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Dynamic changes in metabolic syndrome components and chronic kidney disease risk: a population-based prospective cohort study

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Abstract

Objective To investigate the relationships between dynamic changes in metabolic syndrome (MetS) components and chronic kidney disease (CKD) risk.

Methods Data from the UK Biobank, including baseline assessments from 2006 to 2010, repeat assessments in 2012–2013, and linked national health records, were analyzed. MetS components consisted of abdominal obesity, elevated blood pressure (BP), fasting blood glucose (FBG), serum uric acid (SUA), and lipid abnormalities. The Kaplan-Meier method and log-rank test were used to analyze CKD incidence and group differences. Cox regression models assessed the association between dynamic changes in MetS components and CKD risk.

Results The study enrolled 455,060 participants (45.7% male, 18.4% aged 65 years or older) with a median follow-up of 12.68 years. Those with MetS had a significantly higher 10-year CKD cumulative incidence probability of CKD than those without MetS (4.14% VS 1.14%). Multivariate analysis showed all baseline metabolic abnormalities were linked to CKD risk with HRs from 1.40(1.35–1.45) to 1.85 (1.78–1.92), and MetS strongly associated with CKD (HR: 2.31). CKD risk rose with more MetS components and progression stages. Notably, with FBG being the exception, the four MetS components that shifted from normal at baseline to abnormal at follow - up were associated with elevated CKD risk, with HRs (95% CI) ranging from 1.21 (1.00–1.48) to 1.73 (1.34–2.24). Participants with high baseline SUA, even if it normalized at follow - up, still faced a 1.30 - fold higher CKD risk (95% CI: 1.25–1.35), distinct from other components. For those developing one and ≥ 2 new MetS components at follow - up, the CKD risk HRs (95% CI) were 1.49 (1.00–2.35) and 2.26 (1.21–4.24) respectively.

Conclusion MetS and its component changes are significantly associated with CKD risk, in a dose - response pattern. Incorporating SUA into MetS assessments enhances risk identification, especially noting females' higher susceptibility to elevated SUA. Dynamic monitoring of MetS components is crucial for assessing and predicting CKD risk.

Clinical trial number Not applicable.

Keywords Chronic kidney disease, Metabolic syndrome, Dynamic changes, UK biobank, Cohort study

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Introduction

Chronic kidney disease (CKD) had become a major global public health challenge with a prevalence of 10–15% worldwide [1–3]. It had high risk of progression to end-stage renal disease (ESRD) [3] and cardiovascular diseases [4, 5] which pose significant threats to human health. CKD was ranked as the seventh leading cause of death worldwide in the Global Burden of Disease study [6]. The risk of CKD being particularly pronounced in populations with metabolic risk factors, such as hypertension, hyperglycemia and lipid abnormalities [7, 8].

Metabolic syndrome (MetS) was defined as a cluster of metabolic components abnormalities, commonly including abdominal obesity, hypertension, hyperglycemia, elevated triglycerides (TG), low high-density lipoprotein cholesterol (HDL-C), elevated total cholesterol (TC) or high low-density lipoprotein cholesterol (LDL-C) [9, 10]. The increasing prevalence of MetS had further exacerbated the global burden of CKD [11]. In African Americans and Brazilian individuals, hyperglycemia, abdominal obesity and elevated TG were identified as key MetS components linked to CKD. The combinations of three or four MetS components were demonstrated a cumulative effect, further increasing the CKD risk compared to single MetS component [12, 13]. In Iranian population, MetS was associated with 32% increased risk of incident CKD. Furthermore, individuals with four or five MetS components had a significantly higher risk of CKD compared to those with three MetS components, highlighting the cumulative impact of MetS components on CKD development [14].

As early as 1923, Kylin first described the combination of hypertension, obesity, serum uric acid (SUA) abnormalities and gout as X-syndrome [15]. Uric acid was the end product of purine metabolism from both dietary intake and endogenous synthesis. It accumulated due to impaired excretion and could trigger inflammatory responses. Its low solubility in blood predisposed it to crystal formation, leading to deposition in joints, soft tissues and kidneys [16]. Hyperuricemia, characterized by impaired purine metabolism leading to elevated SUA levels, acted through mechanisms such as oxidative stress, endothelial dysfunction and inflammation, exacerbating the detrimental effects of conditions like hypertension and diabetes on renal function [17, 18]. Elevated SUA levels were intertwined not merely with CKD but also with other MetS components, including obesity, hypertension and dyslipidemia [19].

Although the association between MetS and CKD had been documented, most previous studies focused on baseline measurements or cross-sectional analyses and overlook the impact of temporal changes in MetS components. The dynamic changes in metabolic indicators may also have significant impact on disease outcomes. It was reported that blood pressure (BP) variability and glycemic fluctuations were strong predictors of future micro- and macrovascular complications [20, 21]. Additionally, long-term variability in metabolic parameters, such as TG and HDL-C, was associated with higher risk of stroke [22]. However, the impact of dynamic changes in MetS components on the risk of CKD remains underexplored. Especially, the dynamic changes in MetS components during disease progression, such as transitions from normal to abnormal, persistent abnormalities or recovery, required further investigation to elucidate their impact on CKD risk.

To sum up, elevated SUA was considered as one of MetS components in this study, along with abdominal obesity, hypertension, hyperglycemia and dyslipidemia, to investigate the effect of MetS on the risk of CKD. This study analyzed the associations between different forms of MetS components at baseline and dynamically changing over time and CKD risk. The findings would offer insights into potential strategies for prevention and intervention of CKD.

Methods

Data source and study population

The data of this study was abstracted from UK Biobank which was a large-scale prospective cohort study that recruited over 500,000 participants aged 40–69 years across the United Kingdom between 2006 and 2010. It collected extensive health-related data, including physical measurements, biological samples and health and lifestyle questionnaires [23]. In addition to baseline information, this study also focused on the information from 20,000 participants who attended a repeat assessment visit between 2012 and 2013, approximately 4–5 years after their initial enrollment. All the participants were followed for the development of incident diagnoses through linkage to national health records.

Among 502415 participants, participants with CKD at baseline or missing data on MetS components and relevant covariates were excluded in this study. The CKD was defined as meeting any of the following criteria: self-reported CKD history; a prior diagnosis of CKD based on International Classification of Diseases – 10th Revision (ICD-10) or (International Classification of Diseases – 9th Revision (ICD-9) codes; estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m^2 (calculated using the CKD-EPI equation, accounting for serum creatinine, age, sex, and race [24]), or urine albumin-to-creatinine ratio (UACR) ≥ 30 mg/g at baseline (Fig. 1). This study was conducted under the ethical guidelines approved by the North West Research Ethics Committee (06/MRE08/65), and data access was granted under UK Biobank project approval number 75905. Written informed consent was obtained from all participants prior to enrolment, and

