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## **Determinants of COVID-19 disease severity in** patients with cancer

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As of 10 April 2020, New York State had 180,458 cases of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and 9,385 reported deaths. Patients with cancer comprised 8.4% of deceased individuals1. Population-based studies from China and Italy suggested a higher coronavirus disease 2019 (COVID-19) death rate in patients with cancer<sup>2,3</sup>, although there is a knowledge gap as to which aspects of cancer and its treatment confer risk of severe COVID-194. This information is critical to balance the competing safety considerations of reducing SARS-CoV-2 exposure and cancer treatment continuation. From 10 March to 7 April 2020, 423 cases of symptomatic COVID-19 were diagnosed at Memorial Sloan Kettering Cancer Center (from a total of 2,035 patients with cancer tested). Of these, 40% were hospitalized for COVID-19, 20% developed severe respiratory illness (including 9% who required mechanical ventilation) and 12% died within 30 d. Age older than 65 years and treatment with immune checkpoint inhibitors (ICIs) were predictors for hospitalization and severe disease, whereas receipt of chemotherapy and major surgery were not. Overall, COVID-19 in patients with cancer is marked by substantial rates of hospitalization and severe outcomes. The association observed between ICI and COVID-19 outcomes in our study will need further interrogation in tumor-specific cohorts.

The characterization of COVID-19 in patients with cancer remains limited in published studies and nationwide surveillance analyses. Reports from outside the United States raise the possibility that patients with cancer on active therapy have a higher risk of COVID-19-related severe events<sup>4-7</sup>. In the current study, we report on the epidemiology of COVID-19 experienced at our tertiary care cancer center during the height of incident cases in New York City and offer an analysis of risk factors for severe infection that is pertinent to populations of patients with cancer. From 10 March until 7 May 2020, SARS-CoV-2 was detected in 946 patients at Memorial Sloan Kettering Cancer Center. In comparison with New York City COVID-19 data, the age-stratified rates of hospitalization and

death among 946 laboratory-confirmed cases from 10 March until 7 May 2020 are shown in Supplementary Fig. 1. Clinical characteristics were abstracted for a final study population consisting of 423 case patients diagnosed from 10 March until 7 April 2020, with a follow-up period of at least 30 d or death (Fig. 1).

Table 1 shows the demographic and clinical characteristics of the 423 cases. Most patients were adults over the age of 60 years (234, 56%). The most frequent cancer types included solid tumors such as breast (86, 20%), colorectal (37, 9%) and lung (35, 8%). Lymphoma was the most common hematologic malignancy (48, 11%). Over half of the cases were metastatic solid tumors (238, 56%). At least one of the specified comorbid conditions was present in 248 (59%) individuals: diabetes, hypertension, chronic kidney disease and cardiac disease. Of the presenting symptoms examined, fever (78%) and cough (82%) were the most common, whereas shortness of breath (44%) and diarrhea (26%) were less common but not rare. Chest radiographic findings were varied and are summarized in Supplementary Table 1. In the cohort, 168 (40%) of 423 patients were hospitalized, and 87 (20%) developed severe respiratory illness, including 47 (11%) who required high-flow oxygen and 40 (9%) who required mechanical ventilation. In the absence of approved therapy for COVID-19 during this period, several investigational treatments were administered, including hydroxychloroquine, azithromycin, remdesivir, tocilizumab, convalescent plasma and corticosteroids (Supplementary Table 2). Illness in seven pediatric patients was mild and without complications. The overall case fatality rate was 12% (51 of 423). Case fatality for hospital and intensive care unit (ICU) admittance were 24% (41 of 168) and 35% (17 of 48), respectively.

