Long-term trends in the prevalence of cardiovascular-kidney-metabolic syndrome in South Korea, 2011–2021: a representative longitudinal serial study

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Summary

Background The American Heart Association recently introduced a new framework, known as cardiovascular-kidney-metabolic (CKM) syndrome, aimed at the early prevention of cardiovascular disease. However, this syndrome has not been studied extensively outside of the United States. Thus, this study aimed to examine the long-term trends in CKM syndrome and its associated demographic features in South Korea.

Methods This nationwide, cross-sectional study analyzed data from 61,106 Korean adults aged ≥20 years using the Korea National Health and Nutrition Examination Survey from 2011 to 2021. CKM syndrome was defined using the PREVENT equations, categorizing individuals into five stages (0–4). Age-standardized prevalence rates, annual percent changes (APC), and sociodemographic disparities were analyzed using multinomial logistic regression and Joinpoint regression.

Findings Among the 61,106 participants (50.4% females [95% CI, 50.0–50.8%] and 49.6% males [95% CI, 49.2–50.0%]), stage 2 CKM syndrome was the most prevalent (43.4% [42.9–43.9]), followed by stages 1 (25.4% [25.0–25.8]), 0 (21.1% [20.7–21.6]), 3 (7.3% [7.0–7.5]), and 4 (2.8% [2.6–2.9]). From 2011 to 2021, advanced stages showed significant increases (APC for stage 4: 3.2%; 95% CI, 1.5–5.2), while stage 0 declined (APC: −1.9%; 95% CI, −3.8 to 0.0). Advanced stages were more common among vulnerable subgroups, including males, older adults, rural residents, smokers, drinkers, individuals with obesity, lower education levels, and lower household incomes.

Interpretation This is the first study to investigate the long-term prevalence of CKM syndrome based on stages at the national level in an Asian population. Our findings emphasize the urgent need for tailored public health strategies targeting metabolic risk factors, particularly in vulnerable subgroups, to prevent progression to advanced CKM stages.

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Keywords: Cardiovascular-kidney-metabolic syndrome; Prevalence; South Korea; Trend

Research in context

Evidence before this study

In 2023, the American Heart Association (AHA) introduced the cardiovascular-kidney-metabolic (CKM) syndrome framework, emphasizing the interplay between cardiovascular, renal, and metabolic health. This framework aims to enhance strategies for risk stratification, prevention, and management of these interrelated conditions. A PubMed search was conducted from database inception to August 30, 2024, using the terms "CKM syndrome" or "cardiovascular-kidney-metabolic syndrome" without language restrictions. Previous research has primarily focused on multi-ethnic cohorts in the United States, with limited representation of ethnic groups such as those from the Asia–Pacific region. No studies have investigated CKM syndrome prevalence trends or demographic disparities in non-U.S. populations. This study addresses these gaps by examining CKM syndrome trends and sociodemographic disparities in South Korea.

Added value of this study

This is the first study to investigate CKM syndrome prevalence by stage in an Asian population using nationally representative data from the Korea National Health and Nutrition Examination Survey (KNHANES) spanning 2011–2021. CKM syndrome was categorized into five stages (0–4) based on the AHA's PREVENT equations. Stage 2 was the most prevalent (43.4%), followed by stages 1 (25.4%), 0 (21.1%), 3 (7.3%), and 4 (2.8%). Over the 11 years, advanced stages (3 and 4) increased significantly (e.g., stage 4 annual percent change [APC]: 3.2%; 95% CI, 1.5–5.2), while early stages such as stage 0 declined (APC, −1.9%; 95% CI, −3.8 to 0.0). Vulnerable subgroups, including males, older adults, rural residents, smokers, drinkers, and individuals with obesity, lower education, and lower income, exhibited higher prevalence of advanced stages.

Implications of all the available evidence

This study fills a critical gap in understanding CKM syndrome outside of the U.S., especially in an Asian context. The worsening CKM health and increasing prevalence of advanced stages underscore the need for targeted interventions. Tailored strategies addressing metabolic risk factors like hypertriglyceridemia, hypertension, diabetes, obesity, and alcohol use are vital. Addressing social determinants such as income and education disparities is equally crucial to mitigating CKM syndrome progression in vulnerable subgroups.

Beyond providing foundational data for the Asia–Pacific region, this study demonstrates the global relevance of the AHA's CKM framework. Future research should evaluate these findings in other regions, assess the impact of early-stage interventions, and explore integrated cardiometabolic care strategies. Public health campaigns and community programs focused on behavioral modifications, as outlined in the AHA's Life's Essential 8 framework, are essential to curbing CKM syndrome progression. These findings call for equitable, evidence-based approaches to CKM syndrome management at all stages.

Introduction

Cardiovascular diseases (CVDs) remain a leading cause of death globally, and the associated health and economic costs are projected to rise significantly in the future.[1–4] Recently, the frequent coexistence of CVD, chronic kidney disease (CKD), and metabolic risk factors such as type 2 diabetes mellitus (DM), hypertension, and dyslipidemia has highlighted significant health challenges.[5,6] Poor cardiovascular-kidney-metabolic (CKM) health has profound implications for clinical outcomes, particularly increasing the risk of cardiovascular morbidity and premature mortality.[5] It influences atherogenesis, vascular integrity, hemostasis, myocardial function, and cardiac conduction, thereby contributing to the development of heart failure (HF), ischemic heart disease, stroke, atrial fibrillation, sudden cardiac death, and peripheral artery disease.[5,6] Consequently, there is a pressing need for new approaches to manage risk factors and reduce the burden of CVDs.

