Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.
eMethods

Data Sources

This study was primarily based on data in the VA Corporate Data Warehouse (CDW), which collates electronic health record (EHR) information from Veterans treated at VA facilities nationwide. Information on SARS-CoV-2 vaccination and documented infection was obtained from the VA COVID-19 Shared Data Resource.

Variable Definitions

VA user was defined as patients with at least 1 ICD-10 code in each of the three years prior to 12/15/2020.

Documented SARS-CoV-2 infection and the date of first infection were based on structured information in the VA COVID-19 Shared Data Resource. Since all patients with infection prior to the beginning of study were excluded, only the date of first infection was of relevance.

Date of SARS-CoV-2 vaccination and vaccine type (Moderna, Pfizer, Janssen, or Unknown) were based on structured information in the VA COVID-19 Shared Data Resource.

Age was defined as the age on December 15, 2020 based on birth date recorded in the CDW.

Gender was based on structured data recorded in the CDW.

Race/ethnicity was based on self-reported race and ethnicity data as recorded in the CDW, with categories Hispanic (ethnicity “Hispanic or Latino”), Non-Hispanic White (ethnicity not “Hispanic or Latino”, race “White”), Non-Hispanic Black (ethnicity not “Hispanic or Latino”, race “Black or African American”), Other or Unknown (all others).

Rurality was defined based on a classification of each patient’s home address as recorded in the CDW. The CDW distinguishes “rural” and “highly rural” categories, which we combined to reduce the number of categories for exact matching.

Geographical region was defined based on the VA facility each patient received cancer treatment in. Regions were defined using the following mapping from the CDW: Continental (Arkansas, Colorado, Louisiana, Mississippi, Montana, Oklahoma, Texas, Utah, Wyoming); Midwest (Illinois, Indiana, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, Wisconsin); North Atlantic (Connecticut, Delaware, District Of Columbia, Maine, Maryland, Massachusetts, New Hampshire, New Jersey, New York, North Carolina, Pennsylvania, Rhode Island, Vermont, Virginia, West Virginia); Pacific (Alaska, Arizona, California, Hawaii, Idaho, Nevada, New Mexico, Oregon, Washington); Southeast (Alabama, Florida, Georgia, Kentucky, Puerto Rico, South Carolina, Tennessee).

The Charlson Comorbidity Index was calculated based on ICD-10 codes in the year prior to December 15, 2020 using the R comorbidity package.

Treatment timing prior to vaccination (if in the vaccinated cohort) or prior to entry date (if in the unvaccinated cohort) was defined based on pharmacy records in the CDW. Four treatment timing categories were defined: (1) Distant treatment; (2) Recent treatment; (3) Current treatment; (4) Treatment after vaccine. Regarding category (1), note that all patients in the study population received cancer-directed therapy on or after August 15, 2010, but this treatment ceased at least six months prior to the date of vaccination or matching entry date. The patients in category (2) had received their last dose of systemic therapy sometime in the period between three and six months prior to vaccination or matching. Patients in category (2) therefore represent a group that received systemic therapy more recently than the patients in category (1) but are no longer on active therapy at the time of vaccination or matching. Regarding category (3), patients were included if a patient received any systemic therapy within three months prior to vaccination or matching. Patients in category (4) received their first dose of systemic therapy after vaccination or matching but prior to study end date of May 4, 2021.

Treatment type was defined for the patients on current therapy at the time of vaccination (if in the vaccinated cohort) or entry date (if in the unvaccinated cohort). Patients were considered to be on current therapy if a patient received any systemic therapy within three months prior to vaccination or matching. All agents administered within the three month window were considered. Individual drugs were classified as
chemotherapy, immunotherapy, targeted therapy, or endocrine therapy using the mapping in eTable 13. If all the agents given to a patient in a three month period were the same type, that patient was assigned to that treatment type category. Regimens consisting of combinations of treatment types were prioritized in the following order: if any chemotherapy agent was administered in combination with another agent (e.g., chemoimmunotherapy), it was considered a chemotherapy-containing regimen. If immunotherapy agent was administered in combination with another agent that was not chemotherapy, it was considered an immunotherapy regimen. Targeted regimens contain targeted agents, but not chemotherapy or immunotherapy. Endocrine regimens were composed exclusively of endocrine therapy agents. All routes of cancer treatment were included, including oral, intravenous, intramuscular and subcutaneous.

Cancer type was determined from malignancy ICD-10 codes by the following algorithm for each patient (eFigure 6). For each patient, the most recent malignancy ICD-10 code(s) associated with a cancer-directed systemic treatment was identified. If there was a unique ICD-10 associated with that encounter, then the cancer type associated with that code was used. However, if there were multiple ICD-10 codes, and the ICD-10 codes were associated with different cancer types, ties were broken with the following stepwise algorithm. If one of the ICD-10 codes were for malignancy of brain, bone, or lymph node, the primary site was assumed to be the remaining code(s) since brain, bone, and lymph nodes are common metastatic sites. For example, if a patient was identified by both a colorectal malignancy-associated ICD-10 code and a bone malignancy-associated ICD-10 code, the colorectal malignancy was assumed to be the primary site. If there were still a tie, the primary malignancy was decided by majority vote of the malignancy ICD-10 codes over the past 6 months prior to the most recent treatment-associated malignancy ICD-10 code. Remaining ties were broken via cancer type and treatment matching using a cancer type-treatment matrix. For example, if a patient received antiandrogen therapy and had a prostate malignancy-associated ICD-10 code, that patient was assumed to have prostate cancer. If the patient received a therapy associated with more than one cancer type, the patient was assumed to have the more common cancer type based on SEER national cancer prevalence statistics. If a patient did not receive any of the typical treatments associated with their malignancy ICD-10 code, that patient was assigned to the other malignancy ICD-10 code. Remaining ties were classified as unknown.

