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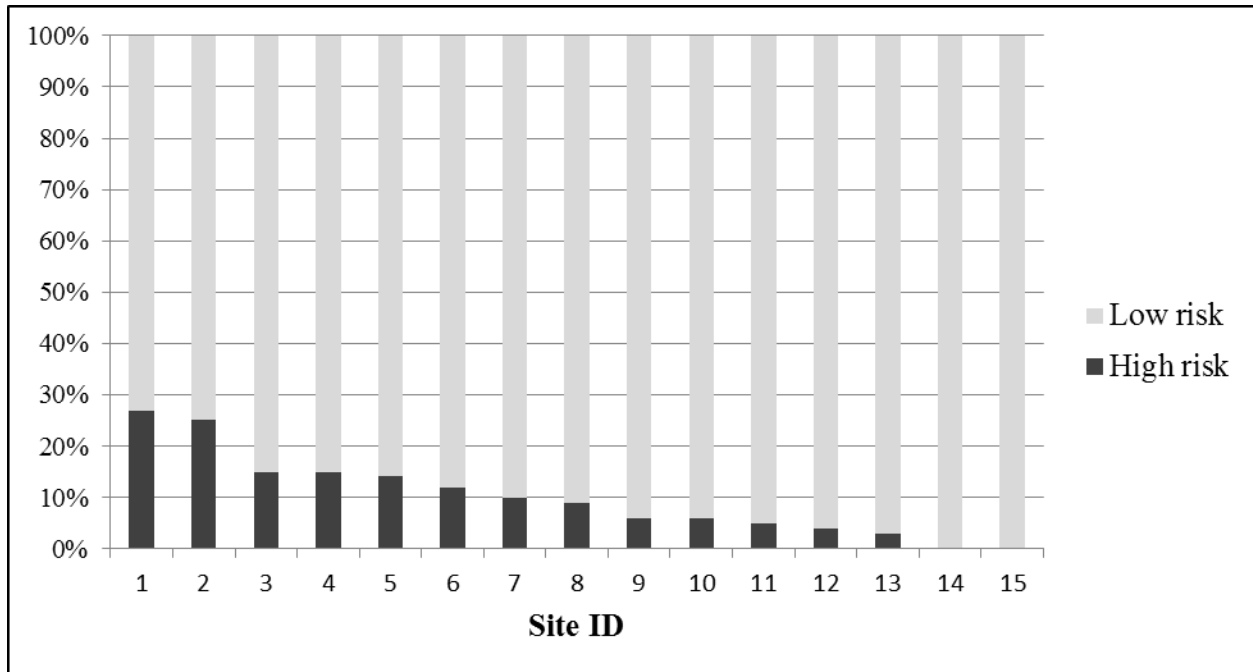


Figure s1 High- and low-risk rates for study sites 1-15 Low-risk: CKD273-classifier below or equal to the cut-off of 0.154. High-risk: CKD273-classifier above the cut-off of 0.154. 1: Leipzig, Germany (n=52); 2: Prague, Czech Republic (n=51); 3: Gentofte, Denmark (n=436); 4: Bergamo, Italy (n=282); 5: Glasgow, United Kingdom (n=219); 6: Skopje, Macedonia (n=177); 7: Ghent, Belgium (n=31); 8: Groningen, Netherlands (n=132); 9: Prague, Czech Republic (n=81); 10: Athens, Greece (n=84); 11: Hoorn, Netherlands (n=118); 12: Hoogeveen, Netherlands (n=24); 13: Marburg, Germany (n=60); 14: Dresden, Germany (n=17); 15: Madrid, Spain (n=13).