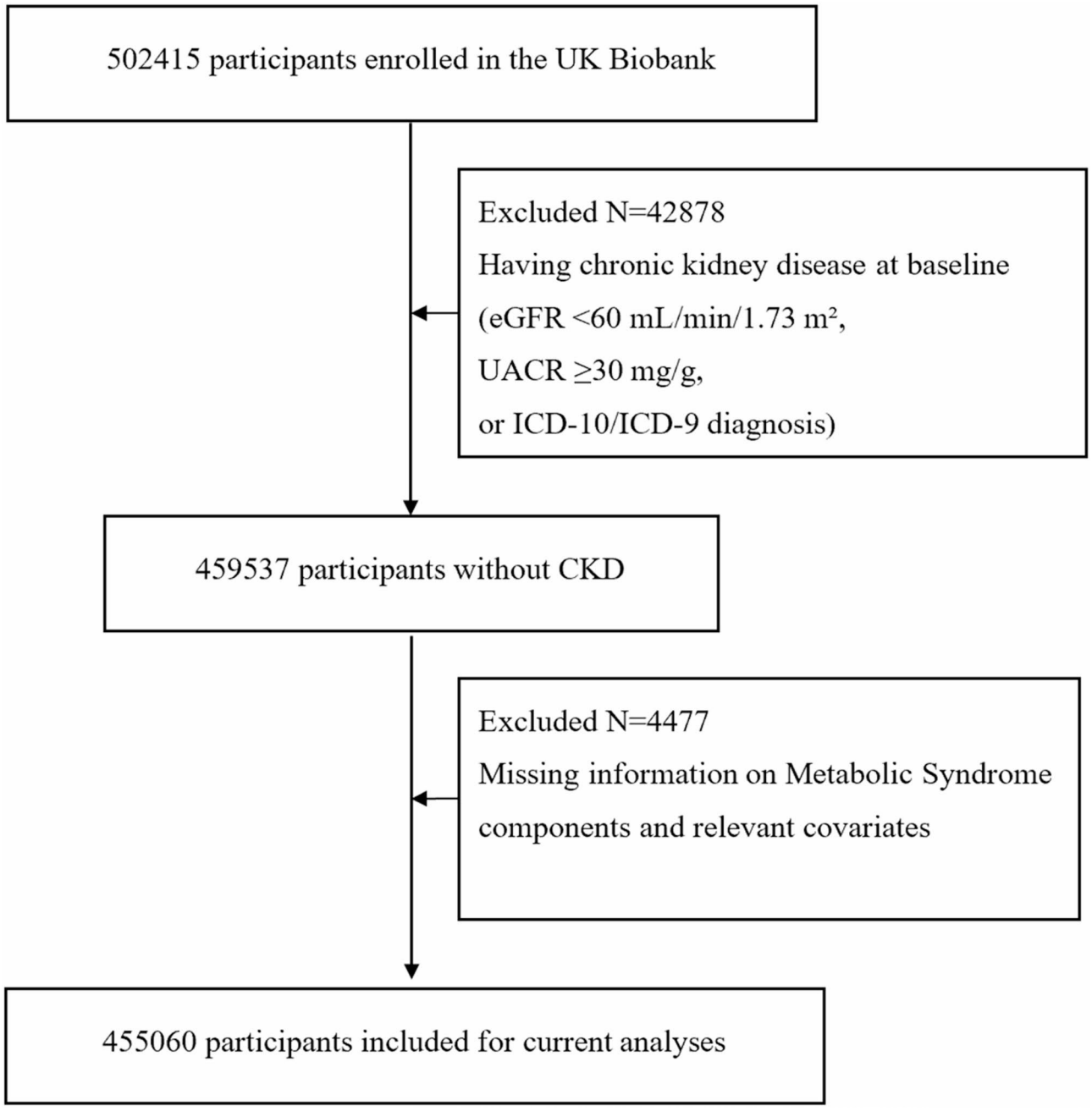

Fig. 1 Flowchart of UK Biobank participants inclusion and exclusion

the study adhered to the principles of the Declaration of Helsinki, ensuring participant confidentiality and data privacy.

Definition of MetS

MetS was defined as having three or more of the following components:

1) Abdominal obesity: Waist circumference (WC) ≥ 102 cm for men or ≥ 88 cm for women.
2) Elevated BP: Systolic blood pressure (SBP) ≥ 130 mmHg and/or diastolic blood pressure (DBP) ≥ 85 mmHg, or a self-reported history of hypertension, or a diagnosis of hypertension according to ICD-10/ICD-9 (Supplementary Table 1) [see Additional file 1], or using antihypertensive medication.
3) Elevated fasting blood glucose (FBG): FBG ≥ 6.1 mmol/L, or self-reported history of diabetes, or a diagnosis of diabetes according to ICD-10/ICD-9 (Supplementary Table 1) [see Additional file 1], or using antidiabetic medication.

4) Elevated SUA: SUA ≥ 420 μmol/L for men or ≥ 360 μmol/L for women, or a self-reported history of gout, or a diagnosis of gout according to ICD-10/ICD-9 (Supplementary Table 1) [see Additional file 1], or using gout medications.
5) Lipid abnormalities: serum TG ≥ 1.7 mmol/L and/or HDL-C < 1.0 mmol/L for men, < 1.3 mmol/L for women, or a self-reported history of hyperlipidemia, or a diagnosis of hyperlipidemia according to ICD-10/ICD-9 (Supplementary Table 1) [see Additional file 1], or using lipid-lowering medication.

Grouping analysis of MetS components and progression stages

To evaluate the impact of the combinations of different MetS components on CKD risk, the participants were categorized into groups based on MetS profiles in two ways:

1) Specific combinations of MetS components: Participants were grouped according to the combinations of two or three MetS components. The groups with two components included abdominal obesity combining with elevated BP, FBG or lipid abnormalities. The groups with three components included elevated BP, FBG and SUA or lipid abnormalities. These specific combinations reflected varying patterns of metabolic dysfunction.
2) Progression stage of metabolic abnormalities: The early stage included simpler combinations of two components, typically abdominal obesity paired with elevated BP or FBG. The intermediate stage involved combinations of three components, commonly elevated BP, FBG and lipid abnormalities, or elevated BP, FBG and SUA. The late stage was characterized by the presence of four major MetS components including elevated BP, FBG, SUA and lipid abnormalities [25]. The stages were designed to capture the increasing complexity and severity of metabolic disturbances.

The classification systems provided structured approaches to assess how different combinations and progression stages of MetS components at baseline influence CKD, offering insights into the cumulative effects of these metabolic risk factors.

Dynamic changes in MetS components

For participants with repeated assessments, their metabolic status was updated using the data collected during the repeated assessment, along with any new information from ICD codes, medication use, or self - reports. For participants without repeated assessments, the metabolic status was updated solely based on ICD codes, medication use, or self - reports. To evaluate the impact of dynamic changes in MetS components over time on CKD risk, three analysis strategies were conducted:

1) The participants were divided into four categories based on changes in single MetS component during the study period: "No-No", representing no abnormality throughout the study period; "No-Yes", indicating a transition from a normal state at baseline to an abnormal state at follow-up; "Yes-No", denoting a transition from an abnormal state at baseline to a normal state at follow-up; and "Yes-Yes", meaning a persistent abnormality throughout the study period.
2) The participants were divided into nine categories based on the changes in the number of MetS components during the study period: participants with no metabolic abnormalities throughout the study period; participants with no metabolic abnormalities at baseline but who developed one or more metabolic abnormalities at follow-up; participants with one or more metabolic abnormalities at baseline but no metabolic abnormalities at follow-up; and participants with one or more metabolic abnormalities at baseline were categorized by the number of abnormal components at the end of the follow-up, ranging from one abnormal component to all five components being abnormal.
3) The final MetS component status was determined based on baseline or follow-up measurements, ICD codes or medication use records. The participants were considered to have a MetS component in the final status if they met the criteria for abnormality at any time throughout the study period. According the combinations of different MetS components, participants were classified into different categories, as described in the section "Grouping Analysis of MetS components and Progression Stages."

The classification systems provided comprehensive understanding of how dynamic changes in MetS components over time influence CKD, encompassing both the emergence of new abnormalities and the resolution of existing abnormalities.

Covariates

The baseline covariates in this study included age (< 65 years or ≥ 65 years), sex (male or female), ethnicity (white, other or unknown), education level (university degree, higher secondary and vocational qualification, secondary school completion, no qualification or prefer not to answer), household income (<£18,000, £18,000–£30,999, £31,000–£51,999, £52,000–£100,000, >£100,000

or Other), smoking status (never, former, current or unknown) and alcohol consumption (never, former, current or unknown).

Study outcome

The study outcome was the new-onset CKD, which was determined based on the ICD-9 (5859) and the ICD-10 (I12.0, I12.9, I13.0, I13.1, I13.2, I13.9, E10.2, E11.2, N18.0, N18.1, N18.2, N18.3, N18.4, N18.5, N18.8 and N18.9). Each participant's follow-up began at their initial assessment visit conducted between 2006 and 2010 at a UK Biobank assessment center. Follow-up time was calculated from the baseline until the earliest of the following: first date of CKD diagnosis, the date of death, date of loss to follow-up or the end of the study period (November 16, 2021). Death, loss to follow-up or no CKD occurred at the end of the study were treated as censored events in the analyses.