Cancer category was determined using the cancer type as defined above. Hematologic malignancies were defined as essential thrombocytopenia, leukemia/myelodysplastic syndrome (MDS)/myelofibrosis (MF), multiple myeloma, mastocytoma, and polycythemia vera. Solid malignancies were defined as brain, breast, colorectal, connective and soft tissue, squamous cell carcinoma of the head and neck (SCCHN)/cutaneous SCC (CSCC)/skin, esophagus/gastric, gynecologic malignancies (Gyn), hepatocellular carcinoma (HCC), lung, lymphoma, melanoma, neuroendocrine, anal/biliary/GIST/pancreas/small intestine (other GI), prostate, renal cell carcinoma (RCC), and urothelial cancer. ICD codes classified as “other/unknown” was split among the solid and hematologic malignancies based on the specific ICD code.

Total death was defined as any death recorded in the CDW occurring on the day of or in the four weeks following SARS-CoV-2 infection or a censoring event. Example: Patient 1, a vaccinated patient was vaccinated with their first dose on December 15th, 2020, infected with COVID-19 on January 1st 2021, and died on January 21st 2021. Patient 2, patient 1’s unvaccinated matched control, was vaccinated on December 20th 2020. Given that patient 2 was vaccinated on December 20th 2020, both Patient 1 and Patient 2 would be censored on that day (Patient 2 censored as control and re-enters study as vaccinated). Although Patient 1 did indeed experience a death, this patient would not be counted in the total death because January 21st 2021 is more than 28 days past Patient 1’s censored date. COVID-19 related death was defined as any death recorded in the CDW within four weeks after documentation of SARS-CoV-2 infection, excluding patients who were censored from the study population prior to infection. In the example above, although Patient 1’s death was within 28 days of a SARS-CoV-2 infection, the death would not be counted as a COVID-19 related death because Patient 1 was censored. On the other hand, if Patient 2 (Patient 1’s matched control) was vaccinated on January 5th 2021, then Patient 1’s death would be counted as a COVID-19 related death.

Matching Algorithm

Vaccinated patients were matched with unvaccinated patients on predictors of SARS-CoV-2 infection and vaccination. These variables included age, race/ethnicity, VA facility, rurality of home address, cancer type, and treatment type/timing. Age was matched with minimum distance matching and all other variables were matched with exact matching. So, a non-Hispanic white veteran with a rural home address and prostate cancer on endocrine therapy at the Boston VA will only be matched with another non-Hispanic white veteran with a rural home address and prostate cancer on endocrine therapy at the Boston VA. If more than one control patient matches the vaccinated patient, the control closest in age to the vaccinated patient is chosen. If there are no
controls available that exactly match the vaccinated patient, the unmatched vaccinated patient is discarded. Matching on additional variables (gender, comorbidity index, BMI) was not included, as their inclusion decreased sample size but did not improve matching quality.

During this matching process, patients who received vaccination after the matching date were eligible to be matched as an unvaccinated control. Excluding these patients would create a bias, since people who are symptomatic from early infection may avoid getting vaccinated and thereby bias the unvaccinated cohort towards a higher early COVID infection rate. If an unvaccinated control was subsequently vaccinated, follow-up for both the control and corresponding case was censored on the date of the control’s vaccination. After the control’s vaccination, the control would cross over to the vaccinated cohort and would be matched to a new unvaccinated control.

To assess for residual confounding, and thereby evaluate matching quality, as in the prior study⁵ we examined the cumulative incidence of infection in the first 14 days of follow-up for both vaccinated and controls. This provides a “negative control” in regard to confounding. During this initial period, vaccinated and unvaccinated groups are expected to exhibit similar rates of infection if exchangeability between the groups holds, i.e., if there is no confounding.

**Statistical Analysis**

For first-dose effectiveness analyses, the index date for each vaccinated patient was set to their vaccination date, and the index date for their matched control was set to this same date. For analyses evaluating effectiveness after the second dose, date of second vaccination was used as the index date for each vaccinated patient and their matched control. For second-dose analyses, matched pairs where (1) the vaccinated patient did not have a second dose, (2) either member was infected before the second-dose index date, (3) the control died before the second-dose index date, or (4) the control was vaccinated before the second-dose index date were excluded.

Curves of cumulative incidence of infection for vaccinated patients and unvaccinated controls were generated using a Fine-Gray adjusted proportional subdistribution hazards model accounting for the competing risk of death⁶, and adjusting for all variables used in matching except for VA facility and cancer type, as these variables introduced too many levels. The Fine-Gray subdistribution hazard function was used to measure risk. These measures were evaluated over pre-defined intervals analogous to those used in the original Pfizer BNT162b2 clinical trial⁷: day 0 after the first dose of vaccine to end of study, day 0 after the first dose to date of second dose, day 0 to day 13 after the second dose and day 14 after the second dose to end of follow-up. As protective immunity is expected to be minimal in the first two weeks after vaccination, a secondary analysis was performed considering the interval day 14 after the first dose to the date of the second dose. Confidence intervals for the effectiveness and cumulative incidence curves were calculated using percentile bootstrapping. Analyses were performed using R version 4.0.2.
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eFigure 1. Flow Diagram of Cohort Selection and Matching.

Veterans with a solid and/or hematologic malignancy who received systemic therapy at the VA between August 15, 2010 and May 4, 2021 alive and without a documented SARS-CoV-2 positive result at beginning of vaccination on December 15, 2020 (n=200,287)

Excluded
- Not meeting definition of a VA user (having at least 1 ICD code in each of the 3 years prior to 2020) (n=11,716)
- Vaccinated with Janssen (n=4,086)

Vaccinated prior to May 5, 2021 (n=113,796)

29,152 (26%) were matched and included in the vaccinated cohort

Not vaccinated prior to May 5, 2021 (n=70,689)

29,152 were matched and included in the unvaccinated cohort
eFigure 2. Cumulative Incidence and Difference in SARS-COV-2 Infection between Matched Vaccinated and Unvaccinated Cohorts Stratified by Vaccination Type.

