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Kidney failure-related excess mortality during the first three years of the COVID-19 pandemic in the United States: a nation-wide, population-based analysis

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Abstract

Background The onset of the COVID-19 pandemic has had a detrimental impact on the healthcare system. Patients with kidney failure and related kidney disease are notably vulnerable to the COVID-19 pandemic. However, it remains unclear how mortality trends associated with kidney failure have evolved over the past three years. In this study, we investigated temporal trends in excess kidney failure-related mortality during the first three years of the pandemic in the United States.

Methods We aim to estimate time-varying excess kidney failure-related mortality, which is defined as the difference between observed mortality and expected mortality predicted by a Poisson log-linear regression model, in the United States (March 2020—March 2023).

Results Our findings revealed two distinct peaks in excess kidney failure-related mortality during the first year (March 2020—February 2021) and the second year (February 2021—March 2022), whereas a notable decline in excess mortality was observed in the third year (March 2022—March 2023). Additionally, disparities in mortality were evident among various demographic groups, including age, sex, racial/ethnic subgroups, and geographic regions. Across all age subgroups, an increase in kidney failure-related mortalities was observed, with individuals aged 85 years and above experiencing the most substantial relative increase, reaching 9595.8 per million persons (95% CI: 9438.8, 9752.9). Moreover, excess kidney failure-related mortalities were recorded at 510.3 per million persons (95% CI: 502.6, 517.9) and 721.8 per million persons (95% CI: 713.4, 730.1) for women and men, respectively. Notably, non-Hispanic Blacks exhibited the highest excess mortality within the racial/ethnic group, registering at 772.6 per million persons (95% CI: 756.3, 788.9).

Conclusions Our study observed high levels of excess kidney failure-related mortality during the first two years of the pandemic, followed by a notable decline in the third year. This highlights the effectiveness of current policies and prevention measures implemented to mitigate the impact of the pandemic.

Keywords COVID-19, Excess mortality, Kidney failure, Temporal pattern

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Introduction

In March 2020, the World Health Organization (WHO) declared the onset of a pandemic characterized by SARS-CoV-2 infection, subsequently named the COVID-19 pandemic. Since then, the pandemic has led to a profound strike on healthcare systems and economic progress, resulting in millions of deaths worldwide [1].

Patients with kidney failure (KF) have proven to be particularly susceptible to both the direct and indirect consequences of the COVID-19 pandemic. Notably, KF is more prevalent among patients with more severe disease, particularly in the intensive care unit (ICU) setting [2, 3]. Emerging evidence suggests that KF patients with COVID-19 infection may experience organ dysfunction due to immune dysregulation and may face the possibility of a direct cytopathic effect of SARS-CoV-2 [4, 5], thereby elevating their risk of mortality. In addition to the reported COVID-19-related deaths, there has been a substantial increase in undetected deaths, attributable to various challenges, including limited access to therapy due to COVID-19 restrictions, thereby increasing the risk of hospitalization and mortality [6–9]. Furthermore, a range of social and economic barriers have disproportionately affected individuals with KF.

While prior research has demonstrated substantial mortality among patients with KF in the early stage of pandemic [10], it remains unclear how mortality within this population has evolved with the widespread availability of prevention measures. It is crucial to track excess mortality among KF patients across the multiple pandemic waves. Such a practice may offer valuable insights into whether the preventive measures have effectively protected patients with KF over this protracted period.

In this study, we investigated temporal trends in excess kidney failure-related mortality during the first three years of pandemic from March 2020 to March 2023 in the US. Additionally, we delve into whether stratification by age, sex, race/ethnicity, and state has modified the patterns of our kidney failure-related mortality.

Methods

Data sources

Weekly data were obtained from the Wide-ranging Online Data for Epidemiologic Research database (WONDER) of the Centers for Disease Control and Prevention (CDC) from January 1, 2018 to March 4, 2023 [11]. Due to the high risk of complications [12], KF may not be recorded as the underlying cause of death by nosologists. Therefore, we included individuals for whom KF was listed as one of the causes of death on their death certificate, recognizing that a decedent could have multiple causes of death [13]. The underlying cause of death referred to individuals for whom KF was listed as the underlying cause of death [14]. Deaths from KF were coded as N17-N19 according to the tenth revision of the International Classification of Diseases (ICD-10). Detailed information regarding the coding procedure for both the multiple and underlying causes of death can be found in the National Vital Statistics System from CDC [13, 14]. For our analysis, we collected demographic data, including age, sex, race/ethnicity, US state and cause of death. In order to estimate the number of deaths, we obtained population size data at the national and states level for the years from 2018 to 2023 from the CDC WONDER [11]. Because all data from CDC WONDER were publicly shared and available, the study was exempted from institutional review board approval.

