Figure S1: Study population at baseline Visit 4 (1996-1998), the Atherosclerosis Risk in Communities (ARIC) Study cohort.

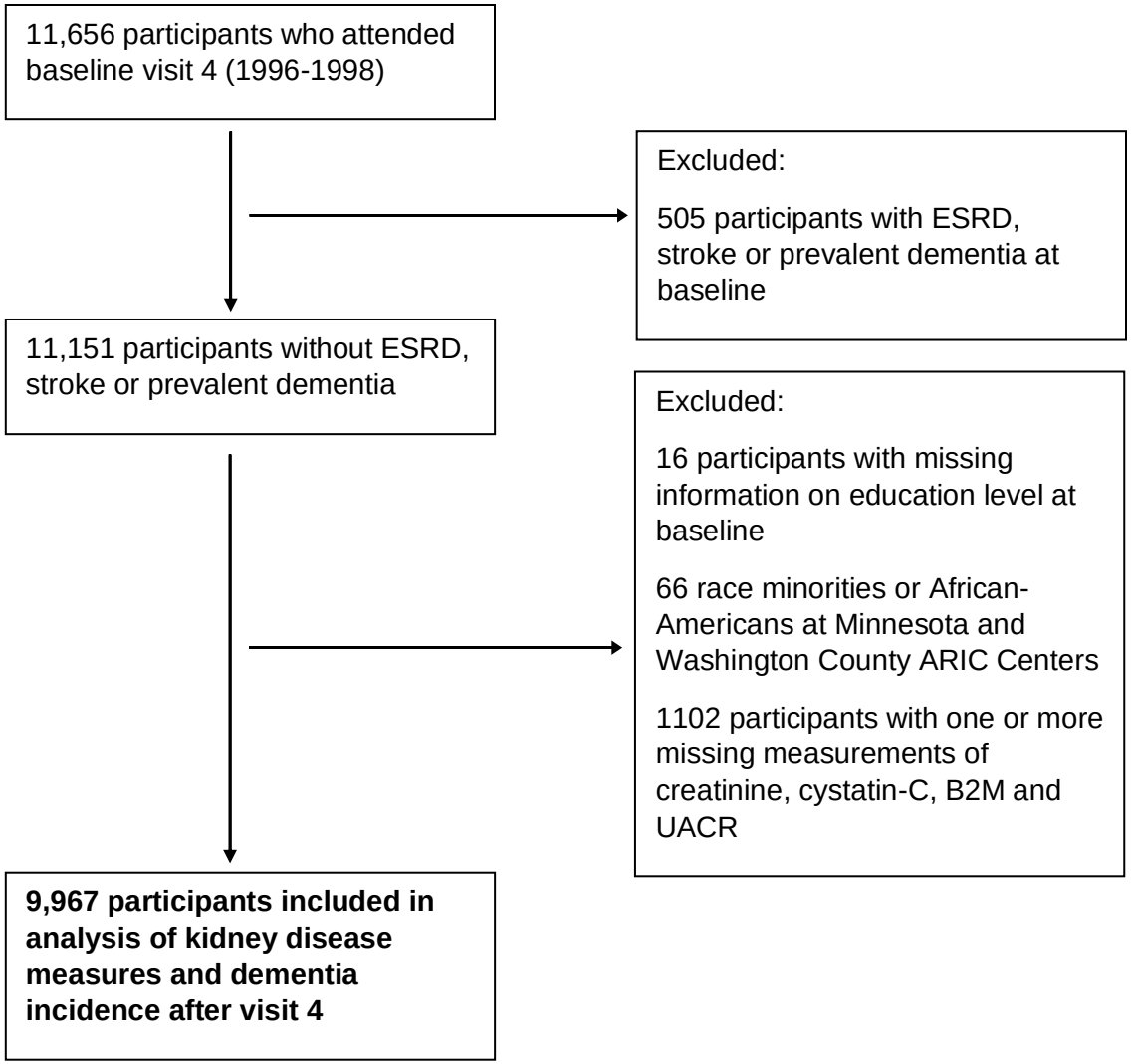

Figure S2: Study population at baseline Visit 5 (2011-2013), the Atherosclerosis Risk in Communities (ARIC) Study cohort

