BMJ Open

Association of cardiovascular-kidney-metabolic syndrome stages with kidney stone prevalence: a population-based analysis of NHANES 2007–2020

Guoliang Lu,[1] Jinjun Tian,[2] Feng Shi,[3] Ding-Guo Zhang,[4] Dawei Wang [1]

To cite: Lu G, Tian J, Shi F, *et al*. Association of cardiovascular-kidney-metabolic syndrome stages with kidney stone prevalence: a population-based analysis of NHANES 2007–2020. *BMJ Open* 2025;**15**:e096533. doi:10.1136/bmjopen-2024-096533

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (https://doi.org/10.1136/bmjopen-2024-096533).

GL, JT, D-GZ and DW contributed equally.

GL and JT are joint first authors.

Received 13 November 2024
Accepted 22 April 2025

[1]Department of Urology, Ruijin Hospital, Shanghai, China
[2]Department of Urology, Shanghai Pudong New Area people's Hospital, Shanghai, China
[3]Civil Aviation Shanghai Hospital, Shanghai, China
[4]Shanghai Pudong New Area People's Hospital, Shanghai, China

Correspondence to
Dr Dawei Wang;
wdwrjhn@163.com

ABSTRACT

Background The prevalence of kidney stones (KSs) has been increasing globally, and their association with cardiovascular disease and metabolic syndrome suggests a shared underlying pathophysiology. However, the impact of different stages of cardiovascular-kidney-metabolic (CKM) syndrome on KS prevalence remains unclear.

Objective This study aimed to investigate the association between the stages of CKM syndrome and the prevalence of KS in a nationally representative sample of adults in the USA.

Methods A total of 15 568 participants aged ≥20 years were included in the National Health and Nutrition Examination Survey 2007–2020 fasting subsample. CKM syndrome stages (0–4) were defined based on the 2023 American Heart Association Presidential Advisory on CKM Health. The KS history was determined using self-reported data. Multivariable logistic regression models were used to assess the association between the CKM syndrome stage and KS prevalence.

Results Of the 15 568 participants, 1501 (9.64%) reported a history of KS. The KS prevalence increased progressively with advancing CKM stage, rising from 5.10% in stage 0 to 16.55% in stage 4 (p<0.001). In the fully adjusted model, the ORs for KS were 1.18 (95% CI 0.83–1.68) for stage 1, 1.72 (95% CI 1.28 to 2.32) for stage 2, 2.00 (95% CI 1.29 to 3.10) for stage 3 and 2.36 (95% CI 1.64 to 3.40) for stage 4, compared with stage 0 (*P* for trend <0.001). Stratified analyses revealed no significant interactions between age, sex, race/ethnicity or other subgroups.

Conclusion This study demonstrated a significant stepwise increase in KS prevalence with the advancing stages of CKM syndrome. These findings highlight the importance of monitoring and managing CKM syndromes to mitigate the risks of KS.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Used a nationally representative National Health and Nutrition Examination Survey cohort (2007–2020) with complex survey weighting to ensure population generalisability.
⇒ Implemented standardised 2023 American Heart Association criteria for cardiovascular-kidney-metabolic syndrome staging, enhancing clinical consistency.
⇒ Adjusted for comprehensive covariates including demographics, socioeconomic status, lifestyle factors and biochemical markers.
⇒ Kidney stone history was based on self-reported data, which may be subject to recall bias.
⇒ The observational nature of the analysis precludes determination of temporal relationships.

INTRODUCTION

Kidney stones (KSs) are hard mineral deposits forming in the renal calyces and pelvis when urine concentrations of substances like calcium, oxalate, uric acid or phosphate become high enough to crystallise.[1] KS affects 10.1% of the US population.[2] Recent research suggests KS is a systemic disorder linked to chronic diseases such as cardiovascular diseases (CVDs), diabetes and obesity, rather than being limited to the kidneys. Stone formation is a complex process influenced by genetic, metabolic and environmental factors.[3]

Cardiovascular-kidney-metabolic (CKM) syndrome, recently defined by the American Heart Association (AHA), represents a systemic disorder characterised by the pathophysiological interplay among metabolic risk factors (eg, obesity, type 2 diabetes, hypertension, dyslipidaemia and insulin resistance), chronic kidney disease (CKD) and CVD.[4] These conditions share common underlying mechanisms, including systemic inflammation and metabolic dysfunction, which create a vicious cycle of organ damage and disease progression. The presence of one condition often exacerbates others, leading to increased risks of adverse outcomes, morbidity and mortality.[5–7] CKM syndrome encompasses individuals at risk for CVD due to metabolic or kidney-related factors, as well as those with established CVD complicated by these conditions. Furthermore, social determinants of health, such as socioeconomic status and environmental factors, exacerbate biological risks

and create barriers to effective lifestyle modification and care.[8] This integrated framework underscores the need for interdisciplinary approaches to address the complex mechanisms, clinical heterogeneity and management challenges associated with CKM syndrome. In this study, we explore the association between CKM syndrome stages and KS prevalence, as both conditions are systemic and share underlying metabolic disturbances.

CKM syndrome comprises interconnected risk factors that elevate the likelihood of developing CVD, type 2 diabetes and other health complications. Metabolic diseases such as obesity, diabetes mellitus and hypertension are associated with an increased risk of KS.[9] An 8-year follow-up study found a correlation between high blood pressure and KS development, with the risk further heightened when hypertension coexists with overweight conditions.[10] These factors can alter urine composition, metabolic processes and kidney function, promoting stone formation. Specifically, increased acid excretion, low citrate levels and high calcium excretion create a conducive environment for KS.[11]

Emerging evidence supports the association between KS and various metabolic risk factors. Unhealthy metabolic status significantly increases KS risk, and combined effects can substantially elevate this risk. Previous studies have identified a broad range of KS risk factors, including biological factors, high sodium intake, metabolic disturbances and genetic predispositions.[12] Observational studies suggest that vascular calcification may also increase KS risk.[13] A growing number of studies indicate a positive association between CVD and KS, suggesting potential shared pathological mechanisms. Therefore, each component of CKM syndrome may influence KS formation.

To better understand these connections, the AHA introduced a model classifying CKM syndrome into distinct stages.[7] Assessing the associations between the combined effects of these factors at various stages and KS prevalence is essential. However, few studies have explored the relationship between this new concept, CKM syndrome and the KS stages. The aim of this study was to investigate the association between CKM syndrome stages and the prevalence of KS in a nationally representative sample of US adults, using data from the National Health and Nutrition Examination Survey (NHANES) from 2007 to 2020.

MATERIALS AND METHODS

Study population

NHANES is a nationally representative health and nutrition survey conducted by the National Center for Health Statistics (NCHS), with data collected through complex sampling methods (available at https://www.cdc.gov/nchs/nhanes). The study protocols were approved by the NCHS Research Ethics Review Board (Protocols #2005–06, #2011–17 and #2018–01) and Ruijin Hospital (2024–177), and all participants provided written informed consent.