Main statistical analysis

For our baseline model of expected deaths, we opted to employ an over-dispersed Poisson model since the over-dispersion feature of the data was detected, using data from January 2018 to February 2020. This model was described in detail elsewhere [15]. This model characterizes death occurrences following Poisson distribution with a seasonal trend, long-term trend, and auto-correlated errors. The seasonal trend was modeled as a yearly periodic function using 1 to 4 harmonics. The long-term trend was modeled using natural cubic splines with 0 to 2 internal knots over the whole period. Therefore, we considered a set of 12 candidate models to identify the optimal one for our baseline model by the time-series cross-validation method, and to estimate the expected number of deaths in 2020 using the model with the best performance (measured by out of sample mean squared error, MSE) from January 2018 to March 2020. According to the minimal value of MSE, harmonics at 4 and internal knots at 1 were chosen in our model, as detailed model selection process can be found in Supplemental Materials Text S1. We utilized this optimal baseline model to predict the expected deaths from March 2020 to March 2023. The projection of KF-related deaths was based on decedent data from January 1, 2018, to March 6, 2020, which was used to model and predict mortality trends from March 7, 2020, to March 4, 2023 (with data from 2018–2020 for model fitting and 2020–2023 for prediction). To quantify the excess deaths, we calculated four key indices: excess deaths (derived from subtracting the expected death counts from observed death counts), weekly average excess deaths (computed as the excess deaths divided by the length of the observational period), excess mortality (expressed as the excess death number per million persons), and excess risk (defined as the ratio between excess death number and expected death number, multiplied by 100%). In order to account for variations in population size, we focused primarily on the excess mortality in our study.

Subgroup analysis

To investigate demographic disparities in excess mortality and their temporal patterns within subgroup populations, we also retrieved weekly death counts for various demographic categories, including age groups (20–64 years, 65–84 years, and 85 + years), sex (male and female), race/ethnicity (non-Hispanic White, non-Hispanic Black, non-Hispanic Asian, and Hispanic), pandemic years, and pandemic waves from the CDC WONDER database. The subgroup data was fitted its own Poisson regression model, integrating identical harmonics and internal knots employed in the overall group analysis. We predefined the categorization of the COVID-19 pandemic years as follows: the first year (from March 7, 2020, to February 27, 2021), the second year (from February 28, 2021 to March 4, 2022), and the third year (from March 5, 2022 to March 4, 2023). In addition, we identified four distinct waves of the pandemic according to the COVID-19 mortality surveillance data from CDC [16]: the early pandemic wave (from March 7, 2020, to October 17, 2020), the Alpha wave (from October 18, 2020, to June 17, 2021), the Delta wave (June 18, 2021, to November 27, 2021), and the Omicron and its subvariants wave (from November 28, 2021, to March 4, 2023).

Sensitivity analysis

Sensitivity analyses were conducted to verify the robustness of the results. First, we employed a seasonal trend incorporating harmonics at 1 and a long-term trend with internal knots at 2 in the model to assess the robustness of the fitting for the time effect. In addition, we refitted our models to operate at the monthly level, which mitigates the potential autocorrelation while potentially reducing precision (Supplemental Tables S4 and S5). To comprehensively analyze the indirect impacts on non-COVID-19 KF mortality, we excluded deaths from COVID-19 (Supplemental Table S6). All analyses were carried out using R statistical software (version 4.2.1).

Results

During the period from March 2020 to March 2023, a total of 808,806 deaths related to KF were recorded in the United States. Of the 10,191,923 all-cause deaths recorded during the three years, 7.94% included kidney failure as a contributing factor. The largest proportion of these deaths occurred among individuals aged 65 to 84 years (405,435 deaths, 50.3%). This was followed by the age group of 85 years and above (230,889 deaths, 28.6%) and the age group of 20 to 64 years (170,372 deaths, 21.1%). In terms of gender distribution, there were 441,394 deaths (54.6%) among males, surpassing the 367,412 deaths (45.4%) among females. Furthermore, more than half of the deaths were attributed to non-Hispanic White individuals within the race/ethnicity category (Table 1).

In the temporal trend analysis (Table 1, Fig. 1), it is evident that although there was a substantial decline in KF-related following the rollout of vaccination program in mid-December 2020, the excess mortality remained notably high throughout the second year of the pandemic, with 255.9 per million persons (95% CI: 252.4, 259.4). Noteworthy is the significant decline observed in the KF-related mortality during the third year of the pandemic, with 178.6 per million persons (95% CI: 174.4, 182.6), coinciding with the emergence of the Omicron variant.

There is a distinct pattern in KF-related mortality across different waves of the pandemic. Notably, there was a significant increase in excess KF-related mortality during the Alpha wave, reaching 145.0 deaths per million persons (95% CI: 142.3, 147.7). Subsequently, following the rollout of vaccines in mid-December 2020, KF-related mortality exhibited a consistent decline throughout the Delta wave, with a rate of 117.7 deaths per million persons (95% CI: 115.5, 119.9). However, the KF-related mortality became notably pronounced during the Omicron and its subvariants wave, surging to 282.5 deaths per million persons (95% CI: 278.1, 286.9) (Table 1, Fig. 1).

Excess KF-related mortality demonstrated notable variations across different demographic factors, including age, sex, and race/ethnicity (Table 1). From March 2020 to March 2023, individuals aged 85 years and above exhibited the highest vulnerability among all age groups, with a rate of 9,595.8 per million persons (95% CI: 252.4, 259.4). Furthermore, there was a significant disparity in mortality between males (721.8 per million persons; 95% CI: 744.4, 761.7) and females (510.3 per million persons; 95% CI: 502.6, 517.9) during the pandemic. Regarding the racial/ethnic subgroups, non-Hispanic Blacks displayed the highest excess KF-related mortality, with a rate of 772.6 deaths per million persons (95% CI: 756.3, 788.9). These excess estimates of age, sex, and race/ethnicity consistently demonstrated variations when KF was considered the underlying cause of death (Supplemental Table S1).

