	3	4	**All**	1	2	3	4	**All**	1	2	3	4	**All**
	>105			0.13	0.75				0.14	0.78				0.00	0.00	
	90-104	0.04		0.05	0.57	*0.06*	0.03		0.06	0.39	*0.05*	0.09		0.00	2.38	*0.11*
	75-89			0.11	2.35				0.11	2.75				0.12	0.00	
	60-74			0.27	2.66				0.18	3.15				0.45	1.81	
eGFR	45-59	0.12	0.77	1.44	5.13	*0.34*	0.02	1.11	1.87	8.42	*0.34*	0.21	0.57	1.19	2.52	*0.33*
mL/min/1.73m²	30-44	1.03	1.55	9.15	27.07	*4.02*	2.71	5.06	18.6	40.3	*10.3*	0.70	0.79	7.19	20.6	*2.59*
	15-29	9.05	19.5	37.7	128.4	*43.0*	25.6	87.9	86.3	195	*113*	6.40	6.19	24.5	85.9	*23.2*
	All	*0.09*		*1.61*	*14.9*	*0.31*	*0.06*		*1.14*	*14.3*	*0.23*	*0.25*		*2.72*	*16.7*	*0.73*

Pooled analysis of cohorts selected for high risk of chronic kidney disease with albumin-to-creatinine ratio or dipstick data

		Overall					Subdivision according to age									
							<65 year					>65 year				
		Albuminuria					Albuminuria					Albuminuria				
		1	2	3	4	**All**	1	2	3	4	**All**	1	2	3	4	**All**
	>105			1.22	6.52				1.34	6.50				0.18	6.37	
	90-104	0.22		0.39	5.00	*0.45*	0.22		0.44	5.29	*0.48*	0.20		0.27	3.07	*0.37*
	75-89			0.30	4.56				0.26	5.02				0.36	3.30	
	60-74			0.36	7.77				0.37	10.28				0.36	4.42	
eGFR	45-59	0.25	0.36	1.65	13.38	*1.44*	0.19	0.31	1.65	19.45	*2.13*	0.31	0.38	1.66	7.24	*1.03*
mL/min/1.73m²	30-44	1.56	2.42	4.33	29.80	*7.35*	1.62	3.09	7.13	49.69	*15.90*	1.59	2.27	3.40	17.34	*4.40*
	15-29	1.57	12.78	20.93	133.0	*60.98*	0.00	28.21	26.77	187.9	*106.8*	1.84	9.15	18.74	97.91	*37.38*
	All	*0.31*		*1.41*	*25.72*	*1.83*	*0.26*		*1.23*	*27.47*	*1.70*	*0.43*		*1.63*	*22.9*	*2.07*

Abbreviations are: ACR. albumin:creatinine ratio; eGFR. estimated glomerular flitration rate, albuminuria 1, ACR <10 mg/g or dipstick negative;, albuminuria 2, ACR 10-29 mg/g or dipstick trace; albuminuria 3, ACR 30-299 mg/g or dipstick 1+; albuminuria 4, ACR≥300 mg/g or dipstick ≥2.

Web appendix Table 3: Incidence rate for acute kidney injury (expressed per 1000 patient years). Shaded areas make up the combined reference groups.

Pooled analysis of general population cohorts with albumin-to-creatinine ratio or dipstick data

		Overall					Subdivision according to age									
							<65 year					>65 year				
		Albuminuria					Albuminuria					Albuminuria				
		1	2	3	4	**All**	1	2	3	4	**All**	1	2	3	4	**All**
	>105			3.55	7.57				3.40	6.67				5.90	25.51	
	90-104	0.98		3.04	5.73	*1.14*	0.59		2.02	3.62	*0.67*	3.68		13.69	39.33	*4.25*
	75-89			3.45	5.86				1.57	5.30				12.90	7.76	
	60-74			6.46	13.77				3.38	6.00				13.29	31.36	
eGFR	45-59	4.73	13.10	21.40	36.08	*6.48*	1.44	7.67	8.24	26.93	*2.47*	7.77	16.42	29.77	44.71	*10.00*
mL/min/1,73m²	30-44	24.49	42.53	52.09	76.62	*32.65*	15.68	66.53	55.60	71.76	*28.72*	26.09	43.59	51.35	81.16	*33.26*
	15-29	69.66	65.82	92.93	109.6	*81.37*	54.68	39.47	63.97	86.44	*68.96*	74.79	74.80	97.10	122.6	*87.38*
	All	*1.69*		*10.15*	*26.26*	*2.21*	*0.70*		*3.83*	*14.67*	*0.91*	*6.93*		*27.04*	*53.87*	*8.77*

Pooled analysis of cohorts selected for high risk of chronic kidney disease with albumin-to-creatinine ratio or dipstick data

