Mortality in Cancer Patients With COVID-19 Who Are Admitted to an ICU or Who Have Severe COVID-19: A Systematic Review and Meta-Analysis

Amogh Rajeev Nadkarni, MBBS1; Swapna C. Vijayakumaran, MD1; Sudeep Gupta, MD, DM2; and Jigeeshu V. Divatia, MD1

abstract

PURPOSE There are scarce data to aid in prognostication of the outcome of critically ill cancer patients with COVID-19. In this systematic review and meta-analysis, we investigated the mortality of critically ill cancer patients with COVID-19.

METHODS We searched online databases and manually searched for studies in English that reported on outcomes of adult cancer patients with COVID-19 admitted to an intensive care unit (ICU) or those with severe COVID-19 between December 2019 and October 2020. Risk of bias was assessed by the Modified Newcastle-Ottawa Scale. The primary outcome was all-cause mortality. We also determined the odds of death for cancer patients versus noncancer patients, as also outcomes by cancer subtypes, presence of recent anticancer therapy, and presence of one or more comorbidities. Random-effects modeling was used.

RESULTS In 28 studies (1,276 patients), pooled mortality in cancer patients with COVID-19 admitted to an ICU was 60.2% (95% CI, 53.6 to 6.7; I² = 80.27%), with four studies (7,259 patients) showing higher odds of dying in cancer versus nonsmoking patients (odds ratio 1.924; 95% CI, 1.596 to 2.320). In four studies (106 patients) of patients with cancer and severe COVID-19, pooled mortality was 59.4% (95% CI, –39.4 to 77.5; I² = 72.28%); in one study, presence of hematologic malignancy was associated with significantly higher mortality compared with nonhematologic cancers (odds ratio 1.878; 95% CI, 1.171 to 3.012). Risk of bias was low.

CONCLUSION Most studies were reported before the results of trials suggesting the benefit of dexamethasone and tocilizumab, potentially overestimating mortality. The observed mortality of 60% in cancer patients with COVID-19 admitted to the ICU is not prohibitively high, and admission to the ICU should be considered for selected patients (registered with PROSPERO, CRD42020207209).

INTRODUCTION

Since December 2019, the world has been gripped by COVID-19, the disease caused by severe acute respiratory syndrome coronavirus 2, with more than 174 million cases and 3.75 million deaths. The spectrum of COVID-19 spans from asymptomatic through moderate to severe. About 5% of all patients and 20% of hospitalized patients with COVID-19 may experience severe manifestations necessitating intensive care unit (ICU) admission.1 Mortality of patients with COVID-19 admitted in the ICU is high. In one meta-analysis,2 31% of patients admitted to the ICU died, whereas in another, mortality ranged from 0% to 84.6%, with a pooled mortality of 41.6%.3

Patients with cancer may be at increased risk of complications and mortality from COVID-19 owing to the systemic effects of malignancy; immune suppression after chemotherapy; treatment-related cardiovascular, renal, and pulmonary toxicities4; as well as the coexistence of comorbidities. Active cancer is associated with increased odds of death among patients with COVID-19.5 In two large series of cancer patients with COVID-19, mortality ranged from 13% to 28%.5,7 Some studies have found that patients with cancer had a higher risk of severe events and in-hospital mortality.7-9

Cancer patients with COVID-19 may develop serious complications necessitating ICU admission. In the setting of a global pandemic, allocation of intensive care resources may require triaging or prioritization of ICU admissions on the basis of outcomes in specific patient populations, such as those with COVID-19 and cancer.

An estimate of the mortality rate in cancer patients with COVID-19 admitted to the ICU on the basis of the available data could help in the planning and
prioritization of patients for ICU admission. Although there are data to suggest that all-cause mortality and the need for ICU admission were higher in COVID-19 patients with cancer than those without cancer,7-10 other studies have found no difference between COVID-19 patients with and without cancer with respect to a composite outcome including death, intubation, or ICU admission.11 Very few studies have specifically reported the mortality of patients with cancer admitted in ICUs, and there are scarce data to aid in selection of critically ill cancer patients with COVID-19 for admission to the ICU or help in prognostication of outcome. Hence, we performed a systematic review and meta-analysis of the available literature to estimate the mortality among cancer patients with COVID-19 admitted to the ICU or those with severe COVID-19.

METHODS
The review was prospectively registered on PROSPERO (CRD42020207209) and conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.12 Ethics committee approval was not required.

Data Sources
We searched for terms related to cancer, COVID-19, and intensive care. Exact search terms are in the Appendix Table A1. Various databases including PUBMED, MEDLINE, SCOPUS, and Web of Science were searched, supplemented by manually searching Cochrane Library and Google Scholar. All articles published from the first report of COVID-19 to October 31, 2020, were eligible to be included in the review.

Study Selection
All studies in English including retrospective and prospective cohort studies, case-control studies, and case series were included if they reported adult patients (age ≥ 18 years) with cancer and COVID-19 who were admitted to the ICU. Where ICU admissions were not specified, patients with cancer and severe or critical COVID-19 were included and their outcomes were analyzed separately. Severe disease included clinical signs of pneumonia plus one of the following: respiratory rate > 30 breaths/min, severe respiratory distress, or SpO2 < 90% on room air. Critical disease included development of the acute respiratory distress syndrome, sepsis, or septic shock.13

In studies that included data on both cancer patients with COVID-19 admitted to the ICU and those with severe COVID-19, only the data for patients admitted to the ICU were extracted. Studies were excluded if the primary outcome was not reported or it was not possible to extract the outcome of cancer patients with COVID-19 from the publication. Preclinical studies, epidemiologic studies, descriptive studies, and randomized controlled trials or studies without a report on mortality outcomes in adult patients with cancer that were admitted to the ICU or had severe COVID-19 were excluded. Studies were imported to Rayyan—a Web and mobile app for systematic reviews—and independently screened by two reviewers14 (A.R.N. and S.C.V.). Disagreements were resolved through mutual discussion, and persistent disagreements were resolved by a third reviewer (J.V.D.). All three literature searchers were clinicians working with critically ill patients. After screening the title and abstracts, full-text studies were identified and were independently assessed by the two primary reviewers.

Data Extraction and Quality Assessment
Data extraction and risk of bias assessment was performed on Microsoft Excel independently by two reviewers (S.C.V. and A.R.N.), with 20% of studies overlapped to assess reliability.
The extracted data points included study setting and design and stratification of patients with cancer on the basis of the severity of disease as defined by WHO criteria.\textsuperscript{13,15} The primary outcome was all-cause mortality in all patients. We also determined the primary outcome in the following subgroups: geographical location, cancer subtypes, presence of recent anticancer therapy (defined as therapy given within 1 month of diagnosis of COVID-19), patients receiving mechanical ventilation in the ICU, and presence of one or more comorbidities. Given the paucity of data and the variable length of follow-up in the included studies, we decided to include mortality regardless of the period of follow-up.

Secondary outcomes included the need for advanced support therapies in patients in the ICU and complications in patients with severe COVID-19. Where available, mortality data in noncancer COVID-19 patients admitted to the ICU from the same cohort were used to determine the odds of death for cancer patients compared with noncancer patients. The risk of bias assessment was carried out using a Modified Newcastle-Ottawa Scale,\textsuperscript{16} which reports three points for selection, two for comparability, and three for outcomes (Appendix Table A2) Funnel plot asymmetry generated using Public Health England tool was used to identify publication bias.\textsuperscript{17}

**Data Synthesis**

Meta-analysis was conducted using Open Meta-Analyst (CEBM, Brown University, Providence, RI).\textsuperscript{18} The pooling of the results was performed using the Der Simonian-Laird random-effects model. Summary of findings tables were constructed using GRADE pro GDT (GRADEpro Guideline Development Tool [Software], McMaster University, 2020 [developed by Evidence Prime Inc.]).\textsuperscript{19} The primary outcome identified for meta-analysis was the pooled mortality rate in patients with COVID-19 admitted to the ICU or cancer patients with severe COVID-19. Subgroup analysis for the primary outcome was performed after grouping of study patients by geographical location (Europe, United States, China, and multinational), hematologic versus other cancers, the use of recent anticancer therapy versus former anticancer therapy, sample size ($\leq 25 \text{ v} > 25\text{ patients}$), and presence of comorbidities. Patients requiring invasive mechanical ventilation were analyzed separately for pooled mortality outcomes. The odds of mortality in COVID-19 patients with cancer versus COVID-19 patients without cancer among patients admitted to the ICU were also estimated. Primary and secondary outcomes were reported and graded using GRADEpro GDT,\textsuperscript{19} tabulated in the summary of findings tables. Meta-regressions for mortality were performed for number of days since December 2019.

