

Deaths Due to COVID-19 in Patients With Cancer During Different Waves of the Pandemic in the US

Alexandra L. Potter, BS; Vedha Vaddaraju; Shivaek Venkateswaran; Arian Mansur, BS; Simar S. Bajaj; Mathew V. Kiang, MPH, ScD; Anupam B. Jena, MD, PhD; Chi-Fu Jeffrey Yang, MD

 Supplemental content

IMPORTANCE With the ongoing relaxation of guidelines to prevent COVID-19 transmission, particularly in hospital settings, medically vulnerable groups, such as patients with cancer, may experience a disparate burden of COVID-19 mortality compared with the general population.

OBJECTIVE To evaluate COVID-19 mortality among US patients with cancer compared with the general US population during different waves of the pandemic.

DESIGN, SETTING, AND PARTICIPANTS This cross-sectional study used data from the Center for Disease Control and Prevention's Wide-Ranging Online Data for Epidemiologic Research database to examine COVID-19 mortality among US patients with cancer and the general population from March 1, 2020, to May 31, 2022. The number of deaths due to COVID-19 during the 2021 to 2022 winter Omicron surge was compared with deaths during the preceding year's COVID-19 winter surge (when the wild-type SARS-CoV-2 variant was predominant) using mortality ratios. Data were analyzed from July 21 through August 31, 2022.

EXPOSURES Pandemic wave during which the wild-type variant (December 2020 to February 2021), Delta variant (July 2021 to November 2021), or Omicron variant (December 2021 to February 2022) was predominant.

MAIN OUTCOMES AND MEASURES Number of COVID-19 deaths per month.

RESULTS The sample included 34 350 patients with cancer (14 498 females [42.2%] and 19 852 males [57.8%]) and 628 156 members of the general public (276 878 females [44.1%] and 351 278 males [55.9%]) who died from COVID-19 when the wild-type (December 2020–February 2021), Delta (July 2021–November 2021), and winter Omicron (December 2021–February 2022) variants were predominant. Among patients with cancer, the greatest number of COVID-19 deaths per month occurred during the winter Omicron period ($n = 5958$): at the peak of the winter Omicron period, there were 18% more deaths compared with the peak of the wild-type period. In contrast, among the general public, the greatest number of COVID-19 deaths per month occurred during the wild-type period ($n = 105\,327$), and at the peak of the winter Omicron period, there were 21% fewer COVID-19 deaths compared with the peak of the wild-type period. In subgroup analyses by cancer site, COVID-19 mortality increased the most, by 38%, among patients with lymphoma during the winter Omicron period vs the wild-type period.

CONCLUSIONS AND RELEVANCE Findings of this cross-sectional study suggest that patients with cancer had a disparate burden of COVID-19 mortality during the winter Omicron wave compared with the general US population. With the emergence of new, immune-evasive SARS-CoV-2 variants, many of which are anticipated to be resistant to monoclonal antibody treatments, strategies to prevent COVID-19 transmission should remain a high priority.

Author Affiliations: Division of Thoracic Surgery, Department of Surgery, Massachusetts General Hospital, Boston (Potter, Vaddaraju, Venkateswaran, Mansur, Bajaj, Yang); Department of Epidemiology and Population Health, Stanford University School of Medicine, Stanford, California (Kiang); Department of Health Care Policy, Harvard Medical School, Boston, Massachusetts (Jena); Department of Medicine, Massachusetts General Hospital, Boston (Jena); National Bureau of Economic Research, Cambridge, Massachusetts (Jena); Mongan Institute Health Policy Research Center, Massachusetts General Hospital, Boston (Yang).

Corresponding Author: Chi-Fu Jeffrey Yang, MD, Massachusetts General Hospital, 55 Fruit St, Boston, MA 02114 (cjyang@mgh.harvard.edu).

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The growing number of US hospitals electing to remove masking requirements that had been in place to control COVID-19 has sparked some debate as to whether it is premature to remove masking mandates, particularly in higher-risk settings, such as hospitals.¹ Compared with the general population, patients with cancer are at increased risk of breakthrough SARS-CoV-2 infection and severe COVID-19.²⁻⁴ With the ongoing relaxation of measures to prevent SARS-CoV-2 transmission, patients with cancer may experience a disparate burden of COVID-19 mortality compared with the general population.