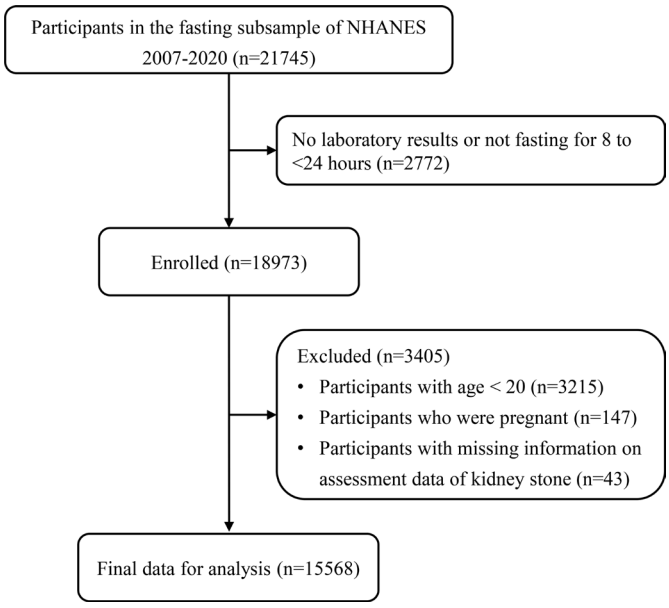

Figure 1 Flowchart of participant selection for the study. NHANES, National Health and Nutrition Examination Survey.

Fasting samples were used to measure key biomarkers (glucose and lipids) essential for CKM syndrome staging. From the NHANES 2007–2020 fasting subsample (n = 21 745), we excluded 2772 participants with missing laboratory data or insufficient fasting duration. Of the remaining 18 973 individuals, we further excluded 3215 under 20 years old, 147 pregnant participants and 43 with missing KS data, yielding a final sample of 15 568 for analysis (figure 1).

Definition of KS

KS history was determined through self-reported data. Participants were classified as having a KS history if they affirmed a prior diagnosis of KS by a healthcare professional in response to the questionnaire item, "Have you/Has sample person (SP) ever had kidney stones?". Additionally, recurrence of KS was defined as having experienced two or more episodes of passing KSs, based on the response to "How many times have you/has SP passed a kidney stone?". This self-report method has been validated in prior studies, demonstrating a 97% accuracy rate in identifying clinically diagnosed KS cases.[14]

Assessment of CKM syndrome stages

CKM syndrome stages (0–4) were classified according to the 2023 AHA Presidential Advisory on CKM Health,[7] with adaptations for NHANES data. The stages were defined as follows: stage 0: no CKM risk factors (eg, absence of hypertension, hyperlipidaemia or metabolic abnormalities). Stage 1: overweight, obesity or dysfunctional adipose tissue without additional metabolic risk factors or CKD. Stage 2: presence of metabolic risk factors (eg, hypertension, dyslipidaemia and insulin resistance) or CKD. Stage 3: high-risk CKD (eg, estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m² or albuminuria ≥300 mg/g) or a high predicted 10-year CVD risk

(≥20% based on validated risk scores). Stage 4: established CVD (eg, coronary artery disease, heart failure or stroke). Detailed NHANES-adapted definitions for each stage, including specific criteria and thresholds, are provided in the online supplemental material.

Assessment of covariates

To account for potential confounding factors, the following covariates were included. Demographics: age (categorised as 20–39, 40–59 and ≥60 years), sex (male and female) and race/ethnicity (non-Hispanic white, non-Hispanic black and other). Socioeconomic status: education level (below high school, high school graduate and above high school) and family poverty-to-income ratio (PIR ≤1.0, 1.1–3.0 and >3.0). Lifestyle factors: drinking status: non-drinkers, low-to-moderate drinkers or heavy drinkers (based on standard alcohol consumption thresholds); smoking status: never, former or current smoker; physical activity (PA): classified as inactive, insufficiently active or active based on self-reported adherence to PA guidelines. Biochemical and nutritional markers: serum calcium, serum phosphorus and urinary creatinine levels were divided into quartiles to account for metabolic variations; total energy intake was assessed using 24-hour dietary recall data and categorised into quartiles. Detailed definitions and measurement protocols for all covariates are provided in the online supplemental materials.

Statistical analysis

All analyses adhered to NHANES guidelines, incorporating sample weights to account for the complex survey design, and were performed using the R 'survey' package (V.4.3.2). Continuous variables were summarised as medians with IQRs, while categorical variables were expressed as weighted percentages. Group comparisons were performed using the Mann-Whitney U test or Kruskal-Wallis H test for continuous variables with non-normal distributions and ordinal categorical variables, while the χ^2 test was applied to nominal categorical variables.

Multivariable logistic regression models estimated the association between CKM stages and KS prevalence, adjusting for covariates, with results reported as ORs and 95% CIs. Subgroup analyses explored interactions between CKM stages and key variables (age, sex, race/ethnicity, smoking status and PA). A two-sided p<0.05 was considered statistically significant.

Patient and public involvement

None.

RESULTS

Baseline characteristics of participants

Table 1 presents the survey-weighted baseline characteristics by KS status. Among 15 568 participants, 1501 (9.64%) reported a history of KS. The median age was 48 years, with females comprising 51.32% of the cohort. Stone formers were significantly older; 38.12% were aged ≥60 years compared with 25.59% of non-stone formers (p<0.001). Males had a higher prevalence of KS (53.27%) than females (46.73%) (p=0.003). Participants with KS were more frequently classified into advanced CKM syndrome stages (stages 3 and 4), with 24.42% versus 14.02% among non-stone formers (p<0.001). Other covariates, including race/ethnicity, smoking status, drinking status and PA, also showed significant differences between the groups.

Table 2 summarises the survey-weighted characteristics across CKM syndrome stages. In stage 0, 66.05% of participants were aged 20–39 years, whereas in stage 4, 69.49% were aged ≥60 years (p<0.001). A higher proportion of males was observed in advanced stages: 54.78% in stage 4 compared with 32.69% in stage 0 (p<0.001). KS prevalence increased consistently with advancing CKM stages, rising from 5.10% in stage 0 to 16.55% in stage 4. As shown in figure 2, the prevalence progressed as follows: 5.10% (stage 0), 6.71% (stage 1), 10.53% (stage 2), 15.00% (stage 3) and 16.55% (stage 4), indicating a significant upward trend with increasing CKM syndrome severity (p<0.001).

Association between CKM syndrome stages and the prevalence of KS

Table 3 illustrates the ORs for KS prevalence across CKM syndrome stages. In the unadjusted model, KS likelihood rose progressively with advancing CKM stages, with stage 4 showing almost 3.7 times the odds compared with stage 0. This association remained robust in model 1, which adjusted for age, sex and race/ethnicity. The trend persisted in model 2 with further adjustments for socioeconomic and lifestyle factors. In model 3, even after additional adjustments for serum calcium, phosphorus and creatinine, the ORs for KS prevalence continued to increase with CKM severity: 1.18 (95% CI 0.83 to 1.68) for stage 1, 1.72 (95% CI 1.28 to 2.32) for stage 2, 2.00 (95% CI 1.29 to 3.10) for stage 3 and 2.36 (95% CI 1.64 to 3.40) for stage 4. This indicates a significant and stepwise rise in KS prevalence with worsening CKM stages (P_{trend}<0.001). To visually summarise the association between CKM syndrome stages and KS prevalence, the ORs and 95% CIs from table 3 are further illustrated in figure 3 using a forest plot.

Data are presented as OR (95% CI) unless indicated otherwise; model 1 was adjusted for age (20–39, 40–59 or ≥60); sex (male or female) and race/ethnicity (Non-Hispanic White, Non-Hispanic Black or Other race); Model 2 was adjusted as model 1 plus education level (below high school, high school or above high school); family PIR (≤1.0, 1.1–3.0 or >3.0); drinking status (non-drinker, low-to-moderate drinker or heavy drinker); smoking status (never smoker, former smoker or current smoker); PA (inactive, insufficiently active or active) and total energy intakes (in quartiles); model 3 was adjusted as model 2 plus serum calcium (in quartiles), serum phosphorus (in quartiles) and urinary creatinine (in quartiles).