**RESULTS**

One thousand three hundred studies were identified on electronic literature search, with 69 studies identified on manual searching. After removing duplicates, 1,238 studies were screened by title and abstract; 74 full-text articles were identified for eligibility, of which 44 studies reporting the primary and other outcomes were included for data extraction. Reasons for exclusion can be identified in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses chart (Fig 1). There were 13 studies from China with potentially overlapping patients.\textsuperscript{29-32} On the basis of overlapping study duration and hospital location, a decision was taken to include only the most recent study (Yang et al)\textsuperscript{29} in the meta-analysis for studies reporting mortality in cancer patients with COVID-19 admitted to the ICU and the largest cohort (Zhang et al)\textsuperscript{25} for studies reporting mortality in cancer patients with severe COVID-19 (Appendix Table A3). Furthermore, two studies detailing outcomes and risk factors for ICU patients with COVID-19 in Lombardy, Italy, were identified.\textsuperscript{33,34} A decision was taken to include the study with the later date of publication.\textsuperscript{34} Twenty-eight studies were included for meta-analysis; these included patients from Asia (three studies),\textsuperscript{29,35,36} the Americas (10 studies),\textsuperscript{5,37-45} Europe (13 studies),\textsuperscript{5,34,46-56} and multinational registries (two studies).\textsuperscript{6,57} The 28 studies that reported mortality in cancer patients with COVID-19 admitted to the ICU included a total of 1,276 patients, with dates of recruitment ranging from January 23 to June 11, 2020. Four studies that included 106 patients and reported mortality in cancer patients with severe COVID-19 were from China (one study),\textsuperscript{25} Spain (two studies),\textsuperscript{58,59} and United Kingdom (one study).\textsuperscript{60} Figure 2 summarizes the studies included and the subgroups studied with the primary and secondary outcomes. Five studies with a total of 131 patients reported mortality outcomes of mechanically ventilated cancer patients in the ICU.\textsuperscript{62,43,51,53,56} Two studies reporting mortality of patients with invasive mechanical ventilation were excluded from the analysis because ICU admission was not mentioned; the numbers including mechanically ventilated patients exceed the number of patients in the ICU cohort, suggesting that not all mechanically ventilated patients may have been admitted to the ICU.\textsuperscript{38,45} Of studies reporting mortality in cancer patients with COVID-19 admitted to the ICU, four studies reported mortality outcomes for noncancer patients with COVID-19,\textsuperscript{26,34,54} and one study reported mortality outcomes on the basis of cancer subtype.\textsuperscript{54} For studies reporting outcomes of cancer patients with severe COVID-19, one study reported mortality outcomes on the basis of cancer subtype, recent anticancer therapy, or presence of one or more comorbidities.\textsuperscript{54} Details of studies included and outcomes are summarized in Table 1.

Mortality was variably reported in the included studies as death in ICU, in hospital, at 28 days, at 30 days, or on a cutoff date (Table 1). The risk of bias assessment on the basis of the Modified Newcastle-Ottawa Scale was a median 7/8 (Appendix Table A4).

**Cancer Patients With COVID-19 Admitted to the ICU**

For cancer patients with COVID-19 admitted to the ICU, the pooled mortality rate was 60.2% (95% CI, 53.6 to 66.7),
The largest study was that of Grasselli et al, with a cohort of 331 cancer patients with COVID-19 admitted to the ICU; however, a sensitivity analysis with the study excluded did not significantly affect mortality (60.2%; 95% CI, 52.8 to 67.6) or heterogeneity ($I^2 = 80.98\%$).

Pooled mortality rate of patients with cancer on invasive mechanical ventilation in the ICU (five studies, 131 patients) was 49.4% (95% CI, 30.9 to 67.9; $I^2 = 78.1\%$). The mortality in cancer patients with COVID-19 admitted to the ICU was significantly higher than that in noncancer patients with COVID-19 admitted to the ICU (59.8% [95% CI, 54.8 to 64.8] vs 42.3% [95% CI, 33.6 to 51.1]; odds ratio [OR] 1.924; 95% CI, 1.596 to 2.320). In one study, mortality of patients with hematologic malignancies as compared with nonhematologic malignancies did not differ significantly (53.8% [95% CI, 26.7 to 80.9] vs 66.7% [95% CI, 42.8 to 90.5]; Table 3). Subgroup analysis on the basis of geographical location revealed significant reduction in heterogeneity and increased mortality for studies from Asia (84.2% [95% CI, 73.7 to 94.6], $I^2 = 0$) and significant reduction in heterogeneity for Europe (57% [95% CI, 50.7 to 63.3], $I^2 = 51.61$). Estimates for mortality by number of centers and sample size are detailed in Appendix Table A5. Funnel plot asymmetry was negative, with two reporting mortality < 3 standard deviations (Appendix Fig A1).
Studies reporting percentage of ICU patients who required advanced respiratory support therapies can be found in Appendix Table A6.

Meta-regressions for ICU mortality showed that mortality in cancer patients with COVID-19 admitted to the ICU did not differ on the basis of the date of recruitment (Appendix Fig A2).

**Cancer Patients With Severe COVID-19**

The pooled mortality rate in cancer patients with severe COVID-19 was 58.4% (95% CI, 39.4 to 77.5) with $I^2$ of 72.28% (Appendix Table A5, Appendix Fig A3). Along with mortality in cancer patients with COVID-19 admitted to the ICU, mortality in cancer patients with severe COVID-19 is reported in Table 2. One study of 246 patients with severe COVID-19 reported higher mortality among patients with hematologic versus those with nonhematologic cancers (77.6% [95% CI, 68.9 to 88.3] v 41.3% [95% CI, 38.2 to 41.4]; OR 1.878; 95% CI, 1.171 to 3.012; Appendix Table A7), but there was no difference among patients with comorbidity compared with those without any comorbidity (49.1% [95% CI, 42.5 to 55.7] v 25% [95% CI, 5 to 49.5]; OR 1.964; 95% CI, 0.542 to 7.104) or in patients who had received recent anticancer therapy compared with those who had not received such therapy (53.5% [95% CI, 42.9 to 64] v 48.1% [95% CI, 40.2 to 55.9]; OR 1.113; 95% CI, 0.708 to 1.748; Appendix Table A7). Our analysis reports the prevalence of pulmonary complications (49.7%), cardiac complications (14.3%), sepsis (11.5%), and renal complications (8.7%; Appendix Table A8).

**DISCUSSION**

Our analysis suggests that the mortality in cancer patients with COVID-19 who are admitted to ICUs or who have severe COVID-19 is nearly 60%. Among cancer patients with severe COVID-19, the odds of death were higher in patients with hematologic malignancies. We also found that cancer patients with COVID-19 in the ICU had a two-fold increase in odds of death compared with COVID-19 patients without cancer.

