RESEARCH LETTER

Prevalence of Cardiovascular-Kidney-Metabolic Syndrome Stages in US Adults, 2011-2020

Cardiovascular, kidney, and metabolic (CKM) diseases are pathophysiologically interrelated,[1] have affected more than 25% of US adults between 2015-2020,[2] and were the leading causes of death in 2021.[3] In 2023, the American Heart Association introduced a novel staging construct, termed *CKM syndrome*,[1] to enhance multidisciplinary approaches to prevention, risk stratification, and management of these disorders. Based on risk factors and established disease, the stages range from 0 (no risk factors) to 4 (established cardiovascular disease [CVD]).

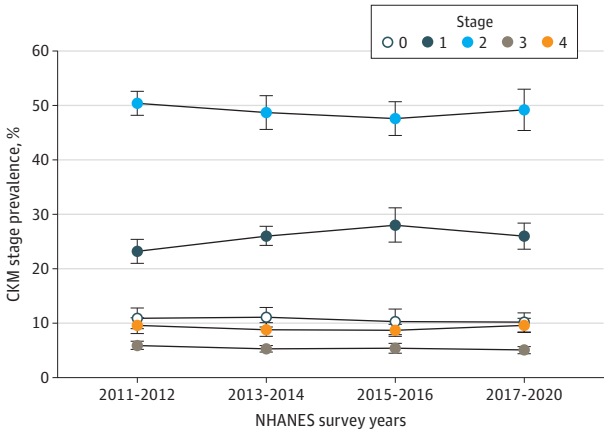
Supplemental content

Few studies have evaluated CKM syndrome stages in the US population; such data may inform health care design, research, training, and policy efforts. In this nationally representative study, we assessed the prevalence and temporal evolution of CKM syndrome stages.

Methods | We used the National Health and Nutrition Examination Survey (NHANES; 2011-March 2020). NHANES includes a nationally representative sample of the US population using a multistage probability design and incorporates interviews, physical examinations, and laboratory measurements. Response rates decreased over the study period (69.5% in 2011-2012 to 46.9% in 2017-March 2020), with survey weights adjusted for nonresponse. We included adults aged 20 years or older who underwent physical examination and fasting laboratory measurements. Missing data were infrequent (<10%). For each participant, we determined the CKM syndrome stage:[1] stage 0 (no CKM risk factors, such as hypertension), 1 (excess or dysfunctional adiposity), 2 (additional metabolic risk factors or moderate- or high-risk chronic kidney disease), 3 (very high-risk chronic kidney disease or high predicted 10-year CVD risk),[4] or 4 (established CVD, such as coronary artery disease). Detailed descriptions of stage definitions, adapted to data available in NHANES, are shown in the eAppendix in the Supplement 1. Advanced CKM syndrome stages were defined as stages 3 or 4 because these identify individuals with or at high risk of CVD.

Temporal trends between 2011-2012 and 2017-March 2020 were assessed by CKM stage and for advanced stages using linear regression. The prevalence of advanced stages also was compared among subgroups (age, sex, race, and ethnicity) using log-binomial regression. All estimates were age-adjusted to the 2010 US Census. Analyses were conducted with R version 4.2.2 (R Foundation). A 2-sided significance threshold of $P < .05$ was used. The Mass General Brigham Institutional Review Board exempted this study because NHANES data are deidentified.

Figure. Temporal Trends of Cardiovascular-Kidney-Metabolic Syndrome Stages Among US Adults, 2011-March 2020



Cardiovascular-kidney-metabolic (CKM) stage estimates (95% CI whiskers) are presented by the National Health and Nutrition Examination Survey (NHANES) cycle. All estimates are age-adjusted to the 2010 census and are nationally representative of the US adult population 20 years or older by use of NHANES survey weights. *P* for trend was >.05 for each stage.

Results | The final study population included 10 762 adults. The mean (SD) age was 47.3 (17.0) years; 51.8%, women; 5.6%, Asian American; 11.5%, Black; 15.3%, Hispanic; 64.4%, White, and 3.3%, other races and ethnicities.

Between 2011 and 2020, 10.6% (95% CI, 9.6%-11.6%) of US adults met criteria for stage 0, 25.9% (95% CI, 24.6%-27.1%) for stage 1, 49.0% (95% CI, 47.4%-50.5%) for stage 2, 5.4% (95% CI, 5.1%-5.8%) for stage 3, and 9.2% (95% CI, 8.5%-9.8%) for stage 4. The prevalence of each stage did not significantly change over the study period (**Figure**; *P* for trend >.05 for each stage). Advanced stages occurred in 14.6% (95% CI, 13.9%-15.3%) and did not significantly change over the study period (*P* for trend = .79).

Adults 65 years or older were more likely to have advanced stages than were those aged 45 through 64 years (55.3% vs 10.7%, $P < .001$) and those aged 20 through 44 years (55.3% vs 2.1%, $P < .001$; **Table**). Only 18.2% (95% CI, 16.5%-19.9%) of adults aged 20 through 44 years had stage 0. Compared with women, men were more likely to have advanced stages (16.9% vs 12.4%; adjusted prevalence ratio [PR], 1.36; 95% CI, 1.24-1.49; $P < .001$). Compared with White adults, Black adults were significantly more likely to have advanced stages (18.9% vs 13.8%; adjusted PR, 1.38; 95% CI, 1.24-1.55; $P < .001$).