Table 1 Survey-weighted characteristics of the general adult population by kidney stone in NHANES 2007–2020

Characteristics	Overall	Non-stone former	Stone former	P value
Participant, N	15568	14067	1501	
Age, years				<0.001
20–39	4893 (35.91)	4618 (37.40)	275 (22.25)	
40–59	5323 (37.27)	4799 (37.01)	524 (39.64)	
≥60	5352 (26.82)	4650 (25.59)	702 (38.12)	
Sex, %				0.003
Female	8020 (51.32)	7344 (51.82)	676 (46.73)	
Male	7548 (48.68)	6723 (48.18)	825 (53.27)	
Race/ethnicity, %				<0.001
Non-Hispanic White	6333 (66.13)	5553 (65.19)	780 (74.76)	
Non-Hispanic Black	3224 (11.31)	3039 (11.94)	185 (5.54)	
Other race	6011 (22.56)	5475 (22.87)	536 (19.70)	
Education level, %				0.604
Below high school	3752 (16.24)	3382 (16.18)	370 (16.85)	
High school	3528 (22.68)	3190 (22.67)	338 (22.74)	
Above high school	8288 (61.08)	7495 (61.15)	793 (60.41)	
Family PIR, %				0.431
≤1.0	3409 (15.40)	3092 (15.53)	317 (14.18)	
1.1–3.0	6577 (36.32)	5943 (36.28)	634 (36.67)	
>3.0	5582 (48.28)	5032 (48.19)	550 (49.15)	
Smoking status, %				0.018
Never smoker	8734 (55.70)	7950 (56.10)	784 (52.09)	
Former smoker	3806 (25.28)	3372 (24.84)	434 (29.31)	
Current smoker	3028 (19.02)	2745 (19.06)	283 (18.60)	
Drinking status, %				0.002
Non-drinker	2067 (10.53)	1867 (10.44)	200 (11.39)	
Former drinker	2052 (11.88)	1800 (11.41)	252 (16.24)	
Current drinker	11449 (77.59)	10400 (78.16)	1049 (72.37)	
Physical activity, %				< 0.001
Inactive	4064 (21.88)	3592 (21.23)	472 (27.81)	
Insufficiently active	4885 (32.66)	4440 (32.79)	445 (31.45)	
Active	6619 (45.46)	6035 (45.98)	584 (40.74)	
Total energy intakes, kcal/day	2007.00 (1495.00, 2655.00)	2007.00 (1493.00, 2667.00)	2005.00 (1541.00, 2585.00)	0.679
Serum calcium, mmol/L	2.33 (2.28, 2.40)	2.33 (2.28, 2.40)	2.33 (2.28, 2.38)	0.029
Serum phosphorus, mmol/L	1.16 (1.07,1.29)	1.16 (1.07,1.29)	1.16 (1.03, 1.26)	<0.001
Urinary creatinine, mg/dL	114.00 (67.00, 168.00)	113.00 (66.00, 168.00)	120.00 (77.00, 168.00)	0.006
Fasting blood glucose, mg/dL	100.00 (93.00, 109.00)	100.00 (93.00, 109.00)	103.000 (95.00, 115.00)	<0.001
Haemoglobin A1c, %	5.50 (5.20, 5.80)	5.40 (5.20, 5.80)	5.600 (5.30, 6.10)	<0.001
LDL cholesterol, mg/dL	111.00 (89.00, 135.00)	111.00 (89.00, 135.00)	113.00 (91.000, 135.00)	0.427
HDL cholesterol, mg/dL	51.000 (43.00, 63.00)	52.00 (43.00, 63.00)	48.00 (41.00, 59.00)	<0.001
CKM syndrome stage, %				<0.001
Stage 0	1457 (11.83)	1390 (12.45)	67 (6.15)	
Stage 1	3211 (23.11)	3014 (23.91)	197 (15.78)	
Stage 2	7735 (50.02)	6968 (49.62)	767 (53.65)	
Stage 3	1385 (5.87)	1198 (5.53)	187 (8.96)	
Stage 4	1780 (9.17)	1497 (8.49)	283 (15.46)	

Continuous variables without a normal distribution are presented as medians (IQRs). Sampling weights were applied for calculation of demographic descriptive statistics; N reflects the study sample, while percentages reflect the survey-weighted data.
CKM, cardiovascular-kidney-metabolic; HDL, high density lipoprotein; LDL, low density lipoprotein; NHANES, National Health and Nutrition Examination Survey; PIR, poverty income ratio.

Table 2 Survey-weighted characteristics of the general adult population by CKM syndrome stages in NHANES 2007–2020

Characteristics	CKM syndrome stage					P value
	Stage 0	Stage 1	Stage 2	Stage 3	Stage 4	
Participant, N	1457	3211	7735	1385	1780	
Age, years						<0.001
20–39	996 (66.05)	1676 (53.78)	2138 (30.22)	9 (0.80)	74 (5.53)	
40–59	382 (28.56)	1134 (35.22)	3345 (46.34)	64 (4.80)	398 (24.98)	
≥60	79 (5.39)	401 (11.01)	2252 (23.45)	1312 (94.40)	1308 (69.49)	
Sex, %						<0.001
Female	974 (67.31)	1728 (51.37)	3921 (48.92)	608 (48.92)	789 (45.22)	
Male	483 (32.69)	1483 (48.63)	3814 (51.08)	777 (51.08)	991 (54.78)	
Race/ethnicity, %						<0.001
Non-Hispanic White	657 (70.46)	1159 (62.34)	2886 (64.89)	713 (72.83)	918 (72.65)	
Non-Hispanic Black	188 (7.34)	686 (12.58)	1672 (11.54)	271 (11.22)	407 (12.03)	
Other race	612 (22.20)	1366 (25.08)	3177 (23.57)	401 (15.95)	455 (15.32)	
Education level, %						<0.001
Below high school	194 (9.48)	613 (12.65)	1898 (16.86)	470 (25.14)	577 (24.98)	
High school	258 (16.68)	671 (21.45)	1773 (23.05)	369 (29.35)	457 (27.22)	
Above high school	1005 (73.84)	1927 (65.90)	4064 (60.09)	546 (45.50)	746 (47.80)	
Family PIR, %						<0.001
≤1.0	271 (12.78)	713 (15.79)	1702 (15.42)	306 (16.63)	417 (16.89)	
1.1–3.0	535 (30.49)	1255 (34.38)	3212 (35.43)	685 (47.18)	890 (46.62)	
>3.0	651 (56.74)	1243 (49.83)	2821 (49.15)	394 (36.19)	473 (36.49)	
Smoking status, %						<0.001
Never smoker	1004 (65.82)	1980 (60.01)	4372 (55.25)	649 (47.09)	729 (39.83)	
Former smoker	185 (15.70)	622 (22.11)	1784 (24.73)	544 (40.90)	671 (38.58)	
Current smoker	268 (18.48)	609 (17.88)	1579 (20.02)	192 (12.01)	380 (21.60)	
Drinking status, %						<0.001
Non-drinker	185 (9.86)	332 (8.67)	1036 (10.29)	265 (18.90)	249 (12.03)	
Former drinker	89 (5.74)	251 (7.36)	966 (11.98)	337 (23.05)	409 (23.48)	
Current drinker	1183 (84.40)	2628 (83.97)	5733 (77.73)	783 (58.05)	1122 (64.49)	
Physical activity, %						<0.001
Inactive	222 (12.18)	569 (16.28)	1915 (21.59)	616 (42.11)	742 (37.13)	
Insufficiently active	470 (31.79)	992 (32.01)	2524 (33.94)	397 (29.85)	502 (30.15)	