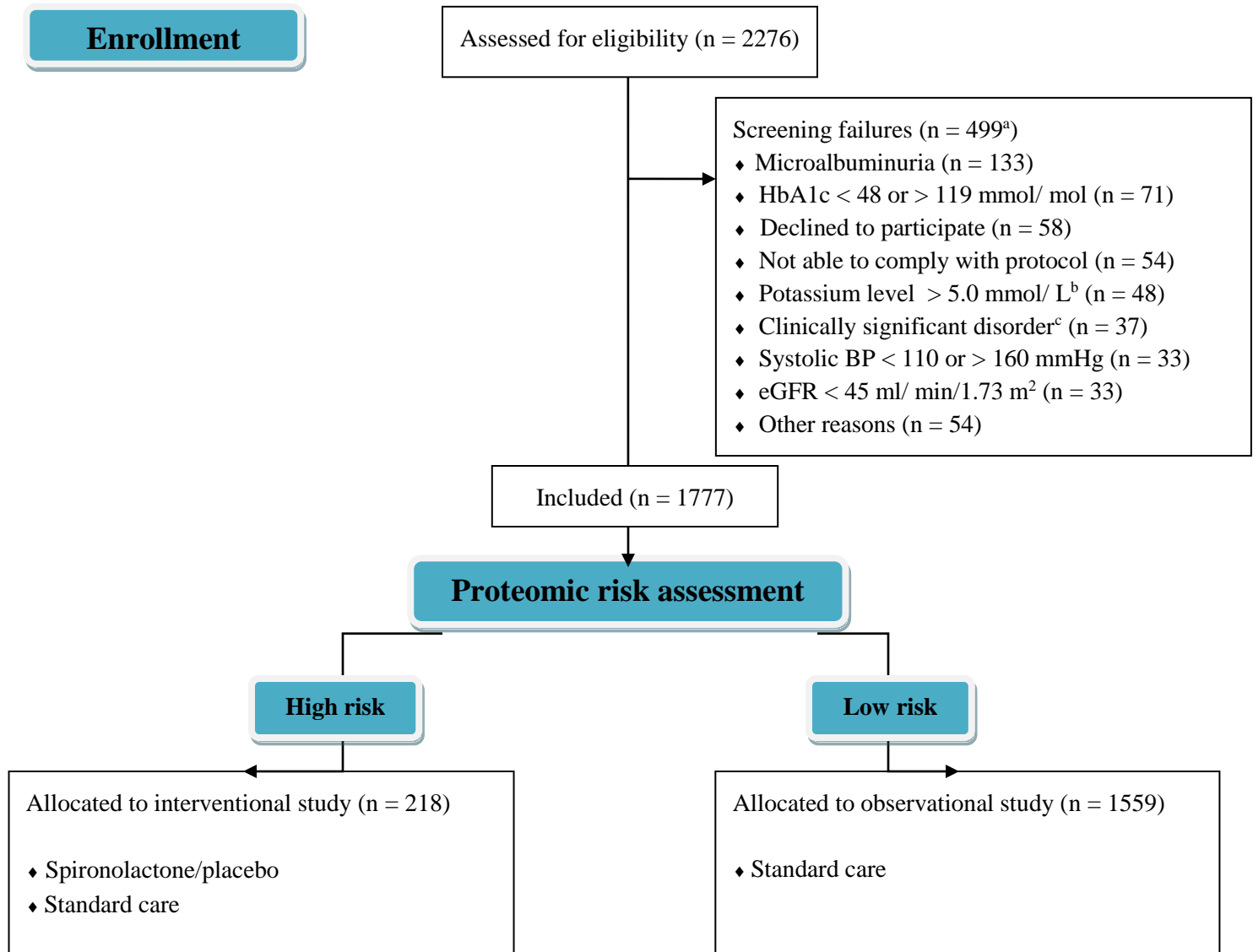


Figure s2 Study flow diagram ^aParticipants may meet more than one exclusion criterion. ^bMeasured in serum or plasma. ^cAny clinically significant disorder which in the investigators opinion could interfere with the results of the trial. BP denotes blood pressure, HbA_{1c} haemoglobin A1c, eGFR estimated glomerular filtration rate.