Examining COVID-19 mortality during previous pandemic waves in which the transmissibility and severity of the SARS-CoV-2 variant predominant at that time, rates of vaccination, and measures to prevent virus transmission varied greatly, may provide insight into future COVID-19 mortality risk among patients with cancer. In the US, the wild-type virus, Delta variant, and Omicron (BA.1) variant were associated with different degrees of transmissibility and severity. For example, compared with the wild-type virus and previous variants, the Delta variant was reported to be more transmissible and to carry a greater risk of severe COVID-19,⁵ whereas the Omicron variant was reported to be significantly more transmissible than both the wild-type virus and Delta variant^{6,7} but was associated with lower risks of COVID-19-related hospitalization and death.⁸⁻¹⁰ The objective of this study was to compare COVID-19 mortality among US patients with cancer compared with the general US population during periods in which the wild-type virus, Delta variant, and Omicron variant were predominant.

Methods

This population-based, retrospective, cross-sectional study was deemed exempt from review and from the informed consent requirement by the Massachusetts General Hospital Institutional Review Board because publicly available deidentified data were used. The study followed the Strengthening of Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline. Individuals who died from COVID-19 from March 1, 2020, to May 31, 2022, in the Wide-Ranging Online Data for Epidemiologic Research (WONDER) system of the Centers for Disease Control and Prevention (CDC)¹¹ (eMethods and eTable 1 in Supplement 1) were identified for analysis. To examine COVID-19 mortality among patients with cancer, we selected individuals with both cancer and COVID-19 identified as causes of death (eMethods and eTable 1 in Supplement 1). To examine COVID-19 mortality among the total US population, we selected all individuals with COVID-19 identified as a cause of death.

Deaths due to COVID-19 among patients with cancer and the general population were grouped according to whether they occurred from December 2020 to February 2021 (wild-type period), July 2021 to November 2021 (Delta period), or December 2021 to February 2022 (winter Omicron period). The date cutoffs for each period were selected based on reports of the dates when the wild-type virus and Delta and Omicron BA.1 variants were widely circulating in the US.^{12,13}

Key Points

Question Did COVID-19 mortality differ between patients with cancer and the general US population depending on which SARS-CoV-2 variant was dominant?

Findings Among 34 350 patients with cancer who died during the COVID-19 pandemic during periods in which wild-type, Delta, and Omicron variants were predominant between March 2020 and May 2022, the number of deaths was higher during the winter Omicron surge compared with the preceding year's winter surge of the wild-type variant. In contrast, there were 29% fewer COVID-19 deaths in the general population during the winter Omicron surge compared with the preceding year's winter surge.

Meaning Findings of this study suggest that patients with cancer experienced a disparate burden of COVID-19 mortality during the winter Omicron wave; strategies to prevent COVID-19 transmission should remain a high priority as new variants arise.

Statistical Analysis

Differences in the characteristics of patients with cancer and differences in the characteristics of members of the general population during the wild-type, Delta, and winter Omicron periods were evaluated using the χ^2 test. Data on race were obtained from death certificates and were collected to evaluate the demographic characteristics of the study cohort during the wild-type, Delta, and winter Omicron periods. Racial categories included in the analysis were American Indian, Asian, Black, multiracial, Native Hawaiian, and White.

The number of COVID-19 deaths per month during the study period was calculated among cancer patients and the general population. The percentage of COVID-19 deaths per month relative to the peak number of COVID-19 deaths per month during the wild-type period was calculated by dividing the number of COVID-19 deaths per month by the peak number of COVID-19 deaths per month during the wild-type period. Subgroup analyses were conducted by age group. To compare the number of COVID-19 deaths between the 3-month winter Omicron period and 3-month wild-type period, mortality ratios were calculated by dividing the number of COVID-19 deaths that occurred during the winter Omicron period by the number of COVID-19 deaths that occurred during the wild-type period. Subgroup analyses were performed by cancer site (eTable 1 in Supplement 1). All *P* values were 2-sided and considered statistically significant at *P* < .05. Data were analyzed from July 21 through August 31, 2022.