In 2023, the American Heart Association (AHA) introduced a novel framework called CKM syndrome, which encompasses interrelations among these conditions. This framework aims to enhance multidisciplinary strategies for risk stratification, prevention, and management of these disorders.[5] A key feature of this framework is the Predicting Risk of Cardiovascular Disease EVENT (PREVENT) equations, which estimate an individual's 10-year risk of CVD using readily available clinical variables such as age, blood pressure, and cholesterol levels. By excluding race as a factor, the equations ensure equitable application across populations.[7] While research on the prevalence of CKM syndrome has primarily been conducted in the United States, these studies predominantly focus on multi-ethnic populations and include limited data on specific ethnic groups, such as Asian individuals. For example, Asian Americans accounted for only 5.6% of the U.S. study population.[8,9] The unique status of South Korea as a predominantly single-ethnic nation provides an optimal setting to examine the prevalence of CKM syndrome specifically within the Asian population. Although the prevalence of metabolic risk factors, CKD, and clinical CVD is well-documented globally, CKM syndrome, encompasses these conditions.

Therefore, this study aimed to examine changes in the prevalence of CKM syndrome over 11 years and investigate the social determinants of health using nationally representative data collected from 2011 to 2021. The results of this study are expected to improve the screening, prevention, and management of CKM risk factors across an individual's life, thereby preventing the syndrome's progression to advanced stages.

Methods

Study design and population

This study analyzed data from the Korea National Health and Nutrition Examination Survey (KNHANES), conducted by the Korea Disease Control and Prevention Agency (KDCA) from 2011 to 2021.[10] The KNHANES employed a two-stage stratified cluster sampling design, stratified by administrative regions (provinces), housing types, and demographic characteristics, to ensure national representativeness.[11] During the COVID-19 pandemic, data collection methods were adapted to maintain continuity, with remote interviews replacing face-to-face household interviews during temporary suspensions.[12] Despite these challenges, the survey maintained a high completion rate, displaying methodological resilience.[12] To address potential biases from nonresponse and unequal sampling probabilities, post-stratification weights were applied using inverse probability weighting, aligning the survey data with population control totals (Supplementary Methods 1.1).

The dataset included a range of demographic variables, such as sex, age group, region of residence, body mass index (BMI), educational background, household income, smoking status, and drinking status. It also encompassed detailed information on various disease statuses and laboratory measurements. Given that older adults are the primary risk group for CKM syndrome, this study focused on long-term prevalence trends within a nationally representative sample of 61,106 individuals aged 20 years or older in South Korea.

The research protocol was approved by the Institutional Review Boards of the KDCA (2007-02CON-04-P, 2008-04EXP-01-C, 2009-01CON-03-2C, 2010-02CON-21-C, 2011-02CON-06-C, 2012-01EXP-01-2C, 2013-07CON-03-4C, 2013-12EXP-035C) in compliance with the local regulations specified in Article 2, Paragraph 1 of the Bioethics and Safety Act and Article 2, Paragraph 2, Item 1 of its Enforcement Regulation, as mandated by the Korean government. All participants provided written informed consent before participation. Additionally, KNHANES data are publicly accessible and serve as a valuable resource for various epidemiological studies (https://knhanes.kdca.go.kr/knhanes/main.do).[13] This study was conducted in accordance with the principles of the Declaration of Helsinki.

Handling missing data and multiple imputation

This study assessed missing data in predictor variables from 2011 to 2021. Variables with less than 5% missing data were excluded.[14] For the remaining missing data, multiple imputation by chained equations (MICE) was applied, assuming data were missing at random. MICE generated five imputed datasets, iteratively refining estimates to minimize bias and preserve variable relationships. This method effectively addressed missing data, enhancing the dataset's overall quality and reliability (Supplementary Methods 1.2).

Covariate definitions

Eight covariates representing participant characteristics were included to examine their association with CKM syndrome. These covariates comprised age (treated as a continuous variable for detailed analysis),[15] sex, region of residence (urban and rural),[16] body mass index (BMI) categories based on Asian-Pacific guidelines (underweight: <18.5 kg/m^2, normal: 18.5–22.9 kg/m^2, overweight: 23.0–24.9 kg/m^2, and obese: ≥25.0 kg/m^2),[17,18] educational background (high school or lower and college or higher), household income (low, lower-middle, upper-middle, and high), smoking status (smoker and non-smoker), and drinking (drinker and non-drinker). The variable of the region of residence was classified into two categories: urban (Seoul, Busan, Daegu, Incheon, Gwangju, Daejeon, Ulsan, Sejong, and Gyeonggi) and rural (Gangwon, Chungbuk, Chungnam, Jeonbuk, Jeonnam, Gyeongbuk, Gyeongnam, and Jeju).[16] Household income was divided into quartiles based on standardized income data from the KNHANES sample households and the population.[19–21] These covariates were assessed as potential contributing factors to CKM syndrome.

Definition of cardiovascular-kidney-metabolic syndrome

CKM syndrome was categorized into five stages based on guidelines provided by the AHA.[5] This classification reflects the complex interplay of cardiovascular, renal, and metabolic risk factors, which result in multiorgan dysfunction and a high incidence of cardiovascular outcomes.

- Stage 0: Individuals with no evidence of CKD, no typical risk factors, a normal BMI (<23 kg/m^2), waist circumference (<80 cm in women and <90 cm in men), and no metabolic risk factors or symptoms of CKD.
- Stage 1: Early risk factors such as BMI ≥23 kg/m^2 or waist circumference ≥80 (women) or ≥90 cm (men), indicating potential metabolic changes like prediabetes.
- Stage 2: Presence of CKD or clear metabolic risk factors, including hypertriglyceridemia, hypertension, metabolic syndrome, or diabetes.

- Stage 3: Subclinical CVD or severe CKD, identified by a predicted 10-year total CVD risk of ≥20% using the PREVENT equations.
- Stage 4: Clinically approved CVDs (e.g., coronary heart disease, HF, stroke) or severe CKD with additional risk factors such as excess/dysfunctional adiposity.