Patients with cancer may be immunosuppressed because of disease or treatment and have cancer- or treatment-related organ dysfunction. Studies comparing cohorts of cancer and noncancer patients have found that patients with hematologic malignancies have a higher mortality rate and incidence of ICU admissions. Another small study found no significant difference in terms of overall survival between solid-tumor and hematologic patients, although patients with a hematologic malignancy showed a non-significant trend for earlier occurrence of severe events.
| Category | Study With Country | Study Design | Study Period | Length of Follow-Up | Proportion of Cancer Patients With COVID-19 Admitted to the ICU for Whom the Primary Outcome Was Available | Proportion of Cancer Patients With COVID-19 Admitted to the ICU Who Died | Proportion of Cancer Patients With Severe COVID-19 for Whom the Primary Outcome Was Available | Proportion of Cancer Patients With Severe COVID-19 Who Died |
|----------|-------------------|--------------|--------------|---------------------|-----------------------------------------------------------------|------------------------------------------------------------------|----------------------------------------------------------------|--------------------------------------------------|
| Studies reporting patients admitted to the ICU | Fattizzo et al.,47,a Italy | Single-center, retrospective | January 23 to February 13, 2020 | NR | 2/16 | 1/2 | NR | NR |
| | Gonfotti et al.,48,a Italy | Single-center, retrospective | January 29 to March 4, 2020 | Death or discharge from hospital | 2/5 | 2/2 | NR | NR |
| | Krause et al.,49,a United States | Multicenter, retrospective | March 9 to April 1, 2020 | 30-day mortality | NR | 7/11 | NR | NR |
| | Gupta et al.,50,a United States | Multicenter, retrospective | March 4 to April 4, 2020 | 28-day mortality | 112/112 | 60/112 | NR | NR |
| | Malard et al.,51,a France | Single-center, retrospective | March 9 to April 4, 2020 | 10-day mortality | NR | 2/7 | NR | NR |
| | Robilotti et al.,52,a United States | Single-center, retrospective | March 10 to April 7, 2020 | 30 days | 48/168 | 17/48 | NR | NR |
| | Mehta et al.,53,a United States | Multicenter, retrospective | March 18 to April 8, 2020 | NR | 23/218 | 15/23 | NR | NR |
| | Garassino et al.,54,a Europe and United States | Multicenter, retrospective | March 26 to April 12, 2020 | Death or discharge from hospital | 13/200 | 8/13 | NR | NR |
| | Martin-Moro et al.,55,a Spain | Single-center, retrospective | March 9 to April 17, 2020 | Median follow-up of 26 days | 2/34 | 2/2 | 17/34 | 10/17 |
| | Yang et al.,56,a China | Multicenter, retrospective | January 13 to April 20, 2020 | 30 days | 30/205 | 26/30 | 52/153 | 35/52 |
| | Lara et al.,57,a United States | Multicenter, retrospective | March 1 to April 22, 2020 | NR | 20/121 | 17/20 | 20/121 | 17/20 |
| | Grasselli et al.,58,a Italy | Multicenter, retrospective | February 20 to April 22, 2020 | Followed up till May 30 (minimum 38 days) | NR | 202/331 | NR | NR |
| | Lee et al.,59,a United Kingdom | Single-center, retrospective | March 18 to April 26, 2020 | Death or discharge from hospital | 53/800 | 23/53 | 187/800 | 59/187 |
| | Joharatnam-Hogan et al.,60,a United Kingdom | Multicenter, retrospective | March 1 to April 28, 2020 | NR | 1/1 | 1/1 | NR | NR |
| | Wang et al.,61,a China | Single-center, retrospective | March 1 to April 30, 2020 | NR | 7/36 | 6/7 | NR | NR |
| | Lunski et al.,62,a United States | Multicenter, retrospective | March 1 to April 30, 2020 | NR | 48/312 | 31/48 | NR | NR |
| | Lamure et al.,63,a France | Multicenter, retrospective | March 1 to April 30, 2020 | 30-day mortality | 25/89 | 8/25 | NR | NR |
| | Shah et al.,64,a United Kingdom | Single-center, retrospective | March 13 to May 5, 2020 | 30-day mortality | 10/80 | 5/10 | NR | NR |

(Continued on following page)
### TABLE 1. Included Studies (Continued)

| Category | Study With Country | Study Design | Study Period | Length of Follow-Up | Proportion of Cancer Patients With COVID-19 Admitted to the ICU for Whom the Primary Outcome Was Available | Proportion of Cancer Patients With Severe COVID-19 Admitted to the ICU Who Died | Proportion of Cancer Patients With Severe COVID-19 for Whom the Primary Outcome Was Available | Proportion of Cancer Patients With Severe COVID-19 Who Died |
|----------|--------------------|--------------|--------------|---------------------|-----------------------------------------------------------------|---------------------------------------------------------------------------|---------------------------------------------------------------------------|--------------------------------------------------|
|          | Luo et al,40,a United States | Single-center, retrospective | March 12 to May 6, 2020 | Death or discharge from the hospital | 21/102 | 15/21 | 34/102 | NR |
|          | Kuderer et al,6,a United States, Canada, and Spain | Multicenter, retrospective | March 17 to May 7, 2020 | 30 days of diagnosis of COVID-19 | 132/928 | 16/52 | 246/928 | 121/242 |
|          | Singh et al,41,a United States | Single-center, retrospective | NR to May 13, 2020 | Median 31 days of follow-up | 30/85 | 23/30 | NR | NR |
|          | Passamonti et al,50,a Italy | Multicenter, retrospective | February 25 to May 18, 2020 | 28-day mortality | 82/536 | 52/82 | 194/536 | 88/194 |
|          | Haase et al,54,a Denmark | Multicenter, retrospective | March 10 to May 19, 2020 | NR | NR | 17/28 | NR | NR |
|          | Garcia-Suárez et al,55,a Spain | Multicenter, retrospective | March 13 to May 25, 2020 | NR | 139/697 | 92/139 | NR | NR |
|          | de Melo et al,45,a Brazil | Single-center, retrospective | April 30 to May 26, 2020 | NR | 32/181 | 8/32 | NR | NR |
|          | Smith et al,44,a United States | Multicenter, retrospective | March 1 to May 30, 2020 | NR | 29/86 | 25/29 | NR | NR |
|          | Ramaswamy et al,36,a India | Single-center, retrospective | March 23 to June 10, 2020 | 30-day mortality | 8/230 | 5/8 | NR | NR |
|          | Lievre et al,56,a France | Multicenter, retrospective and prospective | March 1 to June 11, 2020 | NR | 110/1,289 | 62/110 | NR | NR |

| Studies reporting severe COVID-19 | Zhang et al,25 China | Multicenter, retrospective | January 5 to March 18, 2020 | NR | NR | NR | 56/107 | 23/56 |
|                                   | Rogado et al,58 Spain | Single-center, retrospective | March 5 to April 7, 2020 | NR | NR | NR | 7/17 | 4/7 |
|                                   | Sanchez-Pina et al,59 Spain | Single-center, retrospective | March 7 to April 7, 2020 | NR | NR | NR | 18/39 | 11/18 |
|                                   | Fox et al,60 United Kingdom | Single-center, retrospective | March 20 to April 20, 2020 | Death or discharge from hospital | 8/52 | NR | 25/52 | 19/25 |

Abbreviations: ICU, intensive care unit; NR, not reported.