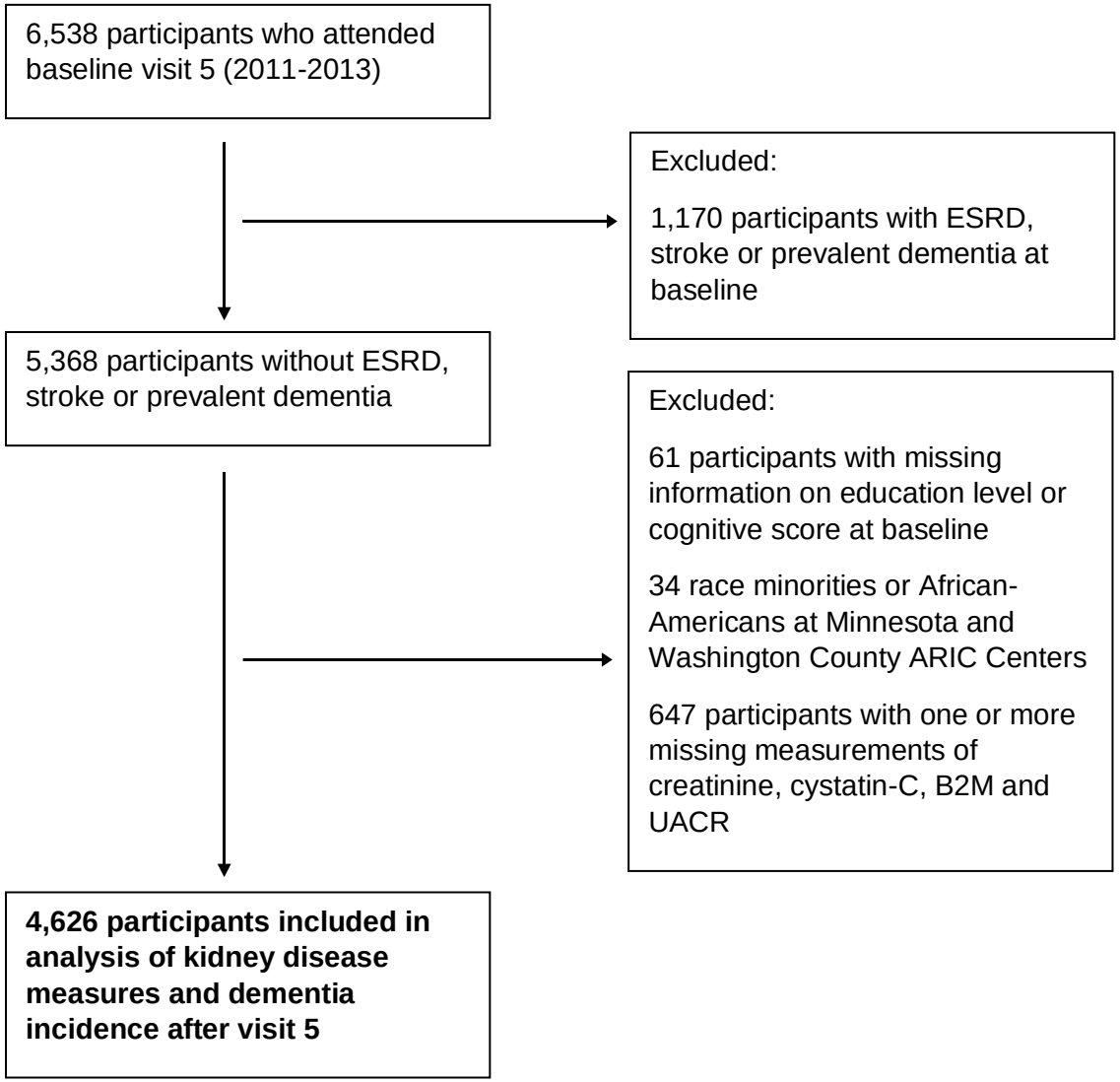

Figure S3: Adjusted relative hazards (95%-CI) of dementia incidence after midlife (baseline visit 4, ages 54-74 years during 1996-1998) and after older age (baseline visit 5, ages 70-90 years during 2011-2013), by eGFR (creatinine) and UACR categories, the Atherosclerosis Risk in Communities (ARIC) Study cohort.

Incident dementia after visit 4 **eGFR CKD-EPI, Creatinine (ml/min)**	**UACR categories (mg/g)** < 10	10 – 30	> 30
≥ 60	reference (n=7,699)	1.11 (0.95–1.30) (n=1,116)	**1.40 (1.16–1.69)*** (n=609)
< 60	1.07 (0.85–1.34) (n=370)	1.01 (0.58–1.76) (n=70)	**1.97 (1.30–2.99)*** (n=103)
Incident dementia after visit 5 **eGFR CKD-EPI, Creatinine (ml/min)**			
≥ 60	reference (n=1,700)	**1.37 (1.00–1.87)*** (n=1,134)	**1.69 (1.17–2.45)*** (n=496)
< 60	0.99 (0.66–1.50) (n=548)	**1.68 (1.15–2.47)*** (n=384)	**2.16 (1.49–3.15)*** (n=364)

Models adjusted for age, sex, race, education level, Apolipoprotein E4 level, smoking, body mass index, diabetes and antihypertensive medication.

***p < 0.05**

Figure S4: Adjusted relative hazards (95%-CI) of dementia incidence after midlife (baseline visit 4, ages 54-74 years during 1996-1998) and after older age (baseline visit 5, ages 70-90 years during 2011-2013), by eGFR (creatinine + cystatin-C) and UACR categories, the Atherosclerosis Risk in Communities (ARIC) Study cohort.

	UACR categories (mg/g)		
Incident dementia after visit 4 **eGFR CKD-EPI, Creatinine and Cystatin-C (ml/min)**	< 10	10 – 30	> 30
≥ 60	reference (n=7,664)	1.10 (0.94–1.29) (n=1,095)	**1.38 (1.14–1.67)*** (n=591)
< 60	1.15 (0.91–1.46) (n=405)	1.25 (0.76–2.05) (n=91)	**2.13 (1.43–3.18)*** (n=121)
Incident dementia after visit 5 **eGFR CKD-EPI, Creatinine and Cystatin-C (ml/min)**			
≥ 60	reference (n=1,550)	**1.43 (1.01–2.01)*** (n=981)	**1.79 (1.18–2.71)*** (n=396)
< 60	1.21 (0.82–1.78) (n=698)	**1.82 (1.26–2.62)*** (n=537)	**2.26 (1.56–3.29)*** (n=464)

Models adjusted for age, sex, race, education level, Apolipoprotein E4 level, smoking, body mass index, diabetes and antihypertensive medication.

***p < 0.05**

Figure S5: Adjusted relative hazards (95%-CI) of dementia incidence after midlife (baseline visit 4, ages 54-74 years during 1996-1998) and after older age (baseline visit 5, ages 70-90 years during 2011-2013), by eGFR (B2M) and UACR categories, the Atherosclerosis Risk in Communities (ARIC) Study cohort.