Next, we assessed risk factors for hospitalization and severe respiratory illness, the latter defined as the requirement for high-flow oxygen supplementation or mechanical ventilation. In the multivariate analysis, the following risk factors were independently associated with hospitalization: non-white race, hematologic malignancy, a composite measure of chronic lymphopenia and/or corticosteroid use and treatment with ICI therapy (Table 2). Age older than 65

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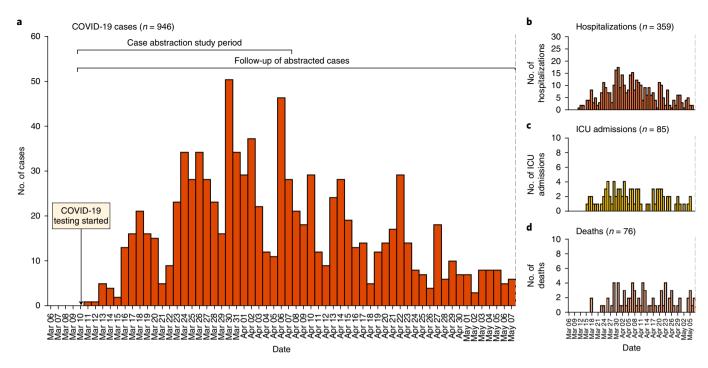


Fig. 1 | Number of SARS CoV-2-positive cases (a), hospitalizations (b), ICU admissions (c) and deaths (d) from 10 March to 7 May 2020. Case abstraction study period was from 10 March to 7 April 2020. Follow-up of abstracted cases was until 7 May 2020.

years, former or current smoker, hypertension and/or chronic kidney disease and history of cardiac disorder were significant predictors in univariate but not in multivariate analysis. The risk factors for severe respiratory illness due to COVID-19 were similar to those for hospitalization but not identical (Table 2). Severe respiratory illness was significantly more common with age older than 65 years. Of note, treatment with ICI also remained an independent predictor of severe respiratory illness. Age and ICI are illustrated by the Kaplan-Meier estimator for this endpoint in Supplementary Figure 2. Notably, metastatic disease, recent chemotherapy or major surgery within the previous 30 d did not show a significant association with either hospitalization or severe respiratory illness. Given the apparent association of ICI with COVID-19 severity, we explored this further by calculating stratum-specific rates of hospitalization and severe respiratory illness (Table 3). Because PD-1 blockade, a type of ICI, is commonly used to treat lung cancer, we examined the occurrence of outcomes by ICI use and underlying cancer (lung versus non-lung) and observed higher frequencies of hospitalization and severe respiratory illness in both ICI-treated groups. Further, we incorporated lung cancer as a covariate with immune checkpoint blockade in a post hoc analysis and found separate, distinct effects of lung cancer and ICI treatment on hospital admission and severe respiratory illness (Supplementary Table 3).

In two separate models, we evaluated the symptoms and laboratory markers as predictors of clinical outcomes of interest. Fever, cough, new onset dyspnea and diarrhea at the time of clinical presentation were associated with a higher risk of hospitalization and severe respiratory illness (Supplementary Table 4), but only dyspnea and diarrhea were independently predictive of severe outcomes. For laboratory biomarkers, evaluated longitudinally and coded as time-dependent predictors, procalcitonin, lymphopenia, interleukin-6, D-dimer and lactate dehydrogenase correlated with subsequent severe respiratory illness (Supplementary Table 5). Finally, we assessed the distribution of first cycle threshold (Ct) values at the time of laboratory diagnosis for both analytic targets of the SARS CoV-2 PCR assay and found no significant association

between Ct values and severe respiratory illness (Supplementary Figure 3).

Patients with cancer are among those most vulnerable to severe illness from respiratory viral infections8. Our early experience with COVID-19 at a large tertiary care cancer center demonstrated severe disease in 20% of patients diagnosed with COVID-19, with an overall case fatality rate of 12%. Similarly to other studies in the general population, we found that age, non-white race, cardiac disease, hypertension and chronic kidney disease correlated with severe outcomes<sup>9,10</sup>. Contrary to early reports, receipt of chemotherapy within 30 d before COVID-19 diagnosis was not associated with a higher risk of complications<sup>6</sup>. Recent major surgery and metastatic disease also did not confer a significant risk of severe COVID-19. Treatment with ICI predicted both hospitalization and severe disease, although there was considerable heterogeneity in ICI-treated tumor types, and disease-specific factors could not be individually addressed. COVID-19 among children with cancer exhibited a milder course, consistent with early reports in children without cancer, but represented a small portion of the evaluated population (7, 2%).

