Integrated Survival Estimates for Cancer Treatment Delay Among Adults With Cancer During the COVID-19 Pandemic

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IMPORTANCE Cancer treatment delay has been reported to variably impact cancer-specific survival and coronavirus disease 2019 (COVID-19)–specific mortality during the severe acute respiratory syndrome coronavirus 2 pandemic. During the pandemic, treatment delay is being recommended in a nonquantitative, nonobjective, and nonpersonalized manner, and this approach may be associated with suboptimal outcomes. Quantitative integration of cancer mortality estimates and data on the consequences of treatment delay is needed to aid treatment decisions and improve patient outcomes.

OBJECTIVE To obtain quantitative integration of cancer-specific and COVID-19–specific mortality estimates that can be used to make optimal decisions for individual patients and optimize resource allocation.

DESIGN, SETTING, AND PARTICIPANTS In this decision analytical model, age-specific and stage-specific estimates of overall survival pre–COVID-19 were adjusted by the probability of COVID-19 (individualized by county, treatment-specific variables, hospital exposure frequency, and COVID-19 infectivity estimates), COVID-19 mortality (individualized by age-specific, comorbidity-specific, and treatment-specific variables), and delay of cancer treatment (impact and duration). These model estimates were integrated into a web application (OncCOVID) to calculate estimates of the cumulative overall survival and restricted mean survival time of patients who received immediate vs delayed cancer treatment. Using currently available information about COVID-19, a susceptible-infected-recovered model that accounted for the increased risk among patients at health care treatment centers was developed. This model integrated the data on cancer mortality and the consequences of treatment delay to aid treatment decisions. Age-specific and cancer stage–specific estimates of overall survival pre–COVID-19 were extracted from the Surveillance, Epidemiology, and End Results database for 691 854 individuals with 25 cancer types who received cancer diagnoses in 2005 to 2006. Data from 5 436 896 individuals in the National Cancer Database were used to estimate the independent impact of treatment delay by cancer type and stage. In addition, data from 275 patients in a nested case-control study were used to estimate the COVID-19 mortality rate by age group and number of comorbidities. Data were analyzed from March 17 to May 21, 2020.

EXPOSURES COVID-19 and cancer.

MAIN OUTCOMES AND MEASURES Estimates of restricted mean survival time after the receipt of immediate vs delayed cancer treatment.

RESULTS At the time of the study, the OncCOVID web application allowed for the selection of up to 47 individualized variables to assess net survival for an individual patient with cancer. Substantial heterogeneity was found regarding the association between delayed cancer treatment and net survival among patients with a given cancer type and stage, and these 2 variables were insufficient to discriminate the net impact of immediate vs delayed treatment. Individualized overall survival estimates were associated with patient age, number of comorbidities, treatment received, and specific local community estimates of COVID-19 risk.

CONCLUSIONS AND RELEVANCE This decision analytical modeling study found that the OncCOVID web-based application can quantitatively aid in the resource allocation of individualized treatment for patients with cancer during the COVID-19 global pandemic.

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Cancer remains a leading cause of mortality, especially in high-income countries, with 607 000 cancer deaths in the US in 2019 alone and more than 9.5 million cancer deaths globally.[1,2] However, the coronavirus disease 2019 (COVID-19) global pandemic, caused by the severe acute respiratory syndrome coronavirus 2, has substantially disrupted cancer care delivery.[3] The pandemic has overwhelmed many health care systems, and rapid policy changes have been implemented to conserve resources. Cancer surgeries with curative intent during the peak of the pandemic were often deemed elective and were reduced or canceled altogether at various institutions.[4] Systemic therapies and radiotherapies have also been variably reduced to encourage physical distancing and allow for staff redeployment. For certain cancers, a delay in the initiation of treatment may be safe[5]; however, for most cancers, the data suggest that treatment delay is associated with worse overall survival (OS).[6]

Further complicating matters, patients with cancer appear to be especially vulnerable to COVID-19.[7] Patients with cancer often have multiple comorbid conditions and risk factors, including older age, diabetes, hypertension, and cardiovascular disease, that are associated with an increase in the risk of COVID-19–specific mortality.[7-9] Thus, a careful and complex balance is necessary to avoid unnecessary mortality in patients with cancer. If such a balance were not optimized, unnecessary cancer or COVID-19 deaths could reduce the net success of the global pandemic response.

Countries and institutions have implemented systems to triage and select patients for immediate vs delayed treatment, most commonly through the use of a 3-tiered system.[10-13] These tiered systems are inherently subjective, do not account for dynamic changes in COVID-19 risk, are unable to discriminate patients with similar risk across cancer types, and are unable to account for individualized COVID-19 mortality risk. To our knowledge, there are no quantitative tools presently available to estimate the individualized risk of death for a patient with cancer during the COVID-19 pandemic. We therefore sought to develop an integrated web-based survival model, termed OncCOVID,[14] to serve as a decision aid by providing personalized quantitative estimates of overall mortality for immediate or delayed cancer treatment conditions.

Methods

Pre–COVID-19 Mortality

Data on patients with invasive cancer were extracted from the Surveillance, Epidemiology, and End Results (SEER) database of the National Cancer Institute. The SEER program collects data from 28% of the US population via a network of population-based incident tumor registries from geographically distinct regions. The SEER 18 registry[15] (which includes cases diagnosed from 2000 through the current data year) was used, and all patients with an invasive cancer diagnosis from 2005 to 2006 were included. Patients with hematologic malignancies and patients with a cancer diagnosis via an autopsy or death certificate (<1.5% of patients) were excluded. The years of diagnoses were chosen to be both representative

Key Points

Question What are the benefits and risks associated with delayed treatment for an individual patient with cancer during the coronavirus disease 2019 pandemic, and does the use of a web-based survival model (OncCOVID) aid treatment decisions?