Incident dementia after visit 4 **eGFR CKD-EPI, Beta-2-microglobulin (ml/min)**	**UACR categories (mg/g)** < 10	10 – 30	> 30
≥ 60	reference (n=7,216)	1.06 (0.90–1.25) (n=999)	**1.36 (1.11–1.68)*** (n=493)
< 60	**1.18 (1.00–1.39)*** (n=853)	**1.65 (1.15–2.35)*** (n=187**)**	**1.89 (1.40–2.57)*** (n=219)
Incident dementia after visit 5 **eGFR CKD-EPI, Beta-2-microglobulin (ml/min)**			
≥ 60	reference (n=1,502)	1.33 (0.94–1.87) (n=950)	1.34 (0.84–2.12) (n=356)
< 60	1.08 (0.74–1.59) (n=746)	**1.84 (1.27–2.65)*** (n=568)	**2.40 (1.67–3.45)*** (n=504)

Models adjusted for age, sex, race, education level, Apolipoprotein E4 level, smoking, body mass index, diabetes, antihypertensive medication and CRP.

***p < 0.05**

Table S1: Number of diagnosed incident dementia events after midlife (baseline visit 4, ages 54-74 years during 1996-1998) and after older age (baseline visit 5, ages 70-90 years during 2011-2013), by ascertainment levels, the Atherosclerosis Risk in Communities (ARIC) Study cohort.

Ascertainment level	**Level 1**	**Level 2**	**Level 3**
Events after visit 4, age 54-74 years	**458**	**1289**	**1821**
Events after visit 5, age 70-90 years	**143**	**322**	**438**

Dementia ascertainment Level 1: in-person cognitive assessment and/or in-person informant interview.
Dementia ascertainment Level 2: All cases from level 1 with additional diagnoses based on telephone interviews.
Dementia ascertainment Level 3: All cases from levels 1 and 2 with additional diagnoses based on hospital records.

Table S2: Characteristics of the study population at baseline visit 4 (1996-1998) stratified by eGFR (cystatin-C) categories, the Atherosclerosis Risk in Communities (ARIC) Study cohort.

	Complete cohort	**eGFR (Cystatin-C) categories (ml/min)**				
Participants	**N = 9967**	eGFR ≥ 90 4000	90 > eGFR ≥ 60 5059	60 > eGFR ≥ 45 629	45 > eGFR ≥ 30 134	30 > eGFR 145
Age, years, mean (SD)	62.8 (5.7)	60.6 (5.1)	63.9 (5.5)	66.7 (5.1)	66.7 (5.1)	64.3 (5.9)
Female	5701 (57.2)	2278 (57.0)	2892 (57.2)	369 (58.7)	85 (63.4)	77 (53.1)
African-American	2029 (20.4)	1101 (27.5)	792 (15.7)	97 (15.4)	24 (17.9)	15 (10.3)
Education						
<High school	1850 (18.6)	633 (15.8)	993 (19.6)	157 (25.0)	43 (32.1)	24 (16.6)
High school or GED	4243 (42.6)	1647 (41.2)	2208 (43.6)	259 (41.2)	59 (44.0)	70 (48.3)
>High school	3874 (38.9)	1720 (43.0)	1858 (36.7)	213 (33.9)	32 (23.9)	51 (35.2)
Smoking						
Current	1413 (14.2)	465 (11.7)	788 (15.6)	104 (16.6)	23 (17.3)	33 (22.9)
Former	4312 (43.5)	1792 (45.0)	2123 (42.1)	282 (44.9)	51 (38.3)	64 (44.4)
Never	4195 (42.3)	1722 (43.3)	2125 (42.2)	242 (38.5)	59 (44.4)	47 (32.6)
Apolipoprotein E4 status						
TT = 0 Alleles	6743 (69.9)	2620 (67.7)	3481 (71.1)	449 (73.8)	96 (73.3)	97 (69.3)
CT = 1 Allele	2651 (27.5)	1146 (29.6)	1290 (26.4)	143 (23.5)	31 (23.7)	41 (29.3)
CC = 2 Alleles	247 (2.6)	103 (2.7)	122 (2.5)	16 (2.6)	4 (3.1)	2 (1.4)

Body mass index (BMI), kg/m^2						
Underweight (<18.5)	73 (0.7)	44 (1.1)	26 (0.5)	1 (0.2)	0 (0.0)	2 (1.4)
Normal weight (18.5 – 25)	2523 (25.3)	1226 (30.6)	1116 (22.1)	116 (18.4)	25 (18.7)	40 (27.6)
Overweight (25 – 30)	3934 (39.5)	1633 (40.8)	1969 (38.9)	233 (37.0)	50 (37.3)	49 (33.8)
Obese (>30)	3437 (34.5)	1097 (27.4)	1948 (38.5)	279 (44.4)	59 (44.0)	54 (37.2)
Diabetes	1543 (15.5)	635 (16.0)	709 (14.1)	127 (20.2)	44 (32.8)	28 (19.4)
Systolic blood pressure, mmHg, mean (SD)	133.9 (21.2)	132.6 (20.4)	134.4 (21.2)	137.2 (25.0)	137.9 (23.5)	139.6 (19.0)
Antihypertensive medication	4165 (41.8)	1354 (33.9)	2210 (43.7)	418 (66.5)	111 (82.8)	72 (49.7)
C-reactive protein (CRP), mg/l, median (IQR)	2.4 (1.1, 5.4)	2.5 (1.1, 5.7)	2.2 (1.0, 5.0)	3.1 (1.3, 6.3)	3.6 (1.6, 7.8)	7.9 (2.4, 10.8)
Measures of kidney function						
Estimated Glomerular Filtration Rate (eGFR), ml/min per 1.73m², median (IQR)						
CKD-EPI, Creatinine	89.2 (76.7, 96.2)	94.7 (88.1, 101.6)	85.3 (74.3, 92.9)	68.4 (59.5, 81.6)	52.1 (43.9, 63.4)	25.9 (7.6, 28.2)
CKD-EPI, Cystatin-C	85.2 (73.0, 97.3)	99.5 (95.0, 104.4)	78.0 (71.1, 83.9)	55.0 (51.0, 58.0)	39.3 (36.3, 42.4)	25.9 (6.2, 30.5)
CKD-EPI, Creatinine + Cystatin-C	87.3 (76.6, 97.1)	99.0 (93.7, 105.1)	81.4 (74.7, 87.6)	61.6 (55.8, 66.8)	45.7 (40.3, 49.6)	25.3 (6.4, 28.2)
CKD-EPI, Beta-2-Microglobulin	75.3 (66.4, 84.6)	85.1 (78.4, 92.6)	70.7 (64.5, 76.6)	55.2 (49.2, 61.6)	42.4 (37.1, 48.7)	22.4 (6.7, 27.7)