There were notable geographic variations in excess KF-related mortality observed during the pandemic. In the first pandemic year, elevated excess mortalities were observed in Alabama, as well as in several Southern states of the US, including Texas, West Virginia, South Carolina, and Mississippi. In the second pandemic year, West Virginia, and Kentucky reported a dramatic increase in KF-related mortality. Of note, most states experienced a

Table 1 Excess mortality associated with kidney failure in the United States from March 2020, to March 2023

Subgroups	Observed deathnumber	Excess death number (95% CI)	Excess death number per week (95% CI)	Excess mortality per million persons (95% CI)	Excess risk % (95% CI)
Overall[a]	808806	204151 (202,124, 206179)	1300.3 (1287.4, 1313.2)	620.5 (614.3, 626.6)	33.8 (33.4, 34.1)
Age group					
Age 20–64	170372	55077 (54,325, 55828)	350.8 (346, 355.6)	284.6 (280.7, 288.4)	47.8 (47.0, 48.5)
Age 65–84	405435	113106 (111,826, 114386)	720.4 (712.3, 728.6)	2278.8 (2253.0, 2304.6)	38.7 (38.2, 39.2)
Age 85 +	230889	59136 (58,169, 60104)	376.7 (370.5, 382.8)	9595.8 (9438.8, 9752.9)	34.4 (33.8, 35.0)
Sex					
Female	367412	85437 (84,157, 86718)	544.2 (536, 552.3)	510.3 (502.6, 517.9)	30.3 (29.8, 30.8)
Male	441394	118228 (116,863, 119592)	753 (744.4, 761.7)	721.8 (713.4, 730.1)	36.6 (36.1, 37.0)
Race/ethnicity					
NH-White	562022	134658 (132,996, 136319)	857.7 (847.1, 868.3)	684.2 (675.7, 692.6)	31.5 (31.1, 31.9)
NH-Black	127976	32249 (31,570, 32928)	205.4 (201.1, 209.7)	772.6 (756.3, 788.9)	33.7 (32.9, 34.4)
NH-Asian	24733	6191 (5890, 6493)	39.4 (37.5, 41.4)	315.9 (300.5, 331.3)	33.4 (31.7, 35.1)
Hispanic	79812	26348 (25,834, 26862)	167.8 (164.5, 171.1)	423.0 (414.8, 431.3)	49.3 (48.2, 50.4)
Pandemic years[b]					
First year	260572	60819 (59,796, 61843)	1169.6 (1149.9, 1189.3)	186.0 (182.9, 189.1)	30.4 (29.9, 31.0)
Second year	284439	84229 (83,083, 85375)	1619.8 (1597.7, 1641.8)	255.9 (252.4, 259.4)	42.1 (41.4, 42.7)
Third year	263795	59103 (57,781, 60426)	1115.2 (1090.2, 1140.1)	178.6 (174.6, 182.6)	28.9 (28.2, 29.5)
Pandemic waves[c]					
Early pandemic	146715	24816 (24,027, 25605)	752 (728.1, 775.9)	75.0 (72.6, 77.4)	20.4 (19.7, 21.0)
Alpha variant	187581	47972 (47,069, 48876)	1370.6 (1344.8, 1396.5)	145.0 (142.3, 147.7)	34.4 (33.7, 35.0)
Delta variant	122251	38929 (38,205, 39654)	1692.6 (1661.1, 1724.1)	117.7 (115.5, 119.9)	43.1 (42.2, 44.0)
Omicron and its subvariants	352259	93457 (91,991, 94922)	1416 (1393.8, 1438.2)	282.5 (278.1, 286.9)	36.0 (35.4, 36.6)

Abbreviation: *CI* Confidence interval

[a] Excess estimates in this table were measured according to the multiple causes of death that kidney failure was listed anywhere on the death certificate

[b] The first year was 7 March 2020 – 27 February 2021; the second year was 28 February 2021—4 March 2022; the third year was 5 March 2022 – 4 March 2023

[c] Early pandemic wave (March 7, 2020, to October 17, 2020); Alpha wave (October 18, 2020, to June 17, 2021); Delta wave (June 18, 2021, to November 27, 2021); Omicron and its subvariants wave (November 28, 2021, to March 4, 2023)

