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The definition of CKM syndrome stages in this study.

In our study, we determined the CKM syndrome stage for each participant. Stage 0 comprised individuals with a normal body mass index (BMI) (Asian ethnicity: $<23 \text{ kg/m}^2$; other racial/ethnic groups: $<25 \text{ kg/m}^2$) and waist circumference thresholds (Asian populations: women $<80 \text{ cm}$, men $<90 \text{ cm}$; other groups: women $<88 \text{ cm}$, men $<102 \text{ cm}$), with the exclusion of individuals meeting the criteria for subsequent stages. Stage 1 included the subjects with the following risk factors for obesity or impaired glucose metabolism: (1) elevated BMI ($\geq 23 \text{ kg/m}^2$ for Asian populations; $\geq 25 \text{ kg/m}^2$ for other racial/ethnic groups); (2) sex-specific abdominal obesity thresholds (Asian populations: women $\geq 80 \text{ cm}$, men $\geq 90 \text{ cm}$; other groups: women $\geq 88 \text{ cm}$, men $\geq 102 \text{ cm}$); and (3) prediabetes, indicated by fasting plasma glucose levels of 100-125 mg/dL and/or hemoglobin A1c (HbA1c) values of 5.7%-6.4%. Stage 2 involved the participants who exhibited metabolic risk factors or moderate-to-high-risk CKD. Metabolic risk factors include elevated fasting serum triglyceride levels (135 mg/dL or higher), hypertension, diabetes, or metabolic syndrome (with at least three of the following conditions: increased waist circumference, a low level of high-density lipoprotein cholesterol (HDL) [$<40 \text{ mg/dL}$ for males or $<50 \text{ mg/dL}$ for females], high fasting serum triglycerides [$\geq 150 \text{ mg/dL}$ or higher], elevated blood pressure [systolic blood pressure of 130 mmHg or higher, diastolic blood pressure of 80 mmHg or higher, and/or the use of blood pressure-lowering medications], or prediabetes). CKD stages, according to the Kidney Disease: Improving Global Outcomes criteria, were identified on the basis of estimated glomerular filtration (eGFR; calculated by using the race-free CKD-EPI 2021 creatinine equation) and urinary albumin to creatinine ratio. Stage 3 encompassed individuals with very-high-risk CKD according to the Kidney Disease: Improving Global Outcomes criteria or a high predicted 10-year risk of CVD ($\geq 20\%$) estimated using the PREVENT equations. Stage 4 consisted of participants with self-reported CVD, including coronary heart disease (CHD), angina, myocardial infarction, heart failure (HF), or stroke. According to the AHA staging framework, stage 4 is further subclassified into 4a (without kidney failure) and 4b (with kidney failure). In line with several previous epidemiological applications of the CKM staging system, we combined Stages 4a and 4b into a single stage 4 category for analytical parsimony and statistical stability. Furthermore, CKM syndrome was categorized into advanced stages (stages 3-4) and nonadvanced stages (stages 0-2) to improve the stratification of disease progression and guide clinical management.

Table S1. Selected variables extracted from the UK Biobank dataset

UKB code	Variable names
31	Sex
21022	Age at recruitment
191	Date lost to follow-up
53	Date of attending assessment centre
21000	Ethnic background
21001	Body mass index (BMI)
48	Waist circumference
26410	Index of Multiple Deprivation (England)
26427	Index of Multiple Deprivation (Scotland)
26426	Index of Multiple Deprivation (Wales)
20116	Smoking status
20117	Alcohol drinker status
6138	Qualifications
22036	At or above moderate/vigorous/walking recommendation
93	Systolic blood pressure, manual reading
94	Diastolic blood pressure, manual reading
4080	Systolic blood pressure, automated reading
4079	Diastolic blood pressure, automated reading
30070	Red blood cell (erythrocyte) distribution width
30740	Glucose
30750	Glycated haemoglobin (HbA1c)
30870	Triglycerides
30690	Cholesterol
30760	HDL cholesterol
30780	LDL direct
30600	Albumin
30700	Creatinine
30500	Microalbumin in urine
30510	Creatinine (enzymatic) in urine
6177	Medication for cholesterol, blood pressure or diabetes
2443	Diabetes diagnosed by doctor
6150	Vascular/heart problems diagnosed by doctor
130706	Date E10 first reported (insulin-dependent diabetes mellitus)
130708	Date E11 first reported (non-insulin-dependent diabetes mellitus)
130710	Date E12 first reported (malnutrition-related diabetes mellitus)
130712	Date E13 first reported (other specified diabetes mellitus)
130714	Date E14 first reported (unspecified diabetes mellitus)
131286	Date I10 first reported (essential (primary) hypertension)

131296	Date I20 first reported (angina pectoris)
131298	Date I21 first reported (acute myocardial infarction)
131300	Date I22 first reported (subsequent myocardial infarction)
131302	Date I23 first reported (certain current complications following acute myocardial infarction)
131304	Date I24 first reported (other acute ischaemic heart diseases)
131306	Date I25 first reported (chronic ischaemic heart disease)
131350	Date I48 first reported (atrial fibrillation and flutter)
131354	Date I50 first reported (heart failure)
131360	Date I60 first reported (subarachnoid haemorrhage)
131362	Date I61 first reported (intracerebral haemorrhage)
131364	Date I62 first reported (other nontraumatic intracranial haemorrhage)
131366	Date I63 first reported (cerebral infarction)
131368	Date I64 first reported (stroke, not specified as haemorrhage or infarction)
131380	Date I70 first reported (atherosclerosis)
131386	Date I73 first reported (other peripheral vascular diseases)

Table S2. Selected variables extracted from the NHANES dataset

Variable description	Data File	Variable code
Age at Screening Adjudicated	DEMO.xpt~DEMO_J.xpt	RIDAGEYR
Gender	DEMO.xpt~DEMO_J.xpt	RIAGENDR
Race/Ethnicity	DEMO.xpt~DEMO_J.xpt	RIDRETH1~RIDRETH3
Education Level-Adults 20+	DEMO.xpt~DEMO_J.xpt	DMDEDUC2
Ratio of family income to poverty	DEMO.xpt~DEMO_J.xpt	INDFMPIR
Are you pregnant now?	RHQ.xpt~RHQ_J.xpt	RHD143
Albumin	LAB18.xpt, L40_B.xpt, L40_2_B.xpt, L40_C.xpt, BIOPRO_D.xpt~BIOPRO_J.xpt	LBXSAL
Serum total cholesterol (mg/dL)	LAB13.xpt, l13_b.xpt, l13_2_b.xpt, l13_c.xpt, TCHOL_D.xpt ~ TCHOL_J.xpt	LBXTC, LB2TC
Red cell distribution width (%)	LAB25.xpt, L25_2_B.xpt, L25_B.xpt, L25_C.xpt, CBC_D.xpt~CBC_J.xpt	LBXRDW
Body Mass Index (kg/m ²)	BMX.xpt~BMX_J.xpt	BMXBMI
Waist Circumference (cm)	BMX.xpt~BMX_J.xpt	BMXWAIST
Glycohemoglobin (%)	LAB10.xpt, L10_B.xpt, L10_2_B.xpt, L10_C.xpt, GHB_D.xpt~GHB_J.xpt	LB2GH, LBXGH
Fasting Glucose (mg/dL)	LAB10AM.xpt, L10AM_B.xpt, L10_2_B.xpt, L10AM_C.xpt, GLU_D.xpt~GLU_J.xpt	LB2GLU
Serum triglycerides (mg/dL)	LAB13AM.xpt, L13AM_B.xpt, L40_B.xpt, L40_2_B.xpt, L13AM_C.xpt, TRIGLY_D.xpt~TRIGLY_J.xpt	LBXTR
Serum HDL cholesterol (mg/dL)	LAB13.xpt, L13_B.xpt, L13_2_B.xpt, L13_C.xpt, HDL_D.xpt~HDL_J.xpt	LBDHDL, LBXHDD, LB2HDL, LBDHDD
Diastolic: Blood pressure mm Hg	BPX.xpt~BPX_J.xpt	BPXDI1~BPXDI4
Systolic: Blood pressure mm Hg	BPX.xpt~BPX_J.xpt	BPXSY1~BPXSY4
Now taking prescribed medicine for HBP	BPQ_B.xpt~BPQ_J.xpt	BPQ050A
Ever told you had high blood pressure	BPQ_B.xpt~BPQ_J.xpt	BPQ020
Serum creatinine (mg/dL)	LAB18.xpt, L40_B.xpt, L40_2_B.xpt, L40_C.xpt, BIOPRO_D.xpt~BIOPRO_J.xpt	LB2SCR, LBDSCR, LBXSCR
Urinary albumin: SI (mg/L)	LAB16.xpt, L16_B.xpt, L16_2_B.xpt, L16_C.xpt, ALB_CR_D.xpt~ALB_CR_E.xpt	URXUMS, UR2UMASI, URXUMASI
Urinary creatinine (mg/dL)	LAB16.xpt, L16_B.xpt, L16_2_B.xpt, L17_C.xpt, ALB_CR_D.xpt~ALB_CR_E.xpt	URXUCR
First albumin creatinine ratio (mg/g)	ALB_CR_F.xpt~ALB_CR_J.xpt	URDACT
Ever told had congestive heart failure	MCQ.xpt~MCQ_J.xpt	MCQ160B
Ever told you had coronary heart disease	MCQ.xpt~MCQ_J.xpt	MCQ160C
Ever told you had angina/angina pectoris	MCQ.xpt~MCQ_J.xpt	MCQ160D
Ever told you had heart attack	MCQ.xpt~MCQ_J.xpt	MCQ160E
Ever told you had a stroke	MCQ.xpt~MCQ_J.xpt	MCQ160F
Generic drug code	RXQ_RX.xpt~RXQ_RX_J.xpt	RXDDRGID
Doctor told you have diabetes	DIQ.xpt~DIQ_J.xpt	DIQ010
Taking insulin now	DIQ.xpt~DIQ_J.xpt	DIQ050