Cumulative incidence curves of SARS-COV-2 infection by vaccination type shown using time zero as the date of the first dose of vaccination. The difference in cumulative incidence is shown below. Confidence intervals were calculated by bootstrapping. The number at risk and cumulative number of events are also shown. A) Patients vaccinated with at least one dose of Pfizer BNT162b2 vaccine. B) Patients vaccinated with at least one dose of Moderna mRNA-1273 vaccine.
eFigure 3. Cumulative Incidence and Difference in SARS-COV-2 Infection between Matched Vaccinated and Unvaccinated Cohorts Stratified by Cancer Category.

Cumulative incidence curves of SARS-COV-2 infection by subgroups by broad cancer category defined in eMethods. Time zero is the date of the first dose of vaccination. The difference in cumulative incidence is shown below. Confidence intervals were calculated by bootstrapping. The number at risk and cumulative number of events are also shown. A) Solid malignancies as defined by cancer type in eMethods. B) Hematologic malignancies as defined by cancer type in eMethods.
eFigure 4. Cumulative Incidence and Difference in SARS-COV-2 Infection between Matched Vaccinated and Unvaccinated Cohorts Stratified by Treatment Timing.

Cumulative incidence curves of SARS-COV-2 infection by subgroups by timing of therapy defined in eMethods. Time zero is the date of the first dose of vaccination. The difference in cumulative incidence is shown below. Confidence intervals were calculated by bootstrapping. The number at risk and cumulative number of events are also shown. A) Distant treatment, defined as systemic therapy received in the ten years prior to vaccination (if in the vaccinated cohort) or prior to entry date (if in the unvaccinated cohort) but not received in the six months prior to vaccination (if in the vaccinated cohort) or prior to entry date (if in the unvaccinated cohort). B) Recent treatment, defined as systemic therapy received in the three to six months prior to vaccination (if in the vaccinated cohort) or prior to entry date (if in the unvaccinated cohort) but not received in the three months prior to vaccination (if in the vaccinated cohort) or prior to entry date (if in the unvaccinated cohort). C) Current treatment, defined as systemic therapy received within the three months prior to vaccination (if in the vaccinated cohort) or prior to entry date (if in the unvaccinated cohort). D) Treatment received after vaccination, defined as first dose of systemic therapy received anytime after vaccination and matching and prior to study end date on May 4, 2021.
**eFigure 5. Cumulative Incidence and Difference in SARS-COV-2 Infection between Matched Vaccinated and Unvaccinated Cohorts Stratified by Additional Treatment Types.**

Cumulative incidence curves of SARS-COV-2 infection by current treatment type as defined in eMethods. shown using time zero as the date of the first dose of vaccination. The difference in cumulative incidence is shown below. Confidence intervals were calculated by bootstrapping. The number at risk and cumulative number of events are also shown. All patients in all panels on are on current treatment, defined as systemic therapy received within the three months prior to vaccination (if in the vaccinated cohort) or prior to entry date (if in the unvaccinated cohort). A) Patients on a targeted therapy at time of vaccination. B) Patients on an immunotherapy regimen.
eFigure 6. Cancer Type Determination Algorithm.

Obtain most recent malignancy ICD code(s) associated with cancer-directed therapy

- Most recent ICD code(s) associated with one cancer type?
  - Yes: Cancer type determined by most recent malignancy ICD code
  - No: Remove "bone", "brain", and "lymph node" ICD codes

Is there one cancer type?

- Yes: Cancer type determined by remaining type
- No: Obtain all malignancy ICD code(s) associated with cancer-directed therapy in prior six months

Is there one cancer type in the majority of ICD codes?

- Yes: Cancer type determined by majority
- No: Match last cancer-directed therapy with specific therapies used for common cancer types

Did the patient receive therapy consistent with one cancer type?

- Yes: Cancer type determined by treatment association
- No: Remove ICD codes associated with cancer types included prior cancer-treatment matching

Is there only one cancer type left?

