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# COVID-19 vaccination: Prioritization of at risk groups

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## 1. News and topics section submission

*Some GU cancer patients are at a substantially increased risk of death if they become infected with COVID-19 infection, and so should be prioritized for vaccination.*

There is currently limited supply of the recently approved COVID-19 vaccines. Given this supply side constraint, many territories, states and countries are utilizing a phased vaccine distribution and administration strategy based on the prioritization of various high-risk groups. While strategies vary between regions, nearly all aim for equitable and clinically driven distribution so that those at higher risk of exposure, illness or poor outcome such as death, are prioritized. Examples of such groups prioritized because of increased mortality from COVID-19 include residents of long term care facilities and older adults [1]. There have also been numerous reports demonstrating patients with cancer who are diagnosed with COVID-19, have a higher risk of severe clinical events than those without cancer [2].

With these considerations in mind, and to further inform our own practice and the risks to our own patient population, we examined patient data from the Mount Sinai Healthcare System Data Warehouse (https://msdw.mountsinai.org). Patients presenting to Mount Sinai Healthcare System in New York who underwent testing for SARS-CoV-2 were included in this dataset ($n = 231{,}231$). Vaccination guidelines vary by region; those in older age groups have been prioritized for vaccination first by many. In New York State , the first general population group offered vaccination was those >65 years of age; hence we examined the mortality of those ≤65 years (180,639; 78% of the cohort); who had a recorded cancer diagnosis ($n = 7{,}888$; 4.4%) [3]. For context, New York State estimates of the prevalence of cancer in New York City is 4.7%.

We examined the impact of a positive COVID-19 diagnosis on the 30 day mortality of patients with various malignancies in this cohort. Our study found that there are notable differences in 30-day mortality for a number of malignancies in patients with COVID-19 versus those without, in keeping with the findings of others that the combination of cancer and COVID-19 increases patient mortality. Our finding supports the National Comprehensive Cancer Network recommendation that patients with cancer should be prioritized for vaccination (Center for Disease Control priority group 1b/c) and should be immunized when vaccination is available to them [4].

Both prostate and bladder cancer patients diagnosed with COVID-19, had a higher 30-day mortality as compared to

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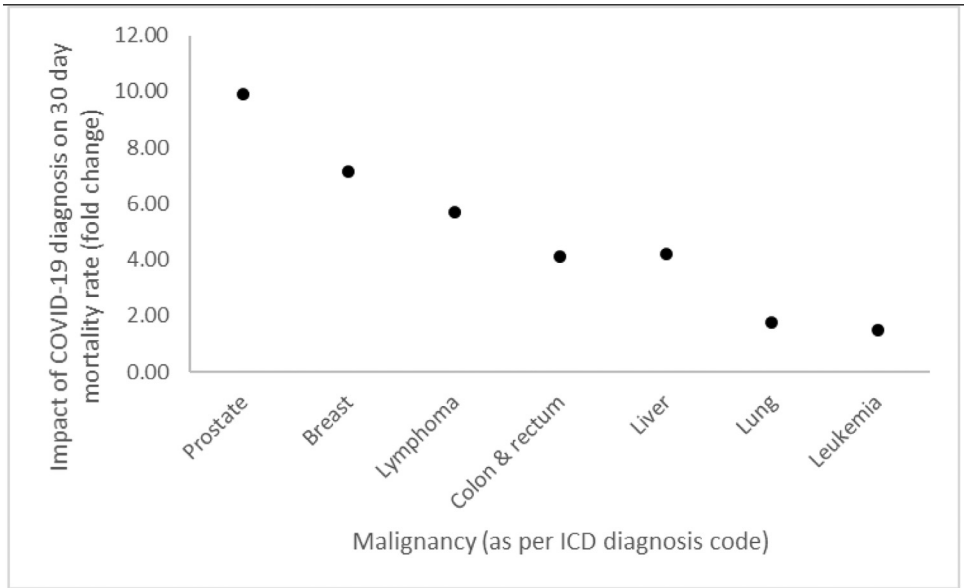


Fig. 1. Relative Increase in 30-Day Mortality Rate for various malignancies in patients who test positive for COVID-19 vs those who test negative for COVID-19. Plot displays only those malignancies for which *N*>=10 for 30-day mortality.

prostate and bladder cancer patients who test negative for COVID-19 in this multi-ethnic cohort from NYC (Fig. 1 and Table 1); where those who test positive for COVID-19 had a 9.9x higher and 26.8x higher 30-day mortality rate respectively, than patients who test negative for COVID-19. The bladder cancer cohort was small relative to the prostate cancer cohort attending our healthcare system, and in turn the absolute number of deaths was smaller (see Table 1). Breast and pancreatic cancers by comparison had 30-day mortality rates which were 7.2x and 5.6x higher respectively in those patients who tested positive for COVID-19 than those who tested negative in this cohort (see Table 1 and Fig. 1).