Continued

Table 2 Continued

Characteristics	CKM syndrome stage					P value
	Stage 0	Stage 1	Stage 2	Stage 3	Stage 4	
Active	765 (56.02)	1650 (51.70)	3296 (44.46)	372 (28.04)	536 (32.72)	
Total energy intakes, kcal/day	1974.00 (1551.00, 2624.00)	2098.00 (1588.00, 2751.00)	2066.00 (1531.00, 2709.00)	1666.00 (1263.00, 2147.00)	1810.00 (1330.00, 2360.00)	<0.001
Serum calcium, mmol/L	2.35 (2.30, 2.40)	2.33 (2.28, 2.38)	2.33 (2.28, 2.40)	2.35 (2.28, 2.40)	2.33 (2.28, 2.40)	<0.001
Serum phosphorus, mmol/L	1.23 (1.13, 1.32)	1.16 (1.07, 1.29)	1.16 (1.07, 1.29)	1.16 (1.07, 1.29)	1.16 (1.07, 1.29)	<0.001
Urinary creatinine, mg/dL	102.00 (57.00, 160.00)	118.00 (69.00, 176.00)	115.00 (69.00, 170.00)	99.00 (65.00, 143.00)	108.00 (67.00, 155.00)	<0.001
Fasting blood glucose, mg/dL	91.00 (86.00, 95.00)	98.00 (92.00, 103.00)	103.00 (96.00, 112.00)	114.00 (100.00, 134.00)	108.00 (98.00, 126.00)	<0.001
Haemoglobin A1c, %	5.200 (5.00, 5.300)	5.300 (5.100, 5.600)	5.500 (5.300, 5.800)	6.00 (5.600, 6.600)	5.800 (5.500, 6.400)	<0.001
LDL-cholesterol, mg/dL	97.00 (79.00,118.00)	112.00 (92.00, 134.00)	118.00 (96.00,142.00)	104.00 (80.00,126.00)	94.00 (74.00,121.00)	<0.001
HDL- cholesterol, mg/dL	62.00 (53.00, 73.00)	55.00 (47.00, 65.00)	48.00 (40.00, 59.00)	50.00 (42.00, 61.00)	48.00 (40.00, 59.00)	<0.001
Kidney stone, %						<0.001
No	1390 (94.90)	3014 (93.29)	6968 (89.47)	1198 (85.00)	1497 (83.45)	
Yes	67 (5.10)	197 (6.71)	767 (10.53)	187 (15.00)	283 (16.55)	

Continuous variables without a normal distribution are presented as medians (IQRs). Sampling weights were applied for calculation of demographic descriptive statistics; N reflects the study sample, while percentages reflect the survey-weighted data.
CKM, cardiovascular-kidney-metabolic; HDL, high density lipoprotein; LDL, low density lipoprotein; NHANES, National Health and Nutrition Examination Survey; PIR, poverty income ratio.

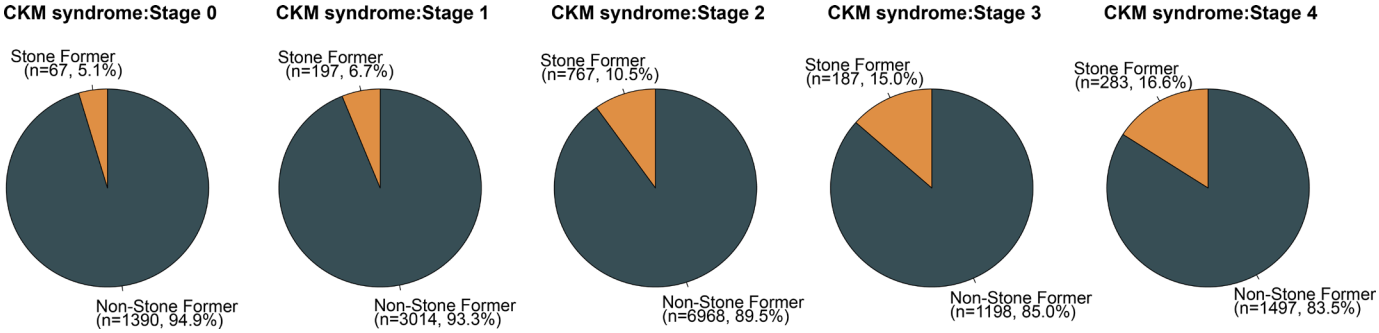

Figure 2 Prevalence of kidney stones across CKM syndrome stages. CKM, cardiovascular-kidney-metabolic.

Stratified analysis

Table 4 presents stratified analyses of the association between CKM syndrome stage and KS prevalence. Among participants aged 20–59, stage 4 was associated with over threefold increased odds of KS compared with stage 0 (OR = 3.14, 95% CI 2.08 to 4.73). In those aged ≥60 years, the association was weaker and non-significant (OR = 1.31, 95% CI 0.45 to 3.80), with no significant age interaction (*P* for interaction = 0.482). Sex-stratified results were similar; in stage 4, females and males had approximately 2.4 times the odds of KS, with no significant sex interaction (*P* for interaction = 0.299). Non-Hispanic Whites showed stronger associations (OR = 2.28, 95% CI 1.45 to 3.60), with weaker trends in other ethnicities. Consistent patterns emerged across subgroups of family PIR, education level, smoking, drinking and PA. Despite varying strengths, the association between CKM syndrome severity and KS prevalence remained consistent across these groups.

Data are presented as OR (95% CI) unless indicated otherwise; analyses were adjusted for age (20–39, 40–59 or ≥60); sex (male or female); race/ethnicity (Non-Hispanic White, Non-Hispanic Black or Other race); education level (below high school, high school or above high school); family PIR (≤1.0, 1.1–3.0 or >3.0); drinking status (non-drinker, low-to-moderate drinker or heavy drinker); smoking status (never smoker, former smoker or current smoker); PA (inactive, insufficiently active or active), total energy intakes (in quartiles); serum calcium (in quartiles); serum phosphorus (in quartiles) and urinary creatinine (in quartiles) when they were not the strata variables. *p-int*, p for interaction.

DISCUSSION

This study explored the relationship between CKM syndrome stages and the prevalence of KS among 15 568 US adults using data from the NHANES 2007–2020. We found that participants with CKM syndrome had significantly higher odds of KS as the CKM stage advanced. Moreover, the association between the CKM syndrome stage and KS prevalence was consistent in the fully adjusted models.