Discussion | Almost 90% of US adults met criteria for CKM syndrome (stage 1 or higher) and 15% met criteria for advanced stages, neither of which improved between 2011 and 2020. The lack of progress, in part, may reflect concomitant improvement and worsening of different risk factors over time.[2,5] Substantial between-subgroup differences

Table. Prevalence of Cardiovascular-Kidney-Metabolic Syndrome Stages Among US Adults by Age, Sex, Race, and Ethnicity, 2011-March 2020

Characteristic	Unweighted No. (%)	Adults 20 years or older by cardiovascular-kidney-metabolic syndrome stage[a] Prevalence, % (95% CI) Stage 0 (n = 867)	Stage 1 (n = 2450)	Stage 2 (n = 5393)	Stage 3 (n = 825)	Stage 4 (n = 1227)	Advanced CKM syndrome (Stages 3 or 4) Prevalence, % (95% CI)	Prevalence ratio (95% CI)[b]	*P* value
Total	10 762	10.6 (9.6-11.6)	25.9 (24.6-27.1)	49.0 (47.4-50.5)	5.4 (5.1-5.8)	9.2 (8.5-9.8)	14.6 (13.9-15.3)		
Age group, y[c]									
20-44	4373	18.2 (16.5-19.9)	36.6 (34.8-38.4)	43.2 (41.0-45.3)	0.1 (0.1-0.2)	1.9 (1.4-2.4)	2.1 (1.6-2.6)	1 [Reference]	
45-64	3838	5.4 (4.1-6.7)	21.2 (19.1-23.3)	62.7 (60.2-65.3)	1.4 (1.0-1.8)	9.2 (8.1-10.4)	10.7 (9.5-11.9)	5.14 (4.05-6.53)	<.001
≥65	2551	1.3 (0.9-1.7)	7.2 (5.8-8.7)	36.2 (34.2-38.2)	27.4 (25.4-29.3)	27.9 (25.8-30.0)	55.3 (53.2-57.4)	26.74 (20.76-34.45)	<.001
Sex[d]									
Men	5200	7.9 (6.7-9.1)	24.9 (23.0-26.8)	50.3 (48.1-52.5)	6.5 (6.0-7.0)	10.4 (9.4-11.4)	16.9 (15.9-17.9)	1.36 (1.24-1.49)	<.001
Women	5562	13.1 (11.8-14.5)	26.8 (25.3-28.2)	47.7 (45.9-49.4)	4.4 (3.9-4.9)	8.0 (7.1-8.9)	12.4 (11.5-13.4)	1 [Reference]	
Race and ethnicity[e]									
Asian	1365	12.2 (10.4-13.9)	26.2 (23.7-28.7)	50.2 (47.4-53.1)	6.5 (5.2-7.7)	4.9 (3.4-6.4)	11.4 (10.0-12.7)	0.83 (0.72-0.96)	.02
Black	2382	6.7 (5.4-8.0)	23.9 (21.7-26.1)	50.5 (48.2-52.7)	7.5 (6.5-8.6)	11.4 (10.1-12.7)	18.9 (17.5-20.3)	1.38 (1.24-1.55)	<.001
Hispanic	2599	6.5 (5.1-7.8)	26.9 (24.9-28.8)	52.0 (50.0-54.1)	7.2 (6.4-8.1)	7.5 (6.4-8.5)	14.7 (13.6-15.7)	1.06 (0.96-1.17)	.28
White	4017	12.2 (10.8-13.5)	26.1 (24.4-27.9)	47.9 (45.8-50.1)	4.6 (4.1-5.0)	9.2 (8.2-10.2)	13.8 (12.7-14.8)	1 [Reference]	
Other race or ethnicity	399	10.1 (6.9-13.4)	22.4 (17.5-27.2)	47.4 (42.6-52.3)	4.6 (2.9-6.2)	15.5 (11.6-19.4)	20.1 (16.3-23.8)	1.46 (1.19-1.78)	.001

[a] Prevalence estimates were age-adjusted to the 2010 US census and nationally representative of the US adult population 20 years or older by use of National Health and Nutrition Examination Survey (NHANES) survey weights. Only adults in the NHANES fasting subsample were included.

[b] Prevalence ratios of advanced cardiovascular-kidney-metabolic syndrome (stages 3 or 4) by subgroup were age and sex adjusted as appropriate.

[c] Age was based on self-report.

[d] Sex was based on self-report.

[e] Race and ethnicity were based on self-report according to categories prespecified in NHANES survey questions. Asian, Black, and White adults only included participants identifying as non-Hispanic. Hispanic includes individuals identifying as Mexican American or non-Mexican Hispanic. Other race or ethnicity included American Indian or Alaska Native, Native Hawaiian or Pacific Islander, multiple races or ethnicities, or unknown. Race and ethnicity were assessed in this analysis to evaluate whether prevalence of cardiovascular-kidney-metabolic stages varied across these groups.

in advanced stages were observed, with older age, men, and Black adults at increased risk.