*Studies were extracted for meta-analysis of mortality outcomes of ICU patients. Wherever data on cancer patients with COVID-19 admitted to the ICU was not available, mortality in cancer patients with severe COVID-19 was meta-analyzed separately.
TABLE 2. Summary of Findings for Cancer Patients With COVID-19 Admitted to the ICU

| No. of Studies | Study Design | Risk of Bias | Inconsistency | Indirectness | Imprecision | Other Considerations | Certainty Assessment | Effect |
|----------------|--------------|--------------|---------------|--------------|-------------|----------------------|----------------------|--------|
|                |              |              |               |              |             |                      |                      |        |
| 1. What is the mortality rate of cancer patients with COVID-19 who get admitted to the ICU? (assessed with mortality rate) | 28 studies | Seriousa | Seriousb | Not serious | Not serious | Strong association; all plausible residual confounding would reduce the demonstrated effect | HIGH | Event rate: 60.2 per 100 ICU admissions (53.6 to 66.7) |
|                |              |              |               |              |             |                      |                      |        |
| 2. What is the mortality rate of cancer patients with COVID-19 who get admitted to the ICU on invasive mechanical ventilation? (assessed with mortality rate) | 5 studies | Seriousa | Seriousb | Seriousc | Not serious | Strong association; all plausible residual confounding would reduce the demonstrated effect | MODERATE | Event rate: 49.4 per 100 ICU admissions (30.9 to 67.9) |

| No. of Studies | Study Design | Risk of Bias | Inconsistency | Indirectness | Imprecision | Other Considerations | Intervention | Comparison | Relative (95% CI) | Absolute (95% CI) | Certainty |
|----------------|--------------|--------------|---------------|--------------|-------------|----------------------|--------------|------------|------------------|------------------|-----------|
| 3. What is the ICU mortality rate in COVID-19–positive cancer versus noncancer patients? | 4 studies | Seriousa | Seriousb | Not serious | Not seriousc | Strong association; all plausible residual confounding would reduce the demonstrated effect | 296/495 (59.8%) | 2,926/6,764 (43.3%) | OR 1.924 (1.596 to 2.320) | 16 more deaths per 100 (from 12 more to 21 more) | LOW |
| 4. Mortality rate in cancer patients admitted to the ICU with COVID-19: hematologic versus nonhematologic | 1 study | Seriousa | Seriousb | Not serious | Seriousc | Strong association; all plausible residual confounding would reduce the demonstrated effect | 7/13 (53.8%) | 10/15 (66.7%) | OR 0.808 (0.239 to 2.731) | 49 fewer deaths per 1,000 (from 343 fewer to 179 more) | VERY LOW |

Abbreviations: ICU, intensive care unit; OR, odds ratio.
*aBaseline data from large observational studies. Large losses to follow-up noted.
*bUnexplained heterogeneity after subgroup analysis.
*cDefinition of outcome of interest, for example, severity of disease is subjective and may vary across study populations.
compared with solid-tumor patients. Among cancer patients with COVID-19, cancer type and active treatment with chemotherapy, immunotherapy, targeted therapies, hormonal therapy, surgery, or radiotherapy within four weeks of diagnosis were not associated with increased adverse outcomes. Unlike these studies that looked at all patients with cancer and COVID-19, our study was focused on cancer patients with COVID-19 admitted to the ICU or those with severe disease. Our analysis too did not reveal a statistically significant difference in mortality in patients with recent anticancer therapy and presence of one or more comorbidities possibly because of paucity in available data.

Before the pandemic, the unadjusted pooled mortality of critically ill cancer patients in studies published between 2005 and 2015 was 47.1%. With advances in oncology and intensive care, mortality rates of critically ill cancer patients have further improved and are below 30% in the ICU and below 40% in hospital. On the basis of such outcomes, most authorities recommend that patients with cancer (with the exception of those with very poor performance status and advanced disease for whom no therapeutic options are available) should be admitted to the ICU for aggressive treatment or a therapeutic ICU trial for about 5 days. During the COVID-19 pandemic, a meta-analysis by Armstrong et al found that the mortality of critically ill patients with COVID-19 has decreased over the course of the pandemic from more than 50% to 40%. The mortality rate of 60% in cancer patients with COVID-19 admitted to the ICU suggests that outcomes in cancer patients with COVID-19 are not prohibitively high. Furthermore, a majority of patients in the included studies were treated before the availability of the results of trials that suggested that dexamethasone and tocilizumab may be beneficial in patients who receive either oxygen or mechanical ventilation. On the basis of such recent advances in care of patients with COVID-19, our meta-analysis may overestimate the true mortality of critically ill cancer patients.

| Studies                  | Estimate (95% CI) Event/Treatment |
|--------------------------|-----------------------------------|
| Fattizzo et al           | 0.500 (−0.193 to 1.193) 1/2       |
| Gonfioi et al            | 0.833 (0.412 to 1.255) 2/2        |
| Malard et al             | 0.286 (−0.049 to 0.620) 2/7      |
| Martin-Moro et al        | 0.833 (0.412 to 1.255) 2/2       |
| Grasselli et al          | 0.610 (0.558 to 0.663) 202/331   |
| Lee et al                | 0.434 (0.301 to 0.567) 23/53     |
| Joharatnam-Hogan et al   | 0.750 (0.150 to 1.350) 1/1       |
| Lamure et al             | 0.320 (0.137 to 0.503) 8/25      |
| Shah et al               | 0.500 (0.190 to 0.810) 5/10      |
| Passamonti et al         | 0.634 (0.530 to 0.738) 52/62     |
| Haase et al              | 0.607 (0.426 to 0.788) 17/28     |
| Garcia Suarez et al      | 0.662 (0.583 to 0.741) 92/139    |
| Lievre et al             | 0.564 (0.471 to 0.656) 62/110    |
| **Subgroup Europe**      | 0.570 (0.507 to 0.633) 469/792   |
| Krause et al             | 0.636 (0.352 to 0.921) 7/11      |
| Gupta et al              | 0.536 (0.443 to 0.628) 60/112    |
| Robilotti et al          | 0.364 (0.219 to 0.489) 17/48     |
| Mehta et al              | 0.652 (0.458 to 0.847) 15/23     |
| Lara et al               | 0.850 (0.694 to 1.006) 17/20     |
| Lunski et al             | 0.646 (0.511 to 0.781) 31/48     |
| Luo et al                | 0.714 (0.532 to 0.908) 15/21     |
| Singh et al              | 0.767 (0.615 to 0.918) 23/30     |
| de Melo et al            | 0.250 (0.100 to 0.400) 8/32      |
| Smith et al              | 0.862 (0.737 to 0.988) 25/29     |
| **Subgroup Americas**    | 0.625 (0.495 to 0.754) 218/374   |
| Garassino et al          | 0.615 (0.351 to 0.880) 8/13      |
| Kuderer et al            | 0.308 (0.182 to 0.433) 16/52     |
| **Subgroup Multinational** | 0.429 (0.140 to 0.737) 24/65 |
| Yang et al               | 0.867 (0.745 to 0.988) 26/30     |
| Ramaswamy et al          | 0.625 (0.290 to 0.960) 5/8       |
| Wang et al               | 0.857 (0.598 to 1.116) 6/7       |
| **Subgroup Asia**        | 0.942 (0.737 to 0.946) 37/45     |
| **Overall**              | 0.602 (0.536 to 0.667) 748/1,276 |

**FIG 3.** Meta-analysis, including subgroup analysis on geographical location.
TABLE 3. Summary of Findings for Cancer Patients With Severe COVID-19

| No. of Studies | Study Design | Risk of Bias | Inconsistency | Indirectness | Imprecision | Other Considerations | Effect |
|----------------|--------------|--------------|---------------|--------------|-------------|----------------------|--------|
| 1              | Observational studies | Serious | Serious | Serious | Not serious | Strong association; all plausible residual confounding would reduce the demonstrated effect | Event rate: 58.4 per 100 patients having severe disease (39.4 to 77.5) | MODERATE |
|                |              |              |              |              |             |                      |        |
|                |              |              |              |              |             |                      |        |
|                |              |              |              |              |             |                      |        |

| No. of Studies | Study Design | Risk of Bias | Inconsistency | Indirectness | Imprecision | Other Considerations | Effect |
|----------------|--------------|--------------|---------------|--------------|-------------|----------------------|--------|
| 1              | Observational studies | Serious | Serious | Not serious | Serious | Strong association; all plausible residual confounding would reduce the demonstrated effect | Relative (95% CI) Absolute (95% CI) |
|                |              |              |              |              |             |                      |        |
|                |              |              |              |              |             |                      |        |
|                |              |              |              |              |             |                      |        |

Abbreviation: OR, odds ratio.