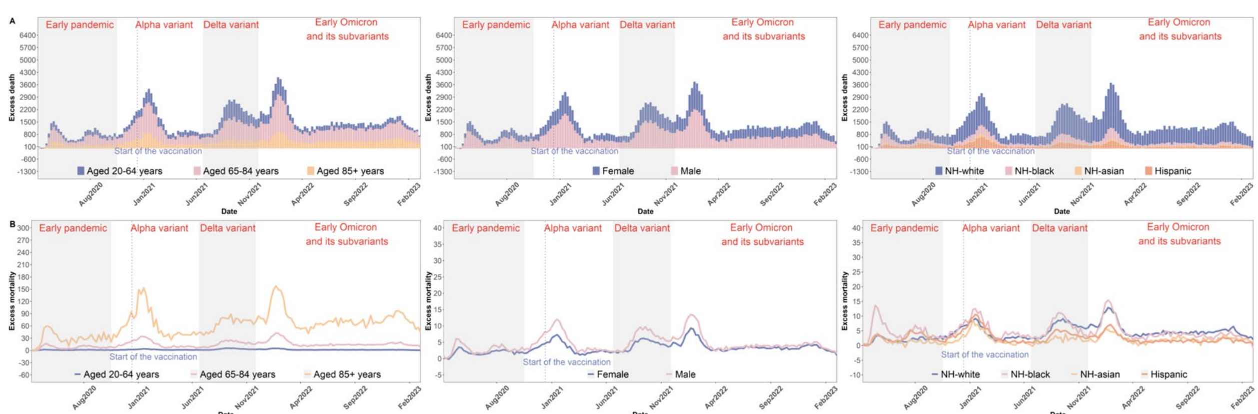

Fig. 1 Excess death and excess mortality (per million persons) for kidney failure by demographic characteristic in the United States. Weekly number of excess deaths by age group (20–64 years, 65–84 years, and 85 + years), sex (male and female) and race/ethnicity (non-Hispanic White, non-Hispanic Black, non-Hispanic Asian, and Hispanic). Early pandemic wave was from 7 March 2020 to 17 October 2020; Alpha variant wave was from 18 October 2020 to 19 June 2021; Delta variant wave was from 20 June 2021 to 27 November 2021; early Omicron and its subvariants wave was from 28 November 2021 to 4 March 2023, according to the COVID-19 mortality surveillance data from CDC. The blue dashed line indicates the start of vaccine rollouts (mid-December 2020)

decline in the third pandemic year. Over the first three years of the pandemic, we found that West Virginia and Alabama were the most affected states. While most states witnessed an increase in excess KF-related mortality during the first two pandemic years, even though they experienced a significant decrease in the third pandemic year, these states still bore had a substantial disease burden (Table 2, Figs. 2, 3). The trends in excess deaths and risk were remarkably similar across these states (Supplemental Table S2, S3 and Supplemental Figure S1, S2).

To evaluate the indirect impacts on non-COVID-19 KF mortality, we excluded deaths from COVID-19. Our analysis revealed a significant increase in excess non-COVID-19 KF-related mortality over the three years of the pandemic. Notably, there was a sharp rise in excess mortality rates during the wave of the Omicron variant and its subvariants, reaching 183.5 per million persons (95% CI: 178.9, 188.2) (Supplemental Table S6).

Discussion

The findings of this study have shed light on the persistent high levels of excess KF-related mortality in the United States during the first and second years of the COVID-19 pandemic, followed by a remarkable decline in the third pandemic year. These declines in excess mortality were observed across all demographic subgroups and states. When further stratified by age and sex, our study revealed a profound high excess mortality in elderly individuals and males. Additionally, the widening disparities in racial/ethnic groups indicated that non-Hispanic Blacks showed disproportionate vulnerability throughout the pandemic. Most states exhibited an increase in excess mortality during the first two pandemic years, followed by a decline in the third pandemic year. Of note, West Virginia and Alabama saw a higher disease burden compared to other states over the three-year period.

The early stages of the COVID-19 pandemic have posed significant challenges for patients with kidney diseases, resulting in disruptions in disease management and healthcare systems worldwide. Patients with KF were uniquely vulnerable to the pandemic, necessitating emergency treatments, mainly kidney replacement therapy (KPT) and routine dialysis services [9, 17, 18]. A previous study has documented considerable excess mortality among individuals with KF during the early stages of the pandemic [10]. Despite the development of prevention, treatment, and vaccination strategies in the first year of the pandemic, the excess KF-related mortality remained elevated in the second pandemic year. There are several potential reasons for this situation. Firstly, patients with KF required access to routine dialysis services or kidney transplantation. Numerous studies have indicated that while COVID-19 vaccination demonstrates immunogenicity, it appears to be less effective for patients with KF receiving dialysis [19, 20]. Secondly, most patients receiving kidney transplant therapy could not generate humoral immunity after two doses of the COVID-19 vaccine [19–21]. The limited efficacy of vaccination in patients with KF may have played a role in this continued excess mortality. Moreover, we found that the Delta wave was associated with the highest excess risk compared to previous pandemic waves. The emergence of the Delta variant in the latter phase of the second pandemic year may exacerbate the mortality risk among individuals with KF.

In contrast to some diseases where excess mortality began to decline in the second pandemic year, excess KF-related mortality exhibited a decline in the third pandemic year, suggesting the downward trend in KF-related mortality rates might have begun later compared to other diseases [22–25]. The decline can be attributed to several factors, primarily the gradual and consistent implementation of prevention strategies and the emergence of less virulent Omicron variants. A prior study has demonstrated improvements in mortality and hospitalization rates among patients with KF receiving KRT since the emergence of the Omicron variant [26]. With reduced restrictions and a greater reopening of society, despite a significant rise in the number of patients experiencing SARS-CoV-2 infection, outcomes for KF patients receiving KRT may have improved. Moreover, in the third pandemic year, the evolvements of policy and healthcare system, including enhanced healthcare services for rural area [27], may have contributed to the declines in excess mortality. In addition, convenient access to COVID-19 antiviral drugs has proven essential in preventing additional excess deaths among individuals with KF. In March 2022, the U.S. government launched a timely one-stop test-to-treat initiative, allowing people to undergo COVID-19 testing and receive a prescription for antiviral drugs at clinics and other health facilities [28]. The selection of appropriate antiviral drugs, such as Remdesivir, Nirmatrelvir with Ritonavir (Paxlovid), Azvudine, and Molnupiravir (Lagevrio) or combinations thereof, has the potential to reduce the risk of death from severe COVID-19 [29, 30].