- Yes: Cancer type determined by remaining type
- No: Remaining ties are unknown

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| Baseline Covariates                      | Overall (N=184485) | Unvaccinated (N=70689) | Vaccinated (N=113796) |
|-----------------------------------------|--------------------|------------------------|-----------------------|
| Age (median [IQR])                      | 73.13 [67.46, 78.12] | 72.48 [65.35, 77.79] | 73.44 [68.62, 78.26] |
| Age (%)                                 |                    |                        |                       |
| <50                                     | 6626 (3.6)         | 4289 (6.1)             | 2337 (2.1)            |
| 50-59                                   | 12707 (6.9)        | 6348 (9.0)             | 6359 (5.6)            |
| 60-69                                   | 40595 (22.0)       | 15921 (22.5)           | 24674 (21.7)          |
| 70-79                                   | 87822 (47.6)       | 30115 (42.6)           | 57707 (50.7)          |
| >=80                                    | 36735 (19.9)       | 14016 (19.8)           | 22719 (20.0)          |
| Gender = M (%)                          | 169645 (92.0)      | 63768 (90.2)           | 105877 (93.0)         |
| Race/Ethnicity (%)                      |                    |                        |                       |
| Non-Hispanic White                      | 126934 (68.8)      | 49371 (69.8)           | 77563 (68.2)          |
| Hispanic                                | 8811 (4.8)         | 2975 (4.2)             | 5836 (5.1)            |
| Non-Hispanic Black                      | 36671 (19.9)       | 13326 (18.9)           | 23345 (20.5)          |
| Other or Unk                            | 12069 (6.5)        | 5017 (7.1)             | 7052 (6.2)            |
| Rurality (%)                            |                    |                        |                       |
| Rural                                   | 62643 (34.0)       | 27900 (39.5)           | 34743 (30.5)          |
| Urban                                   | 120163 (65.1)      | 42157 (59.6)           | 78006 (68.5)          |
| Unknown                                 | 1679 (0.9)         | 632 (0.9)              | 1047 (0.9)            |
| Region (%)                              |                    |                        |                       |
| North Atlantic                          | 40964 (22.2)       | 14120 (20.0)           | 26844 (23.6)          |
| Southeast                               | 42223 (22.9)       | 17258 (24.4)           | 24965 (21.9)          |
| Midwest                                 | 40268 (21.8)       | 14350 (20.3)           | 25918 (22.8)          |
| Continental                             | 29023 (15.7)       | 13130 (18.6)           | 15893 (14.0)          |
| Pacific                                 | 32007 (17.3)       | 11831 (16.7)           | 20176 (17.7)          |
| Charlson Score (%)                      |                    |                        |                       |
| 0-2                                     | 122936 (66.6)      | 50430 (71.3)           | 72506 (63.7)          |
| 3-4                                     | 44988 (24.4)       | 14910 (21.1)           | 30078 (26.4)          |
| 5+                                      | 16561 (9.0)        | 5349 (7.6)             | 11212 (9.9)           |
| Vaccine Type (%)                        |                    |                        |                       |
| Moderna                                 | -                   | -                      | 62376 (54.8)          |
| Pfizer                                  | -                   | -                      | 51389 (45.2)          |
| Unknown                                 | -                   | -                      | 31 (0.0)              |
| Cancer type (%)                         |                    |                        |                       |
| Prostate                                | 66751 (36.2)       | 25198 (35.6)           | 41553 (36.5)          |
| SCCHN/CSCC/skin                        | 29937 (16.2)       | 11343 (16)             | 18594 (16.3)          |
| Lung                                    | 10090 (5.5)        | 3418 (4.8)             | 6672 (5.9)            |
| Leukemia/MDS/MF                         | 9373 (5.1)         | 3727 (5.3)             | 5646 (5)              |
| Colorectal                              | 9307 (5)           | 3698 (5.2)             | 5609 (4.9)            |
| Lymphoma                                | 8676 (4.7)         | 3195 (4.5)             | 5481 (4.8)            |
| Breast                                  | 8291 (4.5)         | 3598 (5.1)             | 4693 (4.1)            |
| Multiple myeloma                        | 6322 (3.4)         | 2241 (3.2)             | 4081 (3.6)            |
| Urothelial                              | 6269 (3.4)         | 2051 (2.9)             | 4218 (3.7)            |
| HCC                                     | 3377 (1.8)         | 1218 (1.7)             | 2159 (1.9)            |
| Esophagus/gastric                       | 2807 (1.5)         | 993 (1.4)              | 1814 (1.6)            |
| Cancer Type                  | Overall | Vaccinated | Unvaccinated |
|-----------------------------|---------|------------|--------------|
| Gyn                         | 2560 (1.4) | 1547 (2.2) | 1013 (0.9)   |
| Melanoma                    | 2496 (1.4) | 950 (1.3)  | 1546 (1.4)   |
| Essential thrombocythemia   | 2333 (1.3) | 971 (1.4)  | 1362 (1.2)   |
| Neuroendocrine              | 2019 (1.1) | 754 (1.1)  | 1265 (1.1)   |
| RCC                         | 1966 (1.1) | 748 (1.1)  | 1218 (1.1)   |
| Polycythemia vera           | 1936 (1)  | 811 (1.1)  | 1125 (1)     |
| Other GI                    | 1453 (0.8) | 559 (0.8)  | 894 (0.8)    |
| Brain                       | 834 (0.5)  | 430 (0.6)  | 404 (0.4)    |
| Connective and soft tissue  | 419 (0.2)  | 181 (0.3)  | 238 (0.2)    |
| Other/unknown/lesser        | 7269 (3.9) | 3058 (4.3) | 4211 (3.7)   |

*Defined based on patient home address.*

*Defined based on VA station at which patient received cancer care.*

*Vaccination type only shown for overall and vaccinated cohort, even though patients in the unvaccinated cohort can be subsequently vaccinated after matching, as those vaccinations are already tabulated in the vaccinated cohort.*

*Cancer type determined by ICD code(s) associated with cancer-directed systemic treatment as detailed in eMethods. Other/unknown/lesser includes cancer of unknown primary, cancer types not included in a predefined category, and cancer types represented by 50 patients or less. CSCC = cutaneous squamous cell carcinoma; Gyn = gynecologic malignancy; HCC = hepatocellular carcinoma; MF = myelofibrosis; MDS = myelodysplastic syndrome; Other GI = anal/biliary/GIST/pancreas/small intestine; RCC = renal cell carcinoma; SCCHN = squamous cell head and neck cancer.*

*Systemic therapy not included in this table as it was a rolling variable defined in relation to vaccination/matching time.*
eTable 2. Demographic and Clinical Characteristics of Vaccinated and Unvaccinated VA Cancer Patients in the Matched Cohort.