Findings In this decision analytical modeling study including data from more than 6 million patients with cancer, the OncCOVID model found heterogeneity regarding the impact of delayed cancer treatment owing to patient and cancer factors that are not currently captured by commonly used triage systems. Whether delayed cancer treatment harms or improves expected survival compared with immediate treatment is dependent on patient, cancer, treatment, and community factors.

Meaning The study's results indicate that the OncCOVID web application may allow clinicians to estimate the net impact of delayed cancer treatment for individual patients and to prioritize patients for immediate treatment in settings with limited treatment capacity.

of contemporary patients with cancer who received diagnoses in the US and to enable the calculation of long-term survival estimates after diagnosis.

A total of 691 854 patients with up to 12 years of follow-up met the eligibility criteria. Mortality codes in the SEER database are assigned from death certificates that are completed by the physician caring for the patient at the time of death. From this data set, 25 cancer types were extracted. Other causes of death were accounted for as competing events for cancer-specific mortality modeling. For each cancer type, Cox proportional hazards and Fine and Gray regression models were used to estimate all-cause mortality and cancer-specific mortality as a function of patient age and cancer stage.

Impact of Treatment Delay

Two approaches were used to provide an estimate of the impact of treatment delay for survival. The first approach used the National Cancer Database and included 5 436 896 patients who received cancer treatment between 2004 and 2014. Time to any treatment from diagnosis was calculated for each patient. Patients were excluded if their time to treatment was missing or greater than 180 days after diagnosis, if their time to death or last contact was missing, or if their clinical cancer stage was missing. Stratified Cox proportional hazards models for each cancer type (with year of diagnosis as stratum) were fit. In addition to clinical stage, the models included covariates for race (White, Black, and other), rurality of treatment facility (urban and rural), age group by decade (<50 years, 50-60 years, 61-70 years, 71-80 years, 81-90 years, and >90 years), insurance status, educational level, household income, treatment facility type, treatment facility location, and distance from patient's residence to hospital. An institutional review board waiver was obtained, and patient consent was deemed not necessary to access publicly available datasets.

The second approach to assess the impact of treatment delay for survival used a rapid semisystematic review of the published literature. Four physicians (D.E.S., R.T.D., W.C.J., and N.K.J.) conducted the review using MEDLINE via PubMed with

the search terms *cancer type* and *treatment delay* and *survival*. This review was performed for each of the 25 cancer types included from the SEER database. Further details are available in eMethods in the Supplement.

Risk of COVID-19 Mortality

To estimate the risk of COVID-19 mortality, we estimated the risk of infection with COVID-19 and the subsequent risk of mortality if infected (ie, the case fatality rate [CFR]). The absolute risk of COVID-19 mortality was calculated as the product of infection probability and conditional mortality rate in patients who were infected.

COVID-19 Risk Estimate

To estimate the risk of infection with COVID-19, a daily risk of infection was calculated based on a susceptible-infected-recovered model. For the present study, default values based on the current literature and real-time data were used; however, all values in the model can be modified by the user as needed. County-level data on the number of people who were infected with COVID-19, recovered from COVID-19, and died of COVID-19 were directly entered into the model from the COVID-19 Case Tracker from Johns Hopkins University.[16] The US county population sizes were obtained from 2019 census estimates.[17] County population size was obtained for the county in which the individual received cancer treatment and, if different, from the county in which the individual resided. The web application allowed for global estimates, but the present study focused only on US estimates.

The mean number of people infected per individual with infection at the current time in the pandemic (ie, effective reproduction number [R_t]) and the mean duration of infectiousness were defaulted to published values (ie, R_t = 1; days of infectiousness = 14) but can be user adjusted.[18,19] Consistent with reports of increased infection rates among health care professionals,[20-24] our model included a different estimated risk of infection for individuals in health care settings. We assumed a higher number of infectious contacts in health care settings, which applied to both health care professionals and patients receiving care that day. A higher infection risk was also assumed for patients who received surgery as a component of their treatment.[25] Further details are available in eMethods in the Supplement.

COVID-19 Mortality Risk Estimate

The CFRs were calculated using a combination of individual patient-level data analysis from a recently reported study on the impact of comorbidities for COVID-19 mortality[26] and published combined estimates of CFRs by age group.[27] Initial estimates of CFRs were obtained from a penalized logistic regression model, with age group by decade and number of comorbidities as categorical covariates with no interaction term. Comorbidities that have been associated to date with increased COVID-19–specific mortality (cancer, diabetes, cardiac disease, obesity, chronic kidney disease, hypertension, and chronic obstructive pulmonary disease) were included.[9,26,28] To obtain improved CFR estimates for each combination of age and comorbidity count, the initial estimates were renormalized so that the weighted mean (across comorbidity counts) for a given age group matched the values reported by the Novel Coronavirus Pneumonia Emergency Response Epidemiology Team[27] while preserving the relative risk associated with the increasing comorbidity counts reported by Gu et al.[26] To estimate the prevalence of comorbidities in the US population, the National Health and Nutrition Examination Survey, a nationally representative survey of the noninstitutionalized civilian population, was used.[30] We used data from the 2005 to 2006 cycle that was restricted to patients older than 40 years who had complete information on age and sex and at least 1 nonmissing entry for the comorbidities we considered. This process yielded a final sample of 3056 adults. Age-specific prevalence values for the presence of 0 to 3 or more comorbidities were used to calculate weighted mean CFRs for each age group. These estimated CFRs were also assumed to increase for patients receiving chemotherapy as part of their cancer treatment or patients who were immunocompromised before receiving treatment based on published relative risk estimates.[29] Cumulative COVID-19 mortality rates over a specified period (with a default of 6 months) were calculated as the cumulative probability of COVID-19 during this period multiplied by the individualized CFR.