		Overall					Subdivision according to age									
							<65 year					>65 year				
		Albuminuria					Albuminuria					Albuminuria				
		1	2	3	4	**All**	1	2	3	4	**All**	1	2	3	4	**All**
	>105			2.99	5.54				2.89	4.04				4.07	26.74	
	90-104	1.41		3.35	5.43	*2.25*	1.23		3.16	5.30	*1.86*	1.97		4.05	6.31	*3.29*
	75-89			3.09	9.92				2.55	9.40				4.08	10.21	
	60-74			6.06	13.73				4.09	13.28				8.10	13.64	
eGFR	45-59	2.28	8.00	13.42	29.03	*8.07*	1.44	7.95	11.79	25.63	*6.86*	2.86	7.71	14.74	31.95	*8.76*
mL/min/1,73m²	30-44	11.2	17.76	36.70	52.09	*27.63*	3.74	16.91	22.62	65.55	*27.38*	13.16	18.53	40.15	45.75	*27.7*
	15-29	25.74	48.66	69.90	104.7	*73.94*	34.01	17.48	21.98	100.0	*55.64*	23.43	56.52	90.11	113.2	*77.22*
	All	*2.33*		*9.08*	*26.59*	*4.88*	*1.51*		*4.70*	*21.08*	*2.84*	*3.80*		*14.53*	*33.83*	*8.15*

Abbreviations are: ACR. albumin:creatinine ratio; eGFR. estimated glomerular flitration rate, albuminuria 1, ACR <10 mg/g or dipstick negative;, albuminuria 2, ACR 10-29 mg/g or dipstick trace; albuminuria 3, ACR 30-299 mg/g or dipstick 1+; albuminuria 4, ACR≥300 mg/g or dipstick ≥2+.

Web appendix Table 4: Incidence rate for progressive chronic kidney disease (expressed per 1000 patient years). Shaded areas make up the combined reference groups.

Pooled analysis of general population cohorts with albumin-to-creatinine ratio or dipstick data

		Overall					Subdivision according to age									
							<65 year					>65 year				
		Albuminuria					Albuminuria					Albuminuria				
		1	2	3	4	**All**	1	2	3	4	**All**	1	2	3	4	**All**
	>105			1.56	12.6				1.76	12.59				0.00	NA	
	90-104	2.02		2.72	7.02	*2.48*	0.83		1.12	7.41	*1.12*	6.97		13.11	4.76	*8.03*
	75-89			5.25	25.21				2.40	22.58				14.45	33.37	
	60-74			16.80	47.50				8.72	39.66				28.44	62.73	
eGFR	45-59	23.91	31.91	63.61	135.1	*28.78*	8.28	12.99	34.96	137.0	*12.72*	36.12	43.13	79.37	133.8	*41.01*
mL/min/1,73m²	30-44	37.53	54.60	82.27	177.5	*55.37*	29.15	63.52	69.60	183.4	*59.62*	39.76	52.70	85.46	173.7	*54.24*
	15-29	33.12	55.36	82.08	178.9	*77.14*	61.11	101.4	118.3	192.2	*128.6*	27.08	44.39	72.02	168.2	*58.84*
	All	*5.62*		*25.93*	*89.59*	*7.55*	*1.62*		*10.13*	*70.54*	*2.71*	*17.36*		*49.74*	*115.9*	*21.27*

Pooled analysis of cohorts selected for high risk of chronic kidney disease with albumin-to-creatinine ratio or dipstick data

		Overall					Subdivision according to age									
							<65 year					>65 year				
		Albuminuria					Albuminuria					Albuminuria				
		1	2	3	4	**All**	1	2	3	4	**All**	1	2	3	4	**All**
	>105			4.43	27.52				4.54	29.71				3.87	10.93	
	90-104	5.51		5.75	14.44	*7.97*	3.01		5.56	12.00	*5.23*	9.65		6.19	24.44	*12.40*
	75-89			8.59	30.90				6.95	35.44				10.82	20.97	
	60-74			19.01	68.77				12.16	67.31				24.82	70.97	
eGFR	45-59	23.75	37.88	57.67	147.1	*43.84*	14.99	25.58	41.38	155.5	*36.33*	29.00	43.19	66.14	136.5	*48.04*
mL/min/1,73m²	30-44	33.55	35.35	64.99	160.3	*65.65*	12.61	35.61	54.37	180.8	*73.04*	39.33	35.13	69.17	148.0	*63.32*
	15-29	12.44	43.16	58.43	209.3	*103.3*	0.00	98.66	75.59	226.8	*147.9*	14.11	28.22	52.64	202.0	*85.94*
	All	*10.40*		*25.96*	*105.0*	*18.44*	*4.86*		*14.82*	*96.48*	*11.68*	*17.42*		*37.48*	*115.4*	*27.41*

Abbreviations are: ACR. albumin:creatinine ratio; eGFR. estimated glomerular flitration rate, albuminuria 1, ACR <10 mg/g or dipstick negative;, albuminuria 2, ACR 10-29 mg/g or dipstick trace; albuminuria 3, ACR 30-299 mg/g or dipstick 1+; albuminuria 4, ACR≥300 mg/g or dipstick ≥2+.

