

COVID-19 and cancer in the United States

COVID-19 e cancro negli Stati Uniti

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The impact of the COVID-19 pandemic, caused by the SARS-CoV-2 virus, in the United States (US) has been enormous. It is the country with the largest number of confirmed COVID-19 infections, 12.6 million reported by November 25, and the greatest number of COVID-19 related deaths, 260,065 to date, representing 18% of deaths globally. COVID-deaths represent the tip of the iceberg of disease severity. The cumulative hospitalization rate in the US is 120.9 per 100,000 people, with those age 50-64 years (182.3 per 100,000 people) and those over the age of 65 (338.2 per 100,000 people) disproportionately hospitalized for COVID-19.¹

During the early parts of the pandemic, the US epicenter was New York City with the majority of cases concentrated in the North East. The North East instituted intense public health efforts including school and business closures, social distancing recommendations, and use of masks. Throughout the prolonged first wave of the infection, other parts of the country have emerged as epicenters including Texas, Florida, California, and Arizona. In these states, public health policies were more variable and work and school reopenings occurred earlier – leading to more recent surges in the Southern, Midwestern, and Western states. Although early in the pandemic the majority of cases were focused in large urban areas, current hotspots include smaller cities as well as more rural settings.

Given the suspected longevity and long-term consequences of the COVID-19 pandemic, studying and understanding its potential impact on vulnerable patients in the US is an important public health concern. One of the largest disparities has been in populations of color. Systemic discrimination, worse healthcare access and utilization, the disproportionate number of people from minority groups being considered essential workers and required to report to work, education inequalities, wealth gaps, and more concentrated living conditions all

contribute to the disproportionate burden the COVID-19 pandemic has on minority groups.¹

There is mounting evidence that COVID-19 severity is greater among cancer patients compared to COVID-19 infected individuals without cancer.² In a study in Wuhan, China, cancer patients infected with COVID-19 had higher risks of ICU admission, ventilation, and death compared to those without cancer. Furthermore, patients with metastatic cancer had a 5-fold elevated risk of dying from their COVID-19 infection in comparison to those patients without cancer.² The cancer patients in this study were within 40 days of treatment. A pressing issue is to understand the extent to which these individuals are at greater vulnerability due to the cancer itself, cancer treatment, or another factor. Cancer patients in the US, and globally, have faced difficult decisions in light of the COVID-19 pandemic. Cancer patients often times rely heavily on a functioning healthcare system, and these very systems are currently treating, and in some highly impacted regions in the country are overwhelmed with, COVID-19 patients. Given that cancer patients are particularly susceptible to severe COVID-19 infection, many cancer patients are having to make the difficult decision between receiving cancer treatment and potentially exposing themselves to COVID-19 or forgoing or delaying necessary cancer treatment possibly contributing to worse cancer outcomes in these cases.

The difficult choice that many cancer patients are having to make presents challenges when it comes to the diagnosis, treatment, and survivorship of cancer patients, and ultimately on mortality. First, in highly affected areas, hospitals and patients have opted to delay diagnostic testing. This delay in screening and diagnostic treatment could result in decreased detection of treatable cancers and this lapsed time could result in disease progression to

more aggressive, metastatic disease by the time diagnostic testing is resumed. This could potentially result in excess cancer mortality.

Furthermore, many cancer patients have opted to delay or alter their treatment regimen to decrease the excess risk of contracting COVID-19 by visiting a hospital. Next, many clinical trials have been temporarily suspended, so for the time being, the development of potentially life saving treatments has been put on pause.³ While the COVID-19 pandemic has the potential to decrease the diagnosis, management, and treatment of cancer in the US, it is the responsibility of epidemiologists to study the impact of COVID-19 on the pandemic and offer up actionable options to mitigate this effect.



It is more important than ever that the epidemiology research community bands together. In response, the Coronavirus Pandemic Epidemiology (COPE) consortium was established to recruit participants in the US and United Kingdom. A key component of COPE is the COVID-19 Symptom Tracker mobile application that collects data on risk factors, daily symptoms, testing, and outcomes from general community members as well as NCI-funded epidemiology cohort participants. The COVID-19 pandemic has raised many questions regarding cancer detection, treatment, and survivorship, and we are optimistic that COPE will be a valuable tool in identifying best cancer care practices amidst the COVID-19 pandemic as well as future directions and lines of research.⁴ This consortium has already led to highly innovative research initiatives. A recent paper produced by COPE found that healthcare workers are more likely to develop COVID-19, which necessitates the need to provide personal protective equipment as well as enforce stringent safety measure.⁵ Prostate cancer specifically has a number of parallels with the COVID-19 infection. First, the risk factors for both illnesses resemble one another: male sex, older age, and racial disparities. One common treatment for men diagnosed with prostate cancer is androgen-deprivation therapy (ADT), which offers a unique intersection between COVID-19 infection mechanisms and prostate tumorigenesis. The *TMPRSS2* protease is required for infection of respiratory cells by COVID-19, while cancer researchers discovered the regulation of *TMPRSS2* expression by androgens in prostate cancer.⁶ Half of men with prostate cancer harbor tumors containing a gene fusion between *TMPRSS2* and members of the ETS family of transcription factors. A lower incidence of COVID-19 among men on ADT is provocative and biologically plausible. Based on the described relationship between ADT, *TMPRSS2*, and SARS-CoV-2 incidence, we suggest an additional direction of inquiry. Leuprolide is the most commonly prescribed ADT for men with prostate cancer and is a modulator

of *TMPRSS2 in vitro*.⁶ An epidemiological study of COVID-19 infection and severity among women exposed to leuprolide for management of endometriosis-associated symptoms could support this potential protective link.

Overall, the US continues to bear a tremendous public health burden of a sustained COVID-19 wave. Given that the COVID-19 pandemic will most likely continue to alter American daily life and pose a threat to much of the population for the foreseeable future, it is important that epidemiologists band together with other scientists, clinicians, and policy makers to better understand the virus and its potential complications and offer up actionable insight into how to mitigate its detriments. Understanding the impact of COVID-19 on cancer care outcomes is urgently needed given the high incidence of both diseases in the US.

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