A raw comparison with New York City cases during the same time period shows that patients with cancer at Memorial Sloan Kettering in the age range of 0–64 years were hospitalized at higher rates than the general New York City COVID-19 population (Supplementary Fig. 1). Crude death rates were similar across age groups at Memorial Sloan Kettering and citywide, except the elderly (≥75 years of age), in which we observed lower rates at Memorial Sloan Kettering. Beyond cancer, it is plausible that competing mortality risks, functional status and socioeconomic disparities contribute to the age-specific differences observed between the Memorial Sloan Kettering and citywide populations.

Very recently, other groups have reported their observations of COVID-19 in cancer-wide patient populations. These include the COVID-19 and Cancer Consortium (CCC19), a multi-institution registry including centers across the United States, Canada and Spain<sup>11</sup>; the United Kingdom Coronavirus Cancer Monitoring

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Table 1   Patient demographics and clinical characteristics
(n=423)

(n=423)	
Characteristic	No. (%)
Age (years)	
<18	7 (2)
18-29	11 (3)
30-39	19 (4)
40-49	51 (12)
50-59	101 (24)
60-69	134 (32)
≥70	100 (24)
Sex	
Male	212 (50)
Female	211 (50)
Race	
White	263 (62)
Black	68 (16)
Asian	36 (9)
Other	56 (13)
Body mass index (BMI, kg/m²)	
<18.5 (underweight)	13 (3)
18.5-24.9 (normal)	135 (32)
25.0-29.9 (overweight)	146 (35)
30.0-39.9 (obese)	109 (26)
≥40 (severely obese)	20 (5)
Smoking status	
Current	10 (2)
Former	157 (37)
Never	249 (59)
Unknown	7 (2)
Underlying cancer <sup>a</sup>	
Hematologic	
Leukemia	32 (8)
Lymphoma	48 (11)
Myeloma	22 (5)
Solid tumor	
Breast	86 (20)
Colorectal	37 (9)
Lung	35 (8)
Prostate	26 (6)
Other	137 (32)
Metastatic disease	238 (56)
Major surgery (30 d) <sup>b</sup>	31 (7)
Asthma	43 (10)
COPD	29 (7)
Diabetes	84 (20)
Cardiac dysfunction <sup>c</sup>	84 (20)
Chronic kidney disease	36 (9)
Hypertension	214 (51)
Systemic chemotherapy (within 30 d) $^{\rm d}$	191 (45)
	Continued

Table 1   Patient demographics and clinical characterist	ics
(n-423) (Continued)	

(11— 125) (65111111464)	
Characteristic	No. (%)
Chronic corticosteroide	66 (16)
Chronic lymphopenia <sup>f</sup>	9 (2)
ICIg	31 (7)
Symptoms at onset	
Fever	331 (78)
Shortness of breath	186 (44)
Cough	347 (82)
Diarrhea	109 (26)
Outcomes (30 d)	
Hospitalization status	
Not admitted	243 (57)
Admitted	168 (40)
Already hospitalized	12 (3)
Oxygen requirements <sup>h</sup>	
None <sup>i</sup>	279 (66)
Low-flow oxygen	57 (13)
High-flow oxygen <sup>j</sup>	47 (11)
Mechanical ventilation	40 (9)
Death	51 (12)