Both CKM syndrome and KS are systemic conditions affecting multiple organs. This study shows KS prevalence is closely linked to advanced CKM syndrome, characterised by insulin resistance, obesity, dyslipidaemia and hypertension. These contribute to stone formation and reflect metabolic dysfunction. CKM syndrome begins early in life,[15] inducing dysfunctional adipose tissue, inflammation, oxidative stress and insulin resistance,[16] leading to hypertension, hypertriglyceridaemia, metabolic syndrome and type 2 diabetes.[7] As these conditions progress, they burden the kidneys, causing CKD and worsening CKM syndrome.[3]

Metabolic syndrome is a known risk factor for KS development. Type 2 diabetes patients have an elevated risk of urinary KS due to increased urinary oxalate excretion, enhancing calcium oxalate stone formation.[17] Their urinary profiles—high oxalate excretion and low pH—make them more prone to uric acid and calcium oxalate stones.[17] Uric acid stone formers face a higher risk of diabetes and glucose intolerance than non-stone

Table 3 OR (95% CIs) of the prevalence of kidney stone according to CKM syndrome stages among adults in NHANES 2007–2020

	CKM syndrome stage					
	Stage 0	Stage 1	Stage 2	Stage 3	Stage 4	P_{trend}
Crude	1.00 (reference)	1.34 (0.94, 1.91)	2.19 (1.64, 2.93)	3.28 (2.29, 4.71)	3.69 (2.68, 5.09)	<0.001
Model 1	1.00 (reference)	1.27 (0.89, 1.82)	1.84 (1.37, 2.48)	2.24 (1.48, 3.40)	2.63 (1.87, 3.72)	<0.001
Model 2	1.00 (reference)	1.25 (0.88, 1.79)	1.80 (1.34, 2.42)	2.08 (1.35, 3.22)	2.45 (1.71, 3.51)	<0.001
Model 3	1.00 (reference)	1.18 (0.83, 1.68)	1.72 (1.28, 2.32)	2.00 (1.29, 3.10)	2.36 (1.64, 3.40)	<0.001

CKM, cardiovascular-kidney-metabolic; NHANES, National Health and Nutrition Examination Survey.

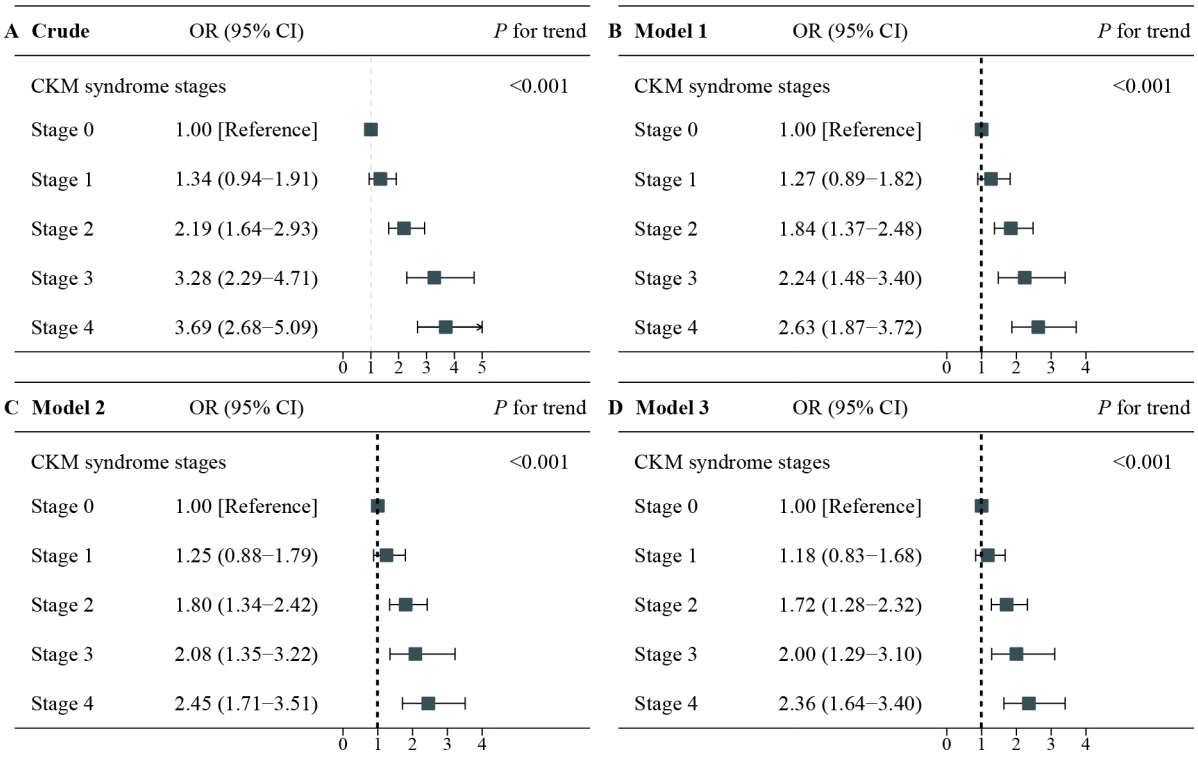

Figure 3 Forest plot illustrating the ORs and 95% CIs for kidney stone prevalence across CKM syndrome stages. Data are presented as OR (95% CI) unless indicated otherwise; Model 1 was adjusted as age (20–39, 40–59 or ≥60); sex (male or female) and race/ethnicity (Non-Hispanic White, Non-Hispanic Black or Other race); model 2 was adjusted as model 1 plus education level (below high school, high school or above high school); family PIR (≤1.0, 1.1–3.0 or >3.0); drinking status (non-drinker, low-to-moderate drinker or heavy drinker); smoking status (never smoker, former smoker or current smoker); physical activity (inactive, insufficiently active or active) and total energy intakes (in quartiles); model three was adjusted as model 2 plus serum calcium (in quartiles), serum phosphorus (in quartiles) and urinary creatinine (in quartiles). CKM, cardiovascular-kidney-metabolic; PIR, poverty-to-income ratio.

formers;[18] increasing HbA1c levels correlate with lower urinary pH, further contributing to KS risk.[19]

Obesity is another significant factor associated with KS. Excess caloric intake results in greater metabolic waste and altered urinary composition.[20] Studies show that waist circumference and body mass index are linked to higher KS risk among adults over 46 years of age.[21] In obese individuals, insulin resistance impairs renal ammonium excretion, [9]and obesity induces a pro-inflammatory state contributing to KS via oxidative stress and altered renal function. Dyslipidaemia is also linked to KS, particularly uric acid stone formation.[22] Masterson *et al* found individuals with dyslipidaemia are over twice as likely to develop KS,[23] and Inci *et al* reported that KS formers have significantly higher serum lipid levels.[24]

A large longitudinal cohort study in Taiwan confirmed a strong relationship between metabolic syndrome and KS formation, with hypertension identified as the strongest predictor of metabolic syndrome components.[25] Metabolic dysfunction has been independently associated with a higher risk of KS, especially in individuals with both obesity and metabolic dysfunction.[26] A meta-analysis confirmed a positive correlation between the number of metabolic syndrome components (such as hypertension, obesity and dyslipidaemia) and risk of KS development.[27] In 694 ageing males, Yung *et al* found metabolic syndrome and particularly hypertension strongly associated with nephrolithiasis.[28] Kohjimoto *et al* reported hypertension and dyslipidaemia significantly linked to KS severity, while other metabolic traits showed less consistent associations.[29] While relationships between CKM syndrome components and KS vary across populations, our study found no significant demographic interactions, indicating a consistent association between CKM stages and KS prevalence across these groups.