Web appendix Table 5: Distribution of subjects for analysis of incident end-stage renal disease (expressed as percentage of the total population under study). Shaded areas make up the combined reference groups. Absolute numbers of subjects per eGFR-albuminuria category can be calculated by multiplying proportions with the total number of subjects under investigation. For general population cohorts overall 811014, <65 year 667454 and >65 year 143560 subjects were included, whereas for high risk cohorts these numbers were 169222, 110880 and 58342, respectively.

Pooled analysis of general population cohorts with albumin-to-creatinine ratio or dipstick data

		Overall					Subdivision according to age									
							<65 year					>65 year				
		Albuminuria					Albuminuria					Albuminuria				
		1	2	3	4	**All**	1	2	3	4	**All**	1	2	3	4	**All**
	>105			0.30	0.11				0.33	0.12				0.14	0.04	
	90-104	86.3		0.50	0.17	*89.6*	91.7		0.54	0.18	*94.8*	61.3		0.30	0.10	*65.1*
	75-89			0.84	0.29				0.85	0.28				0.84	0.29	
	60-74			0.79	0.30				0.64	0.24				1.45	0.59	
eGFR	45-59	7.36	0.52	0.40	0.23	*8.51*	4.18	0.24	0.18	0.12	*4.72*	22.2	1.82	1.44	0.74	*26.2*
mL/min/1.73m²	30-44	1.13	0.13	0.16	0.15	*1.58*	0.22	0.03	0.04	0.06	*0.34*	5.38	0.64	0.75	0.56	*7.32*
	15-29	0.14	0.03	0.05	0.08	*0.31*	0.02	0.01	0.01	0.04	*0.08*	0.70	0.14	0.24	0.28	*1.36*
	<15	0.01	0.00	0.01	0.02	*0.04*	0.00	0.00	0.00	0.01	*0.02*	0.02	0.01	0.02	0.06	*0.11*
	All	*95.6*		*3.05*	*1.35*	*100*	*96.3*		*2.59*	*1.07*	*100*	*92.1*		*5.17*	*2.64*	*100*

Pooled analysis of cohorts selected for high risk of chronic kidney disease with albumin-to-creatinine ratio or dipstick data

		Overall					Subdivision according to age									
							<65 year					>65 year				
		Albuminuria					Albuminuria					Albuminuria				
		1	2	3	4	**All**	1	2	3	4	**All**	1	2	3	4	**All**
	>105			2.11	0.38				2.87	0.54				0.67	0.08	
	90-104	60.4		2.48	0.45	*78.6*	69.8		3.00	0.57	*88.4*	42.6		1.48	0.21	*59.9*
	75-89			4.53	0.80				4.75	0.94				4.12	0.53	
	60-74			6.25	1.15				4.90	1.01				8.82	1.41	
eGFR	45-59	6.02	4.96	3.44	1.05	*15.47*	4.13	2.42	1.83	0.79	*9.17*	9.60	9.80	6.51	1.54	*27.5*
mL/min/1.73m²	30-44	1.09	1.31	1.56	0.82	*4.78*	0.38	0.40	0.58	0.49	*1.85*	2.43	3.05	3.43	1.43	*10.4*
	15-29	0.09	0.15	0.39	0.45	*1.08*	0.02	0.04	0.15	0.29	*0.50*	0.23	0.35	0.83	0.76	*2.18*
	<15	0.00	0.00	0.01	0.10	*0.12*	0.00	0.00	0.01	0.09	*0.10*	0.00	0.00	0.02	0.14	*0.16*
	All	*74.0*		*20.77*	*5.20*	*100*	*77.2*		*18.1*	*4.73*	*100*	*68.0*		*25.9*	*6.10*	*100*

Abbreviations are: ACR. albumin:creatinine ratio; eGFR. estimated glomerular flitration rate, albuminuria 1, ACR <10 mg/g or dipstick negative; albuminuria 2, ACR 10-29 mg/g or dipstick trace; albuminuria 3, ACR 30-299 mg/g or dipstick 1+; albuminuria 4, ACR≥300 mg/g or dipstick ≥2+.

Web appendix Table 6: Distribution of incident end-stage renal disease events (expressed as percentage of the total population under study). Absolute number of events per eGFR-albuminuria category can be calculated by multiplying proportions with the total number of events under investigation. For general population cohorts overall 860, <65 year 486 and >65 year 374 events were observed, whereas for high risk cohorts these numbers were 1341, 951 and 390, respectively.