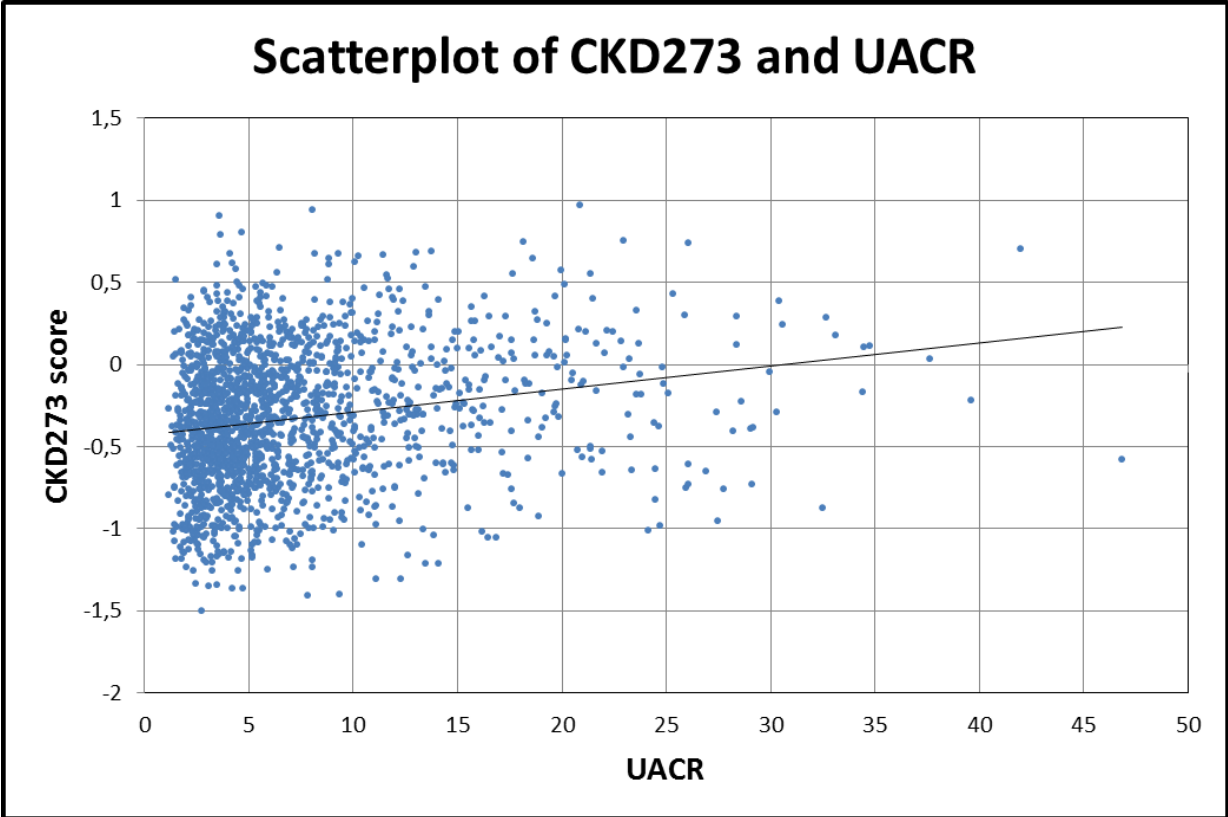


Figure s3 Scatterplot of CKD273 and UACR (urine albumin-to-creatinine ratio) for the whole study population. UACR is shown here as the geometric mean of the three morning void urine samples obtained at screening.