Urine albumin-to-creatinine ratio (UACR), mg/g Creatinine, median (IQR)	3.7 (1.8, 7.5)	3.5 (1.6, 6.7)	3.7 (1.8, 7.4)	4.7 (2.0, 13.3)	4.9 (2.9, 14.8)	7.1 (3.4, 43.2)

Data are presented as number (%) unless otherwise specified.

Table S3: Characteristics of the study population at baseline visit 4 (1996-1998) stratified by UACR categories, the Atherosclerosis Risk in Communities (ARIC) Study cohort.

	Complete cohort	**UACR categories (mg/g)**		
		UACR < 30	UACR 30 – 300	UACR > 300
Participants	**N = 9967**	9255	602	110
Age, years, mean (SD)	62.8 (5.7)	62.7 (5.6)	64.3 (5.7)	65.2 (6.3)
Female	5701 (57.2)	5325 (57.5)	321 (53.3)	55 (50.0)
African-American	2029 (20.4)	1794 (19.4)	195 (32.4)	40 (36.4)
Education				
<High school	1850 (18.6)	1648 (17.8)	171 (28.4)	31 (28.2)
High school or GED	4243 (42.6)	3959 (42.8)	236 (39.2)	48 (43.6)
>High school	3874 (38.9)	3648 (39.4)	195 (32.4)	31 (28.2)
Smoking				
Current	1413 (14.2)	1270 (13.8)	124 (20.9)	19 (17.4)
Former	4312 (43.5)	4007 (43.5)	253 (42.6)	52 (47.7)
Never	4195 (42.3)	3940 (42.7)	217 (36.5)	38 (34.9)
Apolipoprotein E4 status				
TT = 0 Alleles	6743 (69.9)	6267 (70.0)	400 (68.3)	76 (73.1)
CT = 1 Allele	2651 (27.5)	2457 (27.4)	168 (28.7)	26 (25.0)
CC = 2 Alleles	247 (2.6)	227 (2.5)	18 (3.1)	2 (1.9)

Body mass index (BMI), kg/m^2				
Underweight (<18.5)	73 (0.7)	61 (0.7)	12 (2.0)	0 (0.0)
Normal weight (18.5 – 25)	2523 (25.3)	2369 (25.6)	133 (22.1)	21 (19.1)
Overweight (25 – 30)	3934 (39.5)	3690 (39.9)	203 (33.7)	41 (37.3)
Obese (>30)	3437 (34.5)	3135 (33.9)	254 (42.2)	48 (43.6)
Diabetes	1543 (15.5)	1263 (13.7)	218 (36.6)	62 (56.9)
Systolic blood pressure, mmHg, mean (SD)	133.9 (21.2)	132.8 (20.4)	147.2 (25.3)	155.7 (25.3)
Antihypertensive medication	4165 (41.8)	3685 (39.8)	385 (64.0)	95 (86.4)
C-reactive protein (CRP), mg/l, median (IQR)	2.4 (1.1, 5.4)	2.3 (1.0, 5.3)	3.4 (1.5, 6.9)	4.8 (1.8, 9.6)
Measures of kidney function				
Estimated Glomerular Filtration Rate (eGFR), ml/min per 1.73m², median (IQR)				
CKD-EPI, Creatinine	89.2 (76.7, 96.2)	89.3 (77.1, 96.1)	87.3 (73.1, 97.0)	76.7 (57.2, 95.6)
CKD-EPI, Cystatin-C	85.2 (73.0, 97.3)	85.8 (73.8, 97.4)	79.5 (65.8, 93.8)	65.2 (47.4, 83.5)
CKD-EPI, Creatinine + Cystatin-C	87.3 (76.6, 97.1)	87.6 (77.2, 97.1)	83.8 (70.4, 95.9)	73.6 (50.8, 90.5)
CKD-EPI, Beta-2-Microglobulin	75.3 (66.4, 84.6)	75.6 (66.9, 84.6)	71.0 (58.9, 82.2)	58.7 (47.5, 72.5)
Urine albumin-to-creatinine ratio (UACR), mg/g Creatinine, median (IQR)	3.7 (1.8, 7.5)	3.4 (1.6, 6.3)	59.6 (41.2, 106.3)	594.0 (407.0, 996.2)

Data are presented as number (%) unless otherwise specified.

Table S4: Characteristics of the study population at baseline visit 5 (2011-2013) stratified by eGFR (cystatin-C) categories, the Atherosclerosis Risk in Communities (ARIC) Study cohort.