KS and CKD are closely related, each potentially exacerbating the other. Stone formation can lead to long-term kidney damage, inducing CKD.[28] Patients with CKD often exhibit altered urinary excretion of calcium, oxalate, phosphate and uric acid—key contributors to stone formation.[30] Impaired kidney function diminishes oxalate filtration and excretion, leading to its accumulation in the bloodstream.[31] The Chronic Renal Insufficiency Cohort study found that as eGFR declined in CKD stages 2–4, urinary oxalate excretion decreased,[32] increasing stone risk due to metabolic imbalance. However, some studies suggest CKD may offer protection against KS.[33] One study observed that CKD patients with an average creatinine clearance of 35–38 mL/min exhibited hypocitraturia without significant differences in other components.[34] Since citrate inhibits calcium stone formation, this could influence stone risk. A single-centre

Table 4 Stratified analyses of the associations between CKM syndrome stage and the prevalence of kidney stone among adults in NHANES 2007–2020

Subgroups	N	CKM syndrome stage					*P-int*
		Stage 0	Stage 1	Stage 2	Stage 3	Stage 4	
Age, years							0.482
20–59	10216	1 (reference)	1.35 (0.92–1.98)	2.10 (1.51–2.91)	2.79 (0.86–9.10)	3.14 (2.08–4.73)	
≥ 60	5352	1 (reference)	0.61 (0.20–1.89)	0.96 (0.32–2.88)	1.15 (0.39–3.41)	1.31 (0.45–3.80)	
Sex, %							0.299
Female	8020	1 (reference)	1.33 (0.85–2.07)	1.82 (1.21–2.74)	1.99 (1.05–3.77)	2.36 (1.40–4.00)	
Male	7548	1 (reference)	1.09 (0.56–2.15)	1.78 (0.99–3.20)	2.09 (1.04–4.21)	2.47 (1.34–4.55)	
Race, %							0.351
Non-Hispanic White	6333	1 (reference)	1.23 (0.79–1.92)	1.68 (1.16–2.43)	2.05 (1.17–3.57)	2.28 (1.45–3.60)	
Non-Hispanic Black	3224	1 (reference)	0.79 (0.36–1.70)	1.50 (0.70–3.18)	1.94 (0.79–4.77)	1.53 (0.56–4.14)	
Other race	6011	1 (reference)	1.10 (0.62–1.94)	1.91 (1.11–3.31)	1.66 (0.84–3.28)	3.02 (1.60–5.69)	
Family PIR, %							0.687
≤1.0	3409	1 (reference)	1.75 (0.76–4.00)	2.42 (1.14–5.18)	3.02 (1.05–8.72)	4.37 (1.90–10.04)	
1.1–3.0	6577	1 (reference)	1.34 (0.78–2.30)	1.84 (1.13–3.00)	1.94 (1.14–3.33)	2.56 (1.59–4.11)	
>3.0	5582	1 (reference)	1.02 (0.62–1.67)	1.54 (1.00–2.39)	2.07 (1.13–3.80)	1.88 (1.05–3.37)	
Education level, %							0.571
Below high school	3752	1 (reference)	1.72 (0.66–4.47)	3.10 (1.31–7.33)	2.78 (1.00–7.73)	4.34 (1.78–10.56)	
High school	3528	1 (reference)	0.92 (0.41–2.07)	1.21 (0.59–2.49)	1.19 (0.47–3.03)	1.42 (0.67–3.01)	
Above high school	8288	1 (reference)	1.22 (0.77–1.93)	1.75 (1.19–2.57)	2.53 (1.48–4.32)	2.47 (1.49–4.09)	
Smoking status, %							0.266
Non-smokers	8734	1 (reference)	1.47 (0.88–2.46)	2.29 (1.46–3.62)	2.40 (1.28–4.51)	3.61 (2.04–6.39)	
Former smokers	3806	1 (reference)	0.84 (0.40–1.73)	1.17 (0.61–2.25)	1.73 (0.78–3.85)	1.63 (0.83–3.20)	
Current smokers	3028	1 (reference)	0.93 (0.47–1.83)	1.23 (0.63–2.42)	1.23 (0.43–3.49)	1.41 (0.61–3.26)	
Drinking status, %							0.336
Non-drinker	2067	1 (reference)	0.58 (0.20–1.74)	1.50 (0.73–3.11)	1.86 (0.66–5.24)	1.95 (0.84–4.52)	
Low-to-moderate drinker	2052	1 (reference)	1.74 (0.51–5.94)	2.40 (0.87–6.66)	2.08 (0.63–6.81)	2.70 (0.82–8.91)	
Heavy drinker	11449	1 (reference)	1.23 (0.82–1.87)	1.72 (1.21–2.43)	2.18 (1.31–3.63)	2.52 (1.63–3.88)	
Physical activity, %							0.575
Inactive	4064	1 (reference)	1.19 (0.48–2.97)	1.47 (0.61–3.56)	1.49 (0.55–4.05)	2.24 (0.89–5.63)	
Insufficiently active	4885	1 (reference)	1.00 (0.48–2.11)	2.06 (1.13–3.75)	2.86 (1.37–5.97)	2.69 (1.27–5.71)	
Active	6619	1 (reference)	1.27 (0.81–1.99)	1.65 (1.10–2.49)	2.08 (1.15–3.78)	2.09 (1.24–3.51)	
Serum calcium, mmol/L							0.395

Continued

Table 4 Continued

Subgroups	N	CKM syndrome stage					*P-int*
		Stage 0	Stage 1	Stage 2	Stage 3	Stage 4	
Quartile 1	4717	1 (reference)	2.10 (1.06–4.16)	2.93 (1.59–5.41)	2.85 (1.22–6.65)	3.01 (1.35–6.70)	
Quartile 2	3638	1 (reference)	1.20 (0.60–2.41)	1.66 (0.90–3.05)	2.01 (0.77–5.26)	3.05 (1.34–6.94)	
Quartile 3	3361	1 (reference)	0.57 (0.29–1.11)	1.24 (0.71–2.17)	1.63 (0.75–3.58)	1.73 (0.80–3.72)	
Quartile 4	3852	1 (reference)	1.24 (0.55–2.78)	1.59 (0.86–2.95)	1.98 (0.91–4.35)	2.41 (1.27–4.57)	
Serum phosphorus, mmol/L							0.408
Quartile 1	4635	1 (reference)	1.16 (0.62–2.16)	1.52 (0.89–2.60)	1.52 (0.74–3.12)	2.23 (1.15–4.35)	
Quartile 2	3543	1 (reference)	1.76 (0.67–4.63)	2.15 (0.82–5.65)	4.16 (1.27–13.63)	3.10 (1.00–9.60)	
Quartile 3	4131	1 (reference)	1.48 (0.75–2.92)	2.28 (1.20–4.36)	2.24 (0.83–6.01)	3.20 (1.32–7.75)	
Quartile 4	3259	1 (reference)	0.53 (0.26–1.08)	1.38 (0.77–2.48)	1.63 (0.72–3.69)	1.97 (1.02–3.83)	
Urinary creatinine, mg/dL							0.393
Quartile 1	3913	1 (reference)	1.58 (0.76–3.28)	1.60 (0.85–3.03)	2.19 (0.95–5.07)	2.89 (1.31–6.39)	
Quartile 2	4038	1 (reference)	1.04 (0.54–1.98)	1.35 (0.80–2.28)	1.69 (0.78–3.66)	2.06 (1.09–3.87)	
Quartile 3	3750	1 (reference)	1.83 (0.89–3.77)	2.85 (1.45–5.59)	2.85 (1.22–6.65)	3.12 (1.60–6.08)	
Quartile 4	3867	1 (reference)	0.68 (0.33–1.42)	1.43 (0.77–2.64)	1.80 (0.74–4.39)	1.69 (0.78–3.67)	

CKM, cardiovascular-kidney-metabolic; NHANES, National Health and Nutrition Examination Survey; PIR, poverty-to-income ratio.

study indicated that urinary components involved in stone formation were positively associated with eGFR,[35] implying that worse kidney function might reduce stone-forming constituents. Although current data suggest a connection, more comprehensive studies are needed to establish a clear pattern of how worsening kidney function affects KS development.