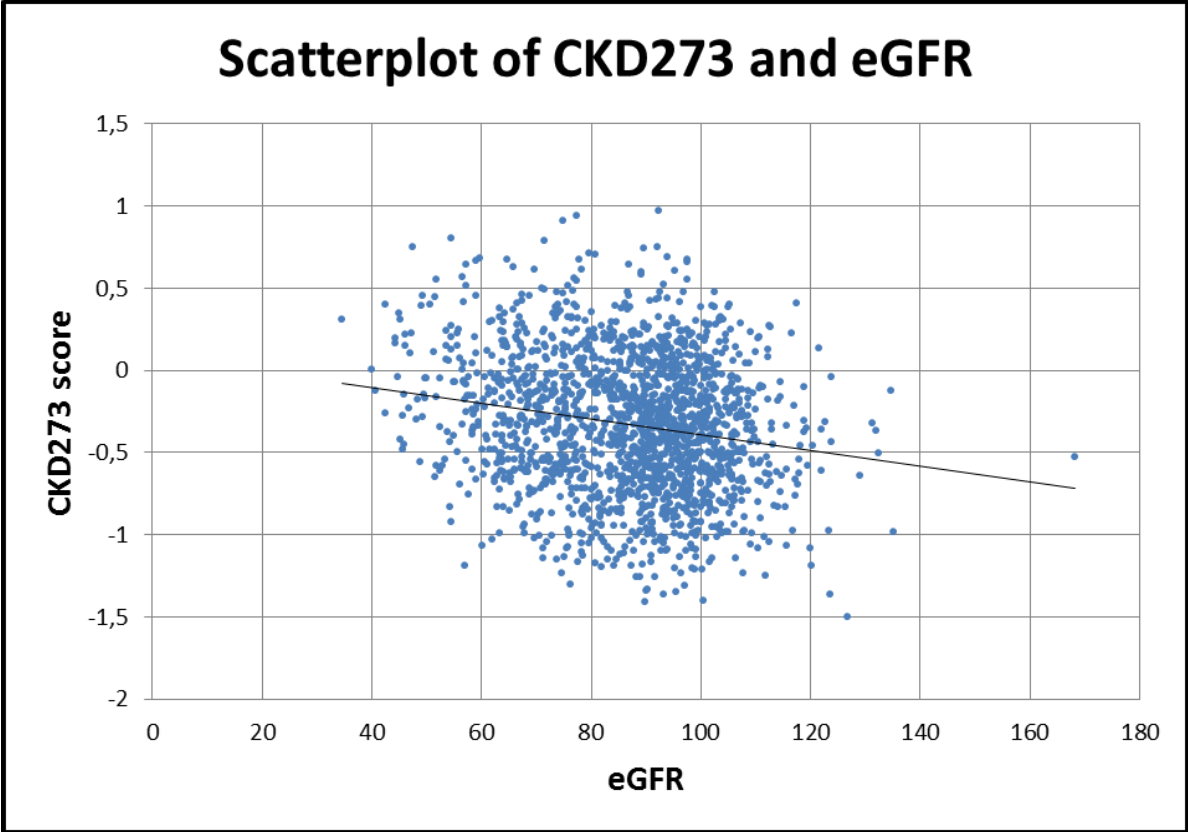


Figure s4 Scatterplot of CKD273 and estimated glomerular filtration rate (eGFR) for the whole study population. eGFR was measured at baseline and calculated by the CKD-EPI equation.

	Included N = 1777	Screening failures N = 499	p-value
Gender, men, n (% ^a)	1106 (62)	324 (65)	0.26 ^b
Age, years	63 [57-68]	63 [57-68]	0.44
Diabetes duration, years	12 (8)	12 (8)	0.49
Body mass index, kg/ m ²	30 (5)	31 (6)	0.06
Systolic blood pressure, mmHg	134 (14)	136 (16)	0.07
Diastolic blood pressure, mmHg	79 (9)	79 (10)	0.12
Heart rate, bpm	74 (11)	75 (12)	0.07
eGFR, ml min ⁻¹ 1.73 m ⁻²	87 (15)	82 (20)	< 0.01
UACR, mg/ g	5 [3-9]	28 [6-52]	< 0.01
Potassium, mmol/ L	4.2 (0.4)	4.3 (0.5)	< 0.01
Sodium, mmol/ L	140 (2)	140 (3)	0.68
HbA1c, mmol/ mol	58 (12)	57 (15)	0.89
HbA1c, %	7.4 (1.1)	7.4 (1.3)	0.89

Table s1: Demographic characteristics of the overall included study cohort and screening failures at time of screening. Mean (SD) or median [IQR], ^aFrequencies are rounded. ^bp-value for chi-square test. eGFR denotes estimated glomerular filtration rate, UACR Urine albumin to creatinine ratio.