| Baseline Covariates | Overall (N=58304) | Unvaccinated (N=29152) | Vaccinated (N=29152) |
|---------------------|-------------------|------------------------|----------------------|
| Age (median [IQR])  | 73.73 [69.43, 78.62] | 73.31 [68.59, 77.87] | 74.14 [70.21, 79.32] |
| Age (%)             |                   |                        |                      |
| <50                 | 943 (1.6)         | 612 (2.1)              | 331 (1.1)            |
| 50-59               | 2830 (4.9)        | 1652 (5.7)             | 1178 (4.0)           |
| 60-69               | 11828 (20.3)      | 6314 (21.7)            | 5514 (18.9)          |
| 70-79               | 30366 (52.1)      | 14978 (51.4)           | 15388 (52.8)         |
| >=80                | 12337 (21.2)      | 5596 (19.2)            | 6741 (23.1)          |
| Gender, Male (%)    |                   |                        |                      |
| Race/ethnicity      |                   |                        |                      |
| Non-Hispanic White  | 41402 (71.0)      | 20701 (71.0)           | 20701 (71.0)         |
| Hispanic            | 2364 (4.1)        | 1182 (4.1)             | 1182 (4.1)           |
| Non-Hispanic Black  | 12334 (21.2)      | 6167 (21.2)            | 6167 (21.2)          |
| Other or Unk        | 2204 (3.8)        | 1102 (3.8)             | 1102 (3.8)           |
| Ruralitya (%)       |                   |                        |                      |
| Rural               | 17740 (30.4)      | 8870 (30.4)            | 8870 (30.4)          |
| Urban               | 40322 (69.2)      | 20161 (69.2)           | 20161 (69.2)         |
| Unknown             | 242 (0.4)         | 121 (0.4)              | 121 (0.4)            |
| Regionb (%)         |                   |                        |                      |
| North Atlantic      | 13234 (22.7)      | 6617 (22.7)            | 6617 (22.7)          |
| Southeast           | 13146 (22.5)      | 6573 (22.5)            | 6573 (22.5)          |
| Midwest             | 14414 (24.7)      | 7207 (24.7)            | 7207 (24.7)          |
| Continental         | 7700 (13.2)       | 3850 (13.2)            | 3850 (13.2)          |
| Pacific             | 9810 (16.8)       | 4905 (16.8)            | 4905 (16.8)          |
| Charlson Score (%)  | 0-2               | 34864 (59.8)           | 18063 (62.0)         |
|                    | 3-4               | 17082 (29.3)           | 8208 (28.2)          |
|                    | 5+                | 6358 (10.9)            | 2881 (9.9)           |
| Vaccine Typec (%)   |                   |                        |                      |
| Moderna             | -                 | -                      | 15716 (53.9)         |
| Pfizer              | -                 | -                      | 13426 (46.1)         |
| Unknown             | -                 | -                      | 10 (0.0)             |
| Systemic therapy receivedd |                 |                        |                      |
| Distant treatment (>6 Months) | 5040 (8.6) | 2520 (8.6) | 2520 (8.6) |
| Recent treatment (3-6 Months) | 15260 (26.2) | 7630 (26.2) | 7630 (26.2) |
| Current chemotherapy-Containing (<3 Months) | 8452 (14.5) | 4226 (14.5) | 4226 (14.5) |
| Current immunotherapy (<3 Months) | 1958 (3.4) | 979 (3.4) | 979 (3.4) |
| Current targeted (<3 Months) | 8584 (14.7) | 4292 (14.7) | 4292 (14.7) |

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| Current endocrine (<3 Months) | 15514 (26.6) | 7757 (26.6) | 7757 (26.6) |
|-------------------------------|--------------|-------------|-------------|
| Treatment after vaccine      | 3496 (6.0)   | 1748 (6.0)  | 1748 (6.0)  |
| Cancer type<sup>c</sup> (%)  |              |             |             |
| Prostate                      | 27848 (47.8) | 13924 (47.8)| 13924 (47.8)|
| SCCHN/SCCC/skin               | 5310 (9.1)   | 2655 (9.1)  | 2655 (9.1)  |
| Leukemia/MDS/MF               | 4986 (8.6)   | 2493 (8.6)  | 2493 (8.6)  |
| Lung                          | 3692 (6.3)   | 1846 (6.3)  | 1846 (6.3)  |
| Multiple myeloma              | 3212 (5.5)   | 1606 (5.5)  | 1606 (5.5)  |
| Breast                        | 2358 (4)     | 1179 (4)    | 1179 (4)    |
| Urothelial                    | 1756 (3)     | 878 (3)     | 878 (3)     |
| Lymphoma                      | 1504 (2.6)   | 752 (2.6)   | 752 (2.6)   |
| Colorectal                    | 1466 (2.5)   | 733 (2.5)   | 733 (2.5)   |
| Essential thrombocytemia      | 904 (1.6)    | 452 (1.6)   | 452 (1.6)   |
| HCC                           | 746 (1.3)    | 373 (1.3)   | 373 (1.3)   |
| Polycythemia vera             | 622 (1.1)    | 311 (1.1)   | 311 (1.1)   |
| Esophagus/gastric             | 510 (0.9)    | 255 (0.9)   | 255 (0.9)   |
| Melanoma                      | 470 (0.8)    | 235 (0.8)   | 235 (0.8)   |
| RCC                           | 450 (0.8)    | 225 (0.8)   | 225 (0.8)   |
| Neuroendocrine                | 420 (0.7)    | 210 (0.7)   | 210 (0.7)   |
| Other GI                      | 316 (0.5)    | 158 (0.5)   | 158 (0.5)   |
| Gyn                           | 102 (0.2)    | 51 (0.2)    | 51 (0.2)    |
| Other/unknown/lesser          | 1632 (2.8)   | 816 (2.8)   | 816 (2.8)   |

<sup>a</sup> Defined based on patient home address.
<sup>b</sup> Defined based on VA station at which patient received cancer care.
<sup>c</sup> Vaccination type only shown for vaccinated cohort, even though patients in the unvaccinated cohort can be subsequently vaccinated after matching, as those vaccinations are already tabulated in the vaccinated cohort.
<sup>d</sup> Systemic therapy received relative to vaccination (if in the vaccinated cohort) or entry date (if in the unvaccinated cohort) with timing determined by the last dose of systemic therapy received. Current treatment, defined as systemic therapy received within three months prior to vaccination, was further subdivided into different treatment types as detailed in eMethods.
<sup>e</sup> Cancer type determined by ICD code(s) associated with cancer-directed systemic treatment as detailed in eMethods. Other/unknown/lesser includes cancer of unknown primary, cancer types not included in a predefined category, and cancer types represented by 50 patients or less. CSCC = cutaneous squamous cell carcinoma; Gyn = gynecologic malignancy; HCC = hepatocellular carcinoma; MF = myelofibrosis; MDS = myelodysplastic syndrome; Other GI = anal/biliary/GIST/pancreas/small intestine; SCCHN = squamous cell head and neck cancer; RCC = renal cell carcinoma.
**eTable 3. Estimated Vaccine Effectiveness against SARS-COV-2 Infection with Alternate Time Periods.**