Take diabetic pills to lower blood sugar	DIQ.xpt~DIQ_J.xpt	DID070, DIQ070
Smoked at least 100 cigarettes in life	SMQ.xpt~SMQ_J.xpt	SMQ020
Do you now smoke cigarettes	SMQ.xpt~SMQ_J.xpt	SMQ040
Had at least 12 alcohol drinks/1 yr?	ALQ.xpt~ALQ_J.xpt	ALQ101
Had at least 12 alcohol drinks/lifetime?	ALQ.xpt~ALQ_J.xpt	ALQ110
How often drink alcohol over past 12 mos	ALQ.xpt~ALQ_J.xpt	ALQ120Q
Moderate activity over past 30 days	PAQ.xpt~PAQ_J.xpt	PAD320
Moderate work activity	PAQ.xpt~PAQ_J.xpt	PAQ620
Moderate recreational activities	PAQ.xpt~PAQ_J.xpt	PAQ665

Table S3. Proportions of missing covariates in two cohorts

Characteristics	NHANES (N = 32,068)		UK Biobank (N = 110,123)		UK Biobank (N = 98,145)	
	n	Percentage, %	n	Percentage, %	n	Percentage, %
Age	0	0	0	0	0	0
Sex	0	0	0	0	0	0
Race	0	0	0	0	0	0
Socioeconomic status	2,816	8.78	0	0	0	0
Education level	38	0.12	0	0	0	0
Smoking status	2	0.01	0	0	0	0
Alcohol status	1,888	5.89	0	0	0	0
Physical activity	500	1.56	0	0	0	0

Table S4. Knots selection of restricted cubic spline analysis

Outcome	Number of knots	Akaike information criterion	Final selected number of knots
Advanced CKM stages in NHANES	3	23654.91	5
	4	23636.26	
	5	23635.16	
	6	23635.48	
Advanced CKM stages in the UK Biobank	3	73351.14	4
	4	73312.12	
	5	73295.52	
	6	73280.08	
Cardiovascular diseases	3	358914.10	4
	4	358896.79	
	5	358891.59	
	6	358891.08	
Atrial fibrillation	3	146829.55	4
	4	146811.88	
	5	146812.66	
	6	146813.94	
Coronary heart disease	3	189008.57	4
	4	189004.25	
	5	189003.49	
	6	189003.87	
Heart failure	3	76886.62	4
	4	76874.01	
	5	76871.20	
	6	76870.43	
STROKE	3	60519.45	4
	4	60521.15	
	5	60522.99	
	6	60524.38	
Peripheral artery disease	3	43890.12	4
	4	43889.35	
	5	43888.34	
	6	43887.46	

Table S5. Baseline characteristics of all participants by CKM syndrome stages in two cohorts

Characteristic	NHANES					P value	Characteristic	UK Biobank					P value
	Stage 0	Stage 1	Stage 2	Stage 3	Stage 4			Stage 0	Stage 1	Stage 2	Stage 3	Stage 4	
No. of participants	1,472	3,413	17,785	4,117	5,281		No. of participants	10,637	14,525	70,318	2,921	11,722	
Age, years, median [IQR]	41.00 [35.00, 50.00]	44.00 [36.00, 53.00]	53.00 [43.00, 63.00]	78.00 [72.00, 80.00]	70.00 [60.00, 78.00]	<0.001	Age, years, mean (SD)	53.96 (8.43)	55.29 (8.33)	57.16 (7.92)	64.38 (5.01)	61.73 (6.31)	<0.001
Gender, n (%)						<0.001	Gender, n (%)						<0.001
Female	925 (62.8)	1,828 (53.6)	9,338 (52.5)	1,761 (42.8)	2,277 (43.1)		Female	7,341 (69.0)	8,169 (56.2)	32,862 (46.7)	497 (17.0)	3,574 (30.5)	
Male	547 (37.2)	1,585 (46.4)	8,447 (47.5)	2,356 (57.2)	3,004 (56.9)		Male	3,296 (31.0)	6,356 (43.8)	37,456 (53.3)	2,424 (83.0)	8,148 (69.5)	
Race and ethnicity, n (%)						<0.001	Race and ethnicity, n (%)						<0.001
Hispanic	249 (16.9)	967 (28.3)	4,937 (27.8)	793 (19.3)	929 (17.6)		Asian or Asian British	95 (0.9)	261 (1.8)	1854 (2.6)	130 (4.5)	356 (3.0)	
Non-Hispanic Black	204 (13.9)	660 (19.3)	3,820 (21.5)	837 (20.3)	1,072 (20.3)		Black or Black British	131 (1.2)	447 (3.1)	1356 (1.9)	68 (2.3)	162 (1.4)	
Non-Hispanic White	877 (59.6)	1,443 (42.3)	7,383 (41.5)	2,249 (54.6)	2,971 (56.3)		Mixed	88 (0.8)	119 (0.8)	405 (0.6)	11 (0.4)	52 (0.4)	
Other Race	142 (9.6)	343 (10.0)	1,645 (9.2)	238 (5.8)	309 (5.9)		Other	95 (0.9)	170 (1.2)	778 (1.1)	34 (1.2)	111 (0.9)	
							White	10,228 (96.2)	13,528 (93.1)	65,925 (93.8)	2,678 (91.7)	11,041 (94.2)	
Qualifications, n (%)						<0.001	Qualifications, n (%)						<0.001
College or above	1,222 (83.0)	2,645 (77.5)	12,922 (72.7)	2,552 (62.0)	3,381 (64.0)		College or above	4,369 (41.1)	4,825 (33.2)	20,212 (28.7)	567 (19.4)	2,358 (20.1)	
High school or equivalent	140 (9.5)	435 (12.7)	2,579 (14.5)	659 (16.0)	957 (18.1)		High school or equivalent	1,359 (12.8)	1,719 (11.8)	7,502 (10.7)	236 (8.1)	1,023 (8.7)	
Less than high school	110 (7.5)	333 (9.8)	2,284 (12.8)	906 (22.0)	943 (17.9)		Less than high school	4,909 (46.2)	7,981 (54.9)	42,604 (60.6)	2,118 (72.5)	8,341 (71.2)	
Socioeconomic status*, n (%)						<0.001	Socioeconomic status*, n (%)						<0.001
Low	310 (21.1)	850 (24.9)	5,231 (29.4)	1,323 (32.1)	1,938 (36.7)		Low	2,809 (26.4)	4,403 (30.3)	23,490 (33.4)	1,175 (40.2)	4,788 (40.8)	
Moderate	478 (32.5)	1,228 (36.0)	6,670 (37.5)	1,914 (46.5)	2,188 (41.4)		Moderate	3,605 (33.9)	4,922 (33.9)	23,557 (33.5)	929 (31.8)	3,707 (31.6)	
High	684 (46.5)	1,335 (39.1)	5,884 (33.1)	880 (21.4)	1,155 (21.9)		High	4,223 (39.7)	5,200 (35.8)	23,271 (33.1)	817 (28.0)	3,227 (27.5)	
Alcohol status, n (%)						<0.001	Alcohol status, n (%)						<0.001
Current	1,038 (70.5)	2,256 (66.1)	10,566 (59.4)	1,715 (41.7)	2,301 (43.6)		Current	9,934 (93.4)	13,514 (93.0)	64,262 (91.4)	2,596 (88.9)	10,140 (86.5)	
Never	321 (21.8)	853 (25.0)	5,023 (28.2)	1,457 (35.4)	1,645 (31.1)		Never	388 (3.6)	601 (4.1)	3563 (5.1)	164 (5.6)	740 (6.3)	
Previous	113 (7.7)	304 (8.9)	2,196 (12.3)	945 (23.0)	1,335 (25.3)		Previous	315 (3.0)	410 (2.8)	2493 (3.5)	161 (5.5)	842 (7.2)	
Smoking status, n (%)						<0.001	Smoking status, n (%)						<0.001
Current	362 (24.6)	638 (18.7)	3,647 (20.5)	590 (14.3)	1,014 (19.2)		Current	1,249 (11.7)	1,495 (10.3)	8,180 (11.6)	850 (29.1)	1,662 (14.2)	
Never	844 (57.3)	2,005 (58.7)	9,521 (53.5)	1,909 (46.4)	2,071 (39.2)		Never	6,469 (60.8)	8,416 (57.9)	36,927 (52.5)	946 (32.4)	4,384 (37.4)	
Previous	266 (18.1)	770 (22.6)	4,617 (26.0)	1,618 (39.3)	2,196 (41.6)		Previous	2,919 (27.4)	4,614 (31.8)	25,211 (35.9)	1,125 (38.5)	5,676 (48.4)	
Moderate activity, n (%)						<0.001	Moderate activity, n (%)						<0.001
Current	810 (55.0)	1,623 (47.6)	7,461 (42.0)	1,412 (34.3)	1,763 (33.4)		Current	7,250 (68.2)	9,393 (64.7)	41,931 (59.6)	1,627 (55.7)	6,414 (54.7)	
Never	844 (57.3)	2,005 (58.7)	9,521 (53.5)	1,909 (46.4)	2,071 (39.2)		Never	6,469 (60.8)	8,416 (57.9)	36,927 (52.5)	946 (32.4)	4,384 (37.4)	
Previous	266 (18.1)	770 (22.6)	4,617 (26.0)	1,618 (39.3)	2,196 (41.6)		Previous	2,919 (27.4)	4,614 (31.8)	25,211 (35.9)	1,125 (38.5)	5,676 (48.4)	
BMI, kg/m², median [IQR]	22.22 [20.61, 23.64]	27.21 [25.11, 30.20]	29.56 [26.04, 34.08]	27.90 [24.66, 31.57]	29.07 [25.60, 33.63]	<0.001	BMI, kg/m², mean (SD)	22.41 (1.76)	27.54 (3.67)	29.20 (5.16)	30.61 (5.18)	30.04 (5.31)	<0.001
Waist circumference, cm, mean (SD)	80.44 (6.81)	95.27 (11.87)	103.07 (15.29)	102.65 (14.21)	105.12 (15.36)	<0.001	Waist circumference, cm, mean (SD)	76.52 (7.95)	89.42 (10.99)	95.88 (13.42)	103.74 (13.20)	100.22 (13.80)	<0.001
HbA1c, %, median [IQR]	5.20 [5.00, 5.40]	5.40 [5.20, 5.60]	5.60 [5.30, 6.00]	5.90 [5.50, 6.60]	5.80 [5.50, 6.50]	<0.001	HbA1c, %, median [IQR]	5.23 [5.04, 5.41]	5.33 [5.11, 5.54]	5.45 [5.21, 5.73]	6.20 [5.59, 7.13]	5.65 [5.36, 6.10]	<0.001
FBG, mg/dL, median [IQR]	91.00 [86.00, 95.00]	97.40 [92.00, 103.00]	103.00 [95.00, 113.20]	111.00 [99.00, 135.05]	108.00 [97.90, 128.90]	<0.001	FBG, mg/dL, median [IQR]	85.88 [80.30, 91.06]	88.90 [83.02, 95.69]	90.61 [83.97, 99.52]	103.21 [88.63, 138.33]	92.84 [84.98, 105.80]	<0.001
TG, mg/dL, median	71.50 [55.00,	83.00 [63.00,	138.00 [91.00,	123.00	125.00 [87.50,	<0.001	TG, mg/dL, median	86.71 [68.91,	97.60 [78.74,	171.83	186.71	156.77 [110.00,	<0.001