Site ID	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Included, n	52	51	436	282	219	177	31	132	81	84	118	24	60	17	13
High-risk (% ^a)	27	25	15	15	14	12	10	9	6	6	5	4	3	0	0
Gender, men (% ^a)	52	75	65	68	69	45	68	58	54	60	71	38	60	41	62
Diabetes duration, years	9 (7)	17 (9)	12 (8)	15 (8)	10 (6)	9 (7)	13 (8)	15 (8)	9 (7)	11 (8)	9.7 (6)	14 (7)	9 (6)	9 (8)	10 (6)
Age, years	65 [60-68]	64 [60-68]	62 [55-68]	65 [61-70]	62 [56-67]	63 [55-67]	63 [58-68]	63 [55-67]	65 [57-69]	63 [58-68]	62 [58-66]	59 [49-65]	60 [55-65]	66 [63-68]	63 [58-68]
Body mass index, kg/m ²	32 (5)	31 (4)	31 (6)	29 (4)	32 (5)	29 (4)	31 (6)	33 (6)	30 (5)	29 (4)	30 (5)	31 (5)	31 (5)	27 (3)	29 (4)
Systolic blood pressure, mmHg	139 (12)	135 (11)	133 (12)	132 (11)	136 (12)	134 (8)	135 (13)	135 (12)	133 (13)	124 (9)	131 (11)	130 (12)	130 (14)	133 (13)	134 (12)
Diastolic blood pressure, mmHg	82 (8)	83 (7)	80 (9)	75 (8)	78 (10)	81 (6)	79 (10)	74 (8)	82 (9)	76 (5)	77 (6)	79 (10)	76 (9)	78 (8)	79 (8)
Heart rate, bpm	75 (12)	75 (12)	76 (12)	72 (10)	79 (12)	76 (5)	74 (13)	74 (12)	72 (10)	72 (5)	75 (12)	75 (11)	72 (9)	62 (9)	69 (9)
eGFR, ml min ⁻¹ 1.73 m ⁻²	79 (17)	81 (12)	87 (16)	85 (16)	87 (14)	99 (13)	81 (17)	87 (17)	80 (14)	88 (12)	82 (14)	87 (13)	84 (16)	94 (9)	93 (11)
UACR, mg/g	5 [3-7]	5 [3-7]	6 [4-10]	5 [3-9]	5 [4-8]	6 [4-11]	5 [3-7]	5 [3-9]	4 [3-6]	5 [4-8]	4 [3-8]	5 [3-11]	4 [3-6]	4 [3-6]	7 [3-8]
Potassium, mmol/L	4.2 (0.5)	4.3 (0.3)	4.2 (0.3)	4.1 (0.4)	4.3 (0.4)	4.1 (0.4)	4.2 (0.4)	4.0 (0.3)	4.2 (0.3)	4.6 (0.4)	4.5 (0.4)	4.1 (0.3)	4.3 (0.5)	4.2 (0.2)	4.1 (0.5)
Sodium, mmol/L	141 (3)	139 (3)	140 (2)	139 (2)	138 (2)	141 (3)	141 (2)	140 (2)	139 (2)	138 (2)	140 (2)	139 (2)	141 (2)	140 (2)	141 (2)
HbA1c, mmol/mol	50 (7)	60 (14)	57 (12)	56 (13)	64 (14)	59 (9)	58 (11)	59 (10)	53 (9)	50 (5)	53 (13)	61 (12)	53 (8)	48 (4)	53 (8)
HbA1c, %	6.7 (0.6)	7.6 (1.3)	7.4 (1.1)	7.3 (1.2)	8.0 (1.2)	7.6 (0.8)	7.5 (1.0)	7.5 (0.9)	7.0 (0.8)	6.7 (0.5)	7.0 (1.2)	7.7 (1.1)	7.0 (0.7)	6.5 (0.4)	7.0 (0.7)
Total cholesterol, mmol/L	5.4 (1.0)	4.5 (0.9)	4.2 (1.0)	4.5 (1.0)	4.3 (1.0)	4.8 (1.2)	4.1 (0.8)	4.2 (0.9)	4.4 (0.9)	4.3 (0.9)	4.1 (0.9)	4.2 (0.9)	4.5 (0.9)	4.7 (1.2)	4.3 (0.7)
HDL cholesterol, mmol/L	1.3 (0.3)	1.3 (0.4)	1.2 (0.4)	1.2 (0.3)	1.2 (0.3)	1.3 (0.4)	1.3 (0.4)	1.2 (0.3)	1.2 (0.3)	1.2 (0.3)	1.1 (0.3)	1.3 (0.2)	1.2 (0.4)	1.4 (0.4)	1.5 (0.7)
LDL cholesterol, mmol/L	3.4 (0.9)	2.5 (0.7)	2.1 (0.9)	2.8 (0.8)	2.3 (0.9)	2.9 (1.0)	2.1 (0.7)	2.1 (0.8)	2.4 (0.8)	2.4 (0.7)	2.1 (0.8)	2.2 (0.8)	2.8 (0.8)	3.0 (0.9)	2.3 (0.4)
Triglycerides, mmol/L	2.2 [1.8-2.8]	1.4 [1.1-1.9]	1.8 [1.3-2.7]	1.3 [0.8-1.8]	1.8 [1.3-2.5]	1.5 [1.1-2.2]	1.4 [1.0-2.0]	1.9 [1.3-2.9]	1.6 [1.2-2.0]	1.3 [1.0-2.0]	1.8 [1.3-2.4]	1.3 [1.1-1.6]	1.8 [1.3-2.4]	1.1 [1.0-1.6]	1.4 [0.8-1.6]
Smoking status, n (% ^a)															
- Current	15	24	14	11	14	15	13	12	7	15	14	25	18	12	8
- Never	71	57	50	49	55	77	52	52	91	43	34	17	77	65	62
- Former	13	16	37	40	31	8	35	33	1	42	52	58	5	24	31
- Unknown	0	4	0	0	0	0	0	3	0	0	0	0	0	0	0