Mortality and Survival Estimates

The estimates of COVID-19 specific mortality ($M_1(t)$) and all-cause pre-COVID-19 mortality ($M_2(t)$) were combined to estimate overall survival at time t as: $S(t)=(1-M_1(t))\times(1-M_2(t))$.[31] We assumed that the risks of COVID-19 and non-COVID-19 mortality were independent, conditional on the patient level covariates and that the COVID-19 mortality risk was 0 after 6 months.

Because of these competing causes of mortality, the assumption of proportional hazards was not valid, and the estimated survival curves for immediate and delayed treatment may have crossed. Thus, restricted mean survival time (RMST) was chosen as a robust summary measure to characterize the net impact of delaying cancer treatment.[32] Restricted mean survival time was interpreted as the mean survival time over a specified period and calculated as the area under the OS curve. Unlike other commonly used measures, such as OS at 5 years, RMST appropriately captured the differential impact of COVID-19 mortality (which typically occurs ≤2 months after infection) and cancer mortality (which typically occurs >6 months after diagnosis). In the presented analyses, RMST was calculated over 1 year or 5 years, as specified, with COVID-19 mortality estimated over a period of 6 months and assumed to be 0 thereafter. This last assumption was based on the uncertainty associated with susceptible-infected-recovered models that are performed for periods more than 6 months in the future.

Statistical Analysis

Statistical analyses were conducted using R software, version 3.6.2 (R Foundation for Statistical Computing). The web application was developed using R Shiny (RStudio). Maps were generated using the tmap, maptools, tmaptools, and sf packages for R software, and the penalized logistic regression analy-

Table 1. Inputs for OncCOVID Model

Category	Default value	Method
Patient age	User defined	NA
No. of comorbidities		
0	Variable by age	Penalized logistic regression analysis normalized using data from the Novel Coronavirus Pneumonia Emergency Response Epidemiology Team (2020)[26,27] and the NHANES[30]
1	Variable by age; RR ≈ 1.23	
≥2	Variable by age; RR ≈ 2.30	
Treatment		
Chemotherapy	Variable by age; RR ≈ 2.50	Estimated RR using data from Williams et al[29]
Surgery[a,b]	RR = 5.73	Estimated RR using data from Wang et al[20] and Zhang and Cheng[25]
Hospital visits, No.[a,b]	3.47-fold increase per day	Estimated increase in number of potentially infectious contacts per day using data from Wang et al[20]
Duration of treatment	User defined	User defined
Duration of treatment delay		
Impact of treatment delay	Variable by cancer type and stage	Multivariable Cox proportional hazards model from the NCDB
Cancer		
No. of types	25	Regression models using SEER data to estimate age-specific CSM and OS by cancer type and stage
Stages	I-IV	
Infection risk[a]		
County-level estimates at residential location	Updated daily	Estimated using data from the COVID-19 Case Tracker[16] and the US Census Bureau[17]
County-level estimates at treatment center location		
No. of people infected per individual with infection at current time in pandemic	1	Time dependent; variable based on current state of pandemic[19]
Duration of infectiousness, d	14	WHO[18] estimates
Infection risk with immediate treatment	Variable	Derived from other inputs using SIR model
Infection risk with delayed treatment		
Health care system		
Hospital system overwhelmed	User defined	User defined
Health care professionals on staff, %[a]	12.00	Estimated using data from the Kaiser Family Foundation[33]
Patients receiving health care per day, %[a]	0.23	CDC[34] estimates
Patients receiving health care and surgery per day, %[a]	17.40	Estimated using data from Zhang and Cheng[25] and the CDC[34]

Abbreviations: CDC, Centers for Disease Control and Prevention; COVID-19, coronavirus disease 2019; CSM, cancer-specific mortality; NA, not applicable; NCDB, National Cancer Database; NHANES, National Health and Nutrition Examination Survey; OS, overall survival; RR, relative risk; SEER, Surveillance, Epidemiology, and End Results; SIR, susceptible-infected-recovered; WHO, World Health Organization.

[a] Risk of COVID-19, not COVID-19–specific mortality.

[b] Risk of contracting COVID-19 in excess of background risk (additional potentially infectious contacts).

sis was conducted using the penalized package for R software. Data were analyzed from March 17 to May 21, 2020.

Results

At the time of the study, the OncCOVID model allowed for the selection of 47 inputs, 18 covariates (eg, age and comorbidities), and 29 parameter estimates (eg, hazard ratio [HR] for delay of treatment) to characterize individual risk estimates for those receiving immediate vs delayed cancer treatment (**Table 1**).

Mortality

Across the 25 cancer types analyzed, substantial variability existed in cancer-specific and overall mortality (pre–COVID-19) by cancer type and stage of disease (**Figure 1**). Five-year cancer-specific mortality ranged from less than 1% to more than 80% based on the cancer type and stage. The impact of delayed cancer treatment varied across cancer type and stage of disease.[14]

For example, treatment delays of up to 6 months were not associated with detrimental consequences for individuals with stage II prostate cancer (HR, 1.000 per month of delay) in our multivariable analysis. However, treatment delays were associated with a substantial survival detriment among individuals with stage I, II, and III head and neck cancers (HR, 1.061-1.161 per month of delay based on stage of disease).