[IQR]	92.00]	104.00]	192.00]	[87.00, 173.00]	181.00]		[IQR]	106.82]	115.32]	[131.62, 235.24]	[133.47, 267.30]	222.49]	
TC, mg/dL, median [IQR]	187.00 [167.00, 211.00]	194.00 [170.00, 216.00]	203.00 [177.00, 231.00]	190.00 [164.00, 217.00]	180.00 [152.00, 213.00]	<0.001	TC, mg/dL, mean (SD)	214.99 (38.10)	219.01 (38.73)	224.53 (46.20)	193.00 (46.97)	186.26 (44.82)	<0.001
HDL, mg/dL, median [IQR]	63.00 [52.00, 74.25]	56.00 [48.00, 66.00]	48.00 [40.00, 60.00]	49.00 [41.00, 60.00]	47.00 [39.00, 58.00]	<0.001	HDL, mg/dL, mean (SD)	65.55 (15.30)	60.39 (13.88)	51.72 (13.57)	44.00 (11.03)	47.77 (13.25)	<0.001
UACR, mg/g, median [IQR]	5.67 [3.96, 8.93]	5.33 [3.82, 7.91]	7.57 [4.81, 15.36]	15.53 [7.60, 46.01]	12.62 [6.38, 38.40]	<0.001	UACR, mg/g, median [IQR]	8.29 [5.56, 13.43]	7.31 [5.00, 11.70]	9.57 [5.87, 20.22]	19.71 [9.45, 63.84]	11.36 [6.48, 26.67]	<0.001
eGFR, mL/min/1.73 m², mean (SD)	101.19 (15.63)	100.54 (15.32)	93.93 (17.68)	66.76 (21.48)	73.19 (23.97)	<0.001	eGFR, mL/min/1.73 m², median [IQR]	99.40 [90.81, 106.28]	97.37 [87.96, 104.11]	96.81 [85.82, 103.52]	86.64 [61.36, 97.19]	91.31 [77.50, 99.22]	<0.001
Hypertension, n (%)	0 (0.0)	0 (0.0)	11,664 (65.6)	3,648 (88.6)	4,624 (87.6)	<0.001	Hypertension, n (%)	0 (0.0)	0 (0.0)	30,957 (44.0)	2,458 (84.1)	8,754 (74.7)	<0.001
DM, n (%)	0 (0.0)	0 (0.0)	3,644 (20.5)	1,820 (44.2)	2,083 (39.4)	<0.001	DM, n (%)	0 (0.0)	0 (0.0)	5,374 (7.6)	1,865 (63.8)	2,657 (22.7)	<0.001
Pre-DM, n (%)	0 (0.0)	1,638 (48.0)	8,524 (48.0)	1,846 (44.9)	2,454 (46.5)	<0.001	Pre-DM, n (%)	0 (0.0)	3609 (24.8)	20,818 (29.6)	430 (14.7)	3,722 (31.8)	<0.001
CKD risk, n (%)						<0.001	CKD risk, n (%)						<0.001
low risk	1,472 (100.0)	3,413 (100.0)	14,658 (82.4)	1,840 (45.7)	2,783 (55.3)		low risk	10,637 (100.0)	14,525 (100.0)	56,924 (81.0)	1,541 (52.8)	8,613 (73.5)	
moderate risk	0 (0.0)	0 (0.0)	2,720 (15.3)	1,154 (28.7)	1,222 (24.3)		moderate risk	0 (0.0)	0 (0.0)	12,332 (17.5)	729 (25.0)	2,411 (20.6)	
high risk	0 (0.0)	0 (0.0)	407 (2.3)	544 (13.5)	548 (10.9)		high risk	0 (0.0)	0 (0.0)	1,062 (1.5)	228 (7.8)	465 (4.0)	
very high risk	0 (0.0)	0 (0.0)	0 (0.0)	486 (12.1)	480 (9.5)		very high risk	0 (0.0)	0 (0.0)	0 (0.0)	423 (14.5)	233 (2.0)	
10-year CVD risk, median [IQR]	0.01 [0.01, 0.02]	0.01 [0.01, 0.03]	0.06 [0.02, 0.11]	0.25 [0.22, 0.29]	0.19 [0.10, 0.27]	<0.001	10-year CVD risk, median [IQR]	0.03 [0.02, 0.06]	0.04 [0.02, 0.08]	0.07 [0.04, 0.11]	0.22 [0.21, 0.25]	0.11 [0.08, 0.16]	<0.001
RDW, %, median [IQR]	12.50 [12.10, 13.10]	12.80 [12.30, 13.50]	13.00 [12.40, 13.70]	13.30 [12.70, 14.10]	13.40 [12.70, 14.30]	<0.001	RDW, %, median [IQR]	13.30 [12.90, 13.84]	13.40 [12.98, 13.91]	13.39 [12.93, 13.90]	13.60 [13.10, 14.20]	13.60 [13.10, 14.26]	<0.001
Albumin, g/dL, median [IQR]	4.30 [4.20, 4.50]	4.20 [4.00, 4.40]	4.20 [4.00, 4.40]	4.10 [3.90, 4.40]	4.10 [3.90, 4.40]	<0.001	Albumin, g/dL, mean (SD)	4.55 (0.26)	4.51 (0.26)	4.53 (0.27)	4.48 (0.31)	4.48 (0.29)	<0.001
RAR, median [IQR]	2.89 [2.72, 3.10]	3.02 [2.83, 3.28]	3.07 [2.86, 3.34]	3.21 [3.00, 3.53]	3.26 [3.00, 3.59]	<0.001	RAR, median [IQR]	2.94 [2.78, 3.11]	2.98 [2.82, 3.15]	2.96 [2.80, 3.14]	3.03 [2.85, 3.25]	3.04 [2.86, 3.27]	<0.001
RAR quartiles, n (%)						<0.001	RAR quartiles, n (%)						<0.001
Q1	698 (47.4)	1,046 (30.6)	4,887 (27.5)	596 (14.5)	790 (15.0)		Q1	3,042 (28.6)	3,355 (23.1)	18,494 (26.3)	537 (18.4)	2,103 (17.9)	
Q2	398 (27.0)	971 (28.5)	4,643 (26.1)	950 (23.1)	1,055 (20.0)		Q2	2,850 (26.8)	3,690 (25.4)	17,853 (25.4)	689 (23.6)	2,451 (20.9)	
Q3	238 (16.2)	806 (23.6)	4,394 (24.7)	1,159 (28.2)	1,420 (26.9)		Q3	2,568 (24.1)	3,887 (26.8)	17,439 (24.8)	701 (24.0)	2,934 (25.0)	
Q4	138 (9.4)	590 (17.3)	3,861 (21.7)	1,412 (34.3)	2,016 (38.2)		Q4	2,177 (20.5)	3,593 (24.7)	16,532 (23.5)	994 (34.0)	4,234 (36.1)	

Abbreviations: CKM, cardiovascular-kidney-metabolic syndrome; NHANES, National Health and Nutrition Examination Survey; BMI, body mass index; HbA1c, hemoglobin A1c; FBG, fasting blood glucose;

TG, triglyceride; TC, total cholesterol; HDL, high-density lipoprotein; UACR, urine albumin-creatinine ratio; eGFR, estimated glomerular filtration rate; DM, diabetes mellitus; CKD, chronic kidney disease;

CVD, cardiovascular disease; RDW, red blood cell distribution width; RAR, ratio of red blood cell distribution width to albumin concentration.

^aSocioeconomic status in the NHANES study was measured by family income to poverty ratios and was divided into three categories: high (≥ 3.5), medium (>1.3 to <3.5), and low (≤ 1.3); Socioeconomic status in the UK Biobank cohort was measured by Index of Multiple Deprivation categorized into 3 quartiles: low (Q3), medium (Q2), and high (Q1).