COPD, chronic obstructive pulmonary disease. <sup>a</sup> In patients with multiple malignancies, the most active and recently treated malignancy was used to define the underlying cancer. <sup>b</sup> Defined as any surgical procedure requiring general anesthesia. <sup>c</sup> Heart failure, myocardial infarction, valvular replacement or cardiomyopathy. <sup>d</sup> Systemic, parenteral chemotherapy. <sup>e</sup> Corticosteroids (equivalent of prednisone 20 mg or higher) for at least 10 d. <sup>f</sup> Absolute lymphocyte count <500 per microliter over five previous consecutive measurements. <sup>g</sup> ICI therapy consisted of the following, given within 90 d: pembrolizumab (18), nivolumab (5), atezolizumab (3), avelumab (1), durvalumab (1), ipilimumab (1), nivolumab + ipilimumab (1) and pembrolizumab followed by nivolumab (1). <sup>h</sup> Highest oxygen requirement over 30 d is shown. <sup>1</sup> Note: two patients had chronic tracheostomy because of prior medical issues but did not require supplemental oxygen during COVID-19 infection. <sup>1</sup> Includes the following oxygen delivery routes: non-rebreather mask, high-flow nasal oxygen and bilevel positive airway pressure.

Project (UKCCMP), a registry spanning the United Kingdom<sup>12</sup>; and two studies from large healthcare systems in New York City, one at Montefiore<sup>13</sup> and another at Mount Sinai<sup>14</sup>.

Our reported case fatality rate of 12% was similar to those reported by CCC19 (13%) and Mount Sinai (11%). Interestingly, Montefiore and UKCCMP both reported a 28% case fatality rate in their populations of patients with cancer. The reasons for this finding are unclear, but these two studies might have had patients who were both older (both reported a median age of 69) and sicker. In the Montefiore study, most patients with cancer who died were residents of nursing homes or shelters (36%), not on active cancer therapy, and had prominent comorbid conditions (69% of the deceased had at least one other severe comorbid disease). It is possible that differences in the use of critical care resources might have contributed to variation in outcomes in patients with cancer. Socioeconomic and racial disparities described in study populations add further complexity to the interpretation of the relationship between cancer and COVID-19 outcomes. Similar to our findings, these studies found no increased risk with chemotherapy treatment or with metastatic disease.

A notable finding of our study is the association of checkpoint inhibitor immunotherapy as a risk factor for severe outcomes in patients treated with ICI, which was independent of age, cancer type, and other comorbid conditions. Although we observed more severe COVID-19 in ICI recipients with underlying lung cancer, patients