The excess KF-related mortality varied in different age groups. Our study shows the highest mortality in people aged 85 years and above, a pattern that aligns with common knowledge that age represents a significant risk factor for mortality during the COVID-19 pandemic. This heightened risk in older individuals may be attributed to a diminished immune response, rendering them more susceptible to COVID-19 [31, 32].

Our study also highlighted racial/ethnic disparities in excess KF-related deaths, which were consistent with

Table 2 Excess kidney failure-related mortality (per million persons) stratified by the COVID-19 pandemic years in the United States over the period

Jurisdiction	Overall (95% CI)	Year One (95% CI)	Year Two (95% CI)	Year Three (95% CI)
Alabama	1089.2 (1050.4, 1128.1)	302.2 (280.0, 324.3)	414.4 (392.2, 436.6)	371.5 (348.5, 394.5)
Arizona	689.5 (659.1, 720.0)	241.6 (225.3, 258.0)	279.6 (262.2, 297.0)	168.0 (149.1, 187.0)
Arkansas	774.3 (712.4, 836.2)	191.3 (157.9, 224.6)	326.7 (291.4, 361.9)	256.4 (218.1, 294.8)
California	568.3 (553.4, 583.2)	208.8 (200.9, 216.7)	207.2 (198.7, 215.7)	152.3 (142.8, 161.7)
Colorado	769.0 (732.1, 805.8)	135.5 (115.4, 155.6)	349.5 (328.5, 370.5)	283.9 (261.3, 306.5)
Connecticut	380.2 (330.8, 429.6)	121.8 (95.1, 148.5)	132.1 (104.0, 160.2)	126.3 (95.6, 156.9)
District of Columbia	194.0 (67.1, 320.9)	43.6 (-15.3, 102.6)	54.7 (-13.7, 123.1)	96.5 (6.6, 186.4)
Florida	575.1 (554.8, 595.4)	111.4 (100.7, 122.2)	279.4 (267.9, 291.0)	184.1 (171.3, 196.9)
Georgia	630.9 (605.1, 656.7)	191.7 (177.6, 205.8)	247.6 (232.9, 262.3)	191.4 (175.6, 207.3)
Hawaii	194.6 (114.9, 274.2)	14.3 (-27.7, 56.4)	113.5 (68.1, 158.9)	65.8 (15.7, 115.9)
Idaho	382.4 (316.0, 448.7)	71.8 (36.1, 107.5)	208.3 (170.8, 245.8)	100.4 (59.1, 141.7)
Illinois	388.5 (362.2, 414.9)	111.1 (96.9, 125.3)	144.5 (129.5, 159.5)	132.9 (116.5, 149.2)
Indiana	469.9 (426.2, 513.5)	199.2 (175.6, 222.7)	208.6 (183.8, 233.5)	62.4 (35.3, 89.4)
Iowa	195.8 (130.0, 261.5)	102.1 (68.8, 135.5)	122.7 (85.6, 159.7)	-28.7 (-71.6, 14.2)
Kansas	556.4 (497.4, 615.4)	169.2 (136.9, 201.4)	230.2 (196.5, 263.8)	157.0 (120.8, 193.2)
Kentucky	1059.5 (1004.7,1114.4)	172.8 (143.6, 202.1)	508.7 (477.5, 539.8)	377.0 (342.6, 411.3)
Louisiana	759.2 (721.2, 797.3)	217.2 (195.5, 238.9)	314.3 (292.5, 336.2)	227.8 (205.4, 250.2)
Maine	314.5 (233.5, 395.5)	53.3 (6.9, 99.6)	120.7 (74.4, 167.1)	139.8 (92.3, 187.4)
Maryland	534.0 (493.6, 574.5)	203.0 (181.5, 224.4)	189.9 (167.0, 212.8)	141.6 (116.2, 167.0)