Table S6. Multinomial logistic regression models for association between RAR and CKM syndrome stages in two cohorts

Model	CKM stage	NHANES		UK Biobank	
		OR (95% CI)	P value	OR (95% CI)	P value
Model 1	Compare to CKM stage 0				
	CKM stage 1	1.84 (1.68, 2.02)	< 0.001	1.16 (1.12, 1.19)	< 0.001
	CKM stage 2	2.11 (1.94, 2.30)	< 0.001	1.09 (1.06, 1.11)	< 0.001
	CKM stage 3	2.96 (2.71, 3.24)	< 0.001	1.40 (1.35, 1.45)	< 0.001
	CKM stage 4	3.18 (2.91, 3.47)	< 0.001	1.42 (1.39, 1.46)	< 0.001
	Compare to CKM stage 1				
	CKM stage 2	1.15 (1.10, 1.20)	< 0.001	0.94 (0.92, 0.96)	< 0.001
	CKM stage 3	1.61 (1.53, 1.70)	< 0.001	1.21 (1.17, 1.25)	< 0.001
	CKM stage 4	1.73 (1.64, 1.82)	< 0.001	1.23 (1.20, 1.26)	< 0.001
	Compare to CKM stage 2				
	CKM stage 3	1.40 (1.36, 1.45)	< 0.001	1.29 (1.25, 1.33)	< 0.001
	CKM stage 4	1.51 (1.46, 1.55)	< 0.001	1.31 (1.29, 1.33)	< 0.001
	Compare to CKM stage 3				
	CKM stage 4	1.07 (1.04, 1.11)	< 0.001	1.02 (0.98, 1.05)	0.313
Model 2	Compare to CKM stage 0				
	CKM stage 1	1.73 (1.58, 1.90)	< 0.001	1.16 (1.13, 1.19)	< 0.001
	CKM stage 2	1.89 (1.73, 2.06)	< 0.001	1.10 (1.08, 1.13)	< 0.001
	CKM stage 3	2.60 (2.36, 2.86)	< 0.001	1.36 (1.31, 1.42)	< 0.001
	CKM stage 4	2.95 (2.69, 3.23)	< 0.001	1.43 (1.39, 1.47)	< 0.001
	Compare to CKM stage 1				
	CKM stage 2	1.09 (1.04, 1.14)	< 0.001	0.95 (0.93, 0.97)	< 0.001
	CKM stage 3	1.50 (1.41, 1.60)	< 0.001	1.17 (1.13, 1.22)	< 0.001
	CKM stage 4	1.71 (1.62, 1.80)	< 0.001	1.24 (1.21, 1.26)	< 0.001
	Compare to CKM stage 2				
	CKM stage 3	1.38 (1.32, 1.44)	< 0.001	1.23 (1.19, 1.28)	< 0.001
	CKM stage 4	1.56 (1.51, 1.62)	< 0.001	1.30 (1.28, 1.32)	< 0.001
	Compare to CKM stage 3				
	CKM stage 4	1.13 (1.09, 1.18)	< 0.001	1.05 (1.01, 1.09)	0.006

Abbreviations: OR, odds ratio; CI, confidence interval; CKM, cardiovascular-kidney-metabolic syndrome; RAR, ratio of red blood cell distribution width to albumin concentration; NHANES, National Health and Nutrition Examination Survey.

Model specifications: Model 1: an unadjusted model; Model 2: adjusted for age, sex, and race/ethnicity.

Table S7. Multinomial logistic regression models for association between RAR quartiles and CKM syndrome stages in two cohorts

Model	Quartile	NHANES		UK Biobank	
		OR (95% CI)	P value	OR (95% CI)	P value
Model 1	Compare to CKM stage 0				
	CKM stage 1				
	Q 1	Reference		Reference	
	Q 2	1.63 (1.40, 1.89)	< 0.001	1.17 (1.10, 1.26)	< 0.001
	Q 3	2.26 (1.90, 2.69)	< 0.001	1.37 (1.28, 1.47)	< 0.001
	Q 4	2.85 (2.32, 3.51)	< 0.001	1.50 (1.39, 1.61)	< 0.001
	CKM stage 2				
	Q 1	Reference		Reference	
	Q 2	1.67 (1.46, 1.90)	< 0.001	1.03 (0.98, 1.09)	0.284
	Q 3	2.64 (2.26, 3.07)	< 0.001	1.12 (1.06, 1.18)	< 0.001
	Q 4	4.00 (3.31, 4.82)	< 0.001	1.25 (1.18, 1.33)	< 0.001
	CKM stage 3				
	Q 1	Reference		Reference	
	Q 2	2.80 (2.38, 3.28)	< 0.001	1.37 (1.21, 1.55)	< 0.001
	Q 3	5.70 (4.78, 6.81)	< 0.001	1.55 (1.37, 1.75)	< 0.001
	Q 4	11.98 (9.75, 14.72)	< 0.001	2.59 (2.30, 2.92)	< 0.001
	CKM stage 4				
	Q 1	Reference		Reference	
	Q 2	2.34 (2.01, 2.73)	< 0.001	1.24 (1.15, 1.34)	< 0.001
	Q 3	5.27 (4.44, 6.26)	< 0.001	1.65 (1.53, 1.79)	< 0.001
	Q 4	12.91 (10.56, 15.77)	< 0.001	2.81 (2.61, 3.04)	< 0.001
	Compare to CKM stage 1				
	CKM stage 2				
	Q 1	Reference		Reference	
	Q 2	1.02 (0.93, 1.13)	0.639	0.88 (0.83, 0.92)	< 0.001
	Q 3	1.17 (1.06, 1.29)	0.003	0.81 (0.77, 0.86)	< 0.001
	Q 4	1.40 (1.26, 1.56)	< 0.001	0.83 (0.79, 0.88)	< 0.001
	CKM stage 3				
Q 1	Reference		Reference		
Q 2	1.72 (1.50, 1.96)	< 0.001	1.16 (1.03, 1.32)	0.015	
Q 3	2.52 (2.21, 2.89)	< 0.001	1.13 (1.00, 1.27)	0.056	
Q 4	4.20 (3.65, 4.83)	< 0.001	1.73 (1.54, 1.94)	< 0.001	
CKM stage 4					
Q 1	Reference		Reference		
Q 2	1.44 (1.27, 1.63)	< 0.001	1.06 (0.98, 1.14)	0.131	
Q 3	2.33 (2.06, 2.65)	< 0.001	1.20 (1.12, 1.29)	< 0.001	
Q 4	4.52 (3.97, 5.15)	< 0.001	1.88 (1.75, 2.02)	< 0.001	
Compare to CKM stage 2					

CKM stage 3					
	Q 1	Reference		Reference	
	Q 2	1.68 (1.50, 1.87)	< 0.001	1.33 (1.19, 1.49)	< 0.001
	Q 3	2.16 (1.94, 2.41)	< 0.001	1.38 (1.24, 1.55)	< 0.001
	Q 4	3.00 (2.70, 3.33)	< 0.001	2.07 (1.86, 2.30)	< 0.001
CKM stage 4					
	Q 1	Reference		Reference	
	Q 2	1.41 (1.27, 1.55)	< 0.001	1.21 (1.14, 1.28)	< 0.001
	Q 3	2.00 (1.82, 2.20)	< 0.001	1.48 (1.39, 1.57)	< 0.001
	Q 4	3.23 (2.94, 3.54)	< 0.001	2.25 (2.13, 2.38)	< 0.001
Compare to CKM stage 3					
CKM stage 4					
	Q 1	Reference		Reference	
	Q 2	0.84 (0.73, 0.96)	0.012	0.91 (0.80, 1.03)	0.137
	Q 3	0.92 (0.81, 1.05)	0.242	1.07 (0.94, 1.21)	0.301
	Q 4	1.08 (0.95, 1.22)	0.248	1.09 (0.97, 1.22)	0.161
Compare to CKM stage 0					
CKM stage 1					
	Q 1	Reference		Reference	
	Q 2	1.63 (1.40, 1.91)	< 0.001	1.17 (1.09, 1.25)	< 0.001
	Q 3	2.34 (1.95, 2.80)	< 0.001	1.37 (1.28, 1.47)	< 0.001
	Q 4	3.15 (2.52, 3.92)	< 0.001	1.54 (1.43, 1.66)	< 0.001
CKM stage 2					
	Q 1	Reference		Reference	
	Q 2	1.46 (1.28, 1.67)	< 0.001	0.99 (0.93, 1.05)	0.705
	Q 3	2.31 (1.97, 2.72)	< 0.001	1.06 (1.00, 1.13)	0.041
	Q 4	3.97 (3.25, 4.85)	< 0.001	1.27 (1.20, 1.35)	< 0.001
CKM stage 3					
Model 2	Q 1	Reference		Reference	
	Q 2	1.59 (1.32, 1.91)	< 0.001	1.07 (0.94, 1.22)	0.305
	Q 3	2.93 (2.39, 3.60)	< 0.001	1.06 (0.93, 1.21)	0.363
	Q 4	7.85 (6.20, 9.95)	< 0.001	1.88 (1.66, 2.13)	< 0.001
CKM stage 4					
	Q 1	Reference		Reference	
	Q 2	1.62 (1.37, 1.92)	< 0.001	1.06 (0.98, 1.15)	0.130
	Q 3	3.57 (2.96, 4.31)	< 0.001	1.31 (1.21, 1.42)	< 0.001
	Q 4	11.59 (9.29, 14.46)	< 0.001	2.45 (2.26, 2.66)	< 0.001
Compare to CKM stage 1					
CKM stage 2					
	Q 1	Reference		Reference	
	Q 2	0.89 (0.81, 0.99)	0.026	0.85 (0.80, 0.89)	< 0.001
	Q 3	0.99 (0.89, 1.10)	0.859	0.77 (0.73, 0.81)	< 0.001
	Q 4	1.26 (1.12, 1.42)	< 0.001	0.83 (0.78, 0.87)	< 0.001