	Complete cohort	**eGFR (Cystatin-C) categories (ml/min)**				
Participants	**N = 4626**	eGFR ≥ 90 376	90 > eGFR ≥ 60 2023	60 > eGFR ≥ 45 1289	45 > eGFR ≥ 30 738	30 > eGFR 200
Age, years, mean (SD)	75.5 (5.2)	72.5 (3.8)	74.3 (4.6)	76.4 (5.2)	77.8 (5.3)	78.5 (5.6)
Female	2637 (57.0)	199 (52.9)	1090 (53.9)	784 (60.8)	438 (59.3)	126 (63.0)
African-American	1003 (21.7)	127 (33.8)	449 (22.2)	259 (20.1)	128 (17.3)	40 (20.0)
Education						
<High school	599 (12.9)	32 (8.5)	217 (10.7)	176 (13.7)	138 (18.7)	36 (18.0)
High school or GED	1908 (41.2)	128 (34.0)	808 (39.9)	574 (44.5)	320 (43.4)	78 (39.0)
>High school	2119 (45.8)	216 (57.4)	998 (49.3)	539 (41.8)	280 (37.9)	86 (43.0)
Smoking						
Current	256 (5.7)	16 (4.4)	115 (5.8)	86 (6.8)	29 (4.1)	10 (5.1)
Former	2165 (47.9)	188 (51.5)	959 (48.1)	592 (47.0)	343 (48.7)	82 (41.8)
Never	1708 (37.8)	126 (34.5)	765 (38.4)	464 (36.9)	268 (38.0)	85 (43.4)
Apolipoprotein E4 status						
TT = 0 Alleles	3236 (72.2)	235 (64.9)	1376 (70.3)	940 (75.0)	549 (76.3)	136 (71.2)
CT = 1 Allele	1167 (26.1)	116 (32.0)	542 (27.7)	300 (23.9)	160 (22.2)	49 (25.7)
CC = 2 Alleles	80 (1.8)	11 (3.0)	39 (2.0)	13 (1.0)	11 (1.5)	6 (3.1)

Body mass index (BMI), kg/m^2						
Underweight (<18.5)	45 (1.0)	8 (2.1)	24 (1.2)	9 (0.7)	1 (0.1)	3 (1.5)
Normal weight (18.5 – 25)	1091 (23.5)	114 (30.3)	534 (26.4)	277 (21.5)	132 (17.9)	34 (17.0)
Overweight (25 – 30)	1793 (38.8)	163 (43.4)	808 (39.9)	487 (37.8)	267 (36.2)	68 (34.0)
Obese (>30)	1697 (36.7)	91 (24.2)	657 (32.5)	516 (40.0)	338 (45.8)	95 (47.5)
Diabetes	1459 (32.3)	110 (29.6)	558 (28.1)	413 (32.9)	281 (39.7)	97 (50.0)
Systolic blood pressure, mmHg, mean (SD)	130.5 (18.1)	128.6 (17.9)	130.4 (16.9)	131.4 (18.5)	129.6 (18.8)	131.5 (23.6)
Antihypertensive medication	3470 (75.1)	230 (61.3)	1387 (68.6)	1011 (78.5)	655 (89.0)	187 (94.0)
C-reactive protein (CRP), mg/l, median (IQR)	2.0 (1.0 – 4.2)	1.3 (0.7, 2.7)	1.7 (0.8, 3.6)	2.4 (1.1, 4.8)	2.5 (1.3, 5.6)	3.6 (1.9, 6.4)
Measures of kidney function						
Estimated Glomerular Filtration Rate (eGFR), ml/min per 1.73m², median (IQR)						
CKD-EPI, Creatinine	70.9 (58.2, 83.0)	88.4 (81.9, 94.6)	78.6 (69.2, 86.0)	65.8 (57.5, 75.0)	52.4 (45.3, 61.0)	36.0 (29.4, 41.5)
CKD-EPI, Cystatin-C	60.9 (47.9, 74.7)	96.0 (93.2, 100.5)	71.2 (65.3, 78.8)	53.1 (49.3, 56.6)	39.4 (35.6, 42.4)	25.9 (21.7, 28.2)
CKD-EPI, Creatinine + Cystatin-C	66.1 (53.8, 78.3)	94.9 (90.4, 100.0)	75.7 (69.5, 82.1)	59.0 (54.3, 64.2)	44.9 (40.2, 49.3)	29.8 (25.4, 32.9)
CKD-EPI, Beta-2-Microglobulin	64.0 (54.0, 73.4)	85.5 (78.7, 91.6)	71.0 (65.4, 77.0)	58.9 (54.3, 64.0)	47.1 (42.6, 52.2)	33.4 (29.0, 37.4)

Urine albumin-to-creatinine ratio (UACR), mg/g Creatinine, median (IQR)	10.3 (6.3, 21.7)	9.5 (6.3, 16.7)	9.2 (5.9, 17.0)	10.1 (6.0, 22.2)	13.9 (7.1, 35.1)	31.1 (11.8, 100.5)

Data are presented as number (%) unless otherwise specified.

Table S5: Characteristics of the study population at baseline visit 5 (2011-2013) stratified by UACR categories, the Atherosclerosis Risk in Communities (ARIC) Study cohort.

	Complete cohort	**UACR categories (mg/g)**		
		UACR < 30	UACR 30 – 300	UACR > 300
Participants	**N = 4626**	3766	752	108
Age, years, mean (SD)	75.5 (5.2)	75.1 (5.0)	77.0 (5.4)	77.0 (5.5)
Female	2637 (57.0)	2190 (58.2)	399 (53.1)	48 (44.4)
African-American	1003 (21.7)	775 (20.6)	189 (25.1)	39 (36.1)
Education				
<High school	599 (12.9)	450 (11.9)	124 (16.5)	25 (23.1)
High school or GED	1908 (41.2)	1562 (41.5)	305 (40.6)	41 (38.0)
>High school	2119 (45.8)	1754 (46.6)	323 (43.0)	42 (38.9)
Smoking				
Current	256 (5.7)	194 (5.3)	56 (7.7)	6 (5.8)
Former	2165 (47.9)	1759 (47.7)	359 (49.1)	46 (44.7)
Never	1708 (37.8)	1421 (38.6)	253 (34.6)	34 (33.0)
Apolipoprotein E4 status				
TT = 0 Alleles	3236 (72.2)	2618 (71.8)	544 (74.3)	74 (71.2)
CT = 1 Allele	1167 (26.1)	962 (26.4)	177 (24.2)	28 (26.9)
CC = 2 Alleles	80 (1.8)	67 (1.8)	11 (1.5)	2 (1.9)