*Baseline data from large observational studies. Large losses to follow-up noted.

bUnexplained heterogeneity after subgroup analysis.

cDefinition of outcome of interest, for example, severity of disease is subjective and may vary across study populations.
Our meta-regression falls short of showing a statistically significant difference in mortality over the period analyzed, again because of the small numbers of patients studied.

The decision regarding the admission of patients with cancer to the ICU in the setting of the COVID-19 pandemic is dictated by various locoregional factors such as availability of ICU resources, institutional policies, underlying cancer diagnosis, a decision not to escalate to ICU for futility in patients with advanced-stage cancer and end-of-life care decisions during ICU care. In a cohort of 928 patients, patients with progressive cancer died at a numerically higher rate without ICU admission than those who were admitted to an ICU. This suggests that aggressive interventions might have already been restricted in these subpopulations and partially explains the similar mortalities in cancer patients with COVID-19 admitted to the ICU and those classified as severely ill. Studies included in our systematic review have noted refusal of ICU admission or limitation of beds. In one multicenter study, only 10% of eligible patients were admitted to the ICU. Similarly, in another study, patients admitted in the ICU were younger and had a lower Charlson Comorbidity Index, suggesting a selection bias. Hanten et al reported local crisis standards of care in the United States that deprioritize patients with cancer in favor of less aggressive interventions, often without sufficient precision to differentiate different survival patterns of cancer subtypes. Considerations such as these may have resulted in several patients being denied admission to ICUs, explaining the paucity of and lack of granularity in the data.

As the pandemic wanes in several parts of the world, there will be occasions when patients with cancer will require admission to the ICU. We believe that on the basis of the results of our meta-analysis, mortality in critically ill patients with COVID-19 and cancer is not prohibitively high, and patients with COVID-19 must not be denied ICU admission only on the grounds that they have cancer. These decisions will need to be individualized taking into account the performance status of the patient and the potential for cure or significant palliation of the cancer.

To our knowledge, this is the first systematic review exploring mortality in cancer patients with COVID-19 admitted to the ICU, or with severe COVID-19. Furthermore, the median risk of bias for our review is 7/8, and the grade of evidence for the primary outcome using the GRADEpro was moderate to high and there is a low risk of publication bias.

Patients were included in meta-analysis on the basis of data that were available for extraction from studies in English that were published or accepted for publication. We did not contact authors for individual patient data. Most studies were performed before publication of trials of therapies such as dexamethasone and tocilizumab. Our review is based on observational studies, and the high heterogeneity noted across studies suggests that results of this review need to be interpreted with caution. The severity of illness in terms of physiologic parameters such as the Acute Physiology and Chronic Health Evaluation score or the Sequential Organ Failure Assessment score is not available. Mortality data are also limited by the numbers of patients still in ICU or hospital on the cutoff date for estimation of mortality. Furthermore, despite the inclusion of 28 studies, we did not have sufficient granularity in the data to definitively determine differences in outcomes in important subgroups, such as hematologic versus solid-tumor malignancies and patients receiving active chemotherapy versus those not receiving chemotherapy.

In summary, the results of our meta-analysis suggest that cancer patients with COVID-19 who require admission to an ICU or those who have severe COVID-19 experience high mortality. However, denying ICU admission to patients with COVID-19 only because they have cancer may not be justified. Targeted interventions to prevent transmission of severe acute respiratory syndrome coronavirus 2 among patients with cancer and early therapeutic interventions in those with COVID-19 are likely to remain very important in the near future.
REFERENCES