CKM stage 3				
Q 1	Reference		Reference	
Q 2	0.97 (0.83, 1.14)	0.719	0.91 (0.81, 1.04)	0.166
Q 3	1.26 (1.07, 1.48)	0.006	0.77 (0.68, 0.88)	< 0.001
Q 4	2.50 (2.10, 2.97)	< 0.001	1.22 (1.08, 1.38)	0.001
CKM stage 4				
Q 1	Reference		Reference	
Q 2	0.99 (0.86, 1.14)	0.937	0.91 (0.84, 0.98)	0.017
Q 3	1.53 (1.32, 1.76)	< 0.001	0.96 (0.89, 1.03)	0.260
Q 4	3.68 (3.17, 4.29)	< 0.001	1.59 (1.48, 1.71)	< 0.001
Compare to CKM stage 2				
CKM stage 3				
Q 1	Reference		Reference	
Q 2	1.09 (0.95, 1.24)	0.230	1.08 (0.96, 1.22)	0.193
Q 3	1.27 (1.11, 1.45)	< 0.001	1.00 (0.89, 1.12)	0.991
Q 4	1.98 (1.73, 2.26)	< 0.001	1.48 (1.32, 1.65)	< 0.001
CKM stage 4				
Q 1	Reference		Reference	
Q 2	1.11 (1.00, 1.24)	0.057	1.08 (1.01, 1.15)	0.023
Q 3	1.54 (1.39, 1.72)	< 0.001	1.24 (1.16, 1.32)	< 0.001
Q 4	2.92 (2.62, 3.25)	< 0.001	1.93 (1.82, 2.04)	< 0.001
Compare to CKM stage 3				
CKM stage 4				
Q 1	Reference		Reference	
Q 2	1.02 (0.89, 1.18)	0.745	0.99 (0.88, 1.13)	0.937
Q 3	1.22 (1.06, 1.40)	0.006	1.24 (1.09, 1.41)	< 0.001
Q 4	1.48 (1.29, 1.69)	< 0.001	1.30 (1.16, 1.47)	< 0.001

Abbreviations: OR, odds ratio; CI, confidence interval; CKM, cardiovascular-kidney-metabolic syndrome; RAR, ratio of red blood cell distribution width to albumin concentration; NHANES, National Health and Nutrition Examination Survey.

Model specifications: Model 1: an unadjusted model; Model 2: adjusted for age, sex, and race/ethnicity.

Table S8. Multinomial logistic regression models for association between RAR and CKM syndrome stages in the complete-case NHANES population

CKM stage	OR (95% CI)	P value
Compare to CKM stage 0		
CKM stage 1	1.68 (1.52, 1.86)	< 0.001
CKM stage 2	1.76 (1.60, 1.93)	< 0.001
CKM stage 3	2.34 (2.11, 2.60)	< 0.001
CKM stage 4	2.57 (2.32, 2.83)	< 0.001
Compare to CKM stage 1		
CKM stage 2	1.05 (1.00, 1.10)	0.067
CKM stage 3	1.39 (1.30, 1.49)	< 0.001
CKM stage 4	1.53 (1.44, 1.62)	< 0.001
Compare to CKM stage 2		
CKM stage 3	1.33 (1.26, 1.40)	< 0.001
CKM stage 4	1.46 (1.40, 1.52)	< 0.001
Compare to CKM stage 3		
CKM stage 4	1.10 (1.05, 1.15)	< 0.001

Abbreviations: OR, odds ratio; CI, confidence interval; CKM, cardiovascular-kidney-metabolic syndrome; RAR, ratio of red blood cell distribution width to albumin concentration; NHANES, National Health and Nutrition Examination Survey. The model was adjusted for age, sex, race, education level, socioeconomic status, smoking status, alcohol consumption, and physical activity.

Table S9. Logistic regression results for the association between RAR and advanced CKM stages in the complete-case NHANES population

	OR (95% CI)	P value
NHANES		
Per 1 SD increase	1.24 (1.19, 1.30)	< 0.001
RAR quartiles		
Q 1	Reference	
Q 2	1.02 (0.93, 1.12)	0.600
Q 3	1.25 (1.13, 1.38)	< 0.001
Q 4	1.77 (1.58, 1.98)	< 0.001

Abbreviations: CKM, cardiovascular-kidney-metabolic syndrome; OR, odds ratio; CI, confidence interval; RAR, ratio of red blood cell distribution width to albumin concentration; NHANES, National Health and Nutrition Examination Survey.

Reference category: Q1 for quartile comparisons.

The model was adjusted for age, sex, race, education level, socioeconomic status, smoking status, alcohol consumption, and physical activity.

Table S10. Comparison of RAR, RDW, and albumin in relation to CKM syndrome stages

Cohort	CKM stage	RAR		RDW		Albumin	
		OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
NHANES	Compare to CKM stage 0						
	CKM stage 1	1.69 (1.54, 1.85)	< 0.001	1.44 (1.32, 1.58)	< 0.001	0.71 (0.66, 0.76)	< 0.001
	CKM stage 2	1.79 (1.64, 1.96)	< 0.001	1.53 (1.41, 1.67)	< 0.001	0.71 (0.67, 0.75)	< 0.001
	CKM stage 3	2.38 (2.16, 2.62)	< 0.001	1.83 (1.67, 2.01)	< 0.001	0.56 (0.52, 0.61)	< 0.001
	CKM stage 4	2.68 (2.44, 2.94)	< 0.001	2.07 (1.90, 2.27)	< 0.001	0.52 (0.48, 0.55)	< 0.001
	Compare to CKM stage 1						
	CKM stage 2	1.06 (1.01, 1.11)	0.010	1.06 (1.02, 1.11)	0.007	1.00 (0.96, 1.04)	0.937
	CKM stage 3	1.41 (1.32, 1.50)	< 0.001	1.27 (1.19, 1.35)	< 0.001	0.79 (0.75, 0.84)	< 0.001
	CKM stage 4	1.59 (1.50, 1.67)	< 0.001	1.44 (1.36, 1.51)	< 0.001	0.73 (0.69, 0.77)	< 0.001
	Compare to CKM stage 2						
	CKM stage 3	1.33 (1.27, 1.39)	< 0.001	1.19 (1.14, 1.25)	< 0.001	0.79 (0.76, 0.83)	< 0.001
	CKM stage 4	1.49 (1.44, 1.55)	< 0.001	1.35 (1.31, 1.40)	< 0.001	0.73 (0.70, 0.76)	< 0.001
	Compare to CKM stage 3						
	CKM stage 4	1.13 (1.08, 1.17)	< 0.001	1.13 (1.09, 1.18)	< 0.001	0.92 (0.88, 0.96)	< 0.001
UK Biobank	Compare to CKM stage 0						
	CKM stage 1	1.15 (1.12, 1.18)	< 0.001	1.08 (1.05, 1.11)	< 0.001	0.87 (0.84, 0.89)	< 0.001
	CKM stage 2	1.07 (1.05, 1.10)	< 0.001	1.04 (1.02, 1.07)	< 0.001	0.94 (0.92, 0.96)	< 0.001
	CKM stage 3	1.25 (1.20, 1.30)	< 0.001	1.20 (1.15, 1.25)	< 0.001	0.89 (0.85, 0.93)	< 0.001
	CKM stage 4	1.35 (1.31, 1.38)	< 0.001	1.27 (1.24, 1.31)	< 0.001	0.83 (0.80, 0.85)	< 0.001
	Compare to CKM stage 1						
	CKM stage 2	0.93 (0.92, 0.95)	< 0.001	0.97 (0.95, 0.98)	< 0.001	1.09 (1.07, 1.11)	< 0.001
	CKM stage 3	1.09 (1.04, 1.13)	< 0.001	1.11 (1.06, 1.15)	< 0.001	1.03 (0.99, 1.07)	0.184

CKM stage 4	1.17 (1.14, 1.20)	< 0.001	1.18 (1.15, 1.21)	< 0.001	0.96 (0.93, 0.98)	< 0.001
Compare to CKM stage 2						
CKM stage 3	1.16 (1.12, 1.21)	< 0.001	1.15 (1.11, 1.19)	< 0.001	0.94 (0.91, 0.98)	0.004
CKM stage 4	1.25 (1.23, 1.28)	< 0.001	1.22 (1.20, 1.24)	< 0.001	0.88 (0.86, 0.90)	< 0.001
Compare to CKM stage 3						
CKM stage 4	1.08 (1.04, 1.12)	< 0.001	1.06 (1.02, 1.10)	0.001	0.93 (0.89, 0.97)	< 0.001

Abbreviations: OR, odds ratio; CI, confidence interval; CKM, cardiovascular-kidney-metabolic syndrome; RAR, ratio of red blood cell distribution width to albumin concentration; RDW, red blood cell distribution width; NHANES, National Health and Nutrition Examination Survey.

The model was adjusted for age, sex, race, education level, socioeconomic status, smoking status, alcohol consumption, and physical activity.

Table S11. Comparison of RAR, RDW, and albumin in relation to advanced CKM syndrome stages

Exposure	RAR		RDW		Albumin	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
NHANES						
Per 1 SD increase	1.47 (1.42, 1.54)	< 0.001	1.33 (1.28, 1.38)	< 0.001	0.74 (0.72, 0.77)	< 0.001
Quartiles						
Q 1	Reference		Reference		Reference	
Q 2	1.06 (0.95, 1.18)	0.318	1.07 (0.96, 1.20)	0.214	0.69 (0.62, 0.76)	< 0.001
Q 3	1.36 (1.22, 1.52)	< 0.001	1.25 (1.12, 1.40)	< 0.001	0.58 (0.52, 0.64)	< 0.001
Q 4	2.36 (2.11, 2.65)	< 0.001	1.93 (1.73, 2.15)	< 0.001	0.54 (0.48, 0.60)	< 0.001
UK Biobank						
Per 1 SD increase	1.23 (1.21, 1.25)	< 0.001	1.21 (1.19, 1.23)	< 0.001	0.90 (0.88, 0.91)	< 0.001
Quartiles						
Q 1	Reference		Reference		Reference	
Q 2	1.03 (0.97, 1.09)	0.327	1.03 (0.97, 1.09)	0.375	0.81 (0.77, 0.85)	< 0.001
Q 3	1.10 (1.04, 1.16)	0.001	1.09 (1.03, 1.16)	0.002	0.79 (0.75, 0.83)	< 0.001
Q 4	1.61 (1.52, 1.70)	< 0.001	1.60 (1.51, 1.69)	< 0.001	0.79 (0.75, 0.84)	< 0.001

Abbreviations: OR, odds ratio; CI, confidence interval; CKM, cardiovascular-kidney-metabolic syndrome; RAR, ratio of red blood cell distribution width to albumin concentration; RDW, red blood cell distribution width; NHANES, National Health and Nutrition Examination Survey.