The 10-year predicted risk model for CVD used the 'AHA prevent' package provided by the AHA, which implements the PREVENT equations within R software to predict the 10-year risk of total CVD, arteriosclerotic cardiovascular disease (ASCVD), and HF.[5,22] These equations reflect the interactions between the cardiovascular system, CKD, and metabolic health and have been adapted as the basis for the stage 3 classification, which is critical to more accurately assess the long-term risk of CVDs and optimize prevention and management strategies for individual patients. Stages 3 or 4 were defined as advanced CKM syndrome stages because they identify individuals with or at a high risk of CVD. A more detailed definition of the CKM syndrome stages as defined in our study is provided in Supplementary Methods 1.3.

Statistical analysis

Trends in prevalence between 2011 and 2021 were analyzed using age-standardized rates. Annual Percent Changes (APC) were calculated, and statistical significance was assessed using a Monte Carlo Permutation test ($P < 0.05$).[23] The association between age and CKM stage prevalence was analyzed using linear, polynomial, and B-spline regression.[24] Initial analyses indicated patterns suggestive of non-linearity, prompting the use of second-degree polynomial regression, which outperformed linear regression based on a lower mean squared error.[25] B-spline regression with three knots was subsequently applied to capture more complex non-linear trends, modeling dispersed prevalence data within a generalized linear model using a Tweedie distribution.[26] Confidence intervals were visualized around the trend lines to represent the uncertainty in the estimates (Supplementary Methods 1.4 and 1.5).

Associations between predictor variables and CKM syndrome stages (0–4) were analyzed using multinomial and multivariate logistic regression.[27] Survey design features, including stratification, clustering, and sampling weights, were incorporated to ensure representativeness and accuracy. Proportions and prevalence estimates, along with their 95% confidence intervals, were calculated using survey-weighted methods that account for the complex sampling design of the KNHANES. Predictor variables were categorized based on established guidelines or prior studies where applicable, while age was treated as a continuous variable and modeled using regression splines to account for potential non-linear relationships.

Multinomial regression analyzed each stage of CKM syndrome individually, providing detailed insights into stage-specific associations, while multivariate models simultaneously evaluated covariates across all stages using the generalized logit link function.[28–30] This dual approach ensured a comprehensive understanding of the relationships between predictors and CKM syndrome stages, accounting for both individual and aggregate stage effects. Details of these methods are further elaborated in Supplementary Methods 1.6. Statistical analyses were performed using SAS software (version 9.4; SAS Institute, Cary, NC, USA), R (version 4.3.2; R Foundation, Vienna, Austria), Python (version 3.11.4; Python Software Foundation), and Joinpoint Regression Program (version 5.2.0; US National Cancer Institute, Bethesda, MD, USA) with two-tailed tests, and $P < 0.05$ were considered statistically significant.[31]

Role of the funding source

The funders played no role in the study design, data collection, data analysis, data interpretation, or manuscript writing. All authors confirm that they had full access to all the data in the study and had final responsibility to submit for publication.

Results

Among the 86,352 participants initially surveyed in the KNHANES between 2011 and 2021, 61,106 Korean adults (50.4% females [95% CI, 50.0–50.8%] and 49.6% males [95% CI, 49.2–50.0%]) were included in our final analysis. Weighted sociodemographic characteristics, including age, sex, region of residence, BMI, household income, educational background, smoking status, and drinking status are summarized in Table 1.

Fig. 1 illustrates nationwide trends in the prevalence of CKM syndrome among Korean adults from 2011 to 2021. While the prevalence of each CKM stage remained relatively stable, advanced stages showed an increasing trend. Stage 4 exhibited the most significant increase (APC: 3.2%; 95% CI, 1.5–5.2), followed by stage 3 (APC: 1.6%; 95% CI, 0.8–2.4) and stage 2 (APC: 0.7%; 95% CI, −0.2 to 1.6). In contrast, stages 1 and 0 showed decreasing trends, with APCs of −0.2% (95% CI, −1.9 to 1.4) and −1.9% (95% CI, −3.8 to 0.0), respectively.

Fig. 2 shows the age-specific prevalence of CKM syndrome stages from 2011 to 2021. The prevalence of stage 0 decreased with age, while stage 4 increased. Younger individuals were more likely to exhibit early CKM stages, whereas older populations predominantly exhibited advanced stages, with stage 3 peaking in individuals aged 50–60.

The weighted proportions of CKM syndrome stages over the study period, as well as sociodemographic disparities, are shown in Fig. 3 and Supplementary Table S1. Overall, the prevalence of CKM syndrome stages was as follows: stage 0, 21.1% (95% CI,