| Group and period | 1-RR (95% CI) |
|------------------|--------------|
| **Overall**      |              |
| 0 days after first dose to end of study | 42 (28 to 53) |
| 0 days after first dose to day of second dose | 41 (24 to 56) |
| 14 days after first dose to day of second dose | 45 (8 to 66) |
| 0 days to 13 days after second dose<sup>a</sup> | 57 (28 to 76) |
| **Solid malignancy** |          |
| 0 days after first dose to end of study | 44 (30 to 56) |
| 0 days after first dose to day of second dose | 38 (15 to 55) |
| 14 days after first dose to day of second dose | 41 (1 to 66) |
| 0 days to 13 days after second dose<sup>a</sup> | 58 (24 to 79) |
| **Hematologic malignancy** |        |
| 0 days after first dose to end of study | 38 (5 to 59) |
| 0 days after first dose to day of second dose | 53 (16 to 77) |
| 14 days after first dose to day of second dose | 59 (-3 to 90) |
| 0 days to 13 days after second dose<sup>a</sup> | 57 (-38 to 92) |
| **Distant treatment** |          |
| 0 days after first dose to end of study | 56 (13 to 82) |
| 0 days after first dose to day of second dose | 37 (-68 to 83) |
| 14 days after first dose to day of second dose | -- <sup>b</sup> |
| 0 days to 13 days after second dose<sup>a</sup> | -- <sup>b</sup> |
| **Recent treatment** |          |
| 0 days after first dose to end of study | 35 (5 to 56) |
| 0 days after first dose to day of second dose | 17 (-50 to 54) |
| 14 days after first dose to day of second dose | 37 (-51 to 77) |
| 0 days to 13 days after second dose<sup>a</sup> | 57 (-6 to 86) |
| **Current treatment** |          |
| 0 days after first dose to end of study | 41 (23 to 55) |
| 0 days after first dose to day of second dose | 46 (22 to 64) |
| 14 days after first dose to day of second dose | 29 (-29 to 62) |
| 0 days to 13 days after second dose<sup>a</sup> | 54 (12 to 80) |
| **Treatment after vaccine** |          |
| 0 days after first dose to end of study | 56 (13 to 80) |
| 0 days after first dose to day of second dose | 66 (15 to 93) |
| 14 days after first dose to day of second dose | -- <sup>b</sup> |
| 0 days to 13 days after second dose<sup>a</sup> | -- <sup>b</sup> |
| **Current chemotherapy-containing** |        |
| 0 days after first dose to end of study | 24 (-27 to 55) |
| 0 days after first dose to day of second dose | 24 (-60 to 69) |
| 14 days after first dose to day of second dose | -71 (-830 to 43) |
| 0 days to 13 days after second dose<sup>a</sup> | -- <sup>b</sup> |
| **Current targeted** |          |
| 0 days after first dose to end of study | 31 (-9 to 58) |
| 0 days after first dose to day of second dose | 50 (-1 to 79) |
| 14 days after first dose to day of second dose | -- <sup>b</sup> |
| Time After First Dose | Effectiveness (95% CI) |
|-----------------------|------------------------|
| 0 days to 13 days after second dose | 61 (-45 to 100) |

**Current endocrine**

| Time After First Dose | Effectiveness (95% CI) |
|-----------------------|------------------------|
| 0 days after first dose to end of study | 57 (38 to 73) |
| 0 days after first dose to day of second dose | 46 (1 to 72) |
| 14 days after first dose to day of second dose | 64 (8 to 93) |
| 0 days to 13 days after second dose | 72 (23 to 95) |

*a Patients who received a second dose of vaccination prior to 14 days after the first dose excluded.

*b Not enough SARS-COV-2 infection events to estimate effectiveness.
eTable 4. Demographic and Clinical Characteristics of Matched Vaccinated and Unvaccinated VA Cancer Patients with Solid Malignancies.

| Baseline Covariates                  | Overall (N=48185) | Unvaccinated\(^a\) (N=24103) | Vaccinated (N=24082) |
|--------------------------------------|-------------------|-------------------------------|---------------------|
| **Age (median [IQR])**               | 73.78 [69.50, 78.84] | 73.37 [68.72, 78.17]         | 74.18 [70.28, 79.54] |
| Age (%)                              |                   |                               |                     |
| <50                                  | 727 ( 1.5)        | 469 ( 1.9)                    | 258 ( 1.1)          |
| 50-59                                | 2220 ( 4.6)       | 1287 ( 5.3)                   | 933 ( 3.9)          |
| 60-69                                | 9799 (20.3)       | 5252 (21.8)                   | 4547 (18.9)         |
| 70-79                                | 24901 (51.7)      | 12286 (51.0)                  | 12615 (52.4)        |
| >=80                                 | 10538 (21.9)      | 4809 (20.0)                   | 5729 (23.8)         |
| **Gender = M (%)**                   |                   |                               |                     |
|                                      | 45246 (93.9)      | 22555 (93.6)                  | 22691 (94.2)        |
| **Race/Ethnicity (%)**               |                   |                               |                     |
| Non-Hispanic White                   | 33728 (70.0)      | 16877 (70.0)                  | 16851 (70.0)        |
| Hispanic                             | 2035 ( 4.2)       | 1016 ( 4.2)                   | 1019 ( 4.2)         |
| Non-Hispanic Black                   | 10530 (21.9)      | 5265 (21.8)                   | 5265 (21.9)         |
| Other or Unk                         | 1892 ( 3.9)       | 945 ( 3.9)                    | 947 ( 3.9)          |
| **Rurality\(^b\) (%)**               |                   |                               |                     |
| Rural                                | 14525 (30.1)      | 7269 (30.2)                   | 7256 (30.1)         |
| Urban                                | 33434 (69.4)      | 16721 (69.4)                  | 16713 (69.4)        |
| Unknown                              | 226 ( 0.5)        | 113 ( 0.5)                    | 113 ( 0.5)          |
| **Region\(^c\) (%)**                 |                   |                               |                     |
| North Atlantic                       | 10896 (22.6)      | 5453 (22.6)                   | 5443 (22.6)         |
| Southeast                            | 11124 (23.1)      | 5563 (23.1)                   | 5561 (23.1)         |
| Midwest                              | 11772 (24.4)      | 5891 (24.4)                   | 5881 (24.4)         |
| Continental                          | 6247 (13.0)       | 3124 (13.0)                   | 3123 (13.0)         |
| Pacific                              | 8146 (16.9)       | 4072 (16.9)                   | 4074 (16.9)         |
| **Charlson Score (%)**               |                   |                               |                     |
| 0-2                                  | 28155 (58.4)      | 14591 (60.5)                  | 13564 (56.3)        |
| 3-4                                  | 14605 (30.3)      | 7029 (29.2)                   | 7576 (31.5)         |
| 5+                                   | 5425 (11.3)       | 2483 (10.3)                   | 2942 (12.2)         |
| **Vaccine Typed (%)**                |                   |                               |                     |
| Moderna                              | -                  | -                             | 12974 (53.9)        |
| Pfizer                               | -                  | -                             | 11101 (46.1)        |
| Unknown                              | -                  | -                             | 7 ( 0.0)            |
| **Systemic therapy received\(^e\)** |                   |                               |                     |
| Distant treatment (>6 Months)        | 4458 ( 9.3)       | 2234 ( 9.3)                   | 2224 ( 9.2)         |
| Recent treatment (3-6 Months)        | 13345 (27.7)      | 6676 (27.7)                   | 6669 (27.7)         |
| Current chemotherapy-Containing (<3 Months) | 6875 (14.3) | 3439 (14.3)                   | 3436 (14.3)         |
| Current immunotherapy (<3 Months)    | 1958 ( 4.1)       | 979 ( 4.1)                    | 979 ( 4.1)          |
| Current targeted (<3 Months)         | 2863 ( 5.9)       | 1430 ( 5.9)                   | 1433 ( 6.0)         |
| Current endocrine (<3 Months)        | 15505 (32.2)      | 7752 (32.2)                   | 7753 (32.2)         |