Results

Study Population and Data Source

A total of 54 692 patients with cancer and 1 008 510 members of the general public died from COVID-19 from March 1, 2020 to May 31, 2022 (eTable 2 in Supplement 1). The study sample included 34 350 patients with cancer (14 498 females [42.2%] and 19 852 males [57.8%]) and 628 156 members of the general public (276 878 females [44.1%] and 351 278 males [55.9%]) who died from COVID-19 when the wild-type (December 2020-February 2021), Delta (July 2021-November 2021), and winter Omicron (December 2021-February 2022) variants were

predominant. The Table shows the baseline characteristics of individuals included in the study.

COVID-19 Mortality per Month Among Patients With Cancer vs the General Public

Among patients with cancer, the greatest number of COVID-19 deaths per month occurred during the winter Omicron period in January 2022 ($n = 5958$). In January 2022, at the peak of the winter Omicron period, there were 18% more deaths compared with the peak of the wild-type period (January 2021) among patients with cancer (Figure 1).

In contrast, among the general public, the greatest number of COVID-19 deaths per month occurred during the wild-type period in January 2021 ($n = 105\,327$). In January 2022, at the peak of the winter Omicron period, there were 21% fewer COVID-19 deaths compared with the peak of the wild-type period among the general population (Figure 1).

COVID-19 Mortality by Age Group Among Patients With Cancer vs the General Public

Among patients with cancer aged younger than 80 years, the greatest number of COVID-19 deaths per month occurred during the winter Omicron period. Among patients with cancer aged younger than 50 years, 50 to 59 years, 60 to 69 years, and 70 to 79 years, the number of COVID-19 deaths per month at the peak of the winter Omicron period was 64%, 62%, 31%, and 16% greater, respectively, compared with the number of COVID-19 deaths per month at the peak of the wild-type period (eFigure in Supplement 1).

In the general population, the greatest number of COVID-19 deaths per month occurred during the Delta period among individuals aged younger than 50 years and 50 to 59 years. For individuals 60 to 69, 70 to 79, and 80 years or older, the greatest number of COVID-19 deaths per month occurred during the wild-type period (eFigure in Supplement 1).

COVID-19 Mortality During the Winter Omicron Period vs Wild-Type Period

More patients with cancer died from COVID-19 during the 3-month winter Omicron period ($n = 12\,877$) vs the wild-type period ($n = 12\,440$). In contrast, there were 29% fewer COVID-19 deaths in the general population during the winter Omicron period ($n = 178\,509$) vs wild-type period ($n = 251\,714$).

COVID-19 Mortality by Cancer Site

Patients with cancer experienced significantly greater COVID-19 mortality during the Omicron period when compared with the wild-type period (mortality ratio, 1.04; 95% CI, 1.02-1.05), while the general US population experienced decreased mortality during the Omicron period relative to the wild-type period (mortality ratio, 0.69; 95% CI, 0.69-0.70) (Figure 2). This finding was consistent across all cancer sites evaluated with the exception of brain (mortality ratio, 0.77; 95% CI, 0.65-0.90), thyroid (mortality ratio, 0.76 [95% CI, 0.54-0.99], and bladder (mortality ratio, 0.58; 95% CI, 0.52-0.65) cancers. Of note, COVID-19 mortality increased the most, by 38% (mortality ratio, 1.38; 95% CI, 1.31-1.45), among patients with lymphoma during the winter Omicron vs wild-type periods.

Discussion

Although infection with the SARS-CoV-2 Omicron variant has been found to be associated with a lower risk of hospital admission and death compared with previous variants among the general population,^{8,9} more patients with cancer died during the winter Omicron period compared with the wild-type or Delta periods. In contrast, among the general population, COVID-19 mortality was highest during the wild-type period.

We also investigated differences in COVID-19 mortality by age group among patients with cancer and the general population. Among the general population, COVID-19 mortality was highest during the Delta period among individuals aged 60 years or younger and was highest during the wild-type period among individuals aged 60 years or older; these differences are likely explained by lower vaccination rates among younger adults compared with older adults during the Delta period.¹⁴ In contrast with the general population, patients with cancer aged younger than 80 years—who had access to COVID-19 vaccines, boosters, and antiviral agents prior to the winter Omicron period—experienced the highest COVID-19 mortality during the winter Omicron period compared with the wild-type and Delta periods.