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Variable	Un	Univariate		Multivariate	
	OR (95% CI)	P value	OR (95% CI)	P value	
Predictors of hospitalization, by logistic regression (	(n = 411a)				
Age (>65 years)	1.81 (1.20-2.72)	0.004	1.53 (0.96-2.43)	0.072	
Sex (female)	0.89 (0.60-1.32)	0.575			
Race (non-white)	1.36 (0.91-2.04)	0.135	1.62 (1.05-2.51)	0.029	
BMI (≥30 kg/m²)	0.89 (0.58-1.36)	0.585			
Smoking (current/former)	1.60 (1.07-2.40)	0.022	1.37 (0.88-2.13)	0.169	
Asthma/COPD	1.39 (0.81-2.37)	0.226	1.07 (0.59-1.92)	0.828	
Cancer (non-metastatic solid)	1.00 (Ref)	-	1.00 (Ref)		
Cancer (metastatic solid)	0.89 (0.53-1.50)	0.647	0.76 (0.43-1.34)	0.338	
Cancer (hematologic)	2.24 (1.25-4.06)	0.007	2.49 (1.35-4.67)	0.003	
Major surgery (within 30 d)	1.24 (0.53-2.84)	0.612			
Diabetes	1.20 (0.73-1.96)	0.467			
Cardiac disorder	1.86 (1.13-3.07)	0.015	1.35 (0.77-2.36)	0.297	
HTN/chronic kidney disease	1.84 (1.24-2.75)	0.003	1.51 (0.96-2.39)	0.077	
Systemic chemotherapy (within 30 d)	1.04 (0.70-1.54)	0.845			
Chronic lymphopenia or corticosteroids	1.86 (1.11-3.15)	0.019	1.85 (1.06-3.24)	0.030	
ICI	2.53 (1.18-5.67)	0.017	2.84 (1.24-6.72)	0.013	
Predictors of severe respiratory illness, by Cox prop	ortional hazard (n = 423)				
Variable	Univariate		Multivariate		
	HR (95% CI)	P value	HR (95% CI)	P value	
Age (>65 years)	2.02 (1.33-3.08)	0.001	1.67 (1.07-2.60)	0.024	
Sex (female)	1.04 (0.68-1.58)	0.859			
Race (non-white)	1.20 (0.79-1.84)	0.394			
BMI (≥30 kg/m²)	1.01 (0.64-1.59)	0.965			
Smoking (current/former)	1.78 (1.17-2.72)	0.007	1.39 (0.89-2.17)	0.148	
Asthma/COPD	1.63 (0.98-2.71)	0.059	1.24 (0.72-2.13)	0.436	
Cancer (non-metastatic solid)	1.00 (Ref)	-	1.00 (Ref)	-	
Cancer (metastatic solid)	0.87 (0.48-1.59)	0.658	0.75 (0.40-1.41)	0.371	
Cancer (hematologic)	1.69 (0.92-3.10)	0.092	1.79 (0.97-3.32)	0.063	
Major surgery (within 30 d)	1.31 (0.63-2.71)	0.464			
Diabetes	1.09 (0.65-1.83)	0.745			
Cardiac disorder	2.02 (1.28-3.19)	0.002	1.44 (0.88-2.37)	0.147	
HTN/chronic kidney disease	1.68 (1.09-2.58)	0.020	1.18 (0.73-1.89)	0.505	
Systemic chemotherapy (within 30 d)	1.19 (0.78-1.82)	0.407			
Chronic lymphopenia or corticosteroids	1.59 (0.97-2.59)	0.066	1.42 (0.86-2.34)	0.165	
ICI	2.38 (1.29-4.38)	0.005	2.74 (1.37-5.46)	0.004	

CI, confidence interval; COPD, chronic obstructive pulmonary disease; HTN, hypertension; HR, hazard ratio; OR, odds ratio. \*12 patients were excluded from the hospitalization endpoint; they were already hospitalized for other reasons before testing positive for SARS-CoV-2 with RNA PCR testing.

with non-lung cancer who were treated with ICI also demonstrated severe outcomes (Table 3). A possible explanation for this observation is an exacerbation of ICI-related lung injury or ICI-triggered immune dysregulation by T cell hyperactivation, which in turn might facilitate acute respiratory distress syndrome, a dreaded COVID-19 complication<sup>15,16</sup>. The association of ICI treatment with other severe infections is influenced by the use of corticosteroids for control of immune-mediated adverse events<sup>17</sup>. In this study, only one of 31 patients treated with ICI received corticosteroid therapy before the severe illness endpoint, and none had immune-mediated pneumonitis at the time of COVID-19 diagnosis. Thus, corticoste-

roids and immune-mediated adverse events were highly unlikely to influence the association of ICI treatment with COVID-19 severity reported in this study. The findings in our current study should be interpreted with caution due to the limitations of our ICI data set in evaluating tumor-specific risk.