1. Wiersinga WJ, Rhodes A, Cheng AC, et al: Pathophysiology, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19): A review. JAMA 324:782-793, 2020
2. Abate SM, Ali SA, Mantfardo B, et al: Rate of intensive care unit admission and outcomes among patients with coronavirus: A systematic review and meta-analysis. PLoS One 15:e0236563, 2020
3. Armstrong RA, Kane AD, Cook TM: Outcomes from intensive care in patients with COVID-19: A systematic review and meta-analysis of observational studies. Anaesthesia 75:1340-1349, 2020
4. Disis ML: Oncology and COVID-19. JAMA 324:1141-1142, 2020
5. Gupta S, Hayek SS, Wang W, et al: Factors associated with death in critically ill patients with coronavirus disease 2019 in the us. JAMA Intern Med 180:1436-1447, 2020
6. Kuderer NM, Choueiri TK, Shah DP, et al: Clinical impact of COVID-19 on patients with cancer (CCC19): A cohort study. Lancet 395:1907-1918, 2020
7. de Azambuja E, Brandão M, Wildiers H, et al: Impact of solid cancer on in-hospital mortality overall and among different subgroups of patients with COVID-19: A nationwide, population-based analysis. ESMO Open 5:e000947, 2020
8. Liang W, Guan W, Chen R, et al: Cancer patients in SARS-CoV-2 infection: A nationwide analysis in China. Lancet Oncol 21:335-337, 2020
9. Shah V, Ko TK, Zuckerman M, et al: Poor outcome and prolonged persistence of SARS-CoV-2 RNA in COVID-19 patients with haematological malignancies; King’s College Hospital experience. Br J Haematol 190:e279-e282, 2020
10. Liu Y, Lu H, Wang W, et al: Clinical risk factors for mortality in patients with cancer and COVID-19: A systematic review and meta-analysis of recent observational studies. Expert Rev Anticancer Ther 21:107-119, 2021
11. Brar G, Pinheiro LC, Shusterman M, et al: COVID-19 severity and outcomes in patients with cancer: A matched cohort study. J Clin Oncol 38:3914-3924, 2020
12. Liberati A, Altman DG, Tetzlaff J, et al: The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: Explanation and elaboration. PLoS Med 6:e1000100, 2009
13. Clinical management of COVID-19. https://www.who.int/publications-detail-direct/clinical-management-of-covid-19
14. Ouzzani M, Hammady H, Fedorowicz Z, et al: Rayyan—A web and mobile app for systematic reviews. Syst Rev 5:210, 2016
15. Marshall JC, Murthy S, Diaz J, et al: A minimal common outcome measure set for COVID-19 clinical research. Lancet Infect Dis 20:e192-e197, 2020
16. Wells G, Shea B, O’Connell D, et al: The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp
17. Public Health England: Funnel plot for proportions. https://fingertips.phe.org.uk/profile/guidance
18. OpenMeta [Analyst]—CEBM @ Brown. http://www.cebm.brown.edu/openmeta/
19. GRADEpro GDT. GRADEpro Guideline Development Tool [Software]. McMaster University, 2020 (developed by Evidence Prime, Inc.) https://gradrpro.org/cite/
20. Yang F, Shi S, Zhu J, et al: Clinical characteristics and prognosis in cancer patients with COVID-19: A single center’s retrospective study. J Infect 81:318-356, 2020
21. Wang J, Zhang J, Tu Y, et al: Cancer patients in SARS-CoV-2 infection: A singlecenter experience from wuhan. J Cancer 11:6243-6247, 2020
22. Zhang B, Yu Y, Hubert SM, et al: Prognostic value of pro-inflammatory neutrophils and C-reactive protein in cancer patient with coronavirus disease 2019: A multi-center, retrospective study. Front Pharmacol 11:576994, 2020
23. Dai M-Y, Chen Z, Leng Y, et al: Patients with lung cancer have high susceptibility of covid-19: A retrospective study in Wuhan, China. Cancer Control 27, 2020
24. Grasselli G, Zaninotto A, Zanella A, et al: Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy Region, Italy. JAMA 323:1574-1581, 2020
25. Grasselli G, Greco M, Zanella A, et al: Risk factors associated with mortality among patients with COVID-19 in intensive care units in Lombardy, Italy. JAMA Intern Med 180:1345-1355, 2020
26. Wang B, Van Oekelen O, Mouhiedine TH, et al: A tertiary center experience of multiple myeloma patients with COVID-19: Lessons learned and the path forward. J Hematol Oncol 13:94, 2020
36. Ramaswamy A, Nayak L, Roy Moulik N, et al: COVID-19 in cancer patients on active systemic therapy—Outcomes from LMIC scenario with an emphasis on need for active treatment. Cancer Med 9:8747-8753, 2020
37. Robiotti EV, Babady NE, Mead PA, et al: Determinants of COVID-19 disease severity in patients with cancer. Nat Med 26:1218-1223, 2020
38. Mehta V, Goel S, Kabarrth R, et al: Case fatality rate of cancer patients with COVID-19 in a New York Hospital System. Cancer Discov 10:935-941, 2020
39. Lara OD, O’Cearbhaill RE, Smith MJ, et al: COVID-19 outcomes of patients with gynecologic cancer in New York City. Cancer 126:4294-4303, 2020
40. Luo J, Rivzi H, Preeshagul IR, et al: COVID-19 in patients with lung cancer. Ann Oncol 31:1386-1396, 2020
41. Singh SRK, Thanikachalam K, Jabbour-Aida H, et al: Covid-19 and cancer: Lessons learnt from a Michigan hotspot. Cancers (Basel) 12:2377, 2020
42. Krause M, Douin DJ, Kim KK, et al: Characteristics and outcomes of mechanically ventilated covid-19 patients—An observational cohort study. J Intensive Care Med 36:271-276, 2021
43. Lusnki MJ, Burton J, Tawagi K, et al: Multivariate mortality analyses in COVID-19: Comparing patients with and patients without cancer in Louisiana. Cancer 127:266-274, 2021
44. Smith M, Lara OD, O’Cearbhaill R, et al: Inflammatory markers in gynecologic oncology patients hospitalized with COVID-19 infection. Gynecol Oncol 159:618-622, 2020
45. de Melo AC, Thuler LCS, da Silva JL, et al: Cancer inpatients with Covid-19: A report from the brazilian national cancer institute. PLoS One 15:e0241261, 2020
46. Lee LW, Cazier JB, Starkey T, et al: COVID-19 mortality in patients with chemotherapy or other anticancer treatments: A prospective cohort study. Lancet 395:1919-1926, 2020
47. Fattizzo B, Giannotta JA, Sciumé M, et al: Reply to “COVID-19 in persons with haematological cancers”: A focus on myeloid neoplasms and risk factors for mortality. Leukemia 34:1957-1960, 2020
48. Gonfotti A, Gattegna L, Salavicë A, et al: Clinical courses and outcomes of five patients with primary lung cancer surgically treated while affected by severe acute respiratory syndrome coronavirus 2. Eur J Cardiothorac Surg 58:598-604, 2020
49. Martín-Moro F, Marquet J, Piris M, et al: Survival study of hospitalised patients with concurrent COVID-19 and haematological malignancies. Br J Haematol 190:e16-e20, 2020
50. Passamonti F, Cattaneo C, Arcaini L, et al: Clinical characteristics and risk factors associated with COVID-19 severity in patients with haematological malignancies in Italy: A retrospective, multicentre, cohort study. Lancet Haematol 7:e737-e745, 2020
51. Malard F, Genthon A, Brissot E, et al: COVID-19 outcomes in patients with hematologic disease. Bone Marrow Transplant 55:2180-2184, 2020
52. Joharatnam-Hogan N, Hochhauser D, Shiu KK, et al: Outcomes of the 2019 novel coronavirus in patients with or without a history of cancer: A multi-centre North London experience. Ther Adv Med Oncol 12, 2020
53. Lamure S, Duléry R, Blasi RD, et al: Determinants of outcome in Covid-19 hospitalized patients with lymphoma: A retrospective multicentric cohort study. EclinicalMedicine;27:100549, 2020
54. Haase N, Plosving Christensen S, et al: Characteristics, interventions, and long term outcomes of COVID-19 ICU patients in Denmark—A nationwide, observational study. Acta Anaesthesiol Scand 65:68-75, 2021
55. Garcia-Suárez J, de la Cruz J, Cedillo A, et al: Impact of hematologic malignancy and type of cancer therapy on COVID-19 severity and mortality: Lessons from a large population-based registry study. J Hematol Oncol 13:133, 2020
56. Lièvre A, Turpin A, Ray-Coquard I, et al: Risk factors for cancer patients with COVID-19 severity and mortality among solid cancer patients and impact of the disease on anticancer treatment: A French nationwide cohort study (GCO-002 CACOVID-19). Eur J Cancer 141:62-81, 2020
57. Garassino MC, Whisnent JG, Huang LC, et al: COVID-19 in patients with thoracic malignancies (TERAVOLT): First results of an international, registry-based, cohort study. Lancet Oncol 21:914-922, 2020
58. Rogado J, Pangua C, Serrano-Montero G, et al: Covid-19 and lung cancer: A greater mortality rate? Lung Cancer 146:19-22, 2020
59. Sanchez-Pina JM, Rodriguez MR, Quismondo NC, et al: Clinical course and risk factors for mortality from COVID-19 in patients with haematological malignancies. Eur J Haematol 105:597-607, 2020
60. Fox TA, Troy-Barnes E, Kirkwood AA, et al: Clinical outcomes and risk factors for severe COVID-19 in patients with haematological disorders receiving chemo- or immunotherapy. Br J Haematol 191:194-206, 2020
61. Shoumariyeh K, Biavasco F, Ihorst G, et al: Covid-19 in patients with hematological and solid cancers at a Comprehensive Cancer Center in Germany. Cancer Med 9:8412-8422, 2020
62. Darmon M, Bourmaud A, Georges Q, et al: Changes in critically ill cancer patients’ short-term outcome over the last decades: Results of systematic review with meta-analysis on individual data. Intensive Care Med 45:977-987, 2019
63. Azoulay E, Schellongowski P, Darmon M, et al: The Intensive Care Medicine research agenda on critically ill oncology and hematology patients. Intensive Care Med 43:1366-1382, 2017
64. The RECOVERY Collaborative Group: Dexamethasone in hospitalized patients with Covid-19. N Engl J Med 384:693-704, 2021
65. REMAP-CAP Investigators, Gordon AC, Mouncey PR, et al: Interleukin-6 receptor antagonists in critically ill patients with Covid-19. N Engl J Med 384:1491-1502, 2021
66. RECOVERY Collaborative Group: Tocilizumab in patients admitted to hospital with COVID-19 (RECOVERY): A randomised, controlled, open-label, platform trial. Lancet 397:1637-1645, 2021
67. Martin-Moro F, Marquet J, Piris M, et al: Inflammatory markers in gynecologic oncology patients hospitalized with COVID-19 infection. Gynecol Oncol 159:618-622, 2020
68. Charlson ME, Pompei P, Ales KL, et al: A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. J Chronic Dis 40:373-383, 1987
69. Virnig BA, Nikpay SS: How will patients with cancer fare during COVID-19? Many unanswered questions. JAMA Oncol 7:195-196, 2021
70. Knaus WA, Draper EA, Wagner DP, et al: APACHE II: A severity of disease classification system. Crit Care Med 13:818-829, 1985
71. Vincent JL, Moreno R, Takala J, et al: The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. Intensive Care Med 22:707-710, 1996
**FIG A1.** Funnel plot for assessing publication bias. Cancer patients with COVID-19 admitted to the ICU (x-axis) versus ICU mortality rate (y-axis); reports studies within and beyond ±3 SD of pooled proportion of ICU mortality. ICU, intensive care unit; SD, standard deviation.