Our finding that prostate cancer patients who test positive for COVID-19 have a 9.9x higher 30-day mortality rate than patients who test negative, is striking. This finding provides evidence contrary to the National Comprehensive Cancer Network guideline which states that "...prioritization among cancer patients should favor those with active cancer on treatment... except those receiving only hormonal therapies."[4] Our data suggests that prostate and breast cancer (both groups in hormonal treatments are commonly used) have amongst the fold differences in 30-day mortality in those who test negative for COVID-19 and those who test positive (see Fig. 1 and Table 1).

One of the guiding principles of patient care is to protect those who are vulnerable. There is limited vaccination data for cancer patients receiving active therapy at this time. However, it is understood that various oncologic interventions and treatments can lead to an immunocompromised state. For example, the effects of anesthesia and surgery on immune response and complications associated with

Table 1
COVID-19 prevalence and 30-day mortality for patients with a positive COVID-19 test in this cohort; for the 10 most commonly diagnosed malignancies in the USA

| | All patients in cohort | | | All patients in cohort who Test Positive for COVID-19 | | |
|---|---|---|---|---|---|---|
| | N | 30-day mortality (*N*) | % 30 day mortality | ALL | 30-day mortality (N) | % 30 day mortality |
| Bladder | 139 | 2 | 1.4% | 5 | 1 | 20.0% |
| Prostate | 700 | 10 | 1.4% | 29 | 3 | 10.3% |
| Breast | 1,877 | 36 | 1.9% | 51 | 6 | 11.8% |
| Pancreas | 116 | 6 | 5.2% | 4 | 1 | 25.0% |
| Lymphoma | 537 | 21 | 3.9% | 28 | 5 | 17.9% |
| Colon & rectum | 541 | 18 | 6.1% | 16 | 2 | 16.7% |
| Liver | 425 | 45 | 10.6% | 15 | 6 | 40.0% |
| Endometrium | 200 | 6 | 3.0% | 9 | 1 | 11.1% |
| Lung | 408 | 45 | 11.0% | 16 | 3 | 18.8% |
| Leukemia | 281 | 22 | 7.8% | 27 | 3 | 11.1% |

Table 2
Vulnerability of GU Cancer patients vs. Non-GU cancer patients in this cohort of patients

| | [ALL] $N = 4,926$ | GU cancer $N = 855$ | Non-GU cancer $N = 4,071$ | $P$ value |
|---|---|---|---|---|
| Age group: | | | | <0.001 |
| <35 | 293 (5.9%) | 4 (0.47%) | 289 (7.1%) | |
| 35-45 | 550 (11.2%) | 18 (2.11%) | 532 (13.1%) | |
| 45-55 | 1,330 (27.0%) | 142 (16.6%) | 1,188 (29.2%) | |
| 55-65 | 2,753 (55.9%) | 691 (80.8%) | 2,062 (50.7%) | |
| Sex: | | | | <0.001 |
| Male | 2,006 (40.7%) | 819 (95.8%) | 1,187 (29.2%) | |
| COPD: | 149 (3.02%) | 21 (2.46%) | 128 (3.14%) | 0.338 |
| Hypertension: | 1,191 (24.2%) | 266 (31.1%) | 925 (22.7%) | <0.001 |
| Obesity: | 434 (8.81%) | 45 (5.26%) | 389 (9.56%) | <0.001 |
| Diabetes: | 604 (12.3%) | 96 (11.2%) | 508 (12.5%) | 0.339 |
| Chronic kidney disease: | 180 (3.65%) | 49 (5.73%) | 131 (3.22%) | 0.001 |
| HIV: | 212 (4.30%) | 49 (5.73%) | 163 (4.00%) | 0.03 |
| Coronary artery disease: | 246 (4.99%) | 74 (8.65%) | 172 (4.23%) | <0.001 |
| Atrial fibrillation: | 113 (2.29%) | 27 (3.16%) | 86 (2.11%) | 0.084 |
| Heart failure: | 113 (2.29%) | 24 (2.81%) | 89 (2.19%) | 0.329 |
| Chronic viral hepatitis: | 135 (2.74%) | 14 (1.64%) | 121 (2.97%) | 0.04 |
| Alcoholic or nonalcoholic liver disease: | 252 (5.12%) | 17 (1.99%) | 235 (5.77%) | <0.001 |