Reference category: Q1 for quartile comparisons.

The model was adjusted for age, sex, race, education level, socioeconomic status, smoking status, alcohol consumption, and physical activity.

Table S12. Comparison of RAR, RDW, and Albumin in relation to incident cardiovascular diseases in a population with CKM syndrome stages 0-3 in the UK Biobank

Disease	RAR		RDW		Albumin	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
CVD	1.12 (1.10, 1.14)	< 0.001	1.08 (1.07, 1.10)	< 0.001	0.90 (0.89, 0.92)	< 0.001
AF	1.16 (1.13, 1.18)	< 0.001	1.10 (1.08, 1.12)	< 0.001	0.86 (0.84, 0.88)	< 0.001
CHD	1.08 (1.06, 1.10)	< 0.001	1.05 (1.03, 1.07)	< 0.001	0.92 (0.91, 0.95)	< 0.001
HF	1.22 (1.20, 1.25)	< 0.001	1.15 (1.12, 1.17)	< 0.001	0.80 (0.77, 0.82)	< 0.001
PAD	1.16 (1.12, 1.20)	< 0.001	1.12 (1.08, 1.16)	< 0.001	0.88 (0.84, 0.92)	< 0.001
STROKE	1.11 (1.07, 1.15)	< 0.001	1.07 (1.04, 1.11)	< 0.001	0.91 (0.88, 0.95)	< 0.001

Abbreviations: HR, hazard ratio; CI, confidence interval; CKM, cardiovascular-kidney-metabolic syndrome; RAR, ratio of red blood cell distribution width to albumin concentration; CVD, cardiovascular disease; AF, atrial fibrillation; CHD, coronary heart disease; HF, heart failure; PAD, peripheral artery disease.

Model was adjusted for age, sex, race, education level, socioeconomic status, smoking status, alcohol consumption, and physical activity.

Table S13. Time-stratified association of RAR with incident cardiovascular diseases (0-5 vs >5 years) in a population with CKM syndrome stages 0-3 in the UK Biobank

Disease	0-5 years HR (95% CI)	>5 years HR (95% CI)	P for interaction
CVD	1.16 (1.14, 1.19)	1.10 (1.08, 1.12)	< 0.001
HF	1.26 (1.20, 1.33)	1.21 (1.18, 1.24)	0.141
CHD	1.16 (1.12, 1.19)	1.05 (1.02, 1.07)	< 0.001
AF	1.18 (1.13, 1.22)	1.15 (1.12, 1.18)	0.295
PAD	1.20 (1.13, 1.28)	1.14 (1.10, 1.19)	0.185
STROKE	1.13 (1.06, 1.21)	1.10 (1.06, 1.14)	0.437

Abbreviations: HR, hazard ratio; CI, confidence interval; CKM, cardiovascular-kidney-metabolic syndrome; RAR, ratio of red blood cell distribution width to albumin concentration; CVD, cardiovascular disease; AF, atrial fibrillation; CHD, coronary heart disease; HF, heart failure; PAD, peripheral artery disease.

Model was adjusted for age, sex, race, education level, socioeconomic status, smoking status, alcohol consumption, and physical activity.

Table S14. Between-cohort meta-analysis for RAR-CKM associations

Comparison	NHANES OR (95% CI)	UK Biobank OR (95% CI)	Cochran's Q	P for heterogeneity	I ² (%)	tau ²	Pooled OR (95% CI)	P value
Stage 1 vs 0	1.69 (1.54, 1.85)	1.15 (1.12, 1.18)	62.63	< 0.001	98.4	0.073	1.39 (0.95, 2.03)	0.087
Stage 2 vs 0	1.79 (1.64, 1.96)	1.07 (1.05, 1.10)	119.89	< 0.001	99.2	0.131	1.38 (0.83, 2.29)	0.209
Stage 3 vs 0	2.38 (2.16, 2.62)	1.25 (1.20, 1.30)	145.88	< 0.001	99.3	0.206	1.72 (0.92, 3.24)	0.091
Stage 4 vs 0	2.68 (2.44, 2.94)	1.35 (1.31, 1.38)	192.88	< 0.001	99.5	0.234	1.90 (0.97, 3.72)	0.061
Stage 2 vs 1	1.06 (1.01, 1.11)	0.93 (0.92, 0.95)	26.46	< 0.001	96.2	0.008	0.99 (0.87, 1.13)	0.889
Stage 3 vs 1	1.41 (1.32, 1.50)	1.09 (1.04, 1.13)	43.83	< 0.001	97.7	0.032	1.24 (0.96, 1.59)	0.097
Stage 4 vs 1	1.59 (1.50, 1.67)	1.17 (1.14, 1.20)	102.12	< 0.001	99.0	0.047	1.36 (1.01, 1.84)	0.044
Stage 3 vs 2	1.33 (1.27, 1.39)	1.16 (1.12, 1.21)	20.35	< 0.001	95.1	0.009	1.24 (1.09, 1.42)	0.002
Stage 4 vs 2	1.49 (1.44, 1.55)	1.25 (1.23, 1.28)	67.65	< 0.001	98.5	0.015	1.36 (1.15, 1.62)	< 0.001
Stage 4 vs 3	1.13 (1.08, 1.17)	1.08 (1.04, 1.12)	2.65	0.104	62.2	0.001	1.10 (1.06, 1.15)	< 0.001
Advanced stage vs nonadvanced	1.47 (1.42, 1.54)	1.23 (1.21, 1.25)	63.91	< 0.001	98.4	0.016	1.34 (1.13, 1.60)	< 0.001

Abbreviations: RAR, ratio of red blood cell distribution width to albumin concentration; CKM, cardiovascular-kidney-metabolic syndrome; OR, odds ratio; CI, confidence interval; NHANES, National Health and Nutrition Examination Survey; I²: Higgins-Thompson heterogeneity index; tau²: between-study variance.

ORs and 95% CIs for each cohort were derived from fully adjusted multinomial logistic regression models, with the corresponding CKM stage as the reference.

Pooled estimates and P values were derived from random-effects meta-analysis (DerSimonian-Laird) on the log(OR) scale, using Wald tests for significance.

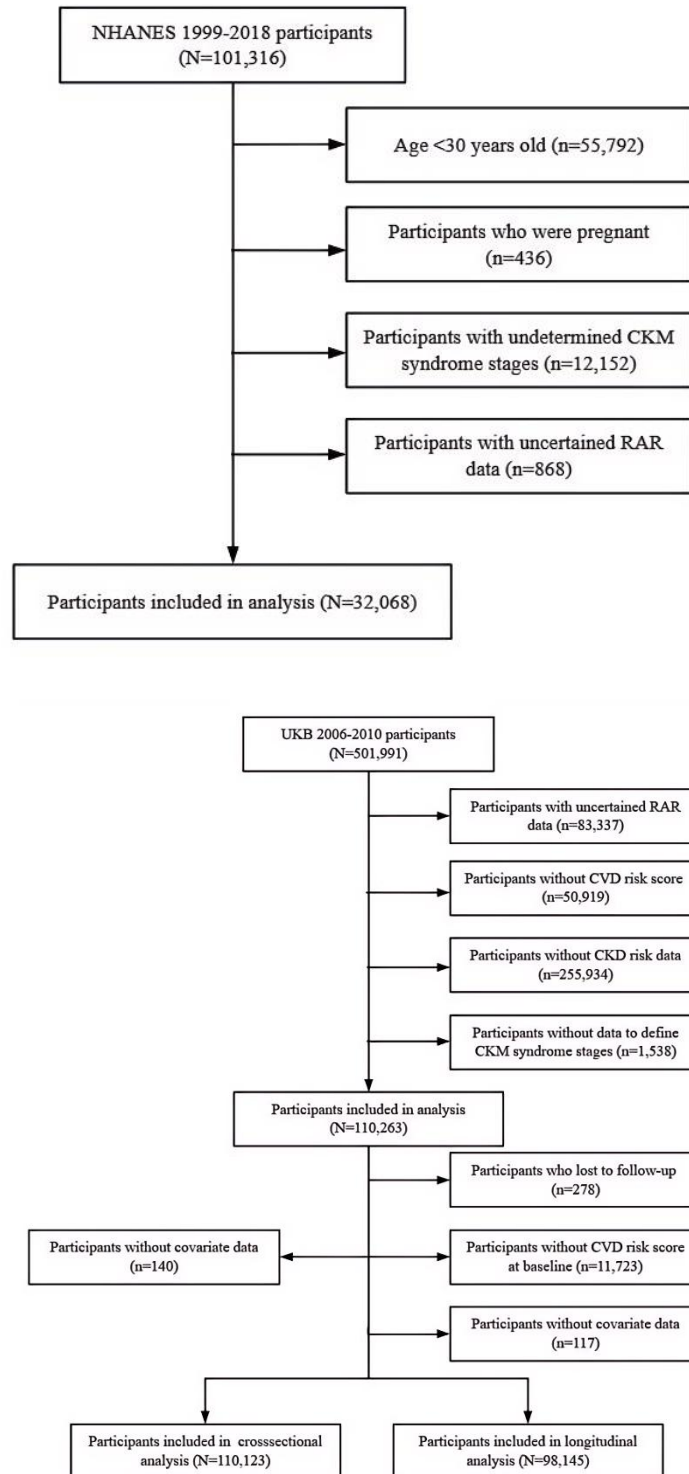


Figure S1. Flowchart of participant selection in two cohorts.

Abbreviations: CKM, cardiovascular-kidney-metabolic syndrome; NHANES, National Health and Nutrition Examination Survey; RAR, ratio of red blood cell distribution width to albumin concentration; UKB, UK Biobank; CKD, chronic kidney disease; CVD, cardiovascular disease.