Statistical analysis

Continuous variables were presented as mean ± standard deviation (SD) for normally distributed data and median (interquartile range (IQR)) for non-normally distributed data. Categorical variables were expressed as number (proportion). To compare differences between groups, the two independent samples t-test was used for normally distributed continuous variables, while the Mann-Whitney U test was applied to non-normally distributed continuous variables. The chi-square test was used for categorical variables. The cumulative incidence of new-onset CKD in different groups was estimated using the Kaplan-Meier (KM) method and compared by log-rank tests. Cox regression models were used to assess the associations between the CKD risk and single MetS component at baseline, the number of MetS components at baseline, the combinations of MetS components at baseline, dynamic changes in single MetS component over time, dynamic changes in the number of MetS components over time and the combinations of MetS component throughout the study period. Cox regression models were tested using Schoenfeld residuals method and no violation of this assumption was detected. All analyses were performed using R software (version 4.4.0, http://www.R-project.org/) and a two-tailed $P < 0.05$ was considered statistically significant.

Stratified and sensitivity analysis

The association between sex and MetS changes was investigated and determined by sex (female or male) in stratified analysis. Sensitivity analyses were conducted to assess the robustness of the study results. First, only participants with complete data of waist circumference, BP, FBG, SUA and blood lipid at baseline (2006–2010) and the first repeat assessment (2012–2013) were included in the analyses. Second, participants who developed CKD within the first two years of follow-up were excluded to minimize the potential confounding effect of early incident CKD. Additionally, participants with less than two years of follow-up were excluded to ensure the stability of the results in individuals with sufficient follow-up duration. Each of these exclusions was independently applied to the entire cohort to evaluate the consistency and reliability of the study results across different subsets of data.

Results

Baseline characteristics of the study population

A total of 455,060 participants were included in the study, with a median follow-up of 12.68 years. During the study period, 13,277 participants were diagnosed with incident CKD, while the remaining 441,783 participants comprised the non-CKD group. Among the study population, 18.4% of participants were 65 years or older and 45.7% were male. The patients with CKD were more likely to be older, male and had higher WC, SBP, TG, SUA levels as well as lower eGFR and HDL-C levels. The prevalence of abdominal obesity, elevated BP, elevated FBG, elevated SUA and lipid abnormalities was significantly higher in CKD patients compared to non-CKD participants (all $P < 0.001$). Additionally, CKD patients tended to have lower income levels and educational attainment (Table 1).

CKD risk

The participants with MetS had a significantly higher 10-year cumulative incidence probability of CKD than those without MetS (4.14% VS 1.14%) (Fig. 2A). The 10-year cumulative incidence probability of CKD increased with the number of MetS components at baseline, ranging from 0.44% in participants with zero components to 10.21% in those with five components (Fig. 2B). Regarding the dynamic changes in MetS components, participants with persistent metabolic abnormalities exhibited the highest 10-year cumulative incidence probability, particularly those with four and five components, with rates of 5.49% and 9.94%, respectively. In contrast, participants without metabolic abnormalities throughout the study period and those with one or more metabolic abnormalities at baseline but no abnormalities at follow-up had the lowest incidence rates of 0.42% and 0.50%, respectively. Additionally, participants developed one or more abnormalities at follow-up had an incidence rate of 0.85% (Fig. 2C). The 10-year cumulative incidence probability of CKD was 1.54% in the early stage, 3.57% in the intermediate stage and 6.12% in the late stage of MetS progression, respectively (Fig. 2D). The differences in the CKD risk across groups were all statistically significance (all $P < 0.001$).

Table 1 Baseline characteristics of the study population

Characteristics	All participants	Non-CKD participants	Incident CKD cases	*P*
N	455,060	441,783	13,277	
Age ≥ 65 years, n (%)	83,555 (18.4)	77,943 (17.6)	5612 (42.3)	< 0.001
Male, n (%)	207,980 (45.7)	201,154 (45.5)	6826 (51.4)	< 0.001
eGFR (mL/min/1.73 m^2)	91.95 ± 11.94	92.33 ± 11.72	79.38 ± 12.31	< 0.001
Ethnicity, n (%)				0.046
White	429,932 (94.5)	417,436 (94.5)	12,496 (94.1)	
Other	23,486 (5.1)	22,767 (5.1)	719 (5.4)	
Unknown	1642 (0.4)	1580 (0.4)	62 (0.5)	
Education level, n (%)				< 0.001
University degree	52,332 (11.5)	51,347 (11.7)	985 (7.4)	
Higher secondary and vocational qualifications	206,600 (45.4)	201,556 (45.6)	5044 (38.0)	
Secondary school completion	115,531 (25.4)	112,748 (25.5)	2783 (21.0)	
No qualifications	75,758 (16.6)	71,498 (16.2)	4260 (32.1)	
Prefer not to answer	4839 (1.1)	4634 (1.0)	205 (1.5)	
Household income, n (%)				< 0.001
<£18,000	87,193 (19.2)	82,761 (18.7)	4432 (33.4)	
£18,000–£30,999	99,036 (21.7)	95,930 (21.7)	3106 (23.4)	
£31,000–£51,999	102,678 (22.6)	100,646 (22.8)	2032 (15.3)	
£52,000–£100,000	80,550 (17.7)	79,512 (18.0)	1038 (7.8)	
>£100,000	21,465 (4.7)	21,299 (4.8)	166 (1.2)	
Other	64,138 (14.1)	61,635 (14.0)	2503 (18.9)	
Smoking status, n (%)				< 0.001
Never	248,807 (54.7)	242,850 (55.0)	5957 (44.9)	
Former	156,634 (34.4)	150,932 (34.1)	5702 (42.9)	
Current	47,844 (10.5)	46,302 (10.5)	1542 (11.6)	
Unknown	1775 (0.4)	1699 (0.4)	76 (0.6)	
Alcohol consumption, n (%)				< 0.001
Never	19,526 (4.3)	18,621 (4.2)	905 (6.8)	
Former	15,913 (3.5)	15,111 (3.4)	802 (6.1)	
Current	418,995 (92.1)	407,457 (92.2)	11,538 (86.9)	
Unknown	626 (0.1)	594 (0.1)	32 (0.2)	
Waist circumference (cm)	90.12 ± 13.39	89.91 ± 13.30	97.09 ± 14.36	< 0.001
Abdominal obesity, n (%)	150,598 (33.1)	143,599 (32.5)	6999 (52.7)	< 0.001
DBP (mmHg)	82.23 ± 10.10	82.22 ± 10.09	82.77 ± 10.47	< 0.001
SBP (mmHg)	137.70 ± 18.57	137.52 ± 18.50	143.83 ± 19.59	< 0.001
Elevated BP, n (%)	306,176 (67.3)	294,723 (66.7)	11,453 (86.3)	< 0.001
FBG (mmol/L)	4.93 (4.60, 5.31)	4.92 (4.59, 5.30)	5.08 (4.69, 5.70)	< 0.001
Elevated FBG, n (%)	70,865 (15.6)	66,582 (15.1)	4283 (32.3)	< 0.001
SUA (μmol/L)	307.18 ± 78.90	306.06 ± 78.46	344.61 ± 84.24	< 0.001
Elevated SUA, n (%)	59,513 (13.1)	55,646 (12.6)	3867 (29.1)	< 0.001
TG (mmol/L)	1.48 (1.04, 2.14)	1.47 (1.04, 2.13)	1.74 (1.24, 2.45)	< 0.001
HDL-C (mmol/L)	1.45 ± 0.38	1.45 ± 0.38	1.33 ± 0.37	< 0.001
Lipid abnormalities, n (%)	243,494 (53.5)	233,496 (52.9)	9998 (75.3)	< 0.001

BP: blood pressure; DBP: diastolic blood pressure; eGFR: estimated glomerular filtration rate; FBG: fasting blood glucose; HDL-C: high-density lipoprotein cholesterol; SBP: systolic blood pressure; SUA: serum uric acid; TG: triglycerides

Associations between single MetS components at baseline and CKD risk

After adjusting for age, sex, eGFR, ethnicity, education level, household income, smoking status and alcohol consumption, all the MetS components were independently associated with an increased risk of CKD (all $P < 0.001$). The hazard ratios (HRs) with 95% confidence intervals (CIs) for abdominal obesity, elevated BP, elevated FBG, elevated SUA and lipid abnormalities were 1.40 (1.35–1.45), 1.69 (1.60–1.78), 1.65 (1.58–1.71), 1.85 (1.78–1.92) and 1.48 (1.42–1.54), respectively (Table 2).