Other studies have examined cancer immunotherapy as a risk factor, and, unlike our study, these did not find an association with poor outcomes<sup>12,13,18</sup>. However, these studies had few patients on immunotherapy and examined death as an endpoint. In this work, we examined an endpoint based on significant oxygen needs, which was more common than death. A disease-specific

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**Table 3** | Stratum-specific point estimates of outcomes by ICI treatment and underlying solid cancer (lung versus non-lung) (n = 275)

Cancer	Endpoint	Non-ICI no./ total no. (%)	ICI <sup>a</sup> no./total no. (%)
Lung cancer—	Hospitalization <sup>b</sup>	12/23 (52)	10/12 (83)
	Severe respiratory illness	8/23 (35)	7/12 (58)
Other solid cancers <sup>c</sup>	Hospitalization <sup>b</sup>	82/216 (38)	8/17 (47)
	Severe respiratory illness	34/221 (15)	5/19 (26)

<sup>&</sup>lt;sup>a</sup> Includes the following non-lung malignancies where ICI was given as therapy: breast (86), lymphoma (48), colorectal (37), prostate (26), kidney (11), genitourinary (9), skin (9), brain (6), uterus (5) and cervix (3). <sup>b</sup> For hospitalization endpoint, seven patients already admitted to the hospital at the time of COVID-19 diagnosis were excluded from calculation. <sup>c</sup> Within 90 d.

analysis of PD-1 blockade in patients with lung cancer from our institution with COVID-19, but treated at multiple hospitals, did not suggest a discernible association<sup>18</sup>. It is unclear whether that study had the statistical power to uncover the effect size reported in this manuscript. It is important to note that these two studies had distinct endpoints and small overlapping study populations. It is possible that patients with lung cancer or other malignancies have confounding effects from other factors that were not fully evaluable in our population. Specifically, in lung cancer, global consortium efforts are underway to understand the observed effect of COVID-19<sup>19</sup>. Until further evidence is available, it is prudent not to alter treatment decisions but to consider increased vigilance with SARS CoV-2 testing in patients initiating or continuing treatment with ICIs, irrespective of symptoms.

There are several other limitations to our study. First, we describe a single-center retrospective analysis in a heterogeneous group of patients with cancer. Second, the effectiveness of experimental therapeutics used for the management of COVID-19 was not explicitly evaluated. With the postponement of all non-essential cancer care during the study period, COVID-19 testing practices were targeted toward symptomatic patients who needed medical evaluation, potentially overestimating the overall severity of COVID-19. Finally, with our study population and design, we are unable to provide a reliable comparison of COVID-19-related outcomes between cancer and non-cancer populations. Such an analysis should be conducted in homogenous cohorts with adequate adjustment for comorbidities, inclusion of patients with cancer on active therapy, a similar testing strategy and the ability to measure the effects of interrupting oncologic care.

Our study has the distinct strength of reporting the most extensive single-institution experience in patients with cancer from the epicenter of the US outbreak. Although we had a high number of COVID-19-related hospitalizations, critical care resources were never in short supply. Further, we describe outcomes on COVID-19-associated respiratory compromise and include a full 30-d follow-up for reporting primary study outcomes and death rates.

In summary, the outcome of COVID-19 is worse among individuals with underlying conditions, including cancer. Our group of 423 patients with cancer had substantial rates of severe respiratory outcomes (20%) and death (12%) with COVID-19 3,13,20-22. In addition, as was seen with the SARS epidemic in 2003, the ongoing risk of contracting the illness and indirect consequences of treatment disruptions are expected to have a lasting effect on the health and safety of patients undergoing treatment for cancer<sup>23</sup>. Continuous preparedness is paramount as routine cancer care is resumed in the coming weeks and months amidst the unpredictable threat posed by COVID-19. Informed approaches with universal screening,

aggressive testing and rigorous control measures will be essential for the safe ongoing delivery of oncologic care.

#### Online content

Any methods, additional references, Nature Research reporting summaries, source data, extended data, supplementary information, acknowledgements, peer review information; details of author contributions and competing interests; and statements of data and code availability are available at https://doi.org/10.1038/s41591-020-0979-0.