vaccination during the perioperative period are still poorly understood [5]. In the era prior to COVID-19, ACIP, a Center for Disease Control advisory committee on immunization practices recommended that vaccines be administered preoperatively, or as soon as a patient's condition stabilizes post operatively [6]. Urologists are very familiar with and regularly rely upon intact immunological responses following surgery; when administering Bacillus Calmette-Guérin (BCG) following a transurethral resection of a bladder tumor; where the benefits of intravesical BCG is an effect of the immunological reaction to the vaccine administered. In the pediatric setting where vaccination occurs more frequently, a common practice is to delay elective surgeries for between 2 to 7 days after administering an inactive vaccine, in situations where significant delay in surgery or vaccination would be harmful [5,7,8] By comparison, radiotherapy, chemotherapy and other causes of hematopoietic cell stress, suppress T cell numbers and function and delayed or defective recovery of the pool of T-cells leads to poor vaccine responses [9].

The optimal timing of vaccination as it relates to Androgen deprivation therapy (ADT) remains poorly understood. Pre-clinical evidence suggests that anti-androgens target the transcriptional regulation of host entry factors for SARS-CoV-2 and their use could prevent infection, and clinical trials addressing this question are ongoing [10]. ADT leads to an increase in the numbers of circulating naïve T-cells and Th1-biased phenotype shortly after starting ADT [11]. However, over time, some androgen receptor antagonists interfere with T-cell priming which could affect the efficacy of COVID vaccination in such subjects receiving ADT [11,12]. A phase 2 clinical trial examining vaccination with a pox-virus based Prostate specific antigen vaccine showed improved survival in those patients who received vaccination before ADT, as compared to those who received vaccination after ADT [13].

The biological mechanisms underpinning this observation are of great importance; and multiple hypothesis abound. Elucidating the reasons and the impact of disease stage and prior treatments are beyond the scope of the current dataset, and remain important topics for further study. However, pragmatism prevailing, mass vaccination will not necessitate such stratification of at risk groups by stage and treatment; rather all such patients will be offered vaccination.

Some further insights into patient vulnerability are available from this dataset though (see Table 2). Those with a diagnosis of a genitourinary (GU) cancer were more likely to be older, male, have co-morbidities such as hypertension, chronic kidney disease, HIV, coronary artery disease and be less likely to be obese, have a chronic viral hepatitis or have liver disease than those with non-GU cancers in this cohort.

The magnitude of the increases in 30-day mortality identified by this work is such that we feel comparison with other patient cohorts is necessary; particularly given the scarcity of data on the effects of vaccination on cancer patients. We believe this communication offers an important data point to discuss with patients so that they may be more fully informed, that guidelines from expert groups may have the necessary data to inform their decisions, and

that those involved in patient care may advocate on behalf of such vulnerable groups, so that they maybe prioritized for access to vaccines, to reduce their risk of death.

The sparsity of data surrounding COVID-19 vaccination and cancer is not surprising given that cancer biology is heterogeneous, cancer prevalence is in the order of 4% and SARS-CoV-2 is a continuously evolving infectious disease, with variable penetrance in different populations. Large clinical trials for COVID-19 vaccination have also highlighted the difficulty in answering such questions, even regarding the primary endpoint of these Phase 3 studies in older adults, where the efficacy of vaccines in patients older than 55 years, a group that compromises approximately 27% of the population in developed nations was deemed to have "not yet enough results" [14] An expedient answer to questions surrounding COVID-19 vaccination and various cancers is only likely to come from larger collaborations and meta-analyses of relevant populations.

Similarly this finding brings to the fore concerns surround the timing of vaccination and therapies for GU cancer patients; where a balance between benefits and harms must be found. There will undoubtedly be debate around avoiding hematopoietic stresses from chemotherapy and radiotherapy vs. anesthesia and surgery: where if the risk of COVID-19 morbidity and mortality outweighs those of the malignancy, the former should be avoided for the 3 to 4 weeks required for COVID-19 vaccination to occur, while there is compelling evidence that the latter has no impact on vaccination efficacy.

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