Body mass index (BMI), kg/m^2				
Underweight (<18.5)	45 (1.0)	33 (0.9)	12 (1.6)	0 (0.0)
Normal weight (18.5 – 25)	1091 (23.5)	908 (24.1)	167 (22.2)	16 (14.8)
Overweight (25 – 30)	1793 (38.8)	1487 (39.5)	272 (36.2)	34 (31.5)
Obese (>30)	1697 (36.7)	1338 (35.5)	301 (40.0)	58 (53.7)
Diabetes	1459 (32.3)	1069 (29.1)	318 (43.5)	72 (67.3)
Systolic blood pressure, mmHg, mean (SD)	130.5 (18.1)	129.0 (17.2)	135.7 (20.0)	144.5 (22.3)
Antihypertensive medication	3470 (75.1)	2739 (72.8)	627 (83.6)	104 (96.3)
C-reactive protein (CRP), mg/l, median (IQR)	2.0 (1.0 – 4.2)	1.9 (0.9, 4.1)	2.4 (1.1, 5.0)	3.1 (1.4, 5.9)
Measures of kidney function				
Estimated Glomerular Filtration Rate (eGFR), ml/min per 1.73m², median (IQR)				
CKD-EPI, Creatinine	70.9 (58.2, 83.0)	71.8 (60.1, 83.4)	66.9 (51.3, 81.1)	50.7 (36.2, 67.0)
CKD-EPI, Cystatin-C	60.9 (47.9, 74.7)	62.8 (50.4, 76.1)	53.1 (41.0, 68.0)	39.4 (28.2, 52.1)
CKD-EPI, Creatinine + Cystatin-C	66.1 (53.8, 78.3)	67.6 (56.1, 79.3)	60.0 (46.9, 74.3)	45.0 (32.3, 57.7)
CKD-EPI, Beta-2-Microglobulin	64.0 (54.0, 73.4)	65.2 (55.8, 74.3)	57.8 (46.9, 68.1)	46.4 (35.8, 57.0)
Urine albumin-to-creatinine ratio (UACR), mg/g Creatinine, median (IQR)	10.3 (6.3, 21.7)	8.3 (5.8, 13.6)	56.0 (38.9, 93.9)	620.1 (379.8, 1343.9)

Data are presented as number (%) unless otherwise specified.

Table S6: Adjusted hazard ratios of dementia incidence (95%-CI) after midlife (baseline visit 4, ages 54-74 years during 1996-1998) and after older age (baseline visit 5, ages 70-90 years during 2011-2013), for linear splines of eGFR measures with a knot at 60 ml/min, the Atherosclerosis Risk in Communities (ARIC) Study cohort.

eGFR	**Baseline visit 4, ages 54-74 years**	**Baseline visit 5, ages 70-90 years**
eGFR CKD-EPI, Creatinine		
per V4-IQR (19.4ml/min) decrease, linear spline		
< 60	1.38 (0.93–2.05)	1.14 (0.87–1.51)
≥ 60	0.95 (0.89–1.02)	1.01 (0.82–1.23)
p-value for spline term difference	0.267	0.390
eGFR CKD-EPI, Cystatin-C		
per V4-IQR (24.3ml/min) decrease, linear spline		
< 60	**1.37 (1.08–1.73)***	**1.39 (1.03–1.89)***
≥ 60	1.07 (0.97–1.18)*	1.23 (0.95–1.60)
p-value for spline term difference	0.151	0.861
eGFR CKD-EPI, Creatinine and Cystatin-C		
per V4-IQR (20.7ml/min) decrease, linear spline		
< 60	**1.47 (1.05–2.04)***	**1.28 (1.01–1.61)***
≥ 60	1.03 (0.95–1.12)	1.09 (0.84–1.40)
p-value for spline term difference	0.121	0.529
eGFR CKD-EPI, Beta-2-Microglobulin		
per V4-IQR (18.3ml/min) decrease, linear spline		
< 60	**1.42 (1.25–1.78)***	**1.49 (1.13–1.97)***
≥ 60	**1.11 (1.02–1.21)***	1.23 (0.96–1.56)*
p-value for spline term difference	0.285	0.315

Models adjusted for age, sex, race, education level, Apolipoprotein E4 level, smoking, body mass index, diabetes, antihypertensive medication and log-UACR. B2M additionally adjusted for CRP.

***p < 0.05**

Table S7: Adjusted relative hazards (95%-CI) of dementia incidence after midlife (baseline visit 4, ages 54-74 years during 1996-1998) and after older age (baseline visit 5, ages 70-90 years during 2011-2013), by eGFR (cystatin-C) categories, the Atherosclerosis Risk in Communities (ARIC) Study cohort.