Pooled analysis of general population cohorts with albumin-to-creatinine ratio or dipstick data

		Overall					**Subdivision according to age**									
							<65 year					**>65 year**				
		Albuminuria					**Albuminuria**					**Albuminuria**				
		1	2	3	4	**All**	1	2	3	4	**All**	1	2	3	4	**All**
	>105			0.23	0.23				0.41	0.41				0.00	0.00	
	90-104	10.4		0.23	0.35	*18.1*	12.4		0.41	0.21	*23.1*	7.75		0.00	0.53	*11.8*
	75-89			0.35	1.98				0.41	3.50				0.27	0.00	
	60-74			1.05	3.37				0.82	4.53				1.34	1.87	
eGFR	45-59	3.37	1.63	3.14	4.77	*12.9*	1.03	1.44	3.09	5.56	*11.1*	6.42	1.87	3.21	3.74	*15.2*
mL/min/1.73m²	30-44	3.84	0.58	5.35	12.7	*22.4*	2.88	0.41	3.09	10.7	*17.1*	5.08	0.80	8.29	15.2	*29.4*
	15-29	2.91	1.16	5.12	20.6	*29.8*	2.06	1.44	4.12	23.1	*30.7*	4.01	0.80	6.42	17.4	*28.6*
	<15	2.09	0.81	2.21	11.6	*16.7*	2.06	1.03	2.26	12.8	*18.1*	2.14	0.53	2.14	10.2	*15.0*
	All	*26.7*		*17.7*	*55.6*	*100*	*24.7*		*14.6*	*60.7*	*100*	*29.4*		*21.7*	*48.9*	*100*

Pooled analysis of cohorts selected for high risk of chronic kidney disease with albumin-to-creatinine ratio or dipstick data

		Overall					**Subdivision according to age**									
							<65 year					**>65 year**				
		Albuminuria					**Albuminuria**					**Albuminuria**				
		1	2	3	4	**All**	1	2	3	4	**All**	1	2	3	4	**All**
	>105			3.80	3.13				5.26	4.21				0.26	0.51	
	90-104	22.7		1.34	2.24	*43.8*	29.8		1.68	2.94	*55.2*	5.64		0.51	0.51	*15.9*
	75-89			1.34	2.68				1.47	3.36				1.03	1.03	
	60-74			1.64	4.85				1.37	5.15				2.31	4.10	
eGFR	45-59	1.64	1.19	2.83	6.04	*11.7*	1.58	0.74	1.47	6.31	*10.1*	1.79	2.31	6.15	5.38	*15.6*
mL/min/1.73m²	30-44	0.82	1.64	2.91	8.95	*14.3*	0.21	0.63	1.68	7.89	*10.4*	2.31	4.10	5.90	11.5	*23.9*
	15-29	0.07	0.67	2.76	16.5	*20.0*	0.00	0.42	1.37	13.3	*15.0*	0.26	1.28	6.15	24.4	*32.1*
	<15	0.00	0.15	0.60	9.47	*10.2*	0.00	0.11	0.74	8.41	*9.25*	0.00	0.26	0.26	12.1	*12.6*
	All	*28.9*		*17.2*	*53.8*	*100*	*33.4*		*15.0*	*51.5*	*100*	*18.0*		*22.6*	*59.4*	*100*

Abbreviations are: ACR. albumin:creatinine ratio; eGFR. estimated glomerular flitration rate, albuminuria 1, ACR <10 mg/g or dipstick negative;, albuminuria 2, ACR 10-29 mg/g or dipstick trace; albuminuria 3, ACR 30-299 mg/g or dipstick 1+; albuminuria 4, ACR≥300 mg/g or dipstick ≥2

Web appendix Table 7: Distribution of incident acute kidney injury events (expressed as percentage of the total population under study). Shaded areas make up the combined reference groups. Absolute number of events per eGFR-albuminuria category can be calculated by multiplying proportions with the total number of events under investigation. For general population cohorts overall 3865, <65 year 1309 and >65 year 2556 events were observed, whereas for high risk cohorts these numbers were 1074, 401 and 673, respectively

Pooled analysis of general population cohorts with albumin-to-creatinine ratio or dipstick data

		Overall					Subdivision according to age									
							<65 year					>65 year				
		Albuminuria					Albuminuria					Albuminuria				
		1	2	3	4	**All**	1	2	3	4	**All**	1	2	3	4	**All**
	>105			0.52	0.41				1.38	1.07				0.08	0.08	
	90-104	38.5		0.72	0.49	*46.7*	59.5		1.30	0.92	*71.5*	27.7		0.43	0.27	*67.0*
	75-89			1.35	0.72				1.53	1.68				1.25	0.23	
	60-74			2.20	1.79				2.52	1.60				2.03	1.88	
eGFR	45-59	14.4	2.25	3.39	2.95	*23.0*	6.19	1.45	1.45	2.90	*12.0*	18.6	2.66	4.38	2.97	*28.6*
mL/min/1,73m²	30-44	11.2	1.76	2.98	4.19	*20.1*	3.59	0.69	1.76	3.90	*9.93*	15.1	2.31	3.60	4.34	*25.4*
	15-29	3.83	0.65	1.63	3.00	*9.11*	1.22	0.23	0.69	3.28	*5.42*	5.16	0.86	2.11	2.86	*11.0*
	All	*72.8*		*13.0*	*14.2*	*100*	*73.2*		*10.8*	*16.0*	*100*	*72.6*		*14.1*	*13.3*	*100*

Pooled analysis of cohorts selected for high risk of chronic kidney disease with albumin-to-creatinine ratio or dipstick data