The CFRs from COVID-19 are provided by age and number of comorbidities (in addition to cancer) in **Table 2**. These estimates ranged from 0.4% for a patient aged 40 to 50 years with no comorbid conditions beyond cancer to 39.3% for a patient older than 80 years with 2 or more comorbid conditions.

Integrated Overall Survival Estimates

The impact of delayed cancer treatment compared with immediate treatment varied substantially across and within cancer types and stages (**Figure 2**A). This variation indicated that individual hypothetical patients had large differences in the harm or benefit associated with delayed treatment based on
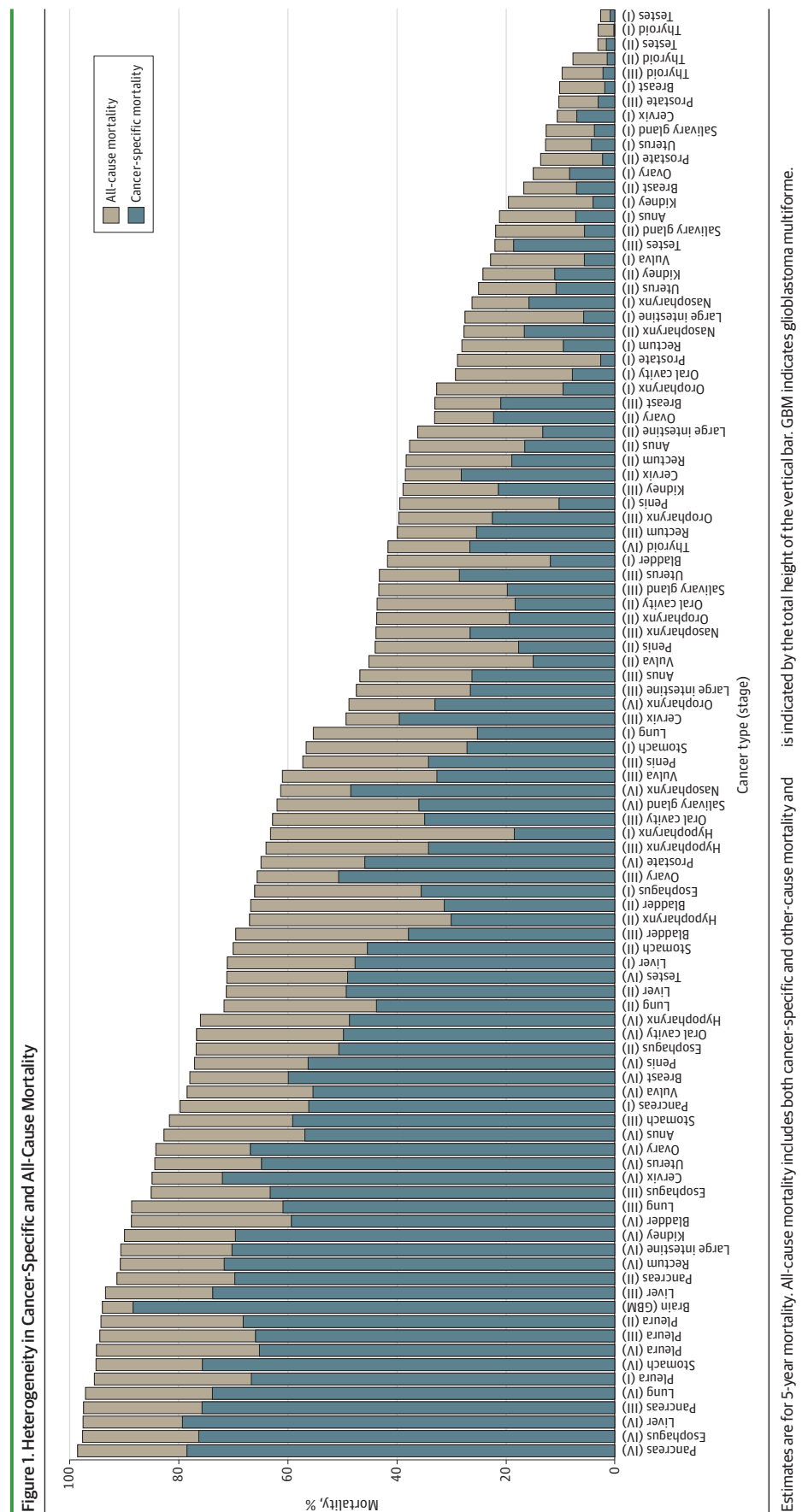
Figure 1. Heterogeneity in Cancer-Specific and All-Cause Mortality

Estimates are for 5-year mortality. All-cause mortality includes both cancer-specific and other-cause mortality and is indicated by the total height of the vertical bar. GBM indicates glioblastoma multiforme.

Table 2. Case Fatality Rates for Patients With Cancer by Age and Number of Additional Chronic Comorbidities

Age group, y	Additional comorbidities, %[a]		
	0	1	≥2
40-50	0.40	0.49	1.15
51-60	1.18	1.45	3.39
61-70	3.01	3.69	8.51
71-80	6.86	8.42	19.43
≥81	14.16	17.34	39.30

[a] Comorbidities include cardiovascular disease, diabetes, hypertension, and obesity.