	eGFR (Cystatin-C) categories (ml/min)				
	eGFR ≥ 90	**90 > eGFR ≥ 60**	**60 > eGFR ≥ 45**	**45 > eGFR ≥ 30**	**30 > eGFR**
Incident dementia after visit 4, age 54-74 years					
eGFR CKD-EPI, Creatinine	reference	0.91 (0.81-1.01)	1.02 (0.83-1.27)	0.91 (0.51-1.62)	**5.89 (1.46-23.76)***
eGFR CKD-EPI, Cystatin-C	reference	1.11 (0.99-1.24)	**1.28 (1.05-1.57)***	**1.76 (1.22-2.54)***	**1.74 (1.11-2.72)***
eGFR CKD-EPI, Creatinine and Cystatin-C	reference	1.02 (0.92-1.14)	**1.38 (1.11-1.72)***	0.96 (0.61-1.50)	**5.42 (1.33-22.08)***
eGFR CKD-EPI, Beta-2-Microglobulin	reference	1.05 (0.91-1.22)	**1.27 (1.04-1.56)***	**1.53 (1.08-2.17)***	**3.80 (1.21-11.98)***
Incident dementia after visit 5, age 70-90 years					
eGFR CKD-EPI, Creatinine	reference	0.96 (0.65-1.43)	1.08 (0.71-1.66)	1.07 (0.64-1.77)	1.49 (0.67-3.29)
eGFR CKD-EPI, Cystatin-C	reference	1.36 (0.83-2.24)	**1.83 (1.10-3.04)***	**1.92 (1.12-3.28)***	**2.40 (1.29-4.43)**
eGFR CKD-EPI, Creatinine and Cystatin-C	reference	1.14 (0.74-1.77)	1.47 (0.93-2.32)	1.08 (0.64-1.83)	**2.17 (1.15-4.10)***

eGFR CKD-EPI, Beta-2-Microglobulin	reference	1.40 (0.71-2.76)	1.87 (0.94-3.75)	1.83 (0.88-3.82)	**3.06 (1.19-7.89)***

Models adjusted for age, sex, race, education level, Apolipoprotein E4 level, smoking, body mass index, diabetes, antihypertensive medication and log-UACR.
***p < 0.05**

Table S8: Adjusted relative hazards (95%-CI) of dementia incidence after midlife (baseline visit 4, ages 54-74 years during 1996-1998) and after older age (baseline visit 5, ages 70-90 years during 2011-2013), by UACR categories, the Atherosclerosis Risk in Communities (ARIC) Study cohort.

	UACR categories (mg/g)		
	< 30	**30 – 300**	**> 300**
Incident dementia after visit 4, age 54-74 years			
	reference	**1.28 (1.05-1.53)***	**3.44 (2.33-5.08)***
Incident dementia after visit 5, age 70-90 years			
	reference	1.27 (0.99-1.63)	**1.93 (1.20-3.11)***

Models adjusted for age, sex, race, education level, Apolipoprotein E4 level, smoking, body mass index, diabetes, antihypertensive medication and eGFR (Cystatin-C).

***p < 0.05**

Table S9: Adjusted hazard ratios of dementia incidence (95%-CI) after midlife (baseline visit 4, ages 54-74 years during 1996-1998) and after older age (baseline visit 5, ages 70-90 years during 2011-2013), by eGFR (creatinine) and significant covariates, the Atherosclerosis Risk in Communities (ARIC) Study cohort.

	Baseline visit 4, ages 54-74 years		**Baseline visit 5, ages 70-90 years**	
	Model 1	Model 2	Model 1	Model 2
eGFR CKD-EPI, Creatinine per V4-IQR (19.4ml/min) decrease	0.98 (0.92 – 1.04)	0.98 (0.91 – 1.04)	1.11 (0.99 - 1.24)	1.03 (0.91 – 1.17)
Education level				
<Highschool	**1.58 (1.38 – 1.79)***	**2.01 (1.51-2.67)***	**1.82 (1.38 – 2.40)***	**1.59 (1.40-1.80)***
Highschool or GED	**1.22 (1.09 – 1.37)***	**1.34 (1.05-1.70)***	**1.29 (1.03 – 1.62)***	**1.19 (1.07-1.33)***
>Highschool	reference	reference	reference	reference
Apolipoprotein E4 Gen				
TT = 0 Alleles	reference	reference	reference	reference
CT = 1 Allele	**1.91 (1.73 – 2.11)***	**1.55 (1.24-1.94)***	**1.63 (1.33 – 2.01)***	**1.96 (1.78-2.16)***
CC = 2 Alleles	**4.10 (3.37 – 4.99)***	**2.36 (1.34-4.17)***	**2.05 (1.19 – 3.53)***	**4.04 (3.33-4.90)***
Body mass index				
Underweight (<18.5)	-	**1.99 (1.27-3.12)***	-	**2.74 (1.45-5.16)***
Normal weight (18.5 – 25)	-	reference	-	reference
Overweight (25 – 30)	-	1.01 (0.89-1.14)	-	**0.73 (0.56-0.95)***
Obese (>30)	-	1.08 (0.95-1.23)	-	**0.68 (0.50-0.91)***
Diabetes	-	**1.46 (1.29-1.65)***	-	1.14 (0.90-1.43)

Antihypertensive medication	-	**1.13 (1.02-1.24)***	-	1.15 (0.91-1.45)

Model 1 adjusted for age, sex, race, education level and Apolipoprotein E4 level.
Model 2 adjusted for age, sex, race, education level, Apolipoprotein E4 level, smoking, body mass index, diabetes, antihypertensive medication and log-UACR.
***p < 0.05**

Table S10: Adjusted hazard ratios (HRs, 95%-CI) of dementia incidence after visit 4 by measures of CKD, the Atherosclerosis Risk in Communities (ARIC) Study cohort. Comparison of HRs with observational period after visit 4 and restricted observational period between visit 4 and visit 5 with right censoring at visit 5.