		Overall					Subdivision according to age									
							<65 year					>65 year				
		Albuminuria					Albuminuria					Albuminuria				
		1	2	3	4	**All**	1	2	3	4	**All**	1	2	3	4	**All**
	>105			0.93	0.28				2.00	0.50				0.30	0.15	
	90-104	18.4		1.86	0.47	*37.2*	29.7		3.74	1.00	*56.1*	11.7		0.74	0.15	*26.0*
	75-89			3.45	1.58				4.99	2.99				2.53	0.74	
	60-74			7.26	2.98				6.73	4.49				7.58	2.08	
eGFR	45-59	3.26	5.87	10.2	5.87	*25.2*	2.24	4.74	7.48	6.48	*21.0*	3.86	6.54	11.9	5.50	*27.8*
mL/min/1,73m²	30-44	2.89	3.82	10.8	7.73	*25.2*	0.50	2.00	3.99	9.48	*16.0*	4.31	4.90	14.9	6.69	*30.8*
	15-29	0.56	1.30	4.47	5.40	*11.7*	0.25	0.25	1.00	5.24	*6.73*	0.74	1.93	6.54	5.50	*14.7*
	All	*36.1*		*39.2*	*24.7*	*100*	*39.7*		*30.2*	*30.2*	*100*	*34.0*		*44.6*	*21.4*	*100*

Abbreviations are: ACR. albumin:creatinine ratio; eGFR. estimated glomerular flitration rate, albuminuria 1, ACR <10 mg/g or dipstick negative;, albuminuria 2, ACR 10-29 mg/g or dipstick trace; albuminuria 3, ACR 30-299 mg/g or dipstick 1+; albuminuria 4, ACR≥300 mg/g or dipstick ≥2+.

Web appendix Table 8: Distribution of incident progressive chronic kidney disease events (expressed as percentage of the total population under study). Shaded areas make up the combined reference groups. Absolute number of events per eGFR-albuminuria category can be calculated by multiplying proportions with the total number of events under investigation. For general population cohorts overall 4797, <65 year 1298 and >65 year 3499 events were observed, whereas for high risk cohorts these numbers were 6347, 2241 and 4106, respectively.

Pooled analysis of general population cohorts with albumin-to-creatinine ratio or dipstick data

		Overall					**Subdivision according to age**									
							<65 year					**>65 year**				
		Albuminuria					**Albuminuria**					**Albuminuria**				
		1	2	3	4	**All**	1	2	3	4	**All**	1	2	3	4	**All**
	>105			0.04	0.17				0.15	0.54				0.00	0.03	
	90-104	23.3		0.15	0.15	*29.4*	29.4		0.23	0.46	*40.1*	21.1		0.11	0.03	*25.5*
	75-89			0.58	0.94				0.77	2.39				0.51	0.40	
	60-74			1.96	2.15				2.23	4.01				1.86	1.46	
eGFR	45-59	32.4	2.40	4.13	5.11	*44.1*	18.1	1.31	2.77	8.63	*30.8*	37.7	2.80	4.63	3.80	*49.0*
mL/min/1,73m²	30-44	10.1	1.19	2.36	5.63	*19.2*	5.86	1.08	1.46	8.40	*16.8*	11.6	1.23	2.69	4.60	*20.1*
	15-29	1.40	0.31	0.96	3.36	*6.02*	1.69	0.39	1.23	6.16	*9.48*	1.29	0.29	0.86	2.31	*4.74*
	<15	0.27	0.08	0.17	0.75	*1.27*	0.62	0.15	0.39	1.62	*2.77*	0.14	0.06	0.09	0.43	*0.71*
	All	*71.4*		*10.3*	*18.2*	*100*	*58.6*		*9.24*	*32.2*	*100*	*76.2*		*10.8*	*13.1*	*100*

Pooled analysis of cohorts selected for high risk of chronic kidney disease with albumin-to-creatinine ratio or dipstick data

		Overall					**Subdivision according to age**									
							<65 year					**>65 year**				
		Albuminuria					**Albuminuria**					**Albuminuria**				
		1	2	3	4	**All**	1	2	3	4	**All**	1	2	3	4	**All**
	>105			0.93	0.77				2.37	2.10				0.15	0.05	
	90-104	19.6		0.93	0.46	*35.9*	20.8		1.92	0.98	*44.9*	18.9		0.39	0.17	*31.0*
	75-89			2.30	1.21				3.12	2.77				1.85	0.37	
	60-74			5.86	3.86				5.04	5.85				6.31	2.78	
eGFR	45-59	10.4	8.07	12.2	8.51	*39.2*	6.92	4.46	8.39	12.1	*31.9*	12.3	10.0	14.3	6.55	*43.2*
mL/min/1,73m²	30-44	2.63	2.22	5.88	7.18	*17.9*	0.62	1.29	3.53	8.79	*12.2*	3.73	2.73	7.16	6.31	*19.9*
	15-29	0.08	0.33	1.24	4.18	*5.83*	0.00	0.49	1.20	5.22	*6.92*	0.12	0.24	1.27	3.60	*5.24*
	<15	0.00	0.02	0.08	1.09	*1.18*	0.00	0.04	0.18	1.87	*2.10*	0.00	0.00	0.02	0.66	*0.68*
	All	*43.3*		*29.5*	*27.3*	*100*	*34.6*		*25.8*	*39.7*	*100*	*48.0*		*31.5*	*20.5*	*100*