Figure 2. Overall Survival Impact of Cancer Treatment Delay
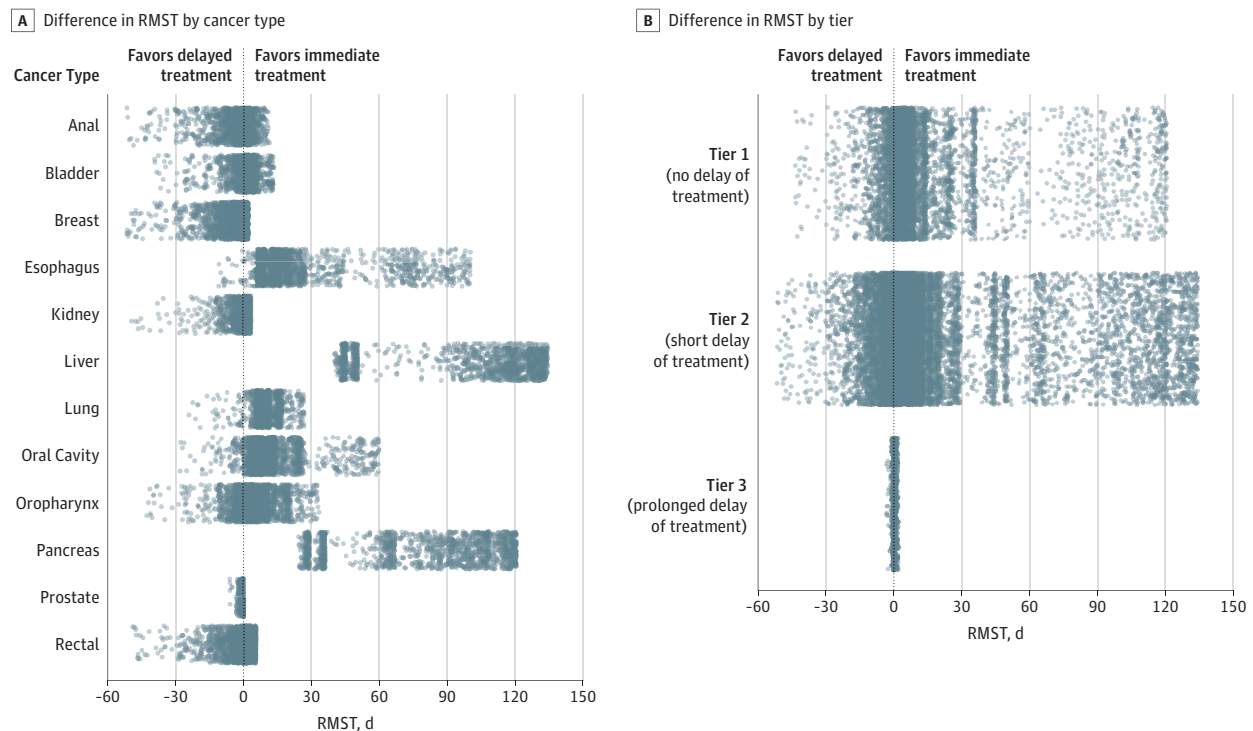
Estimated impact of 3-month treatment delay for restricted mean survival time (RMST) for varying patient factors (eg, age and comorbidities), disease characteristics (eg, cancer type and stage), treatment characteristics (eg, chemotherapy and number of days in hospital), and community factors (eg, effective reproduction number [R_t]). A, Estimated difference in 5-year RMST for immediate vs delayed treatment by cancer type. B, Estimated difference in 5-year RMST for immediate vs delayed treatment by tier.

patient age, cancer type, and cancer stage. This heterogeneity was also a complex function of age, the presence of comorbidities, the receipt of chemotherapy, and other variables in the model. For example, the estimated impact of delayed treatment (relative to immediate treatment) in patients with prostate cancer was minimal, as these patients typically spend only 1 to 2 days in the hospital for surgery (without receipt of chemotherapy) or receive 5 brief outpatient treatments with stereotactic body radiotherapy (also without receipt of chemotherapy). In contrast, among patients with pancreatic cancer, the harm of treatment delay associated with cancer-specific mortality exceeded any decrease in COVID-19–specific mortality (Figure 2A).

Common 3-tiered methods were used to categorize patients with cancer into those who should receive immediate treatment (tier 1 [eg, anal cancer]), those who could delay treat-ment for a brief interval (tier 2 [eg, most cancer types]), and those who could potentially delay treatment until the pandemic has resolved (tier 3 [eg, early-stage prostate cancer]).[13] To illustrate the limitations of this method, the impact of treatment delay across cancer types and stages was classified within each tier (Figure 2B). The tiered system was unable to distinguish between patients who benefited the most from the receipt of immediate vs delayed cancer treatment.

Heterogeneity in the RMST difference between immediate vs delayed treatment was also found across geographic regions based on current county-level COVID-19 case data and population size. **Figure 3** illustrates the spatial heterogeneity across the US counties in a fixed scenario of a patient aged 70 years with stage 3 oropharyngeal cancer, diabetes, and hypertension who will receive concurrent chemotherapy and radiotherapy, with R_t fixed at 2.