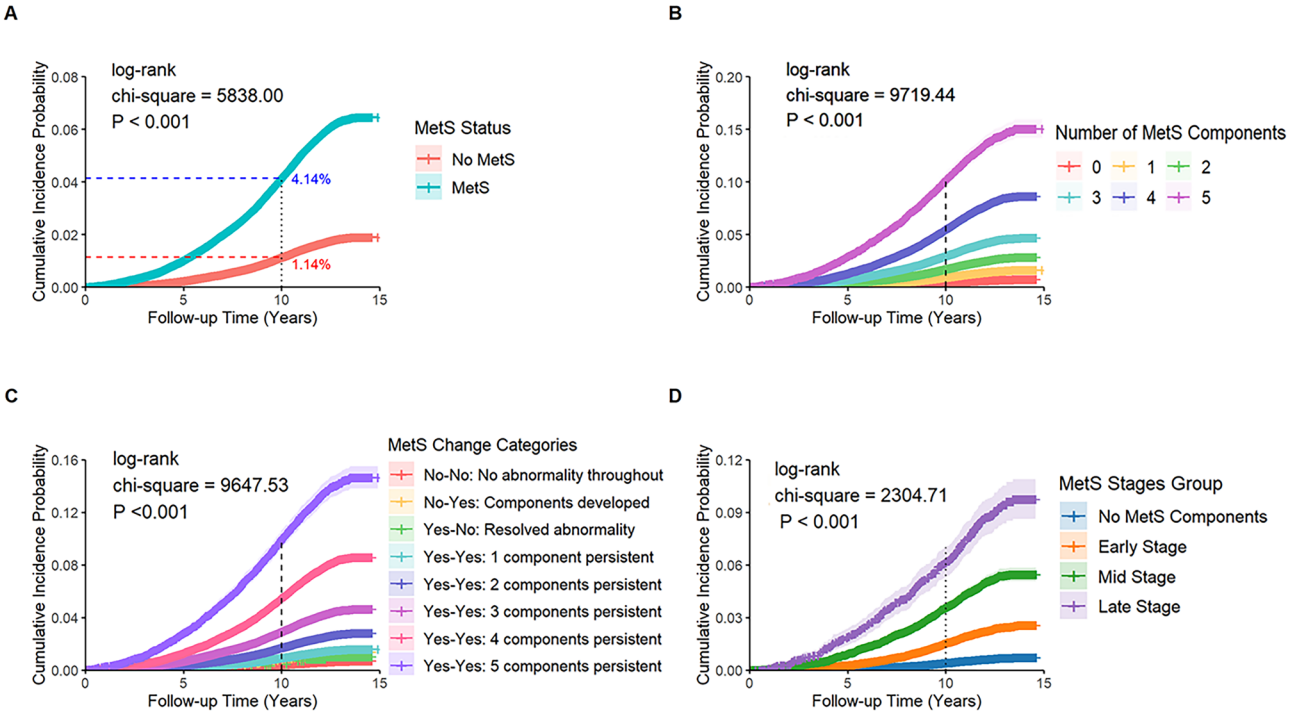

Fig. 2 Cumulative incidence probability of CKD for different classifications related to Metabolic Syndrome. **A**: Stratified by MetS status at baseline; **B**: Stratified by the number of MetS components at baseline; **C**: Stratified by dynamic changes in the number of MetS components over time; **D**: Stratified by the final MetS progression stages throughout the study period. MetS: Metabolic syndrome. MetS components included abdominal obesity, elevated blood pressure, elevated fasting blood glucose, elevated serum uric acid and lipid abnormalities. Shaded areas indicated 95% confidence intervals. log-rank test was used to evaluate the differences across groups

Table 2 Associations between single component, MetS and number of MetS components at baseline and CKD risk

MetS Components	*N*	Model 1		Model 2		Model 3	
		HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Abdominal Obesity	150,598	2.31 (2.24–2.40)	< 0.001	1.50 (1.44–1.55)	< 0.001	1.40 (1.35–1.45)	< 0.001
Elevated BP	306,176	3.17 (3.02–3.33)	< 0.001	1.89 (1.80–1.99)	< 0.001	1.69 (1.60–1.78)	< 0.001
Elevated FBG	70,865	2.71 (2.62–2.82)	< 0.001	1.83 (1.76–1.90)	< 0.001	1.65 (1.58–1.71)	< 0.001
Elevated SUA	59,513	2.83 (2.73–2.94)	< 0.001	1.86 (1.79–1.93)	< 0.001	1.85 (1.78–1.92)	< 0.001
Lipid abnormalities	243,494	2.72 (2.62–2.83)	< 0.001	1.69 (1.62–1.76)	< 0.001	1.48 (1.42–1.54)	< 0.001
MetS	132,991	3.52 (3.40–3.65)	< 0.001	3.09 (2.99–3.20)	< 0.001	2.31(2.23–2.39)	< 0.001
Number of MetS components							
0 component	70,380	Reference		Reference		Reference	
1 component	127,092	2.21 (2.00–2.44)	< 0.001	1.96 (1.77–2.17)	< 0.001	1.66 (1.50–1.83)	< 0.001
2 components	124,597	3.92 (3.56–4.31)	< 0.001	3.20 (2.90–3.52)	< 0.001	2.34 (2.13–2.58)	< 0.001
3 components	85,444	6.56 (5.96–7.21)	< 0.001	5.20 (4.73–5.73)	< 0.001	3.38 (3.07–3.73)	< 0.001
4 components	39,707	12.35 (11.22–13.60)	< 0.001	9.50 (8.62–10.47)	< 0.001	5.42 (4.91–5.97)	< 0.001
5 components	7840	22.44 (20.14–25.00)	< 0.001	16.85 (15.11–18.79)	< 0.001	8.55 (7.66–9.55)	< 0.001

BP: blood pressure; CI: confidence interval; CKD: chronic kidney disease; FBG: fasting blood glucose; HR: hazard ratio; MetS: metabolic syndrome, defined as the presence of three or more components, including abdominal obesity, elevated BP, elevated FBG, elevated SUA and lipid abnormalities. SUA: serum uric acid

Model 1: Univariate analysis; Model 2: Adjusted for age and sex; Model 3: Adjusted for age, sex, eGFR, ethnicity, education level, household income, smoking status and alcohol consumption

Association between the number of MetS components at baseline and CKD risk

After adjusting for covariates, patients with three or more MetS components had significantly higher risk of CKD (HR: 2.31, 95% CI: 2.23–2.39, $P < 0.001$) than participants without MetS. The participants with one, two, three, four and five MetS components were 1.66 (95% CI: 1.50–1.83, $P < 0.001$), 2.34 (95% CI: 2.13–2.58, $P < 0.001$), 3.38 (95% CI: 3.07–3.73, $P < 0.001$), 5.42 (95% CI: 4.91–5.97, $P < 0.001$) and 8.55 (95% CI: 7.66–9.55, $P < 0.001$) times more likely to develop CKD than participants without any MetS components, respectively. The finding

demonstrated a clear dose-response relationship between the number of MetS components and CKD risk. The risk of CKD increased progressively with the number of MetS components (Table 2).