Measure of CKD	**Baseline visit 4, right censored at visit 5**	
	Model 1	Model 2
eGFR CKD-EPI, Creatinine per V4-IQR (19.4ml/min) decrease	0.92 (0.85-1.01)	0.94 (0.87-1.02)
eGFR CKD-EPI, Cystatin-C per V4-IQR (24.3ml/min) decrease	**1.17 (1.06-1.29)***	**1.14 (1.04-1.27)***
eGFR CKD-EPI, Creatinine and Cystatin-C per V4-IQR (20.7ml/min) decrease	1.06 (0.97-1.16)	1.05 (0.96-1.15)
eGFR CKD-EPI, Beta-2-Microglobulin per V4-IQR (18.3ml/min) decrease	**1.22 (1.12-1.32)***	**1.19 (1.10-1.31)***
Log Urine albumin-to-creatinine ratio per V4-IQR (4.2) – fold increase	**1.12 (1.06-1.20)***	**1.09 (1.02-1.16)***

Model 1 adjusted for age, sex, race, education level and Apolipoprotein E4 level.
Model 2 adjusted for age, sex, race, education level, Apolipoprotein E4 level, smoking, body mass index, diabetes and antihypertensive medication. eGFR values adjusted for log-UACR and log-UACR values adjusted for eGFR (cystatin-C). B2M additionally adjusted for CRP.
***p < 0.05**

Table S11: Adjusted hazard ratios (95%-CI) of dementia incidence after visit 4 and after visit 5 by measures of CKD, the Atherosclerosis Risk in Communities (ARIC) Study cohort. Subgroup analysis stratified by ethnicity.

Measure of CKD	**Baseline visit 4**		**Baseline visit 5**	
	Caucasian participants	African-American participants	Caucasian participants	African American participants
eGFR CKD-EPI, Creatinine per V4-IQR (19.4ml/min) decrease	0.98 (0.88-1.09)	0.93 (0.83-1.04)	1.02 (0.87-1.19)	1.08 (0.89-1.31)
eGFR CKD-EPI, Cystatin-C per V4-IQR (24.3ml/min) decrease	**1.17 (1.04-1.31)***	**1.21 (1.03-1.42)***	1.15 (0.95-1.39)	**1.49 (1.16-1.93)***
eGFR CKD-EPI, Creatinine and Cystatin-C per V4-IQR (20.7ml/min) decrease	1.10 (0.98-1.23)	1.06 (0.93-1.21)	1.09 (0.92-1.29)	**1.27 (1.03-1.56)***
eGFR CKD-EPI, Beta-2-Microglobulin per V4-IQR (18.3ml/min) decrease	**1.18 (1.06-1.31)***	**1.25 (1.10-1.43)***	1.16 (0.97-1.38)	**1.59 (1.26-2.02)***
Log Urine albumin-to-creatinine ratio per V4-IQR (4.2) – fold increase	**1.13 (1.05-1.22)***	1.07 (0.98-1.17)	**1.28 (1.11-1.47)***	1.73 (0.97-3.09)

Models adjusted for age, sex, education level, Apolipoprotein E4 level, smoking, body mass index, diabetes and antihypertensive medication. eGFR values adjusted for log-UACR and log-UACR values adjusted for eGFR (cystatin-C). B2M additionally adjusted for CRP.
***p < 0.05**

Table S12: Adjusted hazard ratios (95%-CI) of dementia incidence (according to ascertainment Level 1) after midlife (baseline visit 4, ages 54-74 years during 1996-1998) and after older age (baseline visit 5, ages 70-90 years during 2011-2013), by measures of CKD, the Atherosclerosis Risk in Communities (ARIC) Study cohort.

Measure of CKD	**Baseline visit 4, ages 54-74 years**	**Baseline visit 5, ages 70-90 years**
eGFR CKD-EPI, Creatinine per V4-IQR (19.4ml/min) decrease	0.92 (0.81-1.06)	0.92 (0.74-1.14)
eGFR CKD-EPI, Cystatin-C per V4-IQR (24.3ml/min) decrease	1.04 (0.89-1.23)	1.05 (0.81-1.36)
eGFR CKD-EPI, Creatinine and Cystatin-C per V4-IQR (20.7ml/min) decrease	0.99 (0.85-1.14)	1.00 (0.79-1.24)
eGFR CKD-EPI, Beta-2-Microglobulin per V4-IQR (18.3ml/min) decrease	1.10 (0.96-1.27)	1.04 (0.82-1.33)
Log Urine albumin-to-creatinine ratio per V4-IQR (4.2) – fold increase	**1.14 (1.03-1.26)***	1.60 (0.86-2.98)

Models adjusted for age, sex, race, education level, Apolipoprotein E4 level, smoking, body mass index, diabetes and antihypertensive medication. eGFR values adjusted for log-UACR and log-UACR values adjusted for eGFR (cystatin-C). B2M additionally adjusted for CRP.
***p < 0.05**

Table S13: Adjusted hazard ratios (95%-CI) of dementia incidence after older age (baseline visit 5, ages 70-90 years during 2011-2013), by measures of CKD, the Atherosclerosis Risk in Communities (ARIC) Study cohort. Patients with prevalent mild cognitive impairment (MCI) at visit 5 were excluded.

Measure of CKD	Baseline visit 5
eGFR CKD-EPI, Creatinine per V4-IQR (19.4ml/min) decrease	1.06 (0.89-1.26)
eGFR CKD-EPI, Cystatin-C per V4-IQR (24.3ml/min) decrease	**1.42 (1.14-1.76)***
eGFR CKD-EPI, Creatinine and Cystatin-C per V4-IQR (20.7ml/min) decrease	**1.24 (1.03-1.49)***
eGFR CKD-EPI, Beta-2-Microglobulin per V4-IQR (18.3ml/min) decrease	**1.45 (1.18-1.77)***
Log Urine albumin-to-creatinine ratio per V4-IQR (4.2) – fold increase	**2.70 (1.69-4.34)***

Models adjusted for age, sex, race, education level, Apolipoprotein E4 level, smoking, body mass index, diabetes and antihypertensive medication. eGFR values adjusted for log-UACR and log-UACR values adjusted for eGFR (cystatin C). B2M additionally adjusted for CRP. Baseline visit 5: N = 3,622 patients, 206 events / 16,256 person-years;
***p < 0.05**