Table s2. Baseline characteristics for all included, divided by site. Mean (SD) or median [IQR], P value for chi-square test for categorical variables and unpaired t-test for continuous variables. ^aFrequencies are rounded. eGFR denotes estimated glomerular filtration rate, UACR Urine Albumin-to-Creatinine Ratio. High risk: CKD273-classifier below or equal to the cut-point of 0.154. Site 1: Leipzig, Germany; 2: Prague, Czech Republic; 3: Gentofte, Denmark; 4: Bergamo, Italy; 5: Glasgow, United Kingdom; 6: Skopje, Macedonia; 7: Ghent, Belgium; 8: Groningen, Netherlands; 9: Prague, Czech Republic; 10: Athens, Greece; 11: Hoorn, Netherlands; 12: Hoogeveen, Netherlands; 13: Marburg, Germany; 14: Dresden, Germany; 15: Madrid, Spain

Site ID	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Included, n	52	51	436	282	219	177	31	132	81	84	118	24	60	17	13
Insulin of any kind	37	63	40	24	24	48	58	62	6	21	31	57	35	13	46
Biguanides	73	92	87	87	76	53	87	81	67	94	88	83	80	100	85
Sulphonylureas	8	24	13	41	38	17	35	28	9	18	41	9	9	6	15
GLP-1 analogs	19	14	35	10	16	0	19	13	1	4	1	22	26	6	15
SGLT-2 inhibitors	15	16	8	5	11	0	0	2	1	2	0	13	52	6	8
DDP4 inhibitors	27	35	14	15	12	0	10	8	16	44	3	13	33	38	38
Glitazones	0	18	0	10	10	0	0	1	12	0	1	0	0	0	0
ACE inhibitors	33	53	29	45	52	42	48	26	40	12	24	22	30	6	31
ARB	46	31	35	42	12	15	23	36	33	37	22	48	33	19	54
Alpha-blockers	8	12	2	13	2	2	0	2	0	4	1	0	6	6	8
Beta-blockers	48	41	18	33	22	31	29	36	1	20	37	13	39	44	23
Calcium channel blockers	23	39	27	29	24	12	26	20	16	17	10	30	15	6	8
Loop diuretics	13	4	9	3	3	1	3	4	0	0	3	4	2	0	0
Thiazides	25	27	35	36	19	20	23	33	20	12	31	17	22	6	31
Statins	33	71	81	60	87	37	84	71	47	70	79	57	50	63	77
Fibrates	10	25	2	6	0	4	6	9	21	5	3	13	7	0	23
Aspirin	27	35	49	41	36	12	48	27	0	27	21	9	9	19	31
Other anti-platelet agents ^a	10	12	11	6	5	4	13	9	5	7	12	0	6	0	8

Table s3. Baseline medication for all included, divided by site. Frequencies (% , rounded). ^aOther anti-platelet agents include Warfarin, Non-vitamin K-antagonistic oral anticoagulants (NOAC) and Clopidogrel. Site 1: Leipzig, Germany; 2: Prague, Czech Republic; 3: Gentofte, Denmark; 4: Bergamo, Italy; 5: Glasgow, United Kingdom; 6: Skopje, Macedonia; 7: Ghent, Belgium; 8: Groningen, Netherlands; 9: Prague, Czech Republic; 10: Athens, Greece; 11: Hoorn, Netherlands; 12: Hoogeveen, Netherlands; 13: Marburg, Germany; 14: Dresden, Germany; 15: Madrid, Spain.