Several large-scale epidemiological studies report that individuals with a history of KS have a higher risk of myocardial infarction, coronary heart disease and stroke compared with those without stones.[36 37] Reiner's longitudinal study found that KS history is associated with greater carotid artery wall thickness.[38] Hsi *et al* identified a significant association between recurrent KS formation and coronary artery calcium (CAC), especially in those with higher CAC scores,[39] suggesting a link between recurrent KS and increased coronary artery calcification. CVD-related metabolic factors such as cholesterol, phospholipids and uric acid are associated with KS pathogenesis.[40] Evidence suggests that KS formers with CVD have lower renal alkali excretion and higher acid retention.[41] Hamono *et al* found that CVD risk factors—including smoking, hypertension and overweight—are positively correlated with calcium oxalate stone risk.[42] Abdominal aortic calcification significantly correlates with hypocitraturia; stone formers have notably lower urinary citrate excretion. [43]These findings suggest that hypocitraturia may be a common mechanism for both CVD and KS.

CKM syndrome and increased prevalence of KS is particularly critical in the context of the COVID-19 pandemic, which has exacerbated the burden of CKM syndrome. Individuals with CKM syndrome are at higher risk of severe COVID-19 outcomes. A recent study of 81 051 individuals from a primary care database compared prepandemic (2017–2019) and pandemic (2020–2022) periods, revealing a significant increase in CKM syndrome components during the pandemic. Notably, prediabetes prevalence rose by 170%, while diabetes, hypertension, dyslipidaemia and obesity also showed marked increases. Nearly half of the patients exhibited at least one CKM component, underscoring the growing health burden and the urgent need for targeted interventions to address this escalating public health challenge.[44]

Epidemiological data demonstrate that the progression of CKM syndrome from stage 0 to stage 3 is associated with a significantly higher absolute risk of atherosclerotic CVD and heart failure, both of which remain leading causes of global morbidity and mortality.[8] Our findings further reveal a strong association between advancing CKM stages and increased KS prevalence, underscoring the systemic and interconnected nature of metabolic, cardiovascular and kidney diseases. The COVID-19 pandemic has exacerbated the burden of CKM syndrome, amplifying its underlying mechanisms, including chronic inflammation, oxidative stress and endothelial dysfunction, which collectively accelerate atherosclerosis and cardiovascular complications.[45 46]

The association between CKM syndrome and KS prevalence involves several interconnected mechanisms. Patients with CKM syndrome are at higher risk of developing both calcium oxalate and uric acid stones, with urinary pH playing a critical role in stone composition; acidic urine promotes uric acid stones, while alkaline urine favours calcium phosphate stones. Insulin resistance impairs renal ammoniogenesis in proximal tubules, reducing ammonia production and lowering urinary pH,[47] increasing uric acid stone risk. The inflammatory response also contributes to KS and CKM syndrome progression;[48] elevated urinary oxalate levels—a key risk factor for calcium oxalate stones—are influenced by inflammatory molecules like monocyte chemoattractant protein 1 and immune cell activity.[48] Both KS formation and atherosclerotic plaque development involve macrophage recruitment, releasing inflammatory mediators that cause tissue damage and calcium deposition.[49] Metabolic syndrome may also increase oxalate excretion;[29] elevated urinary oxalate harms renal parenchyma and may be reabsorbed into proximal tubules via passive diffusion.[32] The individual traits of CKM syndrome independently influence stone formation risk and cumulatively further increase the risk of both calcium oxalate and uric acid stones. Future studies are needed to clarify these pathways and identify additional mechanisms.

Our study has several notable strengths, including its novel exploration of the relationship between CKM syndrome stages and KS prevalence, the use of a large, nationally representative sample from NHANES, and rigorous adjustment for multiple confounders to enhance the robustness of our findings. These strengths provide valuable insights into the systemic and interconnected nature of metabolic, cardiovascular and kidney diseases. However, we fully acknowledge the limitations inherent in our study design. The cross-sectional nature of the analysis precludes the ability to infer causality or establish temporal relationships between CKM syndrome and KS development. Additionally, the reliance on self-reported KS history may introduce recall bias or misclassification, potentially affecting the accuracy of our results. While we adjusted for a wide range of covariates, the possibility of unmeasured confounders influencing the observed associations cannot be ruled out. Furthermore, the generalisability of our findings is limited to US adults, and further research in diverse populations is needed to validate and extend these results.

Conclusions

This study demonstrates a clear and progressive association between advancing CKM syndrome stages and increased KS prevalence in a nationally representative US adult population. Individuals with more advanced CKM stages are at a higher risk of developing KS. These findings underscore the critical importance of early detection and effective management of CKM syndrome to mitigate KS risk and burden. Further research is needed to elucidate the underlying mechanisms driving this association

and to develop targeted prevention strategies for at-risk populations.

Acknowledgements We appreciate the contributions of the participants to the NHANES data.

Contributors DW: conceived and designed the study and drafted the initial manuscript. JT: collected and analysed the data and assisted in writing and editing the manuscript. FS: analysed and organised the data. D-GZ: supervised the research and was responsible for the manuscript revision and final approval. GL: provided research resources and was responsible for project management. DW is the guarantor. GL and JT contributed equally to this work as the co-first authors. D-GZ and DW contributed equally as co-corresponding authors.

Funding Establishing an early warning model for renal calculi in civil aviation pilots (No.254).

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, conduct, reporting or dissemination plans of this research.

Patient consent for publication Consent obtained directly from patient(s).

Ethics approval This study involves human participants. All participants provided written informed consent, and study procedures were approved by the National Center for Health Statistics Research Ethics Review Board (protocol number: Protocol #2011-17) and Ruijin Hospital (2024-177). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