**FIG A2.** Meta-regression for proportion of patients who died in the intensive care unit (on the x-axis) versus date of recruitment. (on the y-axis). The circles indicate the proportion of patients dying in each study. The circle size is proportional to the precision of the estimate.
### FIG A3. Meta-analysis of cancer patients with severe COVID-19.

| Studies            | Estimate (95% CI)     | Event/Treatment |
|--------------------|-----------------------|-----------------|
| Zhang et al²⁵      | 0.411 (0.282 to 0.540)| 23/56           |
| Rogado et al⁵⁸     | 0.571 (0.205 to 0.938)| 4/7             |
| Sanchez-Pina et al⁵⁹| 0.611 (0.386 to 0.836)| 11/18           |
| Fox et al⁶⁰        | 0.760 (0.593 to 0.927)| 19/25           |
| Overall (I² = 72.28%, \( P = .013 \)) | 0.584 (0.394 to 0.775) | 57/106          |

### TABLE A1. Search Strategy

| Database          | Search Terms for Electronic Searches                                                                 |
|-------------------|-------------------------------------------------------------------------------------------------------|
| PUBMED             | (coronavirus[Title/Abstract] OR covid-19[Title/Abstract] OR sars-cov-2[Title/Abstract] OR 2019-ncov[Title/Abstract]) AND (mortality[Title/Abstract] OR outcomes[Title/Abstract] OR icu[Title/Abstract] OR intensive care[Title/Abstract]) AND (cancer[Title/Abstract] OR carcinoma[Title/Abstract] OR malignancy[Title/Abstract]) |
| MEDLINE            | (coronaviridae[MeSH Terms]) OR sars related coronavirus[MeSH Terms] AND (cancer[MeSH Terms]) OR malignancies [MeSH Terms]) OR carcinoma[MeSH Terms] AND ((outcome assessment, health care[MeSH Terms]) OR mortality [MeSH Terms]) OR critical care[MeSH Terms] |
| SCOPUS             | TS=(covid-19 OR coronavirus OR sars-cov-2 AND 2019-ncov) AND (mortality OR outcomes OR ICU OR intensive care) AND (cancer OR carcinoma OR malignancy) |
| Web of Science     | (TITLE-ABS-KEY (cancer) OR TITLE-ABS-KEY (carcinoma) OR TITLE-ABS-KEY (malignancy) AND TITLE-ABS-KEY (covid-19) OR TITLE-ABS-KEY (sars-cov-2) OR TITLE-ABS-KEY (2019-ncov) AND TITLE-ABS-KEY (mortality) OR TITLE-ABS-KEY (outcomes) OR TITLE-ABS-KEY (intensive and care) OR TITLE-ABS-KEY (icu)) |
| Cochrane Library   | Manually reviewed by publication date                                                                 |
| Google Scholar     | Manually reviewed by publication date                                                                 |

Abbreviation: ICU, intensive care unit.
### TABLE A2. Risk of Bias Assessment—Modified Newcastle-Ottawa Scale

| Grouping Item | Identifying Item |
|---------------|------------------|
| **Selection (maximum three points)** | |
| Representativeness of exposed cohort (nonsurvivors) | a. Truly representative of the average population of cancer patients with severe COVID-19/requiring ICU admissions  
| | b. Somewhat representative of the average population of cancer patients in the ICU with severe COVID-19  
| | c. Selected group of patients (eg, elderly, cardiac, surgical)  
| | d. No description of derivation of cohort  
| Selection of nonexposed cohort (ie, survivors) | a. Drawn from the same community as the exposed cohort and numbers given  
| | b. Drawn from a different source or numbers not given  
| | c. No description of the nonexposed cohort (ie, numbers not given)  
| Demonstration that outcome of interest was not present at start of study | a. Yes  
| | b. No  
| **Comparability (maximum two points)** | |
| Comparability of cohorts on the basis of patient demographics | a. Study reports patient demographics in survivors and nonsurvivors  
| | b. Survivors and nonsurvivors not separated, or not reported  
| Comparability of cohorts on the basis of clinical details | a. Study reports clinical information in survivors and nonsurvivors  
| | b. Survivors and nonsurvivors not separated, or not reported  
| **Outcome (maximum three points)** | |
| Assessment of outcome | a. Record linkage or method reported  
| | b. No description  
| Was follow-up long enough for outcomes to occur? | a. Yes  
| | b. No  
| Adequacy of follow-up of cohorts (ie, survival from severe disease/completion of patient ICU stay and reporting of ICU outcome) | a. Complete follow-up to completion of ICU stay, all participants accounted for  
| | b. Small number lost to follow-up or description of those without completed ICU stay  
| | c. Low follow-up rate and no description of those lost  
| | d. No statement  

Abbreviation: ICU, intensive care unit.
TABLE A3. Studies With Potentially Overlapping Patients (December 11, 2019 to April 30, 2020)

| Category                              | Study                  | Date of Recruitment | Date Till Recruitment | Mortality | Overlapping Study Centers                                      |
|---------------------------------------|------------------------|---------------------|-----------------------|-----------|-----------------------------------------------------------------|
| Studies reporting ICU mortality       | Guan et al\(^21\)      | December 11, 2019   | January 31, 2020      | 3/5       | 1. Wuhan Jinyintan Hospital, Hubei, China                       |
|                                       | Xie et al\(^26\)       | January 11, 2020    | February 29, 2020     | 17/24     | 2. Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, China |
|                                       | He et al\(^22\)        | January 23, 2020    | February 12, 2020     | 5/5       |                                                                 |
|                                       | Yang et al\(^29\)      | January 13, 2020    | April 10, 2020        | 26/30     |                                                                 |
|                                       | Dai et al\(^30\)       | January 1, 2020     | March 1, 2020         | 3/5       |                                                                 |
|                                       | Wang et al\(^30\)      | NR                  | March 10, 2020        | 3/4       |                                                                 |
|                                       | Zhang et al\(^31\)     | January 1, 2020     | April 30, 2020        | 4/16      |                                                                 |
|                                       | Grasselli et al\(^33\) | February 20, 2020   | March 18, 2020        | NR        | Lombardy ICU Network                                            |
|                                       | Grasselli et al\(^33\) | February 20, 2020   | April 22, 2020        | 202/331   |                                                                 |
| Studies reporting severe disease mortality | Dai et al\(^23\)      | January 1, 2020     | February 24, 2020     | 12/40     | 1. Zhongnan Hospital of Wuhan University, China                 |
|                                       | Zhang et al\(^24\)     | January 13, 2020    | February 26, 2020     | 8/15      | 2. Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, China |
|                                       | Zhang et al\(^25\)     | January 15, 2020    | March 18, 2020        | 23/56     | 3. Renmin Hospital of Wuhan University, Wuhan, China            |
|                                       | Wu et al\(^27\)        | January 9, 2020     | March 20, 2020        | 4/7       |                                                                 |
|                                       | Ma et al\(^28\)        | January 1, 2020     | March 30, 2020        | 5/20      |                                                                 |
|                                       | Yang et al\(^29\)      | January 1, 2020     | April 15, 2020        | 11/19     |                                                                 |

Abbreviations: ICU, intensive care unit; NR, not reported.