Site ID	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Included, n	52	51	436	282	219	177	31	132	81	84	118	24	60	17	13
Diabetic retinopathy															
- No	94	71	79	77	71	94	74	70	96	99	97	83	88	100	85
- Simplex	2	25	14	21	27	2	10	15	4	1	3	8	2	0	8
- Proliferative	0	0	6	2	2	4	10	5	0	0	0	4	3	0	0
- Unknown	4	4	2	1	<1	0	6	9	0	0	0	4	7	0	8
Maculopathy															
- No	96	90	91	93	90	98	81	89	99	100	99	88	93	94	92
- Yes	0	4	7	6	9	2	13	1	1	0	0	8	0	6	0
- Unknown	4	6	2	1	0	0	6	10	0	0	1	4	7	0	8
Laser treatment															
- No	96	92	93	91	96	97	90	87	100	99	98	92	98	100	100
- Yes	0	0	6	8	4	3	10	6	0	1	1	0	0	0	0
- Unknown	4	8	1	1	0	0	0	7	0	0	1	8	2	0	0
Hypertension	87	92	73	95	59	56	74	73	78	54	62	75	68	65	85
Dyslipidemia	38	86	75	72	16	31	74	9	59	85	78	79	40	94	77
Ischemic heart disease	13	12	12	17	15	11	19	17	1	7	13	4	3	6	0
Congestive heart disease	0	0	<1	1	1	0	3	0	0	12	0	0	2	0	0
Other cardiac diseases ^a	8	8	6	26	2	0	23	7	6	1	13	0	2	6	8
Stroke	8	2	6	2	3	1	13	8	0	1	10	0	5	6	0
Peripheral arterial disease ^b	4	4	2	6	2	1	13	5	1	1	4	8	0	6	8

Table s4. Medical history for all included, divided by site. Frequencies (%) are rounded. ^aOther cardiac diseases include arrhythmias, cardiomyopathies, aortic stenosis and valve stenosis. ^bPeripheral arterial disease includes peripheral arterial disease, amputations, aneurisms and carotid stenosis. Site 1: Leipzig, Germany; 2: Prague, Czech Republic; 3: Gentofte, Denmark; 4: Bergamo, Italy; 5: Glasgow, United Kingdom; 6: Skopje, Macedonia; 7: Ghent, Belgium; 8: Groningen, Netherlands; 9: Prague, Czech Republic; 10: Athens, Greece; 11: Hoorn, Netherlands; 12: Hoogeveen, Netherlands; 13: Marburg, Germany; 14: Dresden, Germany; 15: Madrid, Spain.

	β	R ²	P-value
Age, years	0.008	0.02	<0.01
Diabetes duration, years	0.008	0.02	<0.01
Body mass index, kg/m ²	0.006	<0.01	<0.01
Systolic blood pressure, mmHg	0.002	<0.01	<0.01
Diastolic blood pressure, mmHg	-0.001	<0.01	0.51
Heart rate, bpm	0.001	<0.01	0.23
eGFR, ml/min/1.73 m ²	-0.005	0.03	<0.01
UACR mg/g	0.014	0.04	<0.01
Potassium, mmol/L	-0.015	<0.01	0.51
Sodium, mmol/L	-0.004	<0.01	0.28
HbA1c, mmol/mol	0.004	0.01	<0.01
Cholesterol, mmol/L	-0.012	<0.01	0.19
HDL cholesterol, mmol/L	-0.058	<0.01	0.04
LDL cholesterol, mmol/L	-0.019	<0.01	0.07
Triglycerides, mmol/L	0.020	<0.01	0.02

Table s5: Univariate regression analysis of correlation between CKD273 and single baseline variables, in the whole study population. eGFR denotes estimated glomerular filtration rate, UACR Urine Albumin-to-Creatinine Ratio.