Association between the combinations of MetS components at baseline and CKD risk

The risk of CKD associated with different combinations of MetS components was analyzed using participants without metabolic abnormalities ($N = 70380$) as the reference group. Each combination focused on a specific set of MetS components and participants without these specific combinations were excluded from the analyses. In the multivariate analysis, the HRs for the associations between different combinations of MetS components and CKD risk ranged from 1.61 to 3.66 (all $P < 0.05$). Participants with abdominal obesity, elevated BP and SUA had the highest CKD risk with HR (95% CI) of 3.66 (3.11–4.30). The next highest risk was the combinations of abdominal obesity, elevated BP and FBG (HR: 2.90, 95% CI: 2.35–3.57), elevated BP and SUA (HR: 2.44, 95% CI: 2.20–2.71), abdominal obesity and elevated BP (HR: 2.29, 95% CI: 2.02–2.59), respectively. Participants with abdominal obesity and elevated FBG had relatively lower CKD risk with HR (95% CI) of 1.61 (1.06–2.70) (Table 3).

Table 3 also displayed that CKD risk increased progressively with the stage of MetS. The participants at the early stage which was defined as the combinations of abdominal obesity and elevated BP or FBG had 2.31 (95% CI: 2.03–2.61, $P < 0.001$) times more likely to develop CKD than participants without any MetS components. In the intermediate stage, participants with elevated BP, FBG and lipid abnormalities had higher CKD risk with HR (95% CI) of 3.79 (2.95–4.98, $P < 0.001$) and participants with elevated BP, FBG and SUA had higher CKD risk with HR (95% CI) of 4.29 (3.78–4.86, $P < 0.001$). In the late stage, the combination of elevated BP, FBG, SUA and lipid abnormalities showed the highest CKD risk (HR: 4.86, 95% CI: 4.13–5.72, $P < 0.001$).

Association between dynamic changes in single MetS components over time and CKD risk

After adjusting for age, sex, eGFR, ethnicity, education level, household income, smoking status and alcohol consumption, the dynamic changes in single MetS components were significantly associated with CKD risk (Table 4). With the exception of FBG, the other four MetS components that changed from normal state at baseline to abnormal state at follow-up were all associated with higher risk of CKD. The HRs were 1.38 (95%CI: 1.07–1.77, $P = 0.012$) for abdominal obesity, 1.31 (95% CI: 1.01–1.70, $P = 0.044$) for elevated BP, 1.73 (95% CI: 1.34–2.24, $P < 0.001$) for elevated SUA and 1.21 (95% CI: 1.00–1.48, $P = 0.047$) for lipid abnormalities, respectively. The participants with abdominal obesity, elevated BP, elevated FBG or lipid abnormalities at baseline who improved the MetS components to normal state at follow-up had no different risk of developing CKD than participants without metabolic abnormalities throughout the study period (all $P > 0.05$). However, the participants

Table 3 Associations between the combinations of metabolic abnormalities at baseline and CKD risk

Combinations of MetS Components	*N*	Model 1		Model 2		Model 3	
		HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
MetS Components Combination Group							
No MetS Components	70,380	Reference		Reference		Reference	
AO + elevated BP	22,131	3.64 (3.22–4.12)	< 0.001	3.02 (2.66–3.42)	< 0.001	2.29 (2.02–2.59)	< 0.001
AO + elevated FBG	916	2.48 (1.48–4.15)	< 0.001	2.30 (1.37–3.84)	0.001	1.61 (1.06–2.70)	0.043
AO + LA	13,742	2.72 (2.34–3.17)	< 0.001	2.58 (2.21–3.00)	< 0.001	1.86 (1.59–2.17)	< 0.001
Elevated (BP + SUA)	4887	4.99 (4.17–5.97)	< 0.001	4.19 (3.49–5.03)	< 0.001	2.44 (2.20–2.71)	< 0.001
LA + elevated BP	66,222	4.36 (3.94–4.82)	< 0.001	3.39 (3.05–3.77)	< 0.001	2.11 (1.76–2.54)	< 0.001
AO + elevated (BP + FBG)	3363	5.06 (4.11–6.24)	< 0.001	3.89 (3.15–4.80)	< 0.001	2.90 (2.35–3.57)	< 0.001
AO + elevated (BP + SUA)	4075	8.32 (7.09–9.76)	< 0.001	6.91 (5.88–8.12)	< 0.001	3.66 (3.11–4.30)	< 0.001
MetS Progression Stages Group							
No MetS Components	70,380	Reference		Reference		Reference	
Early Stage (AO + elevated BP/FBG)	23,047	3.59 (3.18–4.06)	< 0.001	3.05 (2.70–3.46)	< 0.001	2.31 (2.03–2.61)	< 0.001
Intermediate stage							
Elevated (BP + FBG) + LA	14,141	8.22 (7.32–9.22)	< 0.001	5.86 (5.18–6.64)	< 0.001	3.79 (2.95–4.98)	< 0.001
Elevated (BP + FBG + SUA)	800	6.57 (4.62–9.35)	< 0.001	5.05 (3.53–7.20)	< 0.001	4.29 (3.78–4.86)	< 0.001
Late Stage [elevated (BP + FBG + SUA) + LA]	3026	14.42 (12.41–16.74)	< 0.001	9.97 (8.49–11.70)	< 0.001	4.86 (4.13–5.72)	< 0.001

AO: abdominal obesity; BP: blood pressure; CI: confidence interval; CKD: chronic kidney disease; FBG: fasting blood glucose; HR: hazard ratio; LA: lipid abnormalities; MetS: metabolic syndrome; SUA: serum uric acid

Model 1: Univariate analysis; Model 2: Adjusted for age and sex; Model 3: Adjusted for age, sex, eGFR, ethnicity, education level, household income, smoking status and alcohol consumption

Participants without these specific combinations were excluded from the analyses

Table 4 Association between dynamic changes in single MetS component over time and CKD risk

MetS Components	*N*	Model 1		Model 2		Model 3	
		HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Changes in abdominal obesity							
No-No	302,497	Reference		Reference		Reference	
No-Yes	1965	1.55 (1.22–1.98)	< 0.001	1.36 (1.06–1.75)	0.016	1.38 (1.07–1.77)	0.012
Yes-No	1017	1.07 (0.71–1.61)	0.755	0.93 (0.61–1.40)	0.725	0.92 (0.61–1.40)	0.708
Yes-Yes	149,581	2.33 (2.25–2.41)	< 0.001	1.50 (1.44–1.56)	< 0.001	1.40 (1.35–1.45)	< 0.001
Changes in elevated BP							
No-No	145,700	Reference		Reference		Reference	
No-Yes	3184	1.47 (1.13–1.90)	0.004	1.31 (1.01–1.70)	0.046	1.31 (1.01–1.70)	0.044
Yes-No	1081	0.91 (0.51–1.60)	0.731	0.92 (0.52–1.63)	0.783	0.99 (0.56–1.76)	0.983
Yes-Yes	305,095	3.21 (3.05–3.38)	< 0.001	1.91 (1.81–2.01)	< 0.001	1.70 (1.61–1.79)	< 0.001
Changes in elevated FBG							
No-No	382,128	Reference		Reference		Reference	
No-Yes	2067	1.34 (1.06–1.71)	0.017	0.98 (0.77–1.25)	0.849	1.08 (0.85–1.39)	0.500
Yes-No	933	1.07 (0.72–1.60)	0.736	0.92 (0.61–1.37)	0.670	0.92 (0.61–1.37)	0.672
Yes-Yes	69,932	2.74 (2.64–2.84)	< 0.001	1.83 (1.77–1.90)	< 0.001	1.66 (1.59–1.72)	< 0.001
Changes in elevated SUA							
No-No	394,310	Reference		Reference		Reference	
No-Yes	1237	1.96 (1.52–2.53)	< 0.001	1.68 (1.29–2.18)	< 0.001	1.73 (1.34–2.24)	< 0.001
Yes-No	637	1.74 (1.19–2.54)	0.004	1.49 (1.01–2.18)	0.042	1.30 (1.25–1.35)	< 0.001
Yes-Yes	58,876	2.86 (2.75–2.96)	< 0.001	1.86 (1.79–1.94)	< 0.001	1.86 (1.79–1.93)	< 0.001
Changes in lipid abnormalities							
No-No	206,944	Reference		Reference		Reference	
No-Yes	4622	1.40 (1.15–1.71)	< 0.001	1.21 (0.99–1.47)	0.064	1.21 (1.00–1.48)	0.047
Yes-No	1524	0.87 (0.57–1.34)	0.521	0.85 (0.55–1.31)	0.460	0.80 (0.52–1.23)	0.305
Yes-Yes	241,970	2.76 (2.65–2.87)	< 0.001	1.70 (1.63–1.77)	< 0.001	1.49 (1.43–1.55)	< 0.001