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| Treatment after vaccine | 3181 (6.6) | 1593 (6.6) | 1588 (6.6) |
|------------------------|------------|------------|------------|
| Cancer type\(^f\) (%) |            |            |            |
| Prostate               | 27848 (57.8) | 13924 (57.8) | 13924 (57.8) |
| SCCHN/CSCC/skin        | 5310 (11) | 2655 (11) | 2655 (11) |
| Lung                   | 3692 (7.7) | 1846 (7.7) | 1846 (7.7) |
| Breast                 | 2358 (4.9) | 1179 (4.9) | 1179 (4.9) |
| Urothelial             | 1756 (3.6) | 878 (3.6) | 878 (3.6) |
| Lymphoma               | 1504 (3.1) | 752 (3.1) | 752 (3.1) |
| Colorectal             | 1466 (3) | 733 (3) | 733 (3) |
| HCC                    | 746 (1.5) | 373 (1.5) | 373 (1.5) |
| Esophagus/gastric      | 510 (1.1) | 255 (1.1) | 255 (1.1) |
| Melanoma               | 470 (1.0) | 235 (1.0) | 235 (1.0) |
| RCC                    | 450 (0.9) | 225 (0.9) | 225 (0.9) |
| Neuroendocrine         | 420 (0.9) | 210 (0.9) | 210 (0.9) |
| Other GI               | 316 (0.7) | 158 (0.7) | 158 (0.7) |
| Gyn                    | 102 (0.2) | 51 (0.2) | 51 (0.2) |
| Other/unknown/lesser   | 1237 (2.6) | 629 (2.6) | 608 (2.5) |

\(^a\) The number of vaccinated patients and unvaccinated patients do not match exactly because while “other/unknown” was used as one cancer type for matching, “other/unknown” was split into solid and hematologic malignancies by ICD code for the cancer category subanalysis.

\(^b\) Defined based on patient home address.

\(^c\) Defined based on VA station at which patient received cancer care.

\(^d\) Vaccination type only shown for overall and vaccinated cohort, even though patients in the unvaccinated cohort can be subsequently vaccinated after matching, as those vaccinations are already tabulated in the vaccinated cohort.

\(^e\) Systemic therapy received prior to vaccination (if in the vaccinated cohort) or prior to entry date (if in the unvaccinated cohort) with timing determined by the last dose of systemic therapy received.

Current treatment, defined as systemic therapy received within three months prior to vaccination, was further subdivided into different treatment types as detailed in eMethods.

\(^f\) Cancer type determined by ICD code(s) associated with cancer-directed systemic treatment as detailed in eMethods. Other/unknown/lesser includes cancer of unknown primary, cancer types not included in a predefined category, and cancer types represented by 50 patients or less. CSCC = cutaneous squamous cell carcinoma; Gyn = gynecologic malignancy; HCC = hepatocellular carcinoma; Other GI = anal/biliary/GIST/pancreas/small intestine; RCC = renal cell carcinoma; SCCHN = squamous cell head and neck cancer.
eTable 5. Demographic and Clinical Characteristics of Matched Vaccinated and Unvaccinated VA Cancer Patients with Hematologic Malignancies.