Figure 3. Heat Map of US County-Level Infection Estimates
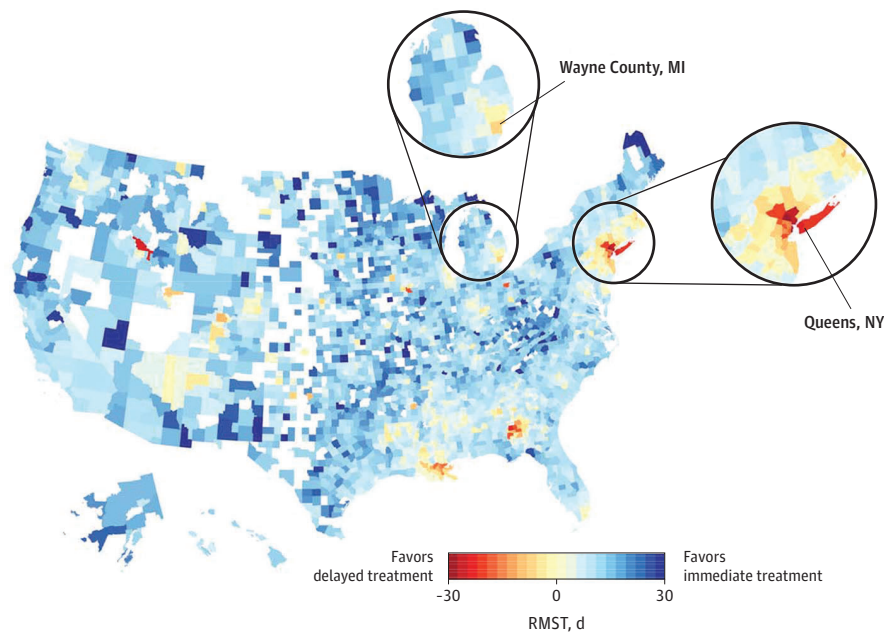
Heat map was based on county-level infection estimates on April 17, 2020, for a patient aged 70 years with stage 3 oropharyngeal cancer, diabetes, and hypertension, who will receive concurrent chemotherapy and radiotherapy. The effective reproduction number (R_t) was set at 2 to calculate the 5-year difference in restricted mean survival time (RMST; calculated as immediate treatment minus delayed treatment conditions) using a 1-month delay.

Discussion

Decisions are currently being made to triage cancer treatment based on qualitative methods for categorizing patients with cancer.[3,10-12,35] These methods are primarily implemented based on perceived urgency, tumor site, and cancer stage and do not account for patient-level factors that impact the risk of COVID-19 mortality (eg, age, comorbidities, location, and treatment) and thus do not provide personalized treatment guidelines. As we indicated, there is potential for net harm associated with immediate or delayed treatment within a given cancer type and stage owing to the complexity of variables that impact each patient's risk. Our model aims to improve current recommendations and provides quantitative estimates to optimize the outcomes of patients with cancer during the global pandemic.

Our model illustrates the challenges of decision-making during the pandemic. An illustrative patient (categorized as tier 2) was a woman aged 70 years from New York City (during the peak of the first wave of the pandemic) who had hypertension and diabetes and a diagnosis of stage II triple-negative breast cancer, for which a standard of care option is breast conservation surgery, chemotherapy, and adjuvant radiotherapy. Compared with a 3-month delay, our model estimated that immediate treatment was associated with an 8% worse 5-year OS or a 5-year RMST decrease of 165 days. In contrast, a patient aged 40 years with no comorbidities and the same stage II breast cancer diagnosis living in Washtenaw County, Michigan, would have a less than 0.1% estimated difference in 5-year OS between immediate and delayed treatment.

Our model is focused on the impact of these decisions for an individual patient rather than the impact for the population or society as a whole. Each day, health care professionals are tasked with either explaining to their patients the safety of delaying cancer treatment or advocating for their patients to receive treatment during the pandemic despite the risks of COVID-19. Our model can also aid in the institutional triage of patients with cancer. Every hospital has a fixed capacity to treat patients with cancer during a given day, and many centers have delayed hundreds to thousands of cancer treatments.[36] Thus, rather than relying on a simple tiered method to evaluate which patients should immediately receive treatment, one could use a model like OncCOVID to more accurately identify which patients will experience the most benefit from immediate treatment and quantitatively estimate the benefits and harms across the population with cancer at a given institution. One could more confidently make institutional policy decisions regarding thresholds for treatment among patients who are likely to experience the greatest net benefit.

Limitations

This study has several limitations. Like all modeling studies, it relies on multiple assumptions. The estimates used in our model are based on currently available data, which are rapidly reported and refined from around the world. Not all patients with COVID-19 are tested, and the extent to which reported case counts are underestimations likely varies between states and over time. In addition, recovered cases are not currently tracked and reported rigorously; however, at this point in the pandemic, this factor has few implications for the model estimates. It is also currently unknown to what extent social distancing impacts model parameters. Many estimates, such

as the impact of the delay of cancer treatment for cancer-specific survival, have their own limitations and potential sources of bias despite the use of multivariable modeling.

There are numerous types and combinations of chemotherapy used clinically; however, in our model, they were treated as 1 binary variable that was age dependent. It is probable that different regimens will have a different impact for COVID-19 mortality; however, these granular data are not yet available. In addition, precise estimates of the cumulative consequences of combining multiple variables that have been reported to impact COVID-19 or COVID-19–specific mortality risk (eg, the receipt of chemotherapy and the presence of specific comorbidities) are unknown. To address these unknown variables, we have made all inputs adjustable by the user, and we are conducting multiple ongoing parallel projects in an attempt to provide more reliable cancer type and stage–specific estimates.

The impact of comorbidities for cancer-specific survival and other-cause mortality (other than COVID-19) has not been incorporated into the model at this time. The current version of the model is designed to evaluate the net impact of a delay in all components of cancer therapy from the time of diagnosis; thus, HR estimates for the impact of only 1 component of therapy (ie, the patient had surgery and is considering a delay in receiving adjuvant breast radiotherapy) are not incorporated into the model. Although the 2005 to 2006 SEER cohort was selected to have 10 years of follow-up, advances in treatment have occurred that may produce small changes in the 5-year survival estimates that were unaccounted for in our models. However, the user can readily adjust all survival estimates as needed. Any model would ideally have independent validation. Although statistically and methodologically desirable, there are no data sets containing 5-year outcomes for patients with COVID-19, and we will continue to work with multiple ongoing prospective COVID-19 registries.