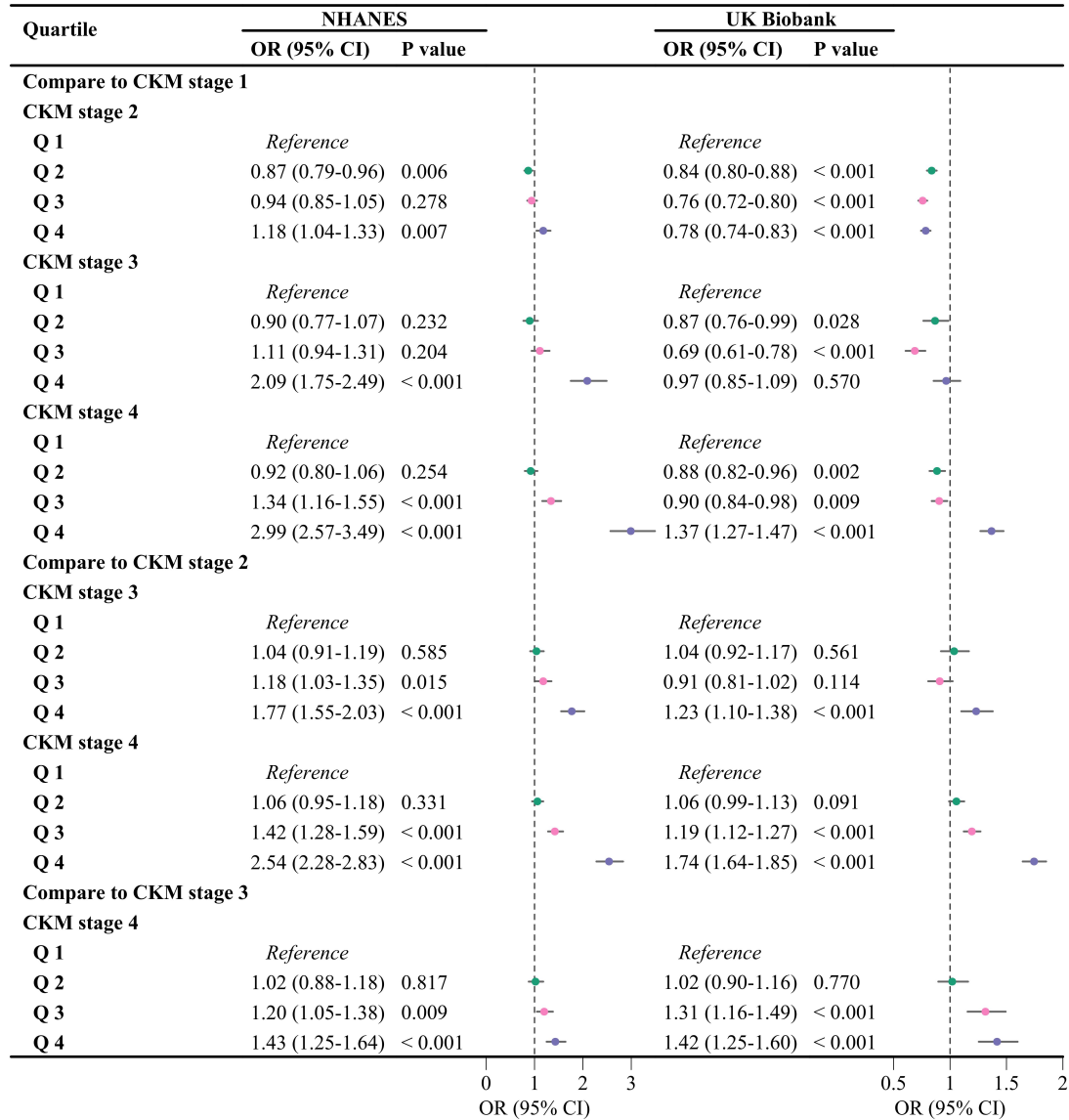
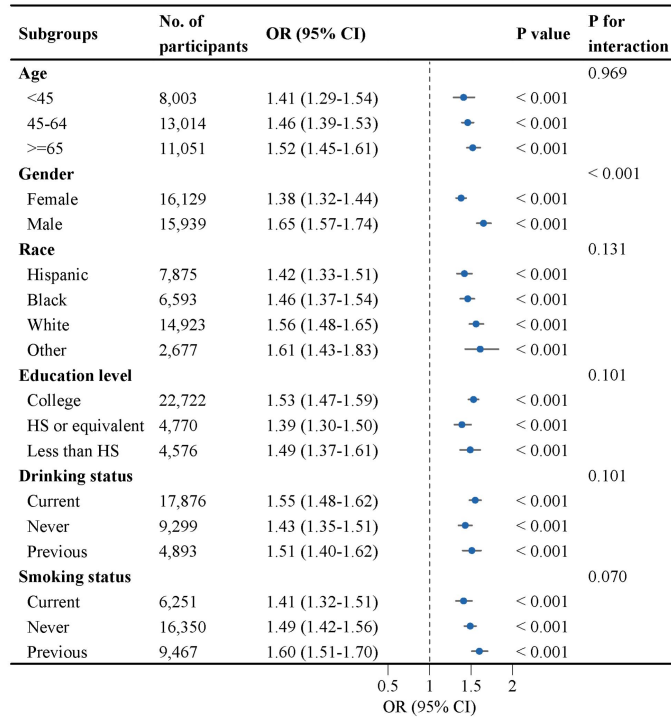


Figure S2. Association between RAR quartiles and CKM syndrome stages in NHANES (A) and UK Biobank (B).

For NHANES: Q1 (2.15-2.88), Q2 (>2.88-3.10), Q3 (>3.10-3.40), and Q4 (>3.40-12.08); for the UK Biobank: Q1 (0.46-2.81), Q2 (>2.81-2.97), Q3 (>2.97-3.16), and Q4 (>3.16-10.08). P values from multinomial logistic regression models adjusted for age, sex, race, education level, socioeconomic status, smoking status, alcohol consumption, and physical activity.

Abbreviations: OR, odds ratio; CI, confidence interval; CKM, cardiovascular-kidney-metabolic syndrome; RAR, ratio of red blood cell distribution width to albumin concentration.

A. NHANES



B. UK Biobank

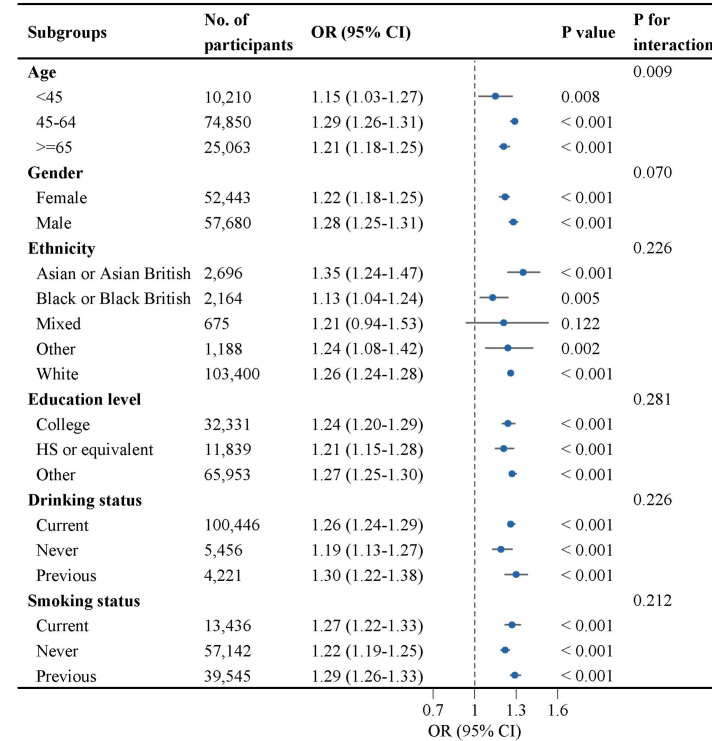


Figure S3. Subgroup analysis of the association between the RAR and advanced CKM stages in NHANES (A) and UK Biobank (B).

The model was adjusted for age, sex, race, education level, socioeconomic status, smoking status, alcohol consumption, and physical activity. The P value for the interaction was calculated using the likelihood ratio test. All P values for interaction in subgroup analyses were adjusted using the Benjamini-Hochberg false discovery rate method.

Abbreviations: OR, odds ratio; CI, confidence interval; HS, high school; NHANES, National Health and Nutrition Examination Survey.

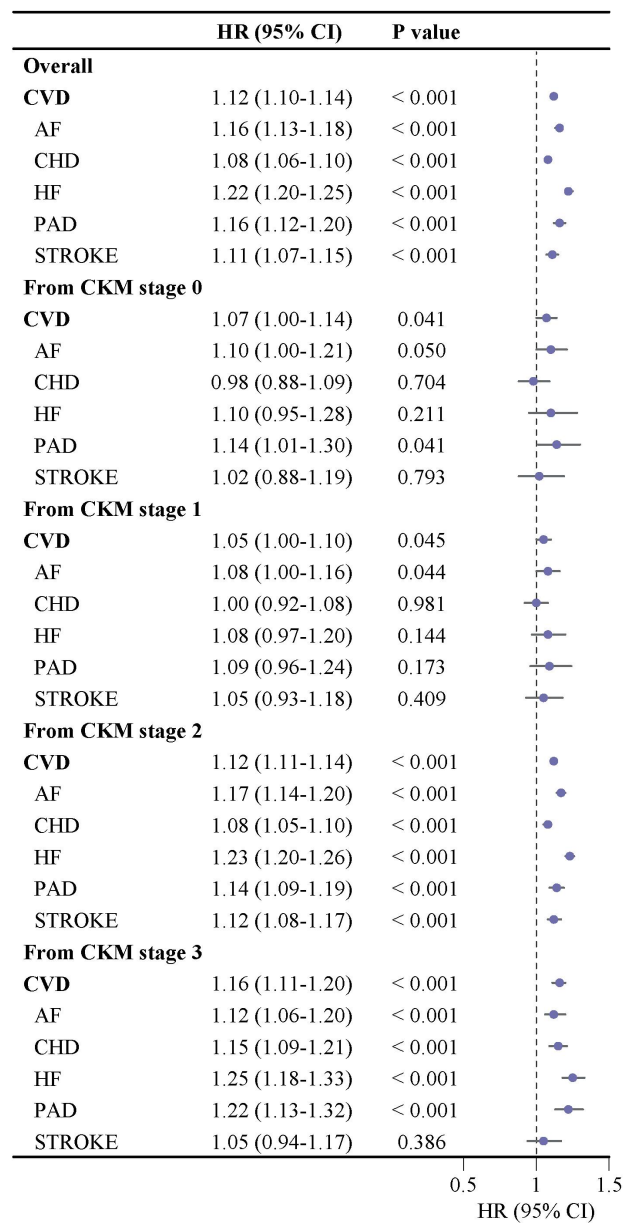


Figure S4. Association between RAR and the risk of incident cardiovascular diseases in a population with CKM syndrome stages 0-3.