Abbreviations are: ACR. albumin:creatinine ratio; eGFR. estimated glomerular flitration rate, albuminuria 1, ACR <10 mg/g or dipstick negative;, albuminuria 2, ACR 10-29 mg/g or dipstick trace; albuminuria 3, ACR 30-299 mg/g or dipstick 1+; albuminuria 4, ACR≥300 mg/g or dipstick ≥2

Web appendix Table 9. Statistical significance for interaction between eGFR and age, and between eGFR and albuminuria in the models adjusted for covariates for end-stage renal disease, acute kidney injury and progressive chronic kidney disease. In case the interaction term eGFR*age reached statistical significance (p<0.05) this indicates that in this cohort the predictive value of eGFR for the outcome under study was less at older age. For the interaction term eGFR*albuminuria statistical significance indicates that the predictive value of higher albuminuria was less at low eGFR.

Study	Interaction	
	eGFR * age (p-value)	eGFR * albuminuria (p-value)
ESRD		
General population cohorts with albumin-to-creatinine ratio data		
- ARIC	0.054	0.051
- HUNT	0.262	0.481
General population cohorts with dipstick data		
- AKDN dip*	NA	NA
- OKINAWA 83	<0.001	0.146
- OKINAWA 93	0.052	0.001
High risk cohorts with albumin-to-creatinine ratio data		
- ADVANCE	0.159	0.117
- AKDN ACR*	0.474	0.470
- ONTARGET	0.910	NA
- Pima	NA	NA
High risk cohorts with dipstick data		
- Hawaii	0.997	0.999
- MRFIT	0.577	0.646
Acute kidney injury		
General population cohorts with albumin-to-creatinine ratio data		
- ARIC	0.034	0.030
- CHS	0.086	0.294
General population cohorts with dipstick data		
- AKDN dip*	<0.001	<0.001
High risk cohorts with albumin-to-creatinine ratio data		
- AKDN ACR*	0.032	<.0001
- ONTARGET	0.985	0.183
Progressive chronic kidney disease		
General population cohorts with albumin-to-creatinine ratio data		
- AusDiab	0.236	0.160
- MESA	0.959	0.023
General population cohorts with dipstick data		
- AKDN dip*	<0.001	<0.001
- Beaver Dam	0.218	0.9101
High risk cohorts with albumin-to-creatinine ratio data		
- ADVANCE	0.261	0.163
- AKDN ACR*	<0.001	0.600
- ONTARGET	0.085	0.002
- Pima	0.013	0.510
- TRANSCEND	0.705	0.253
High risk cohorts with dipstick data		
- CARE	0.846	0.075
- HAWAII	<0.001	<.0001

*Abbreviations: eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; for acronyms of included cohorts see web appendix Table 12; *AKDN delivered two datasets, one on subjects in whom albuminuria was measured as albumin-to-creatinine ratio and one in whom albuminuria was measured by dipstick.*

Web appendix Table 10: Hazard ratio for end-stage renal disease, after adjustment for age, sex and cardiovascular risk factors (Bold: hazard ratio is statistically significant. Italic: hazard ratio shows significant heterogeneity). Shaded areas make up the combined reference groups.

Pooled analysis of general population cohorts with albumin-to-creatinine ratio or dipstick data

		Overall					**Subdivision according to age**									
							<65 year					**>65 year**				
		Albuminuria					**Albuminuria**					**Albuminuria**				
		1	2	3	4	**All**	1	2	3	4	**All**	1	2	3	4	**All**
	>105			**7.82**	**18.1**				**12.4**	**28.6**				0.0	0.0	
	90-104	Ref		**11.3**	**19.7**	Ref	Ref		**14.2**	**13.8**	Ref	Ref		0.0	0.0	Ref
	75-89			**3.83**	**48.1**				**5.81**	**65.2**				0.0	0.0	
	60-74			**7.42**	**67.2**				**5.58**	**87.3**				**6.61**	**18.8**	
eGFR	45-59	**5.16**	**21.8**	**40.3**	**147**	**9.67**	**3.06**	**31.8**	**55.4**	**261**	**9.45**	**3.44**	**9.61**	**16.4**	**41.4**	**4.48**
mL/min/1.73m²	30-44	**55.6**	**74.1**	**294**	**763**	***98.1***	**101**	**293**	**272**	**828**	***110***	**11.5**	**18.1**	**90.8**	**268**	**42.1**
	15-29	**433**	**1044**	**1056**	***2287***	***573***	**999**	**3897**	**2398**	**5081**	***1281***	**131**	**115**	**413**	**1071**	**186**
	All	Ref		***12.0***	***72.1***		Ref		**13.7**	***124***		Ref		***10.3***	***47.5***	