Study limitations include that established CVD was based on self-report. Also, some data recommended to define advanced stages, including cardiac biomarkers, echocardiography, coronary angiography, cardiac computed tomography, atrial fibrillation, and peripheral artery disease, were unavailable, which may lead to underestimation of stages 3 and 4.

Poor CKM health is widespread in the US population, especially among Black adults. Equitable health care approaches prioritizing CKM health are urgently needed.

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Concept and design: All authors.
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Data Sharing Statement: See Supplement 2.

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Substances in Counterfeit Prescription Pills Seized by Law Enforcement, 2017-2022

Counterfeit prescription pills are designed to replicate legitimate pharmaceutical pills in appearance and pharmacologic effects. However, the pharmacology of the active ingredients may be different, and the dose can be uncertain or irregular. In addition, counterfeit prescription pills can be contaminated with fentanyl and, more recently, with xylazine. Thus, counterfeit prescription pills have been associated with adverse outcomes, including fatal overdose.[1,2] Counterfeit drugs obtained during law enforcement seizures undergo comprehensive confirmatory toxicology testing. Results are generally not shared with the public. This descriptive study reports substances identified during testing of counterfeit prescription pills seized by law enforcement in Rhode Island; such documentation can help characterize the local street market.

Supplemental content

Methods | Data were obtained from law enforcement drug seizures reported by the Rhode Island forensic drug chemistry laboratory from January 2017 to December 2022. The number of pills obtained during seizure incidents range from a single pill to thousands; the numbers of incidents and of pills obtained cannot be reported. A representative sample was tested from each incident. If pills of 1 imprint or type were obtained, 1 pill was tested. If there were multiple imprints or types, then 1 of each imprint or type was analyzed. Pills were characterized based on markings. Any pill that yielded a result other than the expected active

Table 1. Laboratory-Identified Counterfeit Pills by Markings in Rhode Island, 2017-2022[a]

	Counterfeit pills tested, No. (%)						
Category, pill marking	2017	2018	2019	2020	2021	2022	Total
Alprazolam							
B 707	0	0	0	1 (1.4)	43 (32.8)	26 (41.9)	70 (22.4)
G 372 2	1 (7.7)	0	2 (7.4)	2 (2.9)	2 (1.5)	3 (4.8)	10 (3.2)
GG 249	3 (23.1)	0	1 (3.7)	4 (5.7)	4 (3.1)	1 (1.6)	13 (4.2)
R 0 3 9	0	0	5 (18.5)	21 (30.0)	20 (15.3)	4 (6.5)	50 (16.0)
S 90 3	4 (30.8)	0	8 (29.6)	26 (37.1)	48 (36.6)	18 (29.0)	104 (33.3)
V 2090	4 (30.8)	0	0	0	1 (0.8)	5 (8.1)	10 (3.2)
XANAX	1 (7.7)	9 (100)	11 (40.7)	16 (22.9)	13 (9.9)	5 (8.1)	55 (17.6)
Total, No.	13	9	27	70	131	62	312
Amphetamine/dextroamphetamine							
AD 30	2 (100)	0	6 (85.7)	16 (33.3)	33 (42.3)	20 (51.3)	77 (44.3)
b 974 30	0	0	0	9 (18.8)	29 (37.2)	13 (33.3)	51 (29.3)
dp 30	0	0	1 (14.3)	3 (6.3)	8 (10.3)	5 (12.8)	17 (9.8)
E 404	0	0	0	20 (41.7)	8 (10.3)	1 (2.6)	29 (16.7)
Total, No.	2	0	7	48	78	39	174
Clonazepam							
R 34	0	0	1 (50.0)	0	0	0	1 (50.0)
TEVA 832	0	0	1 (50.0)	0	0	0	1 (50.0)
Total	0	0	2	0	0	0	2
Oxycodone							
A 215	17 (29.8)	32 (45.7)	32 (32.3)	18 (21.4)	36 (15.9)	21 (14.0)	156 (22.7)
M 30	26 (45.6)	25 (35.7)	27 (27.3)	33 (39.3)	153 (67.7)	105 (70.0)	369 (53.8)
V 4812	9 (15.8)	11 (15.7)	27 (27.3)	25 (29.8)	28 (12.4)	15 (10.0)	115 (16.8)
Other	5 (8.8)	2 (2.9)	12 (12.1)	8 (9.5)	9 (4.0)	9 (6.0)	45 (6.6)
Multiple listed	0	0	1 (1.0)	0	0	0	1 (0.1)
Total, No.	57	70	99	84	226	150	686
Unknown							
200	0	0	1 (50.0)	0	0	0	1 (50.0)
Fragments (unmarked)	0	0	1 (50.0)	0	0	0	1 (50.0)
Total, No.	0	0	2	0	0	0	2

[a] Pills markings are the imprint or text found on a pill.