P values from Cox proportional hazards regression models adjusted for age, sex, race, education level, socioeconomic status, smoking status, alcohol consumption, and physical activity.

Abbreviations: HR, hazard ratio; CI, confidence interval; CKM, cardiovascular-kidney-metabolic syndrome; RAR, ratio of red blood cell distribution width to albumin concentration; CVD, cardiovascular disease; AF, atrial fibrillation; CHD, coronary heart disease; HF, heart failure; PAD, peripheral artery disease.

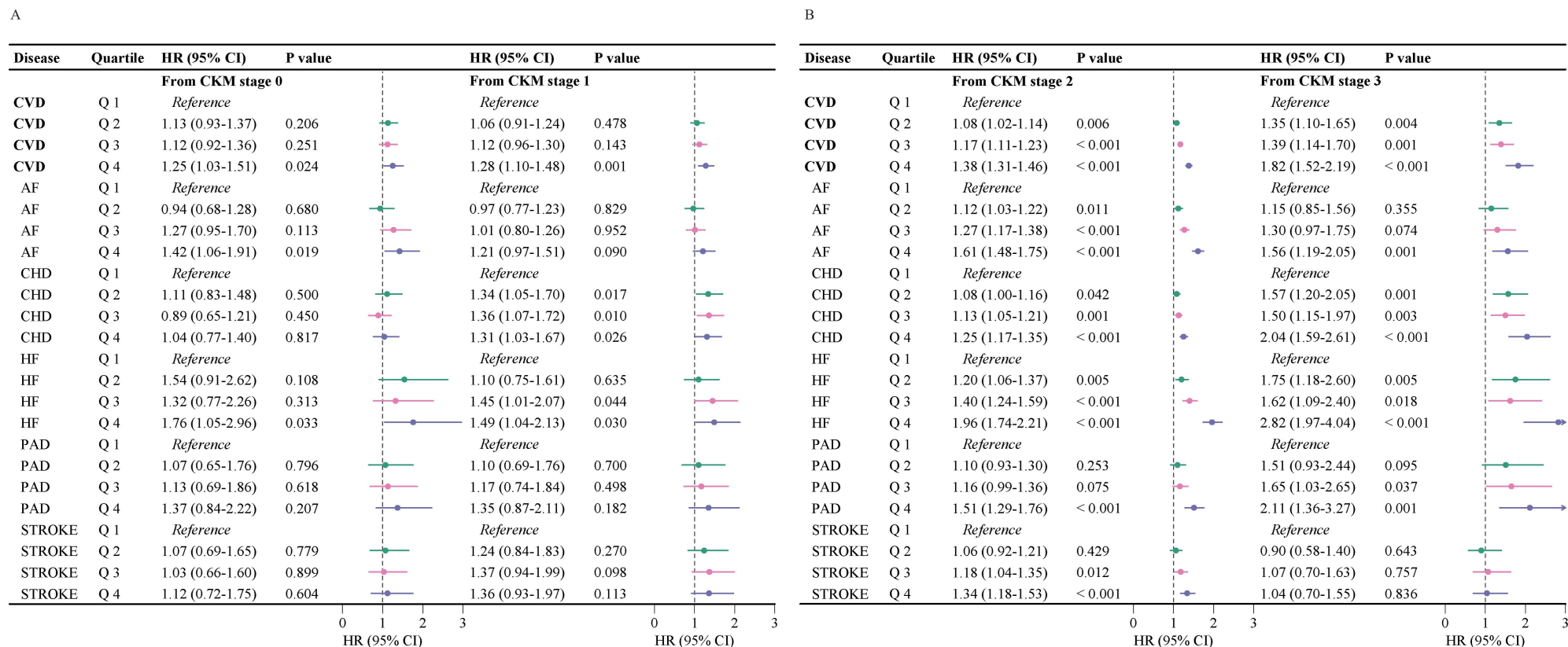


Figure S5. Association between RAR quartiles and the risk of incident cardiovascular diseases in a population with CKM syndrome stages 0-3 (A: stages 0-1; B: stages 2-3).

P values from Cox proportional hazards regression models adjusted for age, sex, race, education level, socioeconomic status, smoking status, alcohol consumption, and physical activity.

Abbreviations: HR, hazard ratio; CI, confidence interval; CKM, cardiovascular-kidney-metabolic syndrome; RAR, ratio of red blood cell distribution width to albumin concentration; CVD, cardiovascular disease; AF, atrial fibrillation; CHD, coronary heart disease; HF, heart failure; PAD, peripheral artery disease.

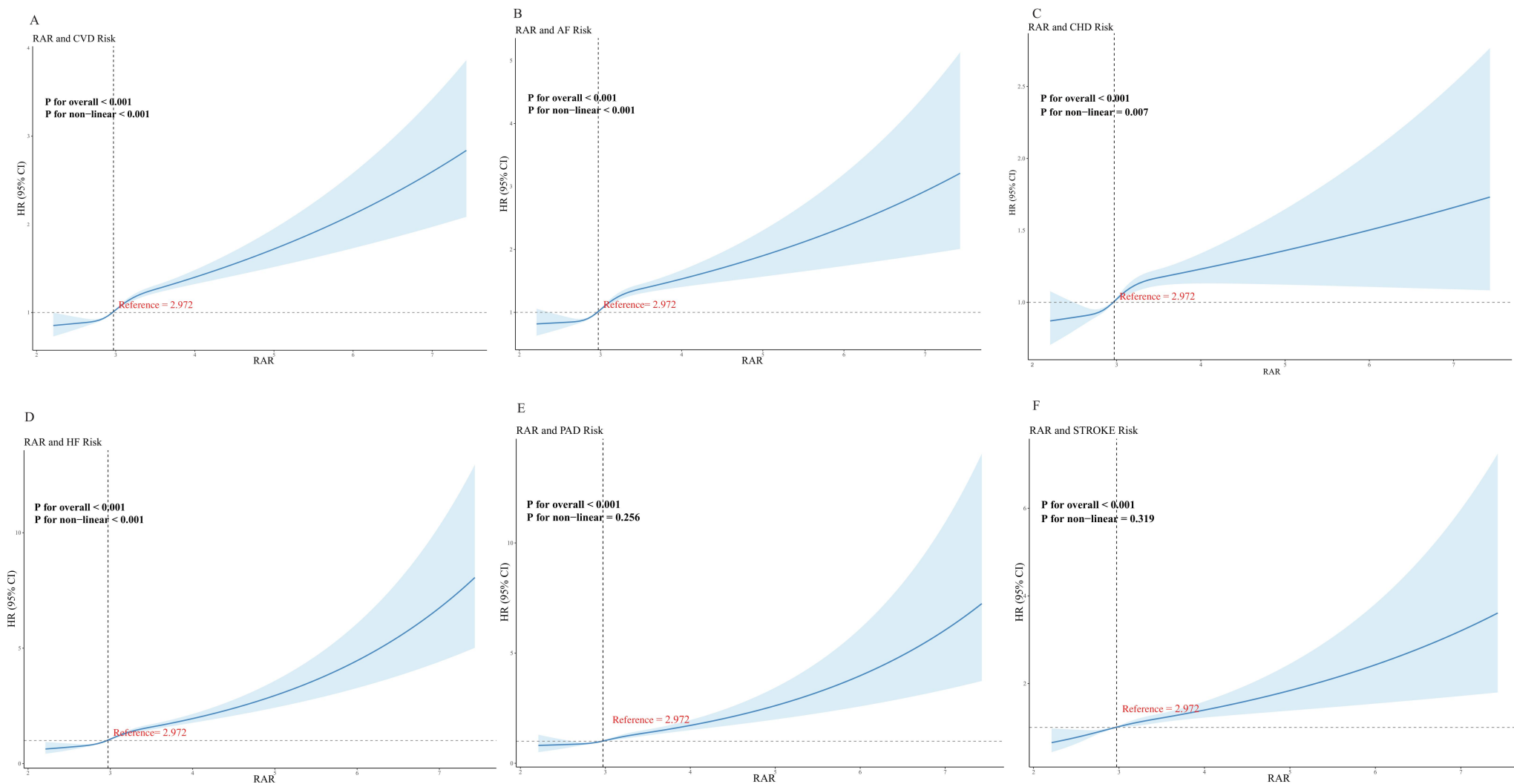


Figure S6. Restricted cubic spline curve for the association between RAR and incident cardiovascular diseases (A: CVD; B: AF; C: CHD; D: HF; E: PAD; F: STROKE).

The model was adjusted for age, sex, race, education level, socioeconomic status, smoking status, alcohol consumption, and physical activity. The vertical dashed line indicates the RAR value used as the reference (HR = 1). Abbreviations: HR, hazard ratio; CI, confidence interval; RAR, ratio of red blood cell distribution width to albumin concentration; CVD, cardiovascular disease; AF, atrial fibrillation; CHD, coronary heart disease; HF, heart failure; PAD, peripheral artery disease.