Pooled analysis of cohorts selected for high risk of chronic kidney disease with albumin-to-creatinine ratio or dipstick data

		Overall					**Subdivision according to age**									
							<65 year					**>65 year**				
		Albuminuria					**Albuminuria**					**Albuminuria**				
		1	2	3	4	**All**	1	2	3	4	**All**	1	2	3	4	**All**
	>105			1.1	2.0				1.1	1.4				0.0	**20.6**	
	90-104	Ref		**2.4**	***10.0***	Ref	Ref		2.6	**10.5**	Ref	Ref		0.0	**15.5**	
	75-89			1.7	***17.3***				1.7	***16.3***				1.9	**16.2**	Ref
	60-74			**3.1**	***32.2***				**4.0**	***39.0***				1.7	**20.7**	
eGFR	45-59	**2.7**	**3.8**	**14.5**	***55.5***	***5.7***	**2.5**	**5.3**	**16.9**	***66.9***	***7.0***	**2.8**	1.8	**10.0**	**31.2**	**3.8**
mL/min/1.73m²	30-44	**23.4**	**33.4**	**56.0**	***140***	***27.4***	**15.9**	**73.6**	**90.9**	***161***	***33.9***	**16.2**	**18.1**	**24.3**	**92.7**	**20.7**
	15-29	**32.6**	**308**	***387***	***463***	***165***	**0.0**	**656**	**792**	***998***	***223***	**25.0**	**175**	**125**	**506**	***146***
	All	Ref		***4.3***	***38.1***		Ref		***4.5***	***43.8***		Ref		**4.1**	***43.3***	

Abbreviations are: ACR. albumin:creatinine ratio; eGFR. estimated glomerular flitration rate, albuminuria 1, ACR <10 mg/g or dipstick negative;, albuminuria 2, ACR 10-29 mg/g or dipstick trace; albuminuria 3, ACR 30-299 mg/g or dipstick 1+; albuminuria 4, ACR≥300 mg/g or dipstick ≥2+.

Web appendix Table 11: Hazard ratio for incident acute kidney injury, after adjustment for age, sex and cardiovascular risk factors (Bold: hazard ratio is statistically significant. Italic: hazard ratio shows significant heterogeneity). Shaded areas make up the combined reference groups.

Pooled analysis of general population cohorts with albumin-to-creatinine ratio or dipstick data

		Overall					**Subdivision according to age**									
							<65 year					**>65 year**				
		Albuminuria					**Albuminuria**					**Albuminuria**				
		1	2	3	4	**All**	1	2	3	4	**All**	1	2	3	4	**All**
	>105			*2.7*	**8.4**				**3.7**	**9.5**				2.4	**6.3**	
	90-104	Ref		**2.4**	**5.8**	Ref	Ref		**3.0**	**6.6**	Ref	Ref		2.5	**5.5**	Ref
	75-89			**2.5**	**4.1**				**2.2**	**6.2**				**2.7**	1.6	
	60-74			**3.3**	**6.4**				**3.8**	**6.0**				**2.7**	**5.9**	
eGFR	45-59	**2.2**	**4.9**	**6.4**	**5.9**	**2.6**	**1.8**	**8.0**	**6.7**	**18.4**	**2.5**	**2.0**	***4.4***	**5.9**	**8.1**	**2.6**
mL/min/1.73m²	30-44	**7.3**	**10.2**	**12.5**	**19.6**	**7.9**	**8.4**	**26.2**	**16.3**	***32.0***	***9.9***	**6.2**	**8.7**	**9.6**	**13.7**	***7.4***
	15-29	**16.8**	**16.8**	**21.5**	**28.8**	**16.7**	**40.0**	**30.7**	**60.9**	***28.5***	***17.8***	**13.5**	**13.6**	**16.8**	**20.9**	**13.0**
	All	Ref		**2.5**	***6.0***		Ref		***3.3***	***10.9***		Ref		**2.4**	**4.7**	

Pooled analysis of cohorts selected for high risk of chronic kidney disease with albumin-to-creatinine ratio or dipstick data

		Overall					**Subdivision according to age**									
							<65 year					**>65 year**				
		Albuminuria					**Albuminuria**					**Albuminuria**				
		1	2	3	4		1	2	3	4		1	2	3	4	
	>105			**2.2**	**3.4**				**2.1**	2.9				2.6	**11.6**	
	90-104	Ref		**2.1**	**3.4**	Ref	Ref		**2.3**	0.0	Ref	Ref		1.7	**2.7**	
	75-89			**1.8**	**5.2**				**1.8**	**6.1**				**1.7**	**3.6**	Ref
	60-74			**2.8**	**6.3**				**2.9**	**8.8**				**2.8**	**4.0**	
eGFR	45-59	**1.7**	**3.5**	**6.6**	**13.0**	**3.0**	1.4	**5.2**	**8.2**	**15.9**	**3.9**	**1.6**	**2.5**	**5.1**	**10.0**	**2.3**
mL/min/1.73m²	30-44	**8.0**	**7.5**	**14.3**	**26.9**	***10.6***	**4.6**	**11.5**	**15.6**	**60.3**	**14.2**	**7.0**	**5.6**	**11.5**	**12.2**	**7.7**
	15-29	**12.2**	1.6	**25.3**	13.7	**16.8**	**20.0**	**10.6**	**15.0**	**39.8**	**23.4**	**9.1**	**14.2**	**21.4**	**1.3**	**12.6**
		Ref		**2.7**	**7.4**		Ref		**2.7**	**13.5**		Ref		**2.7**	**5.1**	