	Total	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Overall, n	61,106	5772	5540	5423	5284	5263	5750	5823	5653	5895	5341	5362
Age, years, median (IQR)	46 (26–62)	43 (22–60)	44 (23–62)	41 (20–58)	44 (23–62)	46 (25–62)	44 (23–61)	46 (25–62)	49 (34–63)	46 (26–63)	51 (34–64)	50 (29–66)
Sex, weighted % (95% CI)												
Male	49.6 (49.2–50.0)	49.1 (47.8–50.4)	49.4 (48.0–50.8)	49.4 (48.3–50.6)	49.2 (47.8–50.7)	49.0 (47.7–50.3)	49.8 (48.6–51.0)	49.6 (48.1–51.0)	50.2 (48.9–51.6)	49.7 (48.5–50.9)	50.2 (49.1–51.4)	49.4 (48.1–50.8)
Female	50.4 (50.0–50.8)	50.9 (49.6–52.2)	50.6 (49.2–52.0)	50.6 (49.4–51.7)	50.8 (49.3–52.2)	51.0 (49.7–52.3)	50.2 (49.0–51.4)	50.4 (49.0–51.9)	49.8 (48.4–51.1)	50.3 (49.1–51.5)	49.8 (48.6–50.9)	50.6 (49.2–51.9)
Region of residence, weighted % (95% CI)												
Urban	46.6 (45.5–47.8)	46.5 (40.3–52.8)	47.9 (41.6–54.3)	47.0 (40.5–53.5)	46.5 (40.1–53.0)	46.7 (40.2–53.3)	47.2 (41.1–53.3)	47.3 (41.1–53.5)	47.4 (43.2–51.6)	45.5 (38.8–52.2)	45.3 (38.2–52.4)	45.8 (39.0–52.6)
Rural	53.4 (52.2–54.5)	53.5 (47.2–59.7)	52.1 (45.7–58.4)	53.0 (46.5–59.5)	53.5 (47.0–59.9)	53.3 (46.7–59.8)	52.8 (46.7–58.9)	52.7 (46.5–58.9)	52.6 (48.4–56.8)	54.5 (47.8–61.2)	54.7 (47.6–61.8)	54.2 (47.4–61.0)
BMI group[a], weighted % (95% CI)												
Underweight	4.1 (3.9–4.3)	4.8 (4.0–5.6)	4.7 (4.1–5.4)	4.3 (3.6–5.0)	4.4 (3.7–5.0)	4.3 (3.6–5.0)	3.8 (3.1–4.4)	3.8 (3.2–4.4)	3.4 (2.8–4.0)	4.0 (3.4–4.7)	3.5 (2.8–4.1)	4.0 (3.3–4.6)
Normal	35.9 (35.4–36.4)	36.7 (35.0–38.3)	36.8 (34.9–38.7)	38.1 (36.5–39.7)	38.4 (36.7–40.0)	35.3 (33.8–36.9)	35.0 (33.5–36.6)	36.0 (34.5–37.5)	36.6 (35.1–38.0)	36.0 (34.4–37.7)	32.0 (30.5–33.6)	34.2 (32.6–35.8)
Overweight	23.8 (23.4–24.2)	24.8 (23.6–26.0)	23.5 (22.1–24.8)	23.8 (22.7–25.0)	23.8 (22.3–25.2)	24.3 (22.9–25.7)	24.0 (22.7–25.3)	23.4 (22.1–24.6)	23.3 (22.0–24.6)	23.9 (22.6–25.2)	24.1 (22.8–25.3)	22.8 (21.4–24.3)
Obese	36.3 (35.8–36.8)	33.8 (32.0–35.5)	35.0 (33.2–36.8)	33.8 (32.2–35.3)	33.5 (31.8–35.2)	36.1 (34.5–37.8)	37.2 (35.4–39.0)	36.8 (35.1–38.4)	36.7 (35.2–38.3)	36.1 (34.5–37.6)	40.4 (38.8–42.1)	39.0 (37.2–40.8)
Household income, weighted % (95% CI)												
Low	15.2 (14.7–15.8)	15.9 (14.1–17.7)	14.9 (12.9–16.9)	16.4 (14.1–18.7)	14.9 (12.9–16.9)	15.6 (13.6–17.5)	16.3 (14.1–18.5)	15.4 (13.2–17.5)	15.3 (13.4–17.2)	15.1 (13.2–17.0)	14.3 (12.2–16.4)	13.9 (11.9–15.9)
Lower-middle	24.5 (23.9–25.1)	28.4 (26.2–30.5)	26.9 (24.3–29.5)	26.2 (24.0–28.4)	25.0 (22.6–27.4)	23.1 (20.8–25.3)	23.3 (21.4–25.3)	23.0 (21.0–25.0)	24.4 (22.3–26.6)	25.4 (23.2–27.6)	21.5 (19.4–23.7)	22.8 (20.7–24.9)
Upper-middle	29.3 (28.6–29.9)	29.3 (27.2–31.4)	28.7 (26.6–30.8)	27.5 (25.5–29.5)	30.3 (27.8–32.7)	30.3 (27.8–32.9)	29.3 (27.0–31.6)	29.6 (27.6–31.6)	29.4 (27.4–31.5)	27.2 (25.2–29.1)	30.0 (27.8–32.1)	30.2 (28.1–32.4)
High	31.0 (30.1–31.9)	26.4 (23.8–29.0)	29.6 (26.8–32.3)	29.9 (26.8–32.9)	29.9 (26.5–33.3)	31.0 (27.9–34.2)	31.0 (27.8–34.3)	32.0 (29.0–35.1)	30.8 (28.1–33.5)	32.3 (29.0–35.5)	34.2 (30.7–37.7)	33.1 (29.3–36.8)
Educational background, weighted % (95% CI)												
High school or lower education	48.1 (47.3–48.8)	58.1 (55.2–60.9)	55.8 (52.9–58.7)	52.8 (50.2–55.5)	48.2 (45.3–51.2)	47.7 (45.0–50.4)	47.1 (44.4–49.9)	44.3 (41.4–47.3)	45.7 (43.0–48.5)	44.0 (41.0–47.0)	42.2 (39.2–45.3)	44.4 (41.4–47.3)
College or higher education	46.6 (45.7–47.4)	40.5 (37.7–43.4)	41.2 (38.3–44.1)	43.2 (40.5–45.9)	43.5 (40.4–46.5)	43.1 (40.3–46.0)	47.3 (44.3–50.2)	49.8 (46.8–52.8)	50.1 (47.2–53.0)	50.3 (47.2–53.5)	51.4 (48.1–54.6)	50.2 (47.1–53.2)
Unknown	5.4 (5.1–5.7)	1.4 (0.9–1.8)	3.0 (2.3–3.7)	4.0 (3.2–4.7)	8.3 (7.1–9.4)	9.1 (7.8–10.5)	5.6 (4.8–6.4)	5.9 (4.7–7.1)	4.1 (3.3–5.0)	5.7 (4.7–6.6)	6.4 (5.2–7.7)	5.5 (4.5–6.4)
Smoking status, weighted % (95% CI)												
Smoker	22.0 (21.6–22.5)	26.9 (25.2–28.6)	25.6 (24.1–27.0)	24.2 (22.5–25.8)	22.9 (21.4–24.5)	21.5 (20.0–23.0)	22.3 (20.7–24.0)	20.8 (19.2–22.4)	21.6 (20.1–23.0)	20.1 (18.6–21.6)	19.4 (17.9–21.0)	18.1 (16.6–19.5)
Non-smoker	78.0 (77.5–78.4)	73.1 (71.4–74.8)	74.4 (73.0–75.9)	75.8 (74.2–77.5)	77.1 (75.5–78.6)	78.5 (77.0–80.0)	77.7 (76.0–79.3)	79.2 (77.6–80.8)	78.4 (77.0–79.9)	79.9 (78.4–81.4)	80.6 (79.0–82.1)	81.9 (80.5–83.4)