BP: blood pressure; CI: confidence interval; CKD: chronic kidney disease; FBG: fasting blood glucose; HR: hazard ratio; MetS: metabolic syndrome; SUA: serum uric acid

Model 1: Univariate analysis; Model 2: Adjusted for age and sex; Model 3: Adjusted for age, sex, eGFR, ethnicity, education level, household income, smoking status and alcohol consumption

No-No: no abnormality throughout the study period; No-Yes: transition from a normal state at baseline to an abnormal state at follow-up; Yes-No: transition from an abnormal state at baseline to a normal state at follow-up; Yes-Yes: persistent abnormality throughout the study period

with elevated SUA at baseline even whose SUA level was reduced to normal state at follow-up still had higher risk of developing CKD than participants with normal SUA throughout the study period (HR: 1.30, 95%CI: 1.25–1.35, $P<0.001$). The participants with persistent metabolic abnormalities throughout the study period (Yes-Yes) had very similar risk of CKD as those with metabolic abnormalities at baseline (Yes) (Table 4 VS Table 2).

Association between dynamic changes in the number of MetS components over time and CKD risk

Table 5 displayed the dynamic changes in the number of MetS components significantly associated with CKD risk. Compared to participants with no metabolic abnormalities throughout the study period, participants without metabolic abnormalities at baseline but who developed one or more metabolic abnormalities at follow-up had significantly higher CKD risk with HR (95% CI) of 1.49 (1.00–2.35, $P=0.047$) and 2.26 (1.21–4.24, $P=0.011$), respectively. The results of the number of abnormal components at the end of the follow-up furthered shown that CKD risk increased as the number of MetS components increased. The participants with one, two, three, four and five MetS components had a 1.69 (95% CI: 1.52–1.87, $P<0.001$), 2.38 (95% CI: 2.16–2.63, $P<0.001$), 3.45 (95% CI: 3.12–3.81, $P<0.001$), 5.56 (95% CI: 5.02–6.14, $P<0.001$) and 8.67 (95% CI: 7.75–9.70, $P<0.001$) times the risk of developing CKD compared to participants without any MetS components, respectively. The participants with one or more metabolic abnormalities at baseline but no metabolic abnormalities at follow-up had no different risk of developing CKD than the reference group (HR: 1.42, 95% CI: 0.71–2.86, $P=0.324$).

Association between the combinations of MetS components throughout the study period and CKD risk

Similar to the baseline analysis, participants without these specific combinations were excluded from the analyses. As shown in Table 6, the combinations of MetS components after change remained significantly associated with CKD risk. In the multivariate analysis, the HRs for the association between different combinations

Table 5 Association between dynamic changes in the number of MetS components over time and CKD risk

MetS Components	*N*	Model 1		Model 2		Model 3	
		HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
No MetS components throughout the study period (No-No)	68,142	Reference		Reference		Reference	
MetS components presented at follow-up (No-Yes)							
1 Component	1730	1.61 (1.02–2.55)	0.042	1.55 (0.98–2.45)	0.062	1.49 (1.00–2.35)	0.047
≥ 2 Components	508	2.86 (1.53–5.35)	0.001	2.61 (1.39–4.88)	0.003	2.26 (1.21–4.24)	0.011
MetS components disappeared at follow-up (Yes-No)	812	1.48 (0.73–2.97)	0.274	1.45 (0.72–2.92)	0.295	1.42 (0.71–2.86)	0.324
MetS components at the end of follow-up (Yes-Yes)							
1 Component	123,746	2.26 (2.03–2.50)	< 0.001	2.00 (1.80–2.22)	< 0.001	1.69 (1.52–1.87)	< 0.001
2 Components	125,111	3.99 (3.61–4.40)	< 0.001	3.25 (2.94–3.59)	< 0.001	2.38 (2.16–2.63)	< 0.001
3 Components	86,466	6.69 (6.07–7.38)	< 0.001	5.30 (4.74–5.86)	< 0.001	3.45 (3.12–3.81)	< 0.001
4 Components	40,392	12.65 (11.46–13.97)	< 0.001	9.74 (8.81–10.76)	< 0.001	5.56 (5.02–6.14)	< 0.001
5 Components	8153	22.50 (20.15–25.12)	< 0.001	16.93 (15.15–18.92)	< 0.001	8.67 (7.75–9.70)	< 0.001

CI: confidence interval; CKD: chronic kidney disease; HR: hazard ratio; MetS: metabolic syndrome

MetS components included abdominal obesity, elevated blood pressure, elevated fasting blood glucose, elevated serum uric acid and lipid abnormalities

Model 1: Univariate analysis; Model 2: Adjusted for age and sex; Model 3: Adjusted for age, sex, eGFR, ethnicity, education level, household income, smoking status and alcohol consumption

No-No: participants with no metabolic abnormalities throughout the study period; No-Yes: participants with no metabolic abnormalities at baseline but who developed one or more metabolic abnormalities at follow-up; Yes-No: participants with one or more metabolic abnormalities at baseline but no metabolic abnormalities at follow-up; Yes-Yes: participants with metabolic abnormalities at baseline were categorized by the number of abnormal components at the end of the follow-up, ranging from one abnormal component to all five components being abnormal

Table 6 Association between the combinations of MetS components throughout the study period and CKD

Combinations of MetS Components	*N*	Model 1		Model 2		Model 3	
		HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
MetS Components Combination Group							
No MetS Components	65,647	Reference		Reference		Reference	
AO + elevated BP	22,302	3.58 (3.15–4.07)	< 0.001	2.97 (2.62–3.38)	< 0.001	2.26 (1.99–2.57)	< 0.001
AO + elevated FBG	873	2.47 (1.45–4.21)	0.001	2.30 (1.35–3.91)	0.002	1.58 (1.13–2.70)	0.040
AO + LA	13,129	2.82 (2.41–3.30)	< 0.001	2.67 (2.28–3.12)	< 0.001	1.91 (1.63–2.23)	< 0.001
Elevated (BP + SUA)	4907	4.99 (4.16–5.99)	< 0.001	4.17 (3.47–5.03)	< 0.001	2.42 (2.17–2.70)	< 0.001
LA + elevated BP	69,231	4.27 (3.85–4.73)	< 0.001	3.33 (2.99–3.71)	< 0.001	2.12 (1.76–2.56)	< 0.001
AO + elevated (BP + FBG)	3425	5.14 (4.17–6.33)	< 0.001	3.96 (3.21–4.89)	< 0.001	2.95 (2.39–3.64)	< 0.001
AO + elevated (BP + SUA)	4068	8.33 (7.07–9.81)	< 0.001	6.90 (5.85–8.14)	< 0.001	3.65 (3.10–4.31)	< 0.001
MetS Progression Stages Group							
No MetS Components	65,647	Reference		Reference		Reference	
Early Stage (AO + elevated BP/FBG)	23,175	3.54 (3.12–4.01)	< 0.001	3.01 (2.65–3.43)	< 0.001	2.28 (2.00–2.60)	< 0.001
Intermediate stage							
Elevated (BP + FBG) + LA	14,884	8.02 (7.13–9.03)	< 0.001	5.76 (5.07–6.54)	< 0.001	3.70 (2.87–4.89)	< 0.001
Elevated (BP + FBG + SUA)	813	6.16 (4.28–8.87)	< 0.001	4.77 (3.30–6.89)	< 0.001	4.23 (3.72–4.81)	< 0.001
Late Stage [elevated (BP + FBG + SUA) + LA]	3231	14.21 (12.23–16.52)	< 0.001	9.89 (8.41–11.62)	< 0.001	4.91 (4.17–5.78)	< 0.001