In addition, the study has multiple limitations owing to the unknown factors of COVID-19. For instance, the long-term health consequences of COVID-19 are unknown among patients who survive the infection. There may also be sudden and unforeseeable changes in policy at either the hospital, community, state, or federal level that could be associated with infection rates and the ability to treat patients with cancer. The OncCOVID application is flexible and fully adjustable by the user, which allows for alteration of any adjustments made. An updated version, which incorporates multiple refined models of cancer-specific survival, hazard estimates of treatment delay, estimates of geographically personalized R_t, and other ongoing upgrades, is being developed based on newly available data. Confidence intervals for the outputs were not provided at this time given the statistical challenges in capturing variance estimates across multiple levels of analysis. Thus, caution is warranted when interpreting model estimate differences as statistically significant or clinically meaningful.

Conclusions

We have developed a resource to assist in the personalization and timing of cancer care during the COVID-19 pandemic. Although it is understandable that patients and health care professionals may experience anxiety about delays in cancer treatment, in many circumstances, a delay in treatment may provide a net benefit or minimal net harm to the individual. However, it may be prudent for organizations and institutions to recognize that many patients with cancer could be substantially harmed from cancer treatment delays and that the benefit to the individual may need to be balanced with that of the population.

REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2018;68(6):394-424. doi:10.3322/caac.21492

2. Dagenais GR, Leong DP, Rangarajan S, et al. Variations in common diseases, hospital admissions, and deaths in middle-aged adults in 21 countries from five continents (PURE): a prospective cohort study. *Lancet*. 2020;395 (10226):785-794. doi:10.1016/S0140-6736(19)32007-0

3. Kutikov A, Weinberg DS, Edelman MJ, Horwitz EM, Uzzo RG, Fisher RI. A war on two fronts: cancer care in the time of COVID-19. *Ann Intern Med*. 2020;172(11):756-758. doi:10.7326/M20-1133

4. Sud A, Torr B, Jones ME, et al. Effect of delays in the 2-week-wait cancer referral pathway during the COVID-19 pandemic on cancer survival in the UK: a modelling study. *Lancet Oncol*. 2020;21(8):1035-1044. doi:10.1016/S1470-2045(20)30392-2

5. van den Bergh RCN, Albertsen PC, Bangma CH, et al. Timing of curative treatment for prostate

cancer: a systematic review. *Eur Urol*. 2013;64(2): 204-215. doi:10.1016/j.eururo.2013.02.024

6. Khorana AA, Tullio K, Elson P, et al. Time to initial cancer treatment in the United States and association with survival over time: an observational study. *PLoS One*. 2019;14(3):e0213209. doi:10.1371/journal.pone.0213209

7. Liang W, Guan W, Chen R, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. *Lancet Oncol*. 2020;21(3):335-337. doi:10.1371/journal.pone.0213209

8. Cho H, Mariotto AB, Mann BS, Klabunde CN, Feuer EJ. Assessing non–cancer-related health status of US cancer patients: other-cause survival and comorbidity prevalence. *Am J Epidemiol*. 2013; 178(3):339-349. doi:10.1093/aje/kws580

9. Richardson S, Hirsch JS, Narasimhan M, et al; the Northwell COVID-19 Research Consortium. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. *JAMA*. 2020; 323(20):2052-2059. doi:10.1001/jama.2020.6775

10. Guckenberger M, Belka C, Bezjak A, et al. Practice recommendations for lung cancer radiotherapy during the COVID-19 pandemic: an ESTRO-ASTRO consensus statement. *Radiother Oncol*. 2020;146:223-229. doi:10.1016/j.radonc.2020.04.001

11. Thomson DJ, Palma D, Guckenberger M, et al. Practice recommendations for risk-adapted head and neck cancer radiotherapy during the COVID-19 pandemic: an ASTRO-ESTRO consensus statement. *Int J Radiat Oncol Biol Phys*. 2020;107(4):618-627. doi:10.1016/j.ijrobp.2020.04.016

12. Antonoff M, Backhus L, Boffa DJ, et al; Thoracic Surgery Outcomes Research Network, Inc. COVID-19 guidance for triage of operations for thoracic malignancies: a consensus statement from Thoracic Surgery Outcomes Research Network. *J Thorac Cardiovasc Surg*. 2020;160(2):601-605. doi:10.1016/j.jtcvs.2020.03.061

13. Ontario Health. *Pandemic Planning Clinical Guidelines for Patients With Cancer*. Ontario Health, Cancer Care Ontario; 2020. Accessed April 15, 2020. https://www.accc-cancer.org/docs/documents/cancer-program-fundamentals/oh-cco-pandemic-planning-clinical-guideline_final_2020-03-10.pdf

14. Hartman H, Schipper M, Spratt D. OncCOVID models. Michigan Medicine, University of Michigan; 2020. Accessed May 21, 2020. http://onccovid.med.umich.edu/

15. Surveillance, Epidemiology, and End Results Program. Registry groupings in SEER data and statistics. National Cancer Institute; 2020. Accessed March 27, 2020. https://seer.cancer.gov/registries/terms.html