(Table 1 continues on next page)

	Total	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
(Continued from previous page)												
Drinking, weighted % (95% CI)												
Drinker	56.6 (56.0–57.1)	58.5 (56.7–60.3)	54.6 (52.8–56.4)	56.1 (54.3–57.9)	55.3 (53.5–57.2)	56.7 (55.0–58.4)	58.3 (56.5–60.1)	58.7 (57.0–60.4)	57.7 (56.0–59.4)	56.9 (55.3–58.5)	56.1 (54.2–58.0)	53.5 (51.4–55.5)
Non-drinker	32.3 (31.9–32.8)	30.3 (28.8–31.8)	32.0 (30.5–33.5)	30.0 (28.4–31.5)	30.6 (29.3–32.0)	31.1 (29.5–32.6)	30.7 (29.3–32.2)	31.2 (29.9–32.5)	33.9 (32.4–35.3)	33.1 (31.7–34.5)	35.2 (33.6–36.8)	36.9 (35.1–38.7)
Unknown	11.1 (10.8–11.4)	11.1 (9.8–12.4)	13.4 (12.2–14.6)	13.9 (12.5–15.4)	14.0 (12.6–15.4)	12.2 (11.0–13.4)	11.0 (9.8–12.2)	10.1 (9.0–11.2)	8.4 (7.4–9.4)	10.0 (9.1–11.0)	8.7 (7.6–9.8)	9.6 (8.5–10.8)

BMI, body mass index; CI, confidence interval; CKM, cardiovascular-kidney-metabolic; KNHANES, Korea National Health and Nutrition Examination Survey. [a]According to the Asian-Pacific guidelines, BMI is divided into four groups: underweight (<18.5 kg/m^2), normal (18.5–22.9 kg/m^2), overweight (23.0–24.9 kg/m^2), and obese (≥25.0 kg/m^2).

***Table 1:* Weighted baseline characteristics of Korean adults from the KNHANES between 2011 and 2021 (n = 61,106).**

20.7–21.6); stage 1, 25.4% (95% CI, 25.0–25.8); stage 2, 43.4% (95% CI, 42.9–43.9); stage 3, 7.3% (95% CI, 7.0–7.5); and stage 4, 2.8% (95% CI, 2.6–2.9). Both males and females exhibited the highest prevalence in stage 2 (48.8% and 38.1%, respectively). Advanced stages (stages 3 and 4) were more common among males (14.0%), rural residents (10.2%), individuals with obesity (BMI ≥ 25 kg/m^2; 15.7%), those in the lowest household income quartile (13.4%), those with lower educational attainment (13.5%), smokers (17.4%), and drinkers (10.8%).

The corresponding APCs for these subgroups are presented in Fig. 4 and Supplementary Table S2. For instance, males had a higher APC in stage 4 (4.0%) compared to females (1.9%), indicating a more pronounced increase in advanced stages. Individuals in stage 0 were more likely to be female and have a college or higher educational background. Stage 3 was more prevalent among males and smokers, while stage 4 was more common among individuals in the lowest household income quartile, those with a lower educational background, smokers, and drinkers.

Supplementary Figs. S2–S5 illustrate the age-specific prevalence of metabolic risk factors, including hypertriglyceridemia, hypertension, diabetes, and metabolic syndrome, across the study population. These metabolic risk factors were more prevalent in older age groups and among males. Supplementary Table S3 further provides a detailed breakdown of these factors by sexes, highlighting the significant influence of sex on the progression of CKM syndrome.

Discussion

This study is the first to investigate the long-term prevalence of CKM syndrome by stage at a national level in an Asian population from 2011 to 2021. Among the CKM stages, stage 2 was the most prevalent (43.4%), followed by stage 1 (25.4%), stage 0 (21.1%), stage 3 (7.3%), and stage 4 (2.8%). Over the study period, an increasing trend was observed in advanced stages, particularly among vulnerable subgroups, including males, older adults, rural residents, individuals with obesity (high BMI), lower education levels, lower household income, smokers, and drinkers. These findings underscore significant disparities in CKM health among vulnerable subgroups and emphasize the urgent need for tailored health interventions. Such efforts could help mitigate progression to stage 4, which corresponds to clinical cardiovascular outcomes, and reduce the overall burden of CKM syndrome.

The impact of metabolic risk factors and kidney function on CVDs has recently been discussed.[5] However, CKM syndrome, which integrates these factors, has been studied for prevalence only in the US population (n = 10,762). Our study represents the first global investigation of the social determinants of this

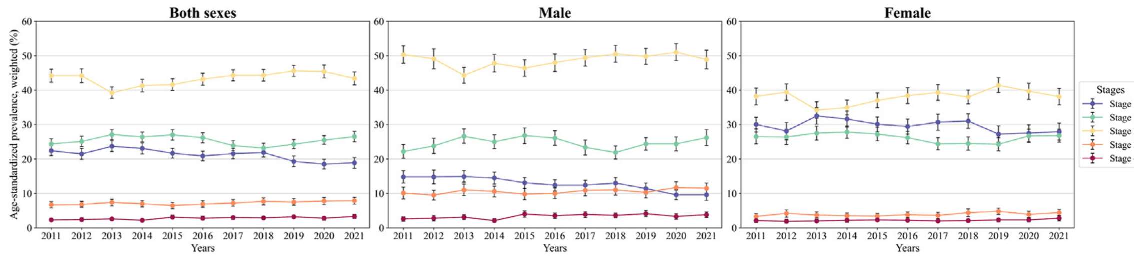

Fig. 1: Nationwide trends in the prevalence of CKM syndrome according to stage and sex among Korean adults, 2011–2021. Error bars indicate 95% confidence intervals calculated using survey-weighted methods. CKM, cardiovascular-kidney-metabolic.