AO: abdominal obesity; BP: blood pressure; CI: confidence interval; CKD: chronic kidney disease; FBG: fasting blood glucose; HR: hazard ratio; LA: lipid abnormalities; MetS: metabolic syndrome; SUA: serum uric acid

Model 1: Univariate analysis; Model 2: Adjusted for age and sex; Model 3: Adjusted for age, sex, eGFR, ethnicity, education level, household income, smoking status and alcohol consumption

Participants without these specific combinations were excluded from the analyses

The final Metabolic component status was determined based on baseline or follow-up measurements, ICD codes or medication use records. The participants were considered to have a Metabolic component in the final status if they met the criteria for abnormality at any time throughout the study period

of MetS components and CKD risk ranged from 1.58 to 3.65 (all $P < 0.05$). Participants with abdominal obesity, elevated BP and SUA had the highest CKD risk with HR (95% CI) of 3.65 (3.10–4.31). The next highest risk was the combinations of abdominal obesity, elevated BP and FBG (HR: 2.95, 95% CI: 2.39–3.64), elevated BP and SUA (HR: 2.42, 95% CI: 2.17–2.70), abdominal obesity and elevated BP (HR: 2.26, 95% CI: 1.99–2.57), respectively. Participants with abdominal obesity and elevated FBG

had relatively lower CKD risk with HR (95% CI) of 1.58 (1.13–2.70).

As MetS progressed, the CKD risk increased. The participants with abdominal obesity and elevated BP or FBG had 2.28 (95% CI: 2.00–2.60, $P<0.001$) times more likely to develop CKD than participants without any MetS components. In the intermediate stage, participants with elevated BP, FBG and lipid abnormalities had higher CKD risk with HR (95% CI) of 3.70 (2.87–4.89, $P<0.001$) and participants with elevated BP, FBG and SUA had higher CKD risk with HR (95% CI) of 4.23 (3.72–4.81, $P<0.001$). In the late stage, the combination of elevated BP, FBG, SUA and lipid abnormalities showed the highest CKD risk (HR: 4.91, 95% CI: 4.17–5.78, $P<0.001$) (Table 6).

After performing the Cox regression analysis for the risk of new-onset CKD, the proportional hazards assumption was tested using the Schoenfeld residuals method, and no violation of this assumption was detected.

Stratified and sensitivity analyses

In the stratified analysis, males exhibited higher risks for elevated BP and FBG. While both males and females showed an increased risk of CKD with the number and changes of MetS components, the overall CKD risk was greater in males. However, for elevated SUA and its changes, the risk was higher in females (Supplementary Tables 2–6) [see Additional file 2]. To ensure the reliability of these findings, this study conducted sensitivity analyses in three ways to assess the robustness of the results. After excluding the participants with incomplete data of five MetS components at baseline and the first repeat assessment, those with follow-up periods of less than two years or those who developed CKD within the first two years of follow-up, the associations between MetS components and CKD risk were similar to the results of the main analyses. The results of this study were stability and reliability (Supplementary Tables 7–11) [see Additional file 2].

Discussions

This study confirmed the strong associations between MetS components and CKD risk, particularly highlighting the dynamic nature of MetS components. The findings extended the existing literatures by focusing on how dynamic changes in MetS components, such as transitions from normal to abnormal states, persistence of abnormalities and improvement or recovery of certain components, impacted the risk of developing CKD. These dynamic changes were critical for understanding CKD progression, underscore the importance of continuous monitoring and timely interventions.

The associations between single MetS component, including abdominal obesity, elevated BP, FBG, SUA and lipid abnormalities, and the risk of CKD was found to be robust and aligned with previous research [26, 27]. However, the contribution of these components to the risk of CKD was different. Notably, elevated SUA exhibited the highest HR (95%CI) of 1.85 (1.78–1.92), highlighting its significant role in metabolic dysfunction and CKD risk, with this impact being more pronounced in females. Hyperuricemia contributed to CKD pathogenesis by stimulating the renin-angiotensin system, inhibiting endothelial nitric oxide release and causing renal vasoconstriction and hypertension [28]. In females, estrogen had modulated urate excretion and endothelial function, potentially amplifying the adverse effects of hyperuricemia when these protective mechanisms were disrupted. Hyperuricemia also induced local inflammation and oxidative stress, exacerbating tubular and interstitial damage, which was more severe in females due to differences in immune response and antioxidant capacity [17]. Urate crystal deposition triggered additional renal injury, perpetuating a cycle that accelerated disease progression [29]. Elevated SUA played a critical role within the MetS framework as both a marker of CKD risk and a key component of metabolic health. Elevated BP and FBG also emerged as significant contributors to CKD development, with HRs (95% CI) of 1.69 (1.60–1.78) and 1.65 (1.58–1.71), respectively. Elevated BP reduced renal blood flow, leading to glomerular hypertension and subsequent kidney damage [30], with this effect being more pronounced in males due to generally higher BP levels. High FBG levels promoted the onset and progression of CKD by increasing glomerular filtration pressure and promoting the formation of advanced glycation end-products (AGEs), further damaging kidney function [31], and males exhibited a greater risk increment associated with elevated FBG compared to females. Both elevated BP and FBG were well-established independent risk factors for CKD, often accelerating the rate and severity of renal damage. Abdominal obesity and lipid abnormalities also contributed to CKD risk, although their impact was less pronounced compared to elevated SUA, BP, and FBG. These findings highlighted the importance of focusing on males with elevated BP and FBG levels, as well as females with elevated SUA levels, for early detection and management.

This study found that MetS significantly correlated with CKD risk, consistent with earlier findings [32, 33]. The comprehensive nature of MetS highlighted its role as a multifactorial syndrome that multiple components collectively impacted renal health. The findings revealed a clear dose-response relationship that as the number of MetS components increased, so did the risk of developing CKD. Compared with participants without MetS components, participants with one, two, three, four and five MetS components had a 0.66-, 1.34-, 2.38-, 4.42- and

7.55- fold increased risk of developing CKD, respectively. This progressive increase in risk underscored the cumulative impact of multiple MetS components on the initiation of CKD, aligning with findings from previous cohort studies [14, 26, 34]. Early identification and targeted interventions focusing on managing these components were critical for reducing CKD risk.

Notably, MetS, as a syndrome composed of multiple metabolic abnormalities, exhibited complex synergistic pathological effects among its components that influenced renal health. Under the premise of the same number of abnormal components, different combinations exerted differential impacts on kidney damage. Therefore, this section further investigated the effects of various combinations of MetS components on CKD risk, providing a more refined dimension for CKD risk assessment. Among the two-component combinations, participants with elevated BP and SUA exhibited the highest CKD risk with HR (95% CI) of 2.44 (2.20–2.71). This combination formed a vicious cycle that elevated BP reduced renal blood flow and impaired SUA excretion, while elevated SUA promoted kidney damage through crystal deposition, inflammation and endothelial dysfunction [18, 35]. Given this close association, early identification and targeted management of BP and UA were crucial for reducing CKD risk. The interventions should focus on controlling both parameters aimed to break the feedback loop that accelerated kidney damage. Lipid abnormalities combined with elevated BP had a HR of 2.11 (1.76–2.54), and this combination accelerated CKD progression by promoting systemic vascular disease. Elevated BP damaged the endothelial cells of the renal vasculature. When combined with lipid abnormalities, it further promoted atherosclerosis, glomerulosclerosis and interstitial fibrosis, leading to additional impairment of renal function [32, 36, 37]. Managing lipid levels alongside BP control was critical to mitigate these effects. For the three-component, the combinations of abdominal obesity, elevated BP and SUA showed a strikingly high HR of 3.66 (3.11–4.30). This triad likely intensified the effects of systemic vascular disease, renal endothelial dysfunction and metabolic dysregulation, resulting in severe renal impairment [19, 38]. Among the combinations of MetS components, those with elevated SUA levels showed a higher CKD risk. Special attention should be given to individuals with elevated SUA, and timely interventions are needed to control SUA within a healthy range to reduce kidney damage risk. Additionally, as MetS advances from early to advanced stages, the complexity of metabolic abnormalities increases, leading to progressively higher CKD risks. In the early stage, abdominal obesity with elevated BP or FBG significantly increased CKD risk. The abdominal obesity triggered chronic low-grade inflammation and insulin resistance. When abdominal obesity paired with elevated BP or FBG, it accelerated kidney damage [39–41]. As MetS progressed to the intermediate stage, the combinations like elevated BP, FBG and lipid abnormalities, or elevated BP, FBG and SUA, showed even greater CKD risk. In this stage, the presence of multiple metabolic disturbances interacted synergistically, creating a feedback loop of vascular and tubular damage that accelerated kidney dysfunction [10, 42, 43]. The cumulative effect of these factors placed additional stress on the kidneys, leading to more rapid progression of CKD. By the advanced stage, elevated BP, FBG, SUA and lipid abnormalities presented higher CKD risk. Multiple metabolic abnormalities interacted to accelerate CKD progression. Elevated BP exacerbated the damage to glomerular and tubular hemodynamics [37]. The AGEs and polyol pathway activation exacerbated metabolic dysregulation [31, 40] The lipid abnormalities caused further endothelial damage and lipid deposition in the kidney [44]. Elevated SUA levels resulted in massive deposition of uric acid crystals, triggering intense inflammation [16]. Based on the number of MetS abnormalities and unique risk profiles associated with different combinations of metabolic components, this study moves beyond traditional broad risk assessment methods for MetS. By identifying high-risk combinations such as elevated SUA and hypertension, our findings facilitate the development of precise intervention strategies and evidence-based screening protocols tailored to individual risk factors. This approach allows for personalized management plans, significantly enhancing the effectiveness of interventions for CKD prevention in high-risk populations.