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#### Methods

Memorial Sloan Kettering Cancer Center is a 514-bed tertiary cancer center in New York City with approximately 25,000 admissions and 173,000 patient days annually. Memorial Sloan Kettering maintains 19 ambulatory sites across New York State and New Jersey, with in excess of 1 million combined yearly outpatient visits. Approximately 23,000 individuals per year are under active treatment. During February and March 2020, a total of 14,067 individuals received parenteral chemotherapy at Memorial Sloan Kettering. Critical care resource allocation was determined by patient-expressed advanced directives and was not subject to shortage during the study period.

**Study population.** From 10 March until 7 April 2020, all consecutive adult and pediatric cases of symptomatic and laboratory-confirmed SARS-CoV-2 infection were included. The only exceptions were asymptomatic patients who were tested before surgery or before receipt of select myeloablative chemotherapy regimens (n=30). Thirty-three patients included in this study cohort were also included in Luo et al. <sup>18</sup>. Identification of case patients and their medical background and clinical course during COVID-19 illness were abstracted from electronic medical records. The Memorial Sloan Kettering Cancer Center Institutional Review Board granted a Health Insurance Portability and Accountability Act waiver of authorization to conduct this study.

Laboratory methods. Nasopharyngeal swab samples were collected using flocked swabs (Copan Diagnostics) and placed in viral transport media. SARS-CoV-2 RNA was detected using the Centers for Disease Control and Prevention protocol targeting two regions of the nucleocapsid gene (N1 and N2), with the following modifications: nucleic acids were extracted from specimens using the NUCLISENS EasyMag (bioMérieux) following an off-board, pre-lysis step<sup>24,25</sup>. Real-time reverse transcription PCR was performed on the ABI 7500 Fast (Applied Biosystems) in a final reaction volume of 20 µl, including 5 µl of extracted nucleic acids. Samples were reported as positive if both the N1 and N2 targets were detected.

**Statistical analysis.** We first assessed patient risk factors for hospitalization as part of the management for COVID-19, using logistic regression. Patients with nosocomial infection  $(n\!=\!12)$  were excluded from this analysis. Next, we assessed risk factors for severe respiratory illness, defined as the requirement for high-flow oxygen supplementation or mechanical ventilation. Cause-specific Cox proportional hazard modeling was applied for this. Analysis time began at the time of COVID-19 diagnosis and was censored at 30 d after diagnosis or death, in the absence of the endpoint beforehand. The proportional hazards assumption was verified by examining Schoenfeld residuals for all predictors.

For the outcomes described above, the following clinical variables were assessed: age, sex, race, diabetes, hypertension cardiovascular disease (myocardial infarction, heart failure, heart valve replacement or cardiomyopathy), chronic obstructive pulmonary disease, asthma, chronic kidney disease, obesity (body mass index  $\geq 30~\text{kg/m}^2$ ), smoking status, underlying cancer, major surgery (surgery requiring general anesthesia), chronic lymphopenia (absolute lymphocyte count  $<\!500~\text{per}$  microliter for at least five measurements, immediately preceding positive COVID-19 PCR test), chronic corticosteroid use (prednisone of 20 mg per day or equivalent, for at least 10 d), systemic parenteral chemotherapy within 30 d, major surgery within 30 d and treatment with an ICI within 90 d. In addition to past underlying conditions, new symptoms at the time of testing were assessed: fever, cough, shortness of breath and diarrhea.

For comparison with New York City data, we derived cases, hospitalization rates and deaths for specified age strata from publicly available data sources maintained by the New York City Department of Health (https://www1.nyc.gov/site/doh/covid/covid-19-data.page) and compared frequencies with Memorial Sloan Kettering counts for the same age groups. Additional evaluation of risk factors was done for symptoms present at the time of diagnosis (fever, cough, dyspnea and diarrhea) and monitoring of clinical laboratory biomarkers (procalcitonin, absolute lymphopenia, interleukin-6, D-dimer and lactate dehydrogenase). The laboratory biomarkers were monitored

over the course of analysis time and encoded as a time-dependent predictor in the time-to-event model.