syndrome, using nationally representative data from an Asian population.[8,9]

The US exhibits a low prevalence of individuals without CKM syndrome, even among young adults, indicating a high burden of risk factors for CVDs.[8] Compared to the US, this study observed a higher prevalence of individuals in stage 0 (South Korea, 21.1% vs. the US, 10.6%), particularly among younger age groups where most were classified as stage 0. In contrast, the prevalence of stage 4 was significantly lower in South Korea (2.8% vs. the U.S., 9.2%), suggesting differences in health outcomes and risk factor profiles between these populations. Additionally, the CKM stage-specific prevalence among Asians residing in the U.S. was like that observed in our study.[8,9]

During the study period (2011–2020), the US did not observe significant changes in the prevalence of each CKM syndrome stage. Although not a significant change, there was an upward trend in stages 3 and 4, potentially reflecting a growing CVD burden. The global burden of CVD study aligns with our findings that while the U.S. has a higher burden than South Korea, the increasing trend observed in South Korea underscores the urgent need for interventions targeting preventable risk factors.[1]

In addition, previous research conducted using the KNHANES data explored individual metabolic risk factors and highlighted the coexistence of comorbidities, suggesting the necessity of organizing these findings into a newly defined staging scheme.[32–34] In patients with HF and ASCVD, hypertension, DM, and dyslipidemia were common comorbidities. Among patients with CKD, DM (23.2%) and hypertension (18.3%) were prevalent comorbidities.[32–34] Therefore, identifying patients with early-stage CKM syndrome and selecting treatments with combined effects (e.g., cardioprotective antihyperglycemic agents and kidney-protective therapies with cardiovascular benefits) can prevent the progression to clinical CVD.

Metabolic risk factors damage blood vessels and lead to inflammation, insulin resistance, and atherosclerosis.[35] CKD exacerbates this by activating the renin-angiotensin-aldosterone system and causing sympathetic nervous system hyperactivity.[36] These interactions create a vicious cycle that imposes additional stress on both the heart and kidneys.[35,36]

The progression of CKM syndrome stages can largely be attributed to the cumulative effects of metabolic risk factors, such as hypertriglyceridemia, hypertension, diabetes, and metabolic syndrome.[37] These risk factors tend to be more prevalent among older adults and males, reflecting demographic disparities that contribute to the observed increases in advanced CKM stages. By accelerating vascular damage, systemic inflammation, and metabolic dysfunction, these factors create a cascade of events that exacerbate CKM syndrome progression. Addressing these risks is crucial to mitigating health disparities and slowing the advancement of CKM stages in vulnerable populations.

While the exact cause of the differences in the prevalence of CKM syndrome between countries cannot be definitively stated, genetic and cultural differences, as well as variations in health status, may significantly influence these disparities.[8] The increasing trend in the prevalence of CKM syndrome in South Korea can be attributed to the westernization of lifestyles, reduced physical activity due to increased indoor activities, and an aging population.[1,38,39] Additionally, while major metabolic risk factors have been increasing, their prevalence remains lower than that in the U.S.[40,41]

Interestingly, the prevalence of stage 3 CKM syndrome was higher among those aged 45–64 years, whereas the prevalence of stage 4 was higher and showed an increasing trend among those aged ≥65 years. Considering that the progression from metabolic syndrome to clinical CVD takes approximately 10 years, it is plausible that individuals may have transitioned from stages 3–4 during this period.[35,42]

South Korea has observed a deterioration in CKM health, highlighting the need for preventive interventions to avert future cardiovascular events and reduce cardiovascular mortality. This study enabled a better understanding of the association between CKM syndrome and different population segments, including males, older adults, urban residents, individuals with