While the baseline assessments provided preliminary insights into MetS-related CKD risk, it did not capture the full dynamic picture. The status of MetS components may change over time. To better understand the impact of MetS on CKD risk, it was essential to consider the dynamic changes in MetS components. As expected, this study found that there were associations between the dynamic changes in MetS components and the risk of CKD. The participants without metabolic abnormalities at baseline but developed metabolic abnormalities during follow-up also had an increased CKD risk. The participants who had metabolic abnormalities at baseline had a reduced risk of CKD when the metabolic abnormalities disappeared at follow-up. It was reported that weight gain trajectories, long-term weight gain and increase of BP were associated with an increased CKD risk [45–47]. These results further emphasized the importance of continuous monitoring and management of MetS components for the prevention and control of CKD risk.

Furthermore, this study further explored the impact of the dynamic changes in the number of MetS components over time on CKD risk. It was also found that there was dose-response relationship between the number

of MetS components and CKD risk. The risk of CKD increased with the increasing number of MetS components. For participants who developed one and ≥ 2 MetS components at follow-up, the HR (95% CI) for CKD risk was 1.49 (1.00–2.35) and 2.26 (1.21–4.24), respectively. Although the risk was lower than that of participants who had persistent metabolic abnormalities during the study period, the finding suggested that participants with normal MetS components at baseline should not be ignored. It was consistent with the previous studies that developed MetS and persistent MetS were both risk factors for CKD [48, 49]. However, the strength of this study was more comprehensive, considering not only different dynamic status of MetS, but also the dynamic changes in single, number and combinations of MetS components. The emphasis on the changes in the cumulative effect of MetS components over time offered a more comprehensive view of CKD risk factors.

Given the role of MetS in the risk of CKD, the following recommendations were suggested. High-risk individuals, particularly those with multiple metabolic abnormalities, should be closely monitored. Lifestyle modifications—such as increased physical activity, maintaining a healthy weight, and reducing intake of high-sugar, high-fat, and high-purine foods—are crucial for preventing new metabolic issues. Pharmacological interventions may be necessary to normalize relevant biomarkers in persistent cases. Regular health screenings should monitor key indicators like blood glucose, lipids, and blood pressure to detect potential metabolic problems early and facilitate prompt intervention. Long-term continuous monitoring is essential for tracking metabolic fluctuations and allowing clinicians to adjust treatment plans swiftly. Given the significant differences in CKD risk associated with various MetS component combinations, developing targeted treatment strategies is critical. Tailored strategies that address gender-specific risk factors can further enhance the effectiveness of these interventions, helping to mitigate the progression of CKD and improve overall renal health outcomes. For example, patients with elevated SUA and hypertension should receive pharmacotherapy that concurrently addresses hyperuricemia and blood pressure control, preferably through agents with dual mechanisms of action. Similarly, for those with abdominal obesity and hyperglycemia, emphasis should be placed on weight control and glycemic regulation through diet, exercise, and antidiabetic medications. This targeted approach not only reduces CKD risk but also improves overall health outcomes, providing a solid foundation for advancing public health efforts towards more precise prevention and management strategies.

Several limitations of the current study should be acknowledged. First, the observational design limited the ability to establish causal relationships between MetS components and CKD risk. Although several potential confounders were adjusted for, residual confounding may still affect the results, which is an inherent limitation of cohort studies. Future prospective studies with more precise metabolic measurements were needed to validate the MetS components in predicting the risk of CKD. Second, the generalizability of the findings was potentially limited. Despite the inclusion of a diverse population in the UK Biobank, the representation of certain ethnic minorities was found to be insufficient. Future research should therefore focus on populations with more diverse ethnic representation to enhance the broader applicability of the results. Third, the study was constrained by data limitations. Follow-up blood measurements for MetS components were available only for participants who attended a repeat assessment visit. For participants without follow-up blood measurements, the metabolic abnormalities determined by baseline blood measurements were assumed to persist during the study period. To address this limitation, a sensitivity analysis was performed, focusing on participants with two assessment visits. This analysis helped mitigate potential bias and strengthen the study's reliability.

Conclusions

In conclusion, the findings strongly supported the notion that MetS, particularly the dynamic changes in MetS components, was closely associated with CKD risk. The risk increased in a dose-response manner with the number of MetS components. Elevated SUA played a pivotal role in increasing CKD risk, with females showing higher susceptibility to elevated SUA compared to males. Including SUA in MetS assessments could improve the risk identification and enabled more effective prevention. Continuous monitoring and intervention were important for managing MetS components. It was necessary to use the dynamic changes in MetS components to dynamically assess and predict the risk of CKD.

Abbreviations

CKD	Chronic kidney disease
ESRD	End-stage renal disease
MetS	Metabolic syndrome
TG	Triglycerides
HDL-C	High-density lipoprotein cholesterol
TC	Total cholesterol
LDL-C	Low-density lipoprotein cholesterol
SUA	Serum uric acid
BP	Blood pressure
ICD-10	International classification of diseases – 10th revision
ICD-9	International classification of diseases – 9th revision
eGFR	Estimated glomerular filtration rate
UACR	Urine albumin-to-creatinine ratio
WC	Waist circumference
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
FBG	Fasting blood glucose
SD	Standard deviation
IQR	Interquartile range

KM	Kaplan-meier
HR	Hazard ratio
CI	Confidence interval
AGEs	Advanced glycation end-products

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

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Author contributions
YH analyzed and interpreted the data and was the primary contributor to writing the manuscript; RF contributed to the research design, acquired funding, study supervision, interpretation of results and manuscript revision; JZ offered statistical insights and helped draft significant portions of the manuscript; JZ assisted in data cleaning and extraction from the UK Biobank database; SC drafted part of the manuscript; ZL provided expertise in methodology and statistical analysis; XX handled data management and provided administrative support; ZH supervised the overall project, coordinated the study design, contributed to the interpretation of results and ensured compliance with ethical standards during manuscript submission.

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Data availability
Data access was granted under UK Biobank project approval number 75905. The datasets used and/or analysed during the current study are available from the UK Biobank repository (https://www.ukbiobank.ac.uk/) under this approval. Access to these datasets is subject to approval by the UK Biobank.

Declarations

Ethics approval and consent to participate
The studies involving human participants were reviewed and approved by North West Research Ethics Committee (06/ MRE08/65). The patients/participants provided their written informed consent to participate in this study.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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