ORCID iD

Dawei Wang http://orcid.org/0000-0003-3063-0874

REFERENCES

1 Khan SR, Pearle MS, Robertson WG, *et al*. Kidney stones. *Nat Rev Dis Primers* 2016;2:16008.
2 Chewcharat A, Curhan G. Trends in the prevalence of kidney stones in the United States from 2007 to 2016. *Urolithiasis* 2021;49:27–39.
3 Peerapen P, Thongboonkerd V. Kidney stone prevention. *Adv Nutr* 2023;14:555–69.
4 Ndumele CE, Rangaswami J, Chow SL, *et al*. Cardiovascular-kidney-metabolic health: a presidential advisory from the American heart association. *Circulation* 2023;148:1606–35.
5 Sun H, Saeedi P, Karuranga S, *et al*. IDF diabetes atlas: global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. *Diabetes Res Clin Pract* 2022;183:109119.
6 Bikbov B, Purcell CA, Levey AS, *et al*. Global, regional, and national burden of chronic kidney disease, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 2020;395:709–33.
7 Ndumele CE, Neeland IJ, Tuttle KR, *et al*. A synopsis of the evidence for the science and clinical management of Cardiovascular-Kidney-Metabolic (CKM) syndrome: a scientific statement from the American heart association. *Circulation* 2023;148:1636–64.
8 Khan SS, Coresh J, Pencina MJ, *et al*. Novel prediction equations for absolute risk assessment of total cardiovascular disease incorporating cardiovascular-kidney-metabolic health: a scientific statement from the American heart association. *Circulation* 2023;148:1982–2004.
9 Carbone A, Al Salhi Y, Tasca A, *et al*. Obesity and kidney stone disease: a systematic review. *Minerva Urol Nefrol* 2018;70:393–400.
10 Borghi L, Meschi T, Guerra A, *et al*. Essential arterial hypertension and stone disease. *Kidney Int* 1999;55:2397–406.
11 Losito A, Nunzi EG, Covarelli C, *et al*. Increased acid excretion in kidney stone formers with essential hypertension. *Nephrol Dial Transplant* 2009;24:137–41.
12 Rule AD, Lieske JC, Pais VM. Management of kidney stones in 2020. *JAMA* 2020;323:1961–2.
13 Huang L, Hu J, Xue C, *et al*. Vascular calcification on the risk of kidney stone: a meta-analysis. *Ren Fail* 2023;45:2183727.
14 Weinberg AE, Patel CJ, Chertow GM, *et al*. Diabetic severity and risk of kidney stone disease. *Eur Urol* 2014;65:242–7.
15 Larqué E, Labayen I, Flodmark C-E, *et al*. From conception to infancy - early risk factors for childhood obesity. *Nat Rev Endocrinol* 2019;15:456–78.
16 Longo M, Zatterale F, Naderi J, *et al*. Adipose tissue dysfunction as determinant of obesity-associated metabolic complications. *Int J Mol Sci* 2019;20:2358.
17 Eisner BH, Porten SP, Bechis SK, *et al*. Diabetic kidney stone formers excrete more oxalate and have lower urine ph than nondiabetic stone formers. *Journal of Urology* 2010;183:2244–8.
18 Sakhaee K, Adams-Huet B, Moe OW, *et al*. Pathophysiologic basis for normouricosuric uric acid nephrolithiasis. *Kidney Int* 2002;62:971–9.
19 Torricelli FCM, De S, Gebreselassie S, *et al*. Type-2 diabetes and kidney stones: impact of diabetes medications and glycemic control. *Urology* 2014;84:544–8.
20 Wollin DA, Skolarikos A, Preminger GM. Obesity and metabolic stone disease. *Curr Opin Urol* 2017;27:422–7.
21 Obesity and weight gain increase risk of kidney stones. *Mayo Clin Womens Healthsource* 2005;9:3.
22 Torricelli FCM, De SK, Gebreselassie S, *et al*. Dyslipidemia and kidney stone risk. *J Urol* 2014;191:667–72.
23 Masterson JH, Woo JR, Chang DC, *et al*. Dyslipidemia is associated with an increased risk of nephrolithiasis. *Urolithiasis* 2015;43:49–53.
24 Inci M, Demirtas A, Sarli B, *et al*. Association between body mass index, lipid profiles, and types of urinary stones. *Ren Fail* 2012;34:1140–3.
25 Chang C-W, Ke H-L, Lee J-I, *et al*. Metabolic syndrome increases the risk of kidney stone disease: a cross-sectional and longitudinal cohort study. *J Pers Med* 2021;11:1154.
26 Ye Z, Wu C, Xiong Y, *et al*. Obesity, metabolic dysfunction, and risk of kidney stone disease: a national cross-sectional study. *Aging Male* 2023;26:2195932.
27 Rahman IA, Nusaly IF, Syahrir S, *et al*. Association between metabolic syndrome components and the risk of developing nephrolithiasis: A systematic review and bayesian meta-analysis. *F1000Res* 2021;10:104.
28 Lee Y-C, Huang S-P, Juan Y-S, *et al*. Impact of metabolic syndrome and its components on kidney stone in aging Taiwanese males. *Aging Male* 2016;19:197–201.
29 Association of metabolic syndrome traits and severity of kidney stones: results from a nationwide survey on urolithiasis in Japan - PubMed, Available: https://pubmed.ncbi.nlm.nih.gov/23433467/
30 Stepanova N. Oxalate homeostasis in non-stone-forming chronic kidney disease: a review of key findings and perspectives. *Biomedicines* 2023;11:1654.
31 Perinpam M, Enders FT, Mara KC, *et al*. Plasma oxalate in relation to eGFR in patients with primary hyperoxaluria, enteric hyperoxaluria and urinary stone disease. *Clin Biochem* 2017;50:1014–9.
32 Waikar SS, Srivastava A, Palsson R, *et al*. Association of urinary oxalate excretion with the risk of chronic kidney disease progression. *JAMA Intern Med* 2019;179:542–51.
33 Uribarri J. Chronic kidney disease and kidney stones. *Curr Opin Nephrol Hypertens* 2020;29:237–42.
34 Uribarri J, Oh MS, Pak CY. Renal stone risk factors in patients with type IV renal tubular acidosis. *Am J Kidney Dis* 1994;23:784–7.
35 Bao D, Zhang H, Wang J, *et al*. Determinants on urinary excretion of oxalate and other key factors related to urolithiasis among patients with chronic kidney disease: a single center study. *Urolithiasis* 2023;51:88.
36 Rule AD, Roger VL, Melton LJ 3rd, *et al*. Kidney stones associate with increased risk for myocardial infarction. *J Am Soc Nephrol* 2010;21:1641–4.
37 Kim SY, Bang WJ, Min C, *et al*. Association of nephrolithiasis with the risk of cardiovascular diseases: a longitudinal follow-up study using a national health screening cohort. *BMJ Open* 2020;10:e040034.

38 Reiner AP, Kahn A, Eisner BH, *et al*. Kidney stones and subclinical atherosclerosis in young adults: the CARDIA study. *J Urol* 2011;185:920–5.
39 Hsi RS, Spieker AJ, Stoller ML, *et al*. Coronary artery calcium score and association with recurrent nephrolithiasis: the multi-ethnic study of atherosclerosis. *J Urol* 2016;195:971–6.
40 Devarajan A. Cross-talk between renal lithogenesis and atherosclerosis: an unveiled link between kidney stone formation and cardiovascular diseases. *Clin Sci (Lond)* 2018;132:615–26.
41 Bargagli M, Moochhala S, Robertson WG, *et al*. Urinary metabolic profile and stone composition in kidney stone formers with and without heart disease. *J Nephrol* 2022;35:851–7.
42 Hamano S, Nakatsu H, Suzuki N, *et al*. Kidney stone disease and risk factors for coronary heart disease. *Int J Urol* 2005;12:859–63.
43 Patel ND, Ward RD, Calle J, *et al*. Vascular disease and kidney stones: abdominal aortic calcifications are associated with low urine pH and hypocitraturia. *J Endourol* 2017;31:956–61.
44 Trimarco V, Izzo R, Pacella D, *et al*. Increased prevalence of cardiovascular-kidney-metabolic syndrome during COVID-19: A propensity score-matched study. *Diabetes Res Clin Pract* 2024;218:111926.
45 Sebastian SA, Padda I, Johal G. Cardiovascular-Kidney-Metabolic (CKM) syndrome: A state-of-the-art review. *Curr Probl Cardiol* 2024;49:102344.
46 Shaito A, Aramouni K, Assaf R, *et al*. Oxidative stress-induced endothelial dysfunction in cardiovascular diseases. *Front Biosci (Landmark Ed)* 2022;27:105.
47 Strohmaier WL, Wrobel BM, Schubert G. Overweight, insulin resistance and blood pressure (parameters of the metabolic syndrome) in uric acid urolithiasis. *Urol Res* 2012;40:171–5.
48 Khan SR. Crystal-induced inflammation of the kidneys: results from human studies, animal models, and tissue-culture studies. *Clin Exp Nephrol* 2004;8:75–88.
49 Yencilek E, Sarı H, Yencilek F, *et al*. Systemic endothelial function measured by flow-mediated dilation is impaired in patients with urolithiasis. *Urolithiasis* 2017;45:545–52.