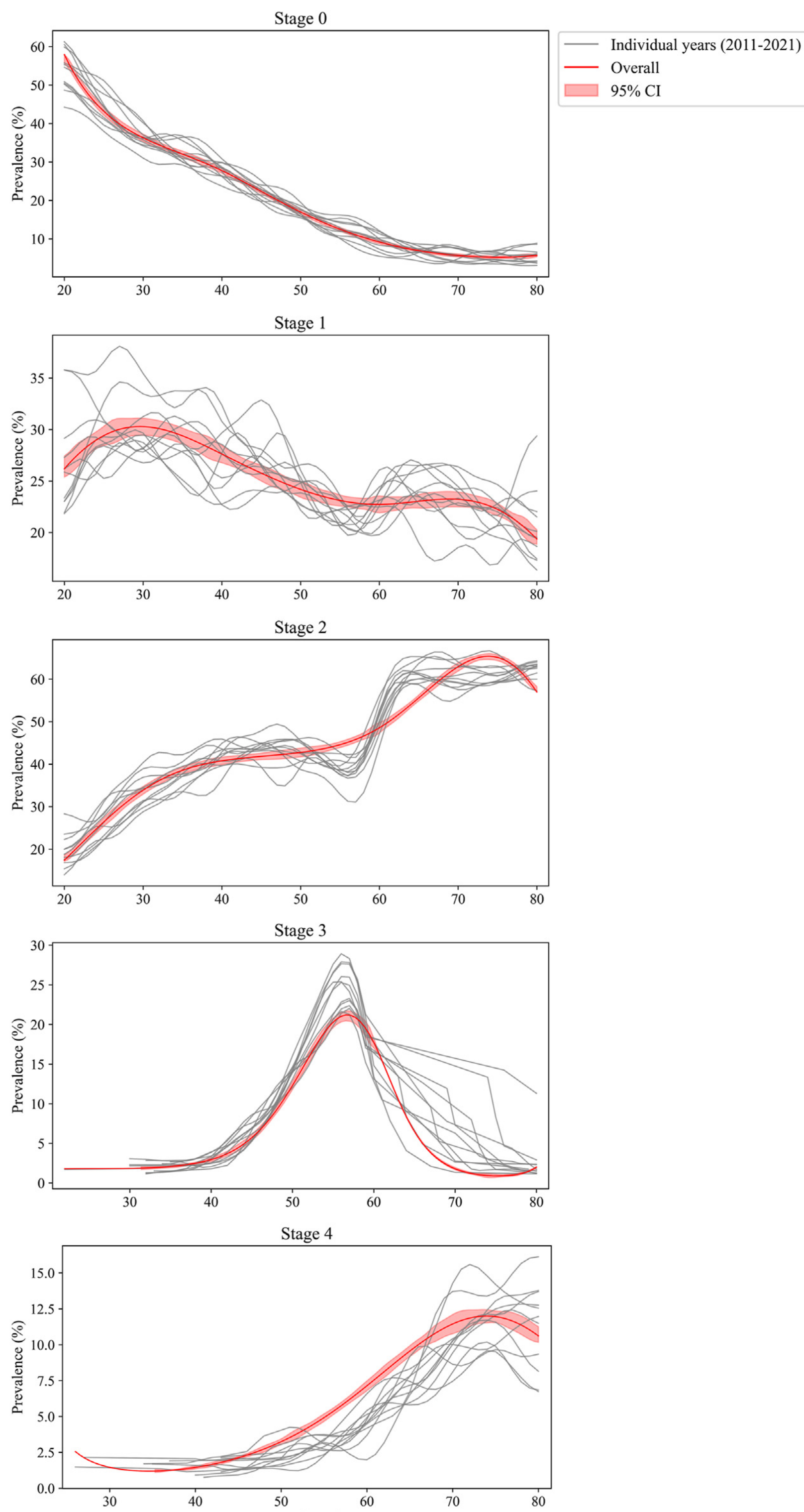

Fig. 2: Age-specific prevalence of CKM syndrome by stages, 2011–2021. CI, confidence interval; CKM, cardiovascular-kidney-metabolic.

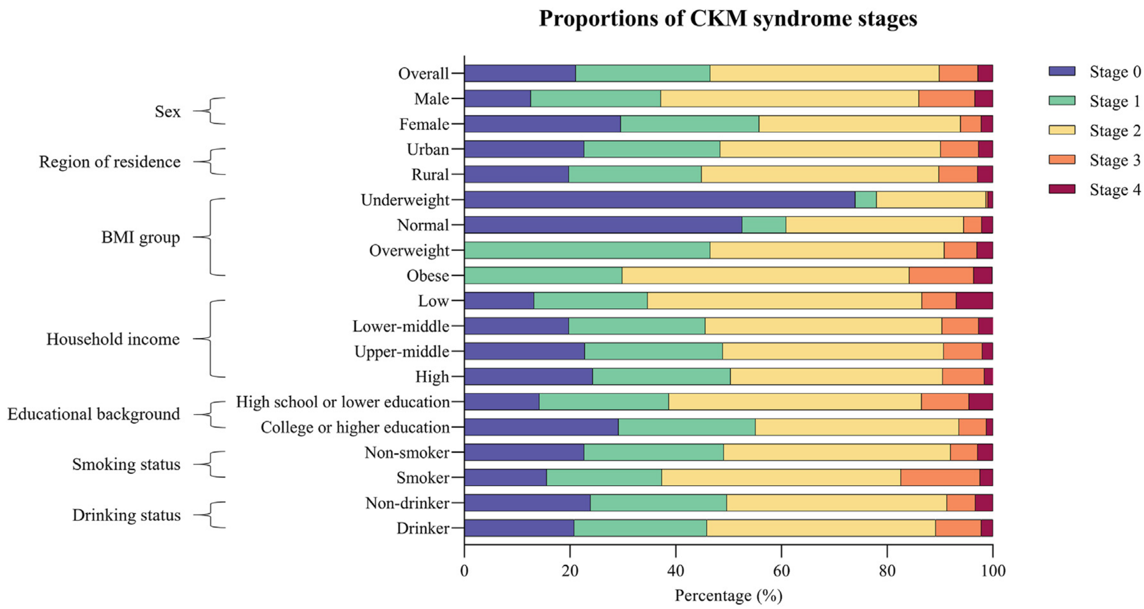

Fig. 3: Proportions of CKM syndrome stages by sociodemographic characteristics from 2011 to 2021. BMI, body mass index; CKM, cardio-vascular-kidney-metabolic.

low educational backgrounds, and those with low incomes. Raising awareness among high-risk groups provides valuable insights for public health authorities to formulate effective policies to address public health emergencies.

The new diagnostic framework for CKM syndrome facilitates the understanding that patients with metabolic risk factors or CKD are in an intermediate stage on the pathway to CVD. In the future, this framework may empower patients to assess their CVD risk and actively engage in patient-centered risk discussions, fostering shared decision-making for therapeutic strategies once acceptable risk thresholds are established in clinical guidelines.