The disparate burden of COVID-19 mortality experienced by patients with cancer compared with the general public during the winter Omicron period is likely explained by the combined effects of greater SARS-CoV-2 exposure during the winter Omicron period (owing to the increased transmissibility of the Omicron variant^{6,7} and the relaxation of policies to prevent SARS-CoV-2 transmission), reduced effectiveness of COVID-19 vaccines in patients with cancer,^{4,15} and greater risk of severe COVID-19 among patients with cancer.²⁻⁴ Patients with lymphoma had the largest increase in COVID-19 mortality during the winter Omicron vs wild-type periods, which is consistent with literature reporting reduced vaccine effectiveness against the Omicron variant in this population.^{4,16}

Limitations

A limitation of this study is that the number of patients with cancer who died from COVID-19 in the CDC WONDER database is likely an underestimate, as patients with a remote history of cancer may not have had cancer recorded in their death certificate and may not have been included in the study cohort. Additionally, the CDC WONDER database does not include information on individuals' vaccination status or cancer staging. Lastly, COVID-19-related delays in cancer diagnoses and treatment may have also contributed to an increase in COVID-19 mortality among patients with cancer during the winter Omicron period.

Conclusions

This cross-sectional study found that, while the general US population experienced a large reduction in COVID-19 mortality during the winter Omicron period, patients with cancer

Table. Baseline Characteristics of Patients With Cancer and Members of the General Population who Died of COVID-19 During the Wild-Type, Delta, and Omicron Periods

Characteristic	Patients, No. (%)			P value
	Wild-type period	Delta period	Winter Omicron period	
Patients with cancer				
Total	12 440	9033	12 877	NA
Age, y				
<50	345 (2.7)	379 (4.2)	462 (3.6)	<.001
50-59	858 (6.9)	828 (9.2)	1144 (8.9)	
60-69	2409 (19.4)	2115 (23.4)	2949 (22.9)	
70-79	3940 (31.6)	2942 (32.6)	4108 (31.9)	
>80	4888 (39.3)	2769 (30.7)	4214 (32.8)	
Sex				
Female	5287 (42.5)	3754 (41.6)	5457 (42.4)	.34
Male	7153 (57.5)	5279 (58.4)	7420 (57.6)	
Race				
American Indian	114 (0.9)	75 (0.8)	84 (0.7)	<.001
Asian	375 (3.0)	137 (1.5)	278 (2.2)	
Black	1484 (11.9)	1031 (11.4)	1723 (13.4)	
Multiracial	49 (0.4)	47 (0.5)	58 (0.5)	
Native Hawaiian	11 (0.1)	11 (0.1)	18 (0.1)	
White	10 407 (83.7)	7732 (85.6)	10 716 (83.2)	
Place of death				
Medical facility, inpatient	7500 (60.3)	5804 (64.3)	7955 (61.8)	<.001
Medical facility, outpatient or ED	303 (2.4)	219 (2.4)	387 (3.0)	
Medical facility, dead on arrival	0 (0.0)	0 (0.0)	0 (0.0)	
Home	1695 (13.6)	1430 (15.8)	2219 (17.2)	
Hospice facility	634 (5.1)	587 (6.5)	849 (6.6)	
Nursing home or long-term care facility	2014 (16.2)	740 (8.2)	1175 (9.1)	
Other ^a	286 (2.3)	245 (2.7)	285 (2.2)	
Place of death unknown	8 (0.1)	8 (0.1)	7 (0.1)	
General population				
Total	251 714	197 933	178 509	NA
Age, y				
<50	10 035 (4.0)	26 127 (13.2)	12 749 (7.1)	<.001
50-59	18 654 (7.4)	30 755 (15.5)	18 940 (10.6)	
60-69	43 067 (17.1)	44 956 (22.7)	36 591 (20.5)	
70-79	67 487 (26.8)	46 079 (23.3)	47 060 (26.4)	
>80	112 471 (44.7)	50 016 (25.3)	63 169 (35.4)	
Sex				
Female	112 404 (44.7)	86 112 (43.5)	78 362 (43.9)	<.001
Male	139 310 (55.3)	111 821 (56.5)	100 147 (56.1)	
Race				
American Indian	3130 (1.2)	2479 (1.3)	1938 (1.1)	<.001
Asian	10 551 (4.2)	3498 (1.8)	4369 (2.4)	
Black	29 172 (11.6)	27 230 (13.8)	22 645 (12.7)	
Multiracial	1126 (0.4)	1205 (0.6)	909 (0.5)	
Native Hawaiian	491 (0.2)	703 (0.4)	355 (0.2)	
White	207 244 (82.3)	162 818 (82.3)	148 293 (83.1)	
Place of death				
Medical facility, inpatient	165 715 (65.8)	149 345 (75.5)	123 086 (69)	<.001
Medical facility, outpatient or ED	7718 (3.1)	7472 (3.8)	7439 (4.2)	
Medical facility, dead on arrival	192 (0.1)	214 (0.1)	182 (0.1)	
Home	19 820 (7.9)	20 616 (10.4)	21 905 (12.3)	
Hospice facility	7551 (3.0)	5267 (2.7)	6093 (3.4)	
Nursing home or long-term care facility	45 202 (18.0)	11 005 (5.6)	15 919 (8.9)	
Other ^a	5489 (2.2)	4003 (2.0)	3878 (2.2)	
Place of death unknown	27 (0.1)	11 (0.1)	7 (0.1)	