Massachusetts	332.5 (294.1, 370.9)	146.7 (126.4, 167.1)	111.0 (89.2, 132.7)	75.2 (51.0, 99.4)
Michigan	576.6 (545.6, 607.6)	158.4 (141.7, 175.1)	275.5 (257.8, 293.1)	142.6 (123.3, 161.8)
Minnesota	652.6 (613.1, 692.0)	161.5 (139.8, 183.1)	269.2 (246.7, 291.7)	221.5 (197.4, 245.6)
Mississippi	787.5 (725.6, 849.4)	281.5 (248.2, 314.8)	308.7 (273.4, 344.0)	197.3 (158.8, 235.7)
Missouri	969.9 (932.6, 1007.2)	269.3 (248.1, 290.6)	372.1 (350.7, 393.5)	328.4 (306.4, 350.4)
Montana	360.1 (255.0, 465.1)	83.0 (29.8, 136.2)	240.1 (180.7, 299.5)	36.4 (-31.8, 104.6)
Nebraska	181.3 (101.8, 260.8)	51.2 (9.0, 93.3)	101.5 (56.4, 146.5)	28.5 (-21.5, 78.6)
Nevada	713.9 (670.0, 757.8)	179.7 (155.4, 204.0)	267.2 (242.1, 292.3)	266.9 (240.3, 293.6)
New Hampshire	813.2 (742.5, 883.9)	172.5 (131.2, 213.9)	306.0 (265.5, 346.5)	333.3 (292.7, 373.9)
New Jersey	715.0 (686.2, 743.7)	283.7 (267.4, 300.1)	214.3 (197.9, 230.6)	218.6 (201.6, 235.6)
New Mexico	575.8 (512.4, 639.3)	175.5 (141.2, 209.8)	272.7 (236.5, 308.8)	127.6 (88.4, 166.8)
New York	286.2 (267.7, 304.7)	141.8 (131.8,151.9)	88.9 (78.3, 99.4)	56.5 (45.0, 67.9)
North Carolina	368.8 (335.5, 402.1)	140.2 (122.8,157.5)	193.6 (174.7, 212.5)	35.0 (13.7, 56.2)
Ohio	672.1 (643.6, 700.6)	163.4 (147.9, 179.0)	295.9 (279.6, 312.1)	212.4 (194.9, 229.9)
Oklahoma	645.7 (594.9, 696.6)	246.0 (218.5, 273.5)	288.9 (259.9, 317.9)	110.9 (79.4, 142.4)
Oregon	600.1 (552.7, 647.5)	83.7 (57.9, 109.5)	279.5 (252.4, 306.5)	236.8 (207.7, 265.9)
Pennsylvania	725.9 (696.1, 755.8)	190.9 (174.8, 207.1)	297.2 (280.3, 314.2)	237.2 (218.7, 255.7)
South Carolina	869.6 (824.7, 914.4)	285.9 (261.1, 310.7)	341.0 (315.3, 366.6)	242.7 (215.6, 269.9)
South Dakota	477.0 (358.8, 595.2)	211.9 (150.6, 273.1)	247.5 (179.2, 315.8)	17.9 (-56.7, 92.4)
Tennessee	814.3 (777.5, 851.1)	193.3 (173.1, 213.6)	383.5 (362.5, 404.5)	236.7 (214.2, 259.1)
Texas	925.0 (909.1, 941.0)	301.4 (292.3, 310.5)	352.6 (343.4, 361.7)	271.0 (261.6, 280.4)
Utah	-63.4 (-116.1, -10.8)	39.7 (12.9, 66.5)	6.8 (-22.7, 36.4)	-108.6 (-142.9, -74.3)
Virginia	506.3 (473.9, 538.6)	138.8 (121.5, 156.1)	244.2 (225.8, 262.6)	123.1 (102.9, 143.4)
Washington	703.5 (672.3, 734.7)	94.0 (76.9, 111.1)	291.4 (273.6, 309.2)	317.4 (298.3, 336.4)
West Virginia	1423.6 (1341.8, 1505.5)	289.6 (244.2, 334.9)	666.5 (619.6, 713.3)	467.8 (418.3, 517.3)
Wisconsin	292.2 (244.4, 340.0)	114.4 (89.8, 138.9)	114.8 (87.8, 141.7)	63.2 (32.3, 94.1)
Wyoming	261.7 (-12.6, 535.9)	67.1 (-16.1, 150.3)	180.4 (11.2, 349.6)	14.1 (-185.4, 213.5)