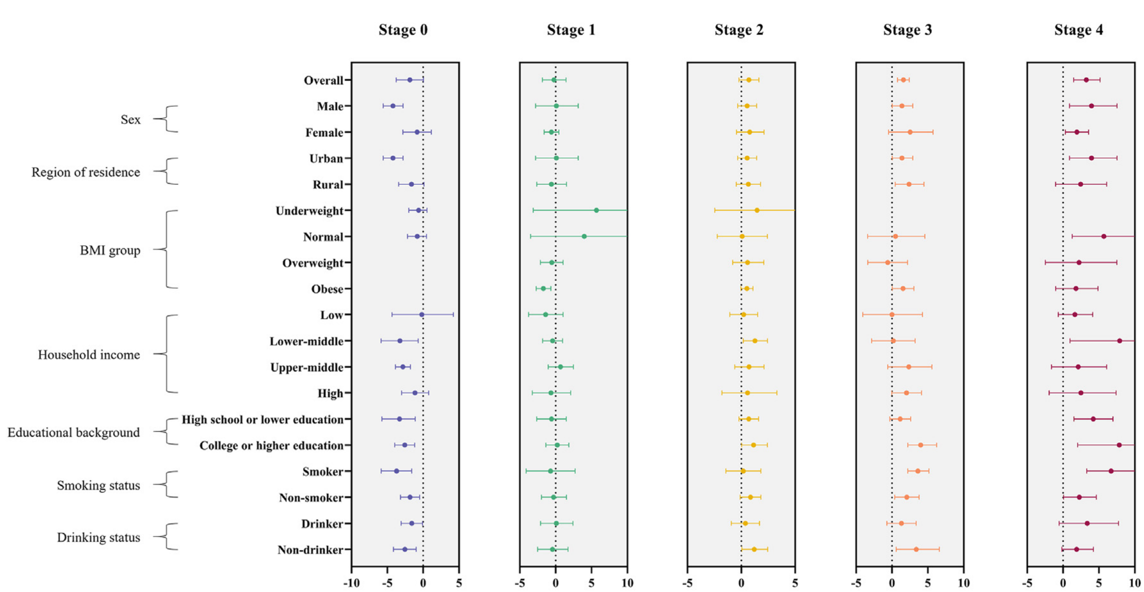

Fig. 4: Annual percent change of CKM syndrome stages by sociodemographic characteristics from 2011 to 2021. Error bars indicate 95% confidence intervals. APC, annual percent change; BMI, body mass index; CKM, cardiovascular-kidney-metabolic.

To address the progression of CKM syndrome, public health policies should prioritize interventions aligned with the AHA's Life's Essential 8 framework, which encompasses behavioral modifications such as improving diet, increasing physical activity, reducing nicotine exposure, and maintaining healthy BMI levels.[43] Care strategies that integrate these components can help improve CKM health outcomes and prevent progression to advanced stages.

Healthcare professionals play a pivotal role in therapy selection, particularly for high-risk individuals with comorbidities such as diabetes.[44] For example, integrating cardioprotective antihyperglycemic therapies with kidney-protective agents may provide dual benefits for managing CKM syndrome. These efforts should be supported by community-based health education campaigns, accessible lifestyle intervention programs, and regular risk monitoring to ensure equitable healthcare delivery across diverse population groups.

This study has certain limitations. First, our data primarily included individuals of a single race, necessitating further analyses of other populations with different races, cultures, lifestyles, and healthcare accessibilities. Although the PREVENT equation was developed using U.S.-based population cohorts, it intentionally excludes race as a predictor to avoid inequitable race-specific treatment decisions. This approach aligns with the growing consensus to remove race from clinical algorithms in medicine and supports the broader applicability of the equation. To further tailor our analysis to the Korean population, we adapted specific metrics, such as BMI, according to the Asia–Pacific guidelines. However, further validation of the PREVENT equation in diverse populations, including predominantly Asian cohorts, is needed to verify its applicability and ensure its accuracy in different contexts.

Second, only clinical characteristics available in the KNHANES dataset were assessed. Because data for CKM stage 3 (subclinical CVDs), such as subclinical ASCVD and subclinical HF, and CKM stage 4 (clinical CVDs), such as peripheral arterial disease and atrial fibrillation, were not available, stages 3 and 4 may have been underestimated. Additionally, changes in diagnostic practices or coding over time may have influenced observed trends, particularly for advanced stages like Stage 4. To mitigate this, we utilized data from the KNHANES dataset, which adheres to consistent data collection protocols. Moreover, we applied weighted analyses and visualized trends with confidence intervals to account for statistical variability and enhance data reliability.

Third, this cross-sectional study design is subject to reverse causality, as the temporal relationship between risk factors and CKM syndrome stages cannot be definitively established. Incidence-prevalence bias may also have influenced our findings, as individuals with advanced stages may be underrepresented due to higher mortality rates. Also, unmeasured confounding variables and potential inaccuracies in self-reported data, such as smoking status or household income, could introduce bias. While we applied robust statistical adjustments to mitigate these effects, the possibility of residual confounding cannot be excluded.

Despite these limitations, our study was the first outside of the US to investigate the prevalence of CKM syndrome using large-scale, long-term nationwide data. Moreover, this comparison with US-based research revealed intriguing differences attributable to national and racial factors. Additionally, this study identified social determinants of health such as region of residence, education level, household income status, and smoking status, in addition to age and sex. These factors are important when formulating effective policies to address CKM syndromes.

This is the first study to investigate the long-term prevalence of CKM syndrome by stages at the national level in an Asian population from 2011 to 2021. During the study period, the prevalence of advanced stages showed a slight increase, while the prevalence of stage 0 and stage 1 may have decreased. These trends were significantly pronounced in vulnerable subgroups, including males, older adults, rural residents, smokers, those with a high BMI, and those with lower education levels and household incomes. In conclusion, it is imperative to develop and implement equitable healthcare approaches that can prevent the progression to stages 3 and 4. Future studies should evaluate the association between early identification of and intervention in CKD syndrome and changes in the clinical burden of CVD.

Contributors

Dr. DKY had full access to all data in the study and assumes responsibility for the integrity of the data and accuracy of the data analysis. All authors approved the final version of the manuscript prior to its submission. *Study concept and design*: YY, JEL, YS, JK, and DKY; *acquisition, analysis, or interpretation of data*: YY, JEL, YS, JK, and DKY; *drafting of the manuscript*: YY, JEL, YS, JK, and DKY; *critical revision of the manuscript for important intellectual content*: all authors; *statistical analysis*: YY, JEL, YS, JK, and DKY; *study supervision*: DKY. DKY supervised the study and served as the guarantor. YY, JEL, and YS contributed equally to this study as first co-authors. DKY is the corresponding author. The corresponding author attests that all listed authors meet the authorship criteria, and that no one meeting the criteria has been omitted.

Data sharing statement

The data are available upon request. Study protocol and statistical codes: available from DKY (yonkkang@gmail.com). Dataset: available from the Korea Disease Control Agency (KDCA) through data use agreements.

Declaration of interests

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanwpc.2025.101474.

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