\(^{a}\)Included in the meta-analysis.
| Study                        | Selection (3) | Comparability (2) | Outcomes (3) | Total (8) |
|-----------------------------|---------------|-------------------|--------------|-----------|
| Fattizzo et al47            | 3             | 2                 | 3            | 8         |
| Gonfiotti et al48           | 2             | 2                 | 2            | 6         |
| Zhang et al45               | 3             | 0                 | 3            | 6         |
| Krause et al42              | 3             | 2                 | 2            | 7         |
| Gupta et al5                | 3             | 2                 | 2            | 7         |
| Malard et al51              | 3             | 2                 | 2            | 7         |
| Rogado et al58              | 3             | 2                 | 3            | 8         |
| Sanchez-Pina et al54        | 3             | 2                 | 3            | 8         |
| Robiotti et al57            | 3             | 2                 | 3            | 8         |
| Mehta et al58               | 3             | 0                 | 2            | 5         |
| Garassino et al57           | 3             | 2                 | 3            | 8         |
| Martin-Moro et al49         | 3             | 0                 | 2            | 5         |
| Yang et al59                | 3             | 0                 | 2            | 5         |
| Fox et al50                 | 3             | 2                 | 2            | 7         |
| Lara et al59                | 3             | 0                 | 3            | 6         |
| Grasselli et al34           | 3             | 2                 | 3            | 8         |
| Lee et al56                 | 3             | 0                 | 3            | 6         |
| Joharatnam-Hogan et al52    | 3             | 2                 | 2            | 7         |
| Wang et al55                | 3             | 2                 | 2            | 7         |
| Lunski et al53              | 3             | 0                 | 2            | 5         |
| Lamure et al53              | 3             | 2                 | 3            | 8         |
| Shah et al5                  | 3             | 2                 | 2            | 7         |
| Luo et al55                 | 3             | 0                 | 2            | 5         |
| Kuderer et al5               | 3             | 0                 | 2            | 5         |
| Singh et al41               | 3             | 2                 | 2            | 7         |
| Passamonti et al50          | 3             | 2                 | 2            | 6         |
| Haase et al49               | 3             | 2                 | 2            | 7         |
| García-Suárez et al56      | 3             | 0                 | 3            | 6         |
| de Melo et al56             | 3             | 0                 | 3            | 6         |
| Smith et al44               | 3             | 0                 | 2            | 5         |
| Ramaswamy et al56           | 3             | 2                 | 2            | 7         |
| Lievre et al56              | 3             | 2                 | 2            | 7         |

NOTE. Rates studies out of a maximum of three points for selection, two for comparability, and three for outcomes. Modified Newcastle-Ottawa Scale reported in Table A2.
### TABLE A5. Subgroup Analysis by Geographical Region, Number of Centers, and Study Size

| Group                     | Studies (No.) | Mortality, % (95% CI)         | Residual Heterogeneity, $I^2$ (%) | $P$        |
|---------------------------|----------------|-----------------------------|----------------------------------|-----------|
| All studies (ICU admissions) | 28             | 60.2 (53.6 to 66.7)         | 80.27                            | <.001     |
| With Grasselli et al34 removed | 27             | 60.2 (52.8 to 67.6)         | 80.98                            | <.001     |
| Asia                      | 3              | 84.2 (73.7 to 94.6)         | 0                                | <.001     |
| Americas                  | 10             | 62.5 (49.5 to 75.4)         | 81.88                            | <.001     |
| Europe                    | 13             | 57 (50.7 to 63.3)           | 51.61                            | <.001     |
| Multinational registries  | 2              | 43.9 (14.0 to 73.7)         | 76.44                            | <.004     |
| Single or multiple centers|                |                             |                                  |           |
| Single                    | 12             | 56.3 (42.6 to 70.0)         | 73.63                            | <.001     |
| Multiple                  | 16             | 62.8 (55.5 to 70.0)         | 86.35                            |           |
| Study size                |                |                             |                                  |           |
| < 25 patients             | 13             | 69.1 (60.5 to 77.7)         | 17.64                            | <.001     |
| > 25 patients             | 15             | 56.4 (45.3 to 67.6)         | 87.77                            |           |
| All studies (severe COVID-19) | 4              | 58.4 (39.4 to 77.5)         | 72.28                            | <.001     |

Abbreviation: ICU, intensive care unit.

### TABLE A6. Advanced Support Therapies—Intensive Care

#### Intensive Care Support Therapies

| Study                | NIV | IMV, No. (% Patients Admitted to the ICU) | CRRT | ECMO | Total Cancer Cohort | Cancer Patients With COVID-19 Admitted to the ICU |
|----------------------|-----|------------------------------------------|------|------|---------------------|-----------------------------------------------|
| Krause et al42       |     | 11 (100)                                 |      |      | 11                  | 11                                            |
| Malard et al51       |     | 7 (100)                                  |      |      | 23                  | 7                                             |
| Robioliti et al37    |     | 40 (83)                                  |      |      | 168                 | 48                                            |
| Garassino et al52    |     | 9 (69)                                   |      |      | 200                 | 13                                            |
| Martín-Moro et al49  |     | 4 (100)                                  |      |      | 34                  | 2                                             |
| Yang et al29         | 11  | 21 (70)                                  |      |      | 205                 | 30                                            |
| Fox et al60          |     | 6 (75)                                   |      |      | 52                  | 8                                             |
| Lara et al39         | 9   | 9 (45)                                   |      |      | 121                 | 20                                            |
| Wang et al35         | 3   | 5 (71)                                   |      |      | 36                  | 7                                             |
| Luo et al46          |     | 18 (86)                                  |      |      | 102                 | 21                                            |
| Larski et al43       |     | 43 (90)                                  |      |      | 312                 | 48                                            |
| Lamure et al43       |     | 21 (84)                                  |      |      | 89                  | 25                                            |
| Kuderer et al56      |     | 55 (42)                                  |      |      | 928                 | 132                                           |
| Singh et al41        |     | 23 (77)                                  |      |      | 7                   | 85                                            |
| Lievre et al56       |     | 49 (45)                                  |      |      | 1,298               | 110                                           |

NOTE. Data expressed as number of patients (%).

Abbreviations: CRRT, continuous renal replacement therapy; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; IMV, invasive mechanical ventilation; NIV, noninvasive ventilation.
### TABLE A7. Subgroup Analysis on the Basis of Presence of Cancer, Cancer Type, Presence of Comorbidities, and Recent Anticancer Therapy

| Outcome                                                                 | Studies | Estimate | Lower | Upper | P    |
|-------------------------------------------------------------------------|---------|----------|-------|-------|------|
| Mortality of IMV patients with COVID-19 admitted to the ICU              | 5       | 49.4     | 30.9  | 67.9  | < .001 |
| Mortality in patients with COVID-19—cancer versus noncancer patients    | 4       | 1.924    | 1.596 | 2.320 | < .001 |
| Mortality rate in cancer patients with severe COVID-19: hematologic versus nonhematologic | 1       | 1.878    | 1.171 | 3.012 | < .05  |

Subgroup analysis: not significant

| Outcome                                                                 | Studies | Estimate | Lower | Upper | P    |
|-------------------------------------------------------------------------|---------|----------|-------|-------|------|
| Mortality rate in cancer patients admitted to the ICU with COVID-19: hematologic versus nonhematologic | 1       | 0.808    | 0.239 | 2.731 | .731  |
| Mortality rate in cancer patients with severe COVID-19: recent anticancer therapy versus anticancer therapy for more than a month-OR | 1       | 1.113    | 0.708 | 1.748 | .644  |
| Mortality rate in cancer patients with severe COVID-19: one or more comorbidities versus no comorbidities-OR | 1       | 1.964    | 0.542 | 7.104 | .303  |

Abbreviations: ICU, intensive care unit; IMV, invasive mechanical ventilation; OR, odds ratio.

### TABLE A8. Complications in Cancer Patients With Severe COVID-19

| Outcome                        | Studies | Estimate | Lower | Upper | P    |
|--------------------------------|---------|----------|-------|-------|------|
| Pulmonary complications        | 4       | 0.497    | 0.063 | 0.931 | .025 |
| Cardiac complications          | 3       | 0.143    | 0.042 | 0.244 | .006 |
| Renal complications            | 3       | 0.087    | 0.013 | 0.161 | .022 |
| Sepsis                         | 3       | 0.115    | 0.046 | 0.184 | .001 |

Pooled Proportion of Complications: Cancer Patients With Severe COVID-19