For both outcomes, predictors were first analyzed separately in a univariate analysis. Predictors with a univariate *P* value of less than 0.25 were incorporated into a multivariate model<sup>26,27</sup>. The Kaplan–Meier estimator was calculated and shown for the cumulative probability of severe respiratory illness, for independent predictors. Details of sample population and statistical tests are provided in the Life Sciences Reporting Summary. All study analyses were performed using R version 3.5 (R Development Core Team).

**Reporting Summary.** Further information on research design is available in the Nature Research Reporting Summary linked to this article.

#### Data availability

All data generated or analyzed during this study are included in this published article (and its supplementary information files).

#### References

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#### **Author contributions**

E.V.R., M.K., Y.T. and M.S.G. made substantial contributions to the study conception and design. Y.T., E.V.R., P.A.M., T.R. and M.K. made substantial contributions to the acquisition of data. Y.T. and T.R. conducted statistical analysis. T.M.H., M.S.G., M.K., Y.T. and E.V.R. made substantial contributions to the interpretation of data. M.K. drafted the first version of the manuscript. E.V.R., N.E.B., P.A.M., T.R., P.P.-J., M.B., Y.B., M.C., C.J.F., M.S.G., A.J., A.K., Y.J.L., A.L., A.M., S.M., T.N., G.A.P., J.P., G.R.-S., E.S., S.K.S., K.S., M.K.S., J.D.W., T.M.H., Y.T. and M.K. contributed to critical revisions and approved the final version of the manuscript. M.K., Y.T., T.M.H. and E.V.R. take responsibility for the integrity of the work.

#### **Competing interests**

The authors declare no competing interests.

#### Additional information

**Supplementary information** is available for this paper at https://doi.org/10.1038/s41591-020-0979-0.

Correspondence and requests for materials should be addressed to M.K.

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# nature research

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For	all statistical an	alyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.			
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$\boxtimes$	For hierare	chical and complex designs, identification of the appropriate level for tests and full reporting of outcomes			
	Estimates of effect sizes (e.g. Cohen's $d$ , Pearson's $r$ ), indicating how they were calculated				
	Our web collection on <u>statistics for biologists</u> contains articles on many of the points above.				
So	ftware and	d code			
Poli	Policy information about <u>availability of computer code</u>				
Da	ata collection	Data was collected from the electronic health record and laboratory informatics system through manual extraction and automated processing.			

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### Data

Data analysis

Policy information about <u>availability of data</u>

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

All study analyses were performed on R version 3.5 (R Development Core Team, Vienna, Austria)

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Life scier	nces s	tudy design		
All studies must dis	sclose on the	ese points even when the disclosure is negative.		
Sample size	No sample	size was calculated because this was a retrospective study		
Data exclusions		s with missing clinical information and asymptomatic individuals tested as part of diagnostic screening protocols before surgery or ive chemotherapy were excluded.		
Replication	Non-experi	mental study design in humans. Replication not feasible		
Randomization	No random	ization was performed on a retrospective cohort		
Blinding	Data and sa	ample collection of clinical specimens occurred before the conception of this study and was therefore blinded.		
Poportin	a for	specific materials, systems and methods		
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Materials & exp	perimenta	al systems Methods		
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		es involving human research participants		
Population chara	cteristics	Study population was patients with cancer receiving care at our institution from March 10 through May 7th 2020.		
Recruitment		This was a retrospective clinical study.		
Ethics oversight		The MSKCC Institutional Review Board granted a HIPAA waiver of authorization to conduct the study.		
Note that full informa	ation on the a	approval of the study protocol must also be provided in the manuscript.		
Clinical data				
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Clinical trial regis	tration No	ot a clinical trial		
Study protocol	No	ot a clinical trial		
Data collection	Cli	nical parameters were extracted from the institutional database and the electronic health record.		

Among COVID-19 patients outcomes included hospitalization and severe COVID-19 illness, defined as the need for high-flow oxygen or ventilator support.

Outcomes