Abbreviation: *CI* Confidence interval

'Overall' refers to the period from 7 March 2020 to 4 March 2023; year one was defined as the first year (from 7 March 2020 to 27 February 2021); year two was defined as the second year (from 28 February 2021 to 4 March 2022); year three was defined as the third year (from 5 March 2022 to 4 March 2023)

Alaska, Delaware, North Dakota, and Rhode Island were not involved in the calculation due to limited data

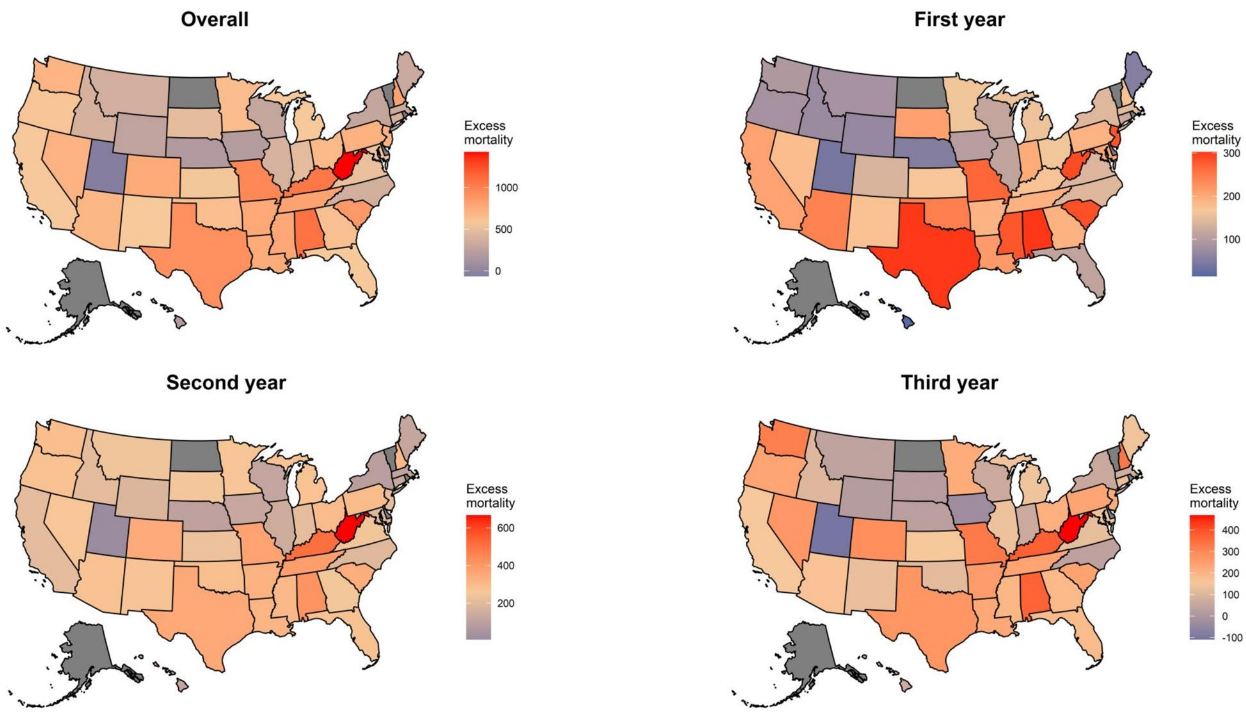

Fig. 2 Maps of excess mortalities of kidney failure (per million persons) stratified by the COVID-19 pandemic years in the United States. 'Overall' refers to the period from 7 March 2020 to 4 March 2023. The three years were defined as the first year (from 7 March 2020 to 27 February 2021); the second year (from 28 February 2021 to 4 March 2022); the third year (from 5 March 2022 to 4 March 2023). * Alaska, Delaware, North Dakota, and Rhode Island were not involved in the calculation due to limited data

other studies demonstrating similar disparities in both COVID-19 or non-COVID-19 excess deaths [33]. Specifically, we found that the non-Hispanic Black individuals exhibited the highest excess KF-related mortality compared to other ethnic groups during the three pandemic years. Previous studies have indicated that racial and ethnic minority populations face a relatively higher mortality rate due to factors such as occupational exposure to COVID-19, living in multigenerational households and densely populated communities, and limited access to healthcare and private transportation [33–36]. These disparities in race and ethnicity appear to have exacerbated the death toll associated with KF within vulnerable populations during the COVID-19 pandemic. The stark disparities and disproportionate burden underscore the need for future government preparedness plans that prioritize addressing racial disparities.

In our geographic analysis, we identified West Virginia and Alabama as having the highest KF-related mortalities, respectively. Most states exhibited elevated KF-related mortality during the first two pandemic years, followed by a decrease in the third pandemic year. Comparatively, the Southern states tended to have relatively higher mortality associated with KF, while the North Central and Northeastern states had the lowest KF-related mortality. This geographic variation likely reflected the disparities in the disease burden from KF, as well as the influence of economic status, local policies enacted in response to the COVID-19 pandemic, and the availability of resources for managing KF. Given the observed global relationship between COVID-19 and renal complications, similar trends in KF-related mortality might be anticipated in other countries or regions experiencing comparable COVID-19 waves.

With the persistent circulation and increased transmissibility of SARS-CoV-2, the long-term indirect impact on non-COVID-19 KF patients may continue to emerge. To evaluate these indirect effects, our study excluded deaths directly associated with COVID-19, focusing on the pandemic's broader impact on non-COVID-19 KF mortality. Over the three pandemic years, we observed a notable increase in excess KF-related mortality, especially during the Omicron variant and its subvariant waves. This trend likely reflects the challenges KF patients faced in accessing routine healthcare services as SARS-CoV-2 spread more widely, intensifying healthcare demand and limiting available resources for non-COVID-19 KF patients.

This study has limitations that should be noted. Firstly, we utilized provisional data for analyzing excess deaths