16. Johns Hopkins University Center for Systems Science and Engineering. COVID-19 data repository by the Center for Systems Science and Engineering

(CSSE) at Johns Hopkins University. Center for Systems Science and Engineering, Johns Hopkins University. Accessed April 15, 2020. https://github.com/CSSEGISandData/COVID-19

17. United States Census Bureau. US census 2019 county estimates. United States Census Bureau. March 26, 2020. Accessed April 15, 2020. https://www2.census.gov/programs-surveys/popest/datasets/2010-2019/counties/totals/

18. World Health Organization. Considerations for Quarantine of Individuals in the Context of Containment for Coronavirus Disease (COVID-19): Interim Guidance, 29 February 2020. World Health Organization; 2020. Accessed April 15, 2020. https://apps.who.int/iris/handle/10665/331299

19. World Health Organization. Q&A on coronaviruses (COVID-19). World Health Organization. April 17, 2020. Accessed April 15, 2020. https://www.who.int/news-room/q-a-detail/q-a-coronaviruses

20. Wang C, Liu L, Hao X, et al Evolving epidemiology and impact of non-pharmaceutical interventions on the outbreak of coronavirus disease 2019 in Wuhan, China. Preprint. Posted online March 6, 2020. medRxiv. doi:10.1101/2020.03.03.20030593

21. Centers for Disease Control and Prevention. Interim operational considerations for public health management of healthcare workers exposed to or with suspected or confirmed COVID-19: non-US healthcare settings. Centers for Disease Control and Prevention. Updated August 27, 2020. Accessed July 30, 2020. https://www.cdc.gov/coronavirus/2019-ncov/hcp/non-us-settings/public-health-management-hcw-exposed.html

22. Vahidy FS, Bernard DW, Boom ML, et al. Prevalence of SARS-CoV-2 infection among asymptomatic health care workers in the greater Houston, Texas, area. *JAMA Netw Open*. 2020;3(7): e2016451. doi:10.1001/jamanetworkopen.2020.16451

23. Wang X, Ferro EG, Zhou G, Hashimoto D, Bhatt DL. Association between universal masking in a health care system and SARS-CoV-2 positivity among health care workers. *JAMA*. 2020;324(7): 703-704. doi:10.1001/jama.2020.12897

24. Nguyen LH, Drew DA, Joshi AD, et al. Risk of COVID-19 among frontline healthcare workers and the general community: a prospective cohort study. Preprint. Posted online May 25, 2020. medRxiv. doi:10.1101/2020.04.29.20084111

25. Zhang Y, Cheng SR. Estimating preventable COVID-19 infections related to elective outpatient surgery in Washington state: a quantitative model. Preprint. Posted online March 27, 2020. medRxiv. doi:10.1101/2020.03.18.20037952

26. Gu T, Chu Q, Yu Z, et al. History of coronary heart disease increases the mortality rate of COVID-19 patients: a nested case-control study. Preprint. Posted online April 3, 2020. medRxiv. doi:10.1101/2020.03.23.20041848

27. The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19)—China, 2020. *China CDC Weekly*. 2020;2:1-10. doi:10.1136/bmjopen-2020-038976

28. Guan WJ, Liang WH, Zhao Y, et al; China Medical Treatment Expert Group for COVID-19. Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. *Eur Respir J*. 2020;55(5):2000547. doi:10.1183/13993003.00547-2020

29. Williams M, Le Calvez K, Mi E, Chen J, Dadhania S, Pakzad-Shahabi L. Estimating the risks from COVID-19 infection in adult chemotherapy patients. Preprint. Posted online March 20, 2020. medRxiv. doi:10.1101/2020.03.18.20038067

30. Centers for Disease Control and Prevention. National Health and Nutrition Examination Survey, NHANES 2005-2006. US Department of Health and Human Services; 2020. Accessed April 15, 2020. https://wwwn.cdc.gov/nchs/nhanes/ContinuousNhanes/Default.aspx?BeginYear=2005

31. Pfeiffer RM, Gail MH. *Absolute Risk: Methods and Applications in Clinical Management and Public Health*. Chapman and Hall/CRC; 2017.

32. Rahmadian AP, Delos Santos S, Parshad S, Everest L, Cheung MC, Chan KK. Quantifying the survival benefits of oncology drugs with a focus on immunotherapy using restricted mean survival time. *J Natl Compr Canc Netw*. 2020;18(3):278-285. doi:10.6004/jnccn.2019.7362

33. Kaiser Family Foundation. Health care employment as a percent of total employment. Kaiser Family Foundation. May 2018. Accessed April 15, 2020. https://www.kff.org/other/state-indicator/health-care-employment-as-total/?currentTimeframe=0&sortModel=%7B%22colId%22:%22Location%22,%22sort%22:%22asc%22%7D

34. National Center for Health Statistics. Ambulatory care use and physician office visits. National Center for Health Statistics, Centers for Disease Control and Prevention. Updated October 10, 2019. Accessed April 15, 2020. https://www.cdc.gov/nchs/fastats/physician-visits.htm

35. COVID-19 Pandemic Breast Cancer Consortium. Recommendations for prioritization, treatment and triage of breast cancer patients during the COVID-19 pandemic: executive summary. American College of Surgeons. March 25, 2020. Accessed April 15, 2020. https://www.facs.org/quality-programs/cancer/executive-summary

36. Bostock N. Patients waiting more than a month for urgent cancer checks amid COVID-19 crisis. GPonline. May 20, 2020. Accessed June 29, 2020. https://www.gponline.com/patients-waiting-month-urgent-cancer-checks-amid-covid-19-crisis/article/1681673