Abbreviations: ED, emergency department; NA, not applicable.

^a Other place of death was not defined in the Centers for Disease Control and Prevention's Wide-Ranging Online Data for Epidemiologic Research database.

Figure 1. Percentage of COVID-19 Deaths per Month Relative to the Peak of COVID-19 Deaths per Month During the Wild-Type Period Among Patients With Cancer and the General Population

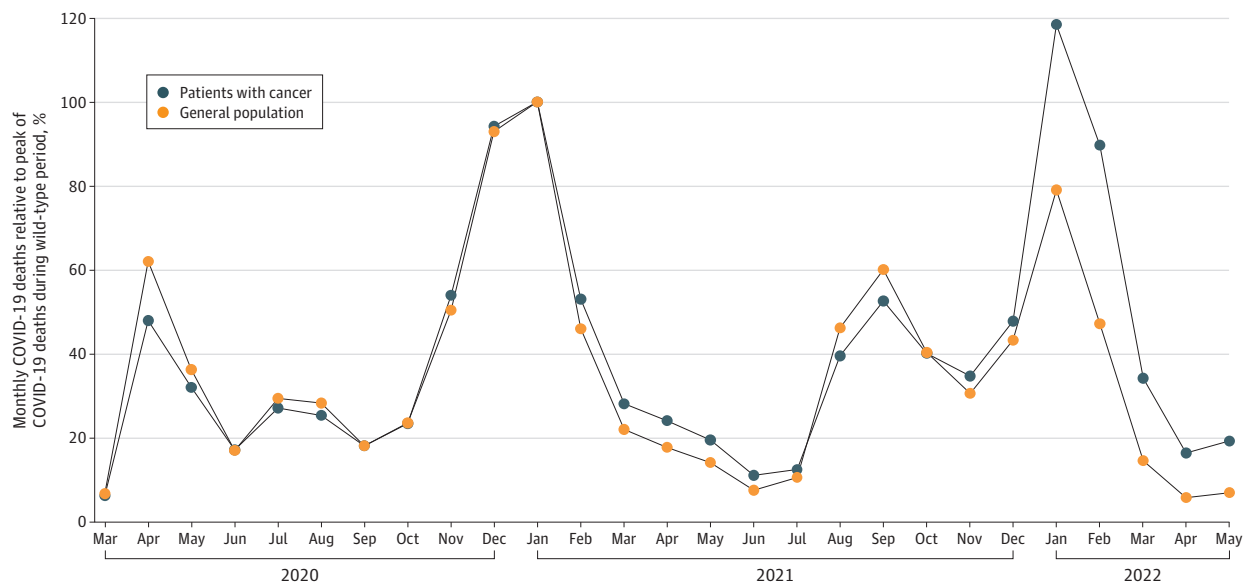
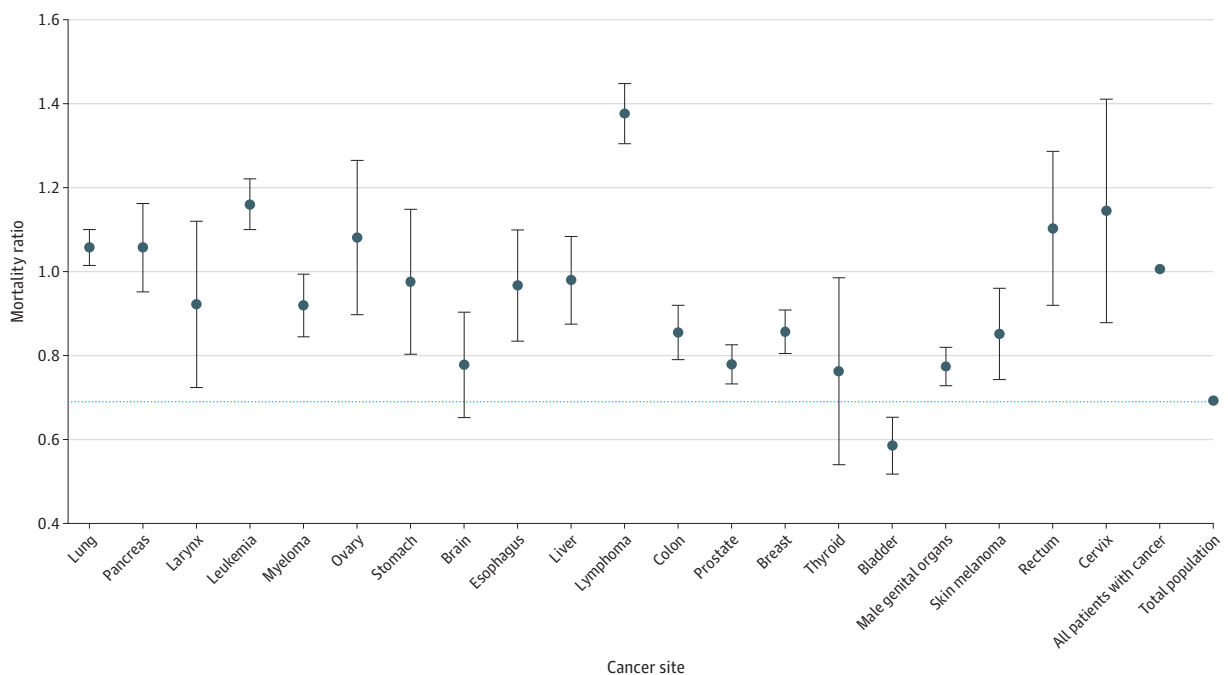


Figure 2. Mortality Ratios of the Number of COVID-19 Deaths During the Winter Omicron Period vs the Wild-Type Period by Cancer Site



The dashed line corresponds with the mortality ratio of the number of COVID-19 deaths during the winter Omicron period vs the number of COVID-19 deaths during the wild-type period among the total US population. Mortality ratios above this line indicate greater-than-expected COVID-19 mortality during the

Omicron vs wild-type periods compared with the general population. Mortality ratios below this line indicate lower-than-expected COVID-19 mortality during the Omicron vs wild-type periods compared with the general population. The error bars indicate 95% CIs.

experienced the highest COVID-19 mortality during the winter Omicron period likely due to increased SARS-CoV-2 exposure during this period combined with the reduced effectiveness of COVID-19 vaccines and increased risk of COVID-19

mortality in this population. With future COVID-19 waves imminent, strategies to protect those at highest risk should remain a high priority, even during future pandemic waves with less virulent SARS-CoV-2 variants.

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Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Potter, Venkateswaran, Yang.

Critical review of the manuscript for important intellectual content: All authors.

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Administrative, technical, or material support: Bajaj.
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