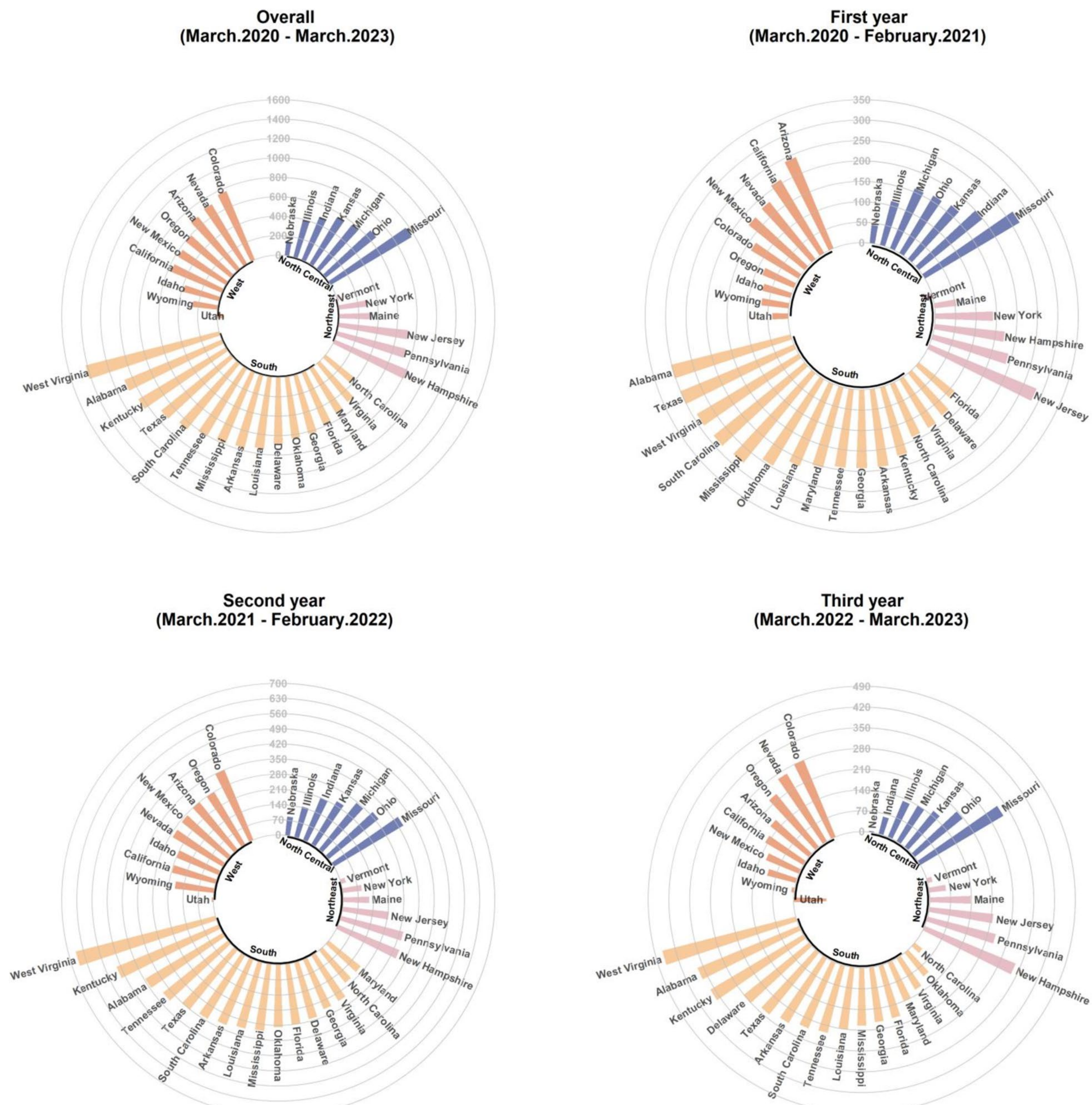

Fig. 3 Annual excess mortalities of kidney failure (per million persons) by states in the United States. 'Overall' refers to the period from 7 March 2020 to 4 March 2023. The three years were defined as the first year (from 7 March 2020 to 27 February 2021); the second year (from 28 February 2021 to 4 March 2022); the third year (from 5 March 2022 to 4 March 2023). * Alaska, Delaware, North Dakota, and Rhode Island were not involved in the calculation due to limited data

associated with KF, and we did not exclude the most recent weeks to mitigate potential unreliability. This may introduce increased statistical uncertainty of excess deaths due to reporting lags. Secondly, our reference baseline data only covered a two-year observation period, which might limit our ability to estimate a long-term variation of excess death. Thirdly, we solely relied on the weekly death data from WONDER, while alternative databases are provided by the National Center for Health Statistics (NCHS) [37]. Although we performed sensitivity analyses in our study, we did not perform a comparative analysis with the NCHS dataset to further validate the robustness of our findings. Fourthly, since KF had to be explicitly recorded as a cause or contributing factor to death, some renal-related mortality cases may not have been captured in our study, potentially leading to an underestimation of renal-related deaths.

Conclusions

In summary, our study revealed temporal trends in excess mortality associated with kidney failure (KF) over the first three years of the COVID-19 pandemic, with a particularly notable decline in the third year, coinciding with the Omicron surge. This reduction in excess KF-related mortality highlights the effectiveness of existing policies and preventive measures in mitigating the pandemic's impact. However, excess non-COVID-19 KF mortality persisted throughout these three years. As COVID-19 continues to challenge public health, it remains crucial to monitor mortality from non-COVID-19 causes and to expand healthcare resources accordingly.

Supplementary Information

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Supplementary Material 1.

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Authors' contributions

Research idea, study design: PC, XC, and JR. Manuscript drafting: ZC, PJ, and PC. Data collec-tion and analysis: ZC, JL, YG, and JX. Manuscript revision and editing: PC, DX, XC, WC, LM, LH, PJ, SZ, and SS. All authors reviewed and approved the final version of the article for submission.

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Data availability

All original data used in this work are publicly available, shown at: https://wonder.cdc.gov/controller/datarequest/D176.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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