Abbreviations are: ACR. albumin:creatinine ratio; eGFR. estimated glomerular flitration rate, albuminuria 1, ACR <10 mg/g or dipstick negative;, albuminuria 2, ACR 10-29 mg/g or dipstick trace; albuminuria 3, ACR 30-299 mg/g or dipstick 1+; albuminuria 4, ACR≥300 mg/g or dipstick ≥2+.

Web appendix Table 12: Odds ratio for progressive chronic kidney disease, after adjustment for age, sex and the cardiovascular risk factors (Bold: hazard ratio is statistically significant. Italic: hazard ratio shows significant heterogeneity). Shaded areas make up the combined reference groups.

Pooled analysis of general population cohorts with albumin-to-creatinine ratio or dipstick data

		Overall					Subdivision according to age									
							<65 year					>65 year				
		Albuminuria					Albuminuria					Albuminuria				
		1	2	3	4	All	1	2	3	4	All	1	2	3	4	All
	>105			**0.7**	*3.0*				**0.9**	**1.7**				**0.5**	2.3	
	90-104	Ref		0.9	*3.3*	Ref	Ref		1.3	*13.1*	Ref	Ref		**1.4**	1.2	Ref
	75-89			1.9	*5.0*				*2.0*	*7.7*				1.6	**3.0**	
	60-74			***3.2***	**8.1**				*4.0*	***14.2***				**2.5**	**11.0**	
eGFR	45-59	**3.1**	***4.1***	***9.4***	***56.6***	**3.9**	*2.5*	4.0	**6.2**	*68.1*	**4.7**	**3.4**	***4.2***	***9.0***	***32.2***	**3.7**
mL/min/1,73m²	30-44	***3.0***	**19.1**	***14.9***	***22.2***	**3.7**	*20.7*	**34.9**	**37.7**	***113***	**13.9**	**3.1**	**9.4**	***13.9***	*2.4*	**3.0**
	15-29	**4.0**	**11.7**	**21.0**	**7.7**	**7.9**	**23.9**	**193.9**	**908.0**	**32.8**	**37.6**	**1.7**	**3.5**	**11.7**	*4.6*	**5.6**
	All	Ref		**3.1**	**11.2**		Ref		**5.2**	**21.3**		Ref		**2.8**	**7.7**	

Pooled analysis of cohorts selected for high risk of chronic kidney disease with albumin-to-creatinine ratio or dipstick data

		Overall					Subdivision according to age									
							<65 year					>65 year				
		Albuminuria					Albuminuria					Albuminuria				
		1	2	3	4		1	2	3	4		1	2	3	4	
	>105			***0.6***	*4.7*				1.1	**7.2**				**0.5**	**0.4**	
	90-104	Ref		*0.9*	*3.5*	Ref	Ref		1.6	***4.5***	Ref	Ref		**0.6**	*1.3*	
	75-89			*1.0*	***3.6***				**2.0**	**9.3**				*1.1*	**1.6**	Ref
	60-74			***2.8***	***9.3***				**3.5**	**22.5**				***2.4***	**6.8**	
eGFR	45-59	***3.0***	***4.8***	***10.1***	***31.4***	**4.7**	**4.8**	***7.2***	***13.0***	***43.7***	**6.3**	***2.8***	**4.3**	***7.1***	***15.4***	**4.0**
mL/min/1,73m²	30-44	***3.3***	***3.4***	***9.8***	***68.7***	**6.4**	**4.7**	***10.9***	***14.2***	***67.1***	**10.3**	**3.4**	**3.2**	**6.7**	***15.6***	**4.8**
	15-29	***0.5***	***3.1***	***9.4***	***38.6***	**8.9**	**#**	**41.7**	**35.4**	**185**	**36.4**	*1.0*	*2.9*	**4.1**	*10.8*	**6.2**
		Ref		**2.2**	**9.9**		Ref		**2.5**	**13.7**		Ref		**2.1**	**7.1**	

Abbreviations are: ACR. albumin:creatinine ratio; eGFR. estimated glomerular flitration rate, albuminuria 1, ACR <10 mg/g or dipstick negative;, albuminuria 2, ACR 10-29 mg/g or dipstick trace; albuminuria 3, ACR 30-299 mg/g or dipstick 1+; albuminuria 4, ACR≥300 mg/g or dipstick ≥2+.