| Baseline Covariates | Overall (N=10119) | Unvaccinated\(^a\) (N=5049) | Vaccinated (N=5070) |
|---------------------|-------------------|-------------------------------|---------------------|
| Age (median [IQR])  | 73.46 [69.02, 77.62] | 73.01 [67.84, 76.83] | 73.92 [69.90, 78.39] |
| Age (%)             |                   |                               |                     |
| <50                 | 216 (2.1)         | 143 (2.8)                     | 73 (1.4)            |
| 50-59               | 610 (6.0)         | 365 (7.2)                     | 245 (4.8)           |
| 60-69               | 2029 (20.1)       | 1062 (21.0)                   | 967 (19.1)          |
| 70-79               | 5465 (54.0)       | 2692 (53.3)                   | 2773 (54.7)         |
| >=80                | 1799 (17.8)       | 787 (15.6)                    | 1012 (20.0)         |
| Gender = M (%)      | 9783 (96.7)       | 4853 (96.1)                   | 4930 (97.2)         |
| Race/Ethnicity (%)  |                   |                               |                     |
| Non-Hispanic White  | 7674 (75.8)       | 3824 (75.7)                   | 3850 (75.9)         |
| Hispanic            | 329 (3.3)         | 166 (3.3)                     | 163 (3.2)           |
| Non-Hispanic Black  | 1804 (17.8)       | 902 (17.9)                    | 902 (17.8)          |
| Other or Unk        | 312 (3.1)         | 157 (3.1)                     | 155 (3.1)           |
| Rurality\(^b\) (%)  |                   |                               |                     |
| Rural               | 3215 (31.8)       | 1601 (31.7)                   | 1614 (31.8)         |
| Urban               | 6888 (68.1)       | 3440 (68.1)                   | 3448 (68.0)         |
| Unknown             | 16 (0.2)          | 8 (0.2)                       | 8 (0.2)             |
| Region\(^c\) (%)    |                   |                               |                     |
| North Atlantic      | 2338 (23.1)       | 1164 (23.1)                   | 1174 (23.2)         |
| Southeast           | 2022 (20.0)       | 1010 (20.0)                   | 1012 (20.0)         |
| Midwest             | 2642 (26.1)       | 1316 (26.1)                   | 1326 (26.2)         |
| Continental         | 1453 (14.4)       | 726 (14.4)                    | 727 (14.3)          |
| Pacific             | 1664 (16.4)       | 833 (16.5)                    | 831 (16.4)          |
| Charlson Score (%)  |                   |                               |                     |
| 0-2                 | 6709 (66.3)       | 3472 (68.8)                   | 3237 (63.8)         |
| 3-4                 | 2477 (24.5)       | 1179 (23.4)                   | 1298 (25.6)         |
| 5+                  | 933 (9.2)         | 398 (7.9)                     | 535 (10.6)          |
| Vaccine Type\(^d\) (%) |             |                               |                     |
| Moderna             | -                 | -                             | 2742 (54.1)         |
| Pfizer              | -                 | -                             | 2325 (45.9)         |
| Unknown             | -                 | -                             | 3 (0.1)             |
| Systemic therapy received\(^e\) |       |                               |                     |
| Distant treatment (>6 Months) | 582 (5.8) | 286 (5.7) | 296 (5.8) |
| Recent treatment (3-6 Months) | 1915 (18.9) | 954 (18.9) | 961 (19.0) |
| Current chemotherapy-Containing (<3 Months) | 1577 (15.6) | 787 (15.6) | 790 (15.6) |
| Current targeted (<3 Months) | 5721 (56.5) | 2862 (56.7) | 2859 (56.4) |
| Current endocrine (<3 Months) | 9 (0.1) | 5 (0.1) | 4 (0.1) |
| Treatment after vaccine | 315 (3.1) | 155 (3.1) | 160 (3.2) |

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| Cancer Type                          | Overall (N) (%) | Unvaccinated (N) (%) | Vaccinated (N) (%) |
|-------------------------------------|-----------------|----------------------|--------------------|
| Leukemia/MDS/MF                     | 4986 (49.3)     | 2493 (49.4)          | 2493 (49.2)        |
| Multiple myeloma                    | 3212 (31.7)     | 1606 (31.8)          | 1606 (31.7)        |
| Essential thrombocytethmia           | 904 (8.9)       | 452 (9)              | 452 (8.9)          |
| Polycythemia vera                   | 622 (6.1)       | 311 (6.2)            | 311 (6.1)          |
| Other/unknown/lesser                | 395 (3.9)       | 187 (3.7)            | 208 (4.1)          |

a The number of vaccinated patients and unvaccinated patients do not match exactly because while “other/unknown” was used as one cancer type for matching, “other/unknown” was split into solid and hematologic malignancies by ICD code for the cancer category subanalysis.

b Defined based on patient home address.

c Defined based on VA station at which patient received cancer care.

d Vaccination type only shown for overall and vaccinated cohort, even though patients in the unvaccinated cohort can be subsequently vaccinated after matching, as those vaccinations are already tabulated in the vaccinated cohort.

e Systemic therapy received prior to vaccination (if in the vaccinated cohort) or prior to entry date (if in the unvaccinated cohort) with timing determined by the last dose of systemic therapy received. Current treatment, defined as systemic therapy received within three months prior to vaccination, was further subdivided into different treatment types as detailed in eMethods.

f Cancer type determined by ICD code(s) associated with cancer-directed systemic treatment as detailed in eMethods. Other/unknown/lesser includes cancer of unknown primary, cancer types not included in a predefined category, and cancer types represented by 50 patients or less. MF = myelofibrosis; MDS = myelodysplastic syndrome.
eTable 6. Demographic and Clinical Characteristics of Matched Vaccinated and Unvaccinated VA Cancer Patients with Distant Treatment (>6 months).

| Baseline Covariates              | Overall (N=5040) | Unvaccinated (N=2520) | Vaccinated (N=2520) |
|----------------------------------|------------------|-----------------------|---------------------|
| Age (median [IQR])              | 74.35 [70.05, 80.53] | 73.84 [69.06, 79.58] | 75.25 [70.94, 81.36] |
| Age (%)                         |                  |                       |                     |
| <50                             | 85 ( 1.7)        | 58 ( 2.3)             | 27 ( 1.1)           |
| 50-59                           | 236 ( 4.7)       | 132 ( 5.2)            | 104 ( 4.1)          |
| 60-69                           | 926 (18.4)       | 510 (20.2)            | 416 (16.5)          |
| 70-79                           | 2452 (48.7)      | 1218 (48.3)           | 1234 (49.0)         |
| >=80                            | 1341 (26.6)      | 602 (23.9)            | 739 (29.3)          |
| Gender = M (%)                  | 4665 (92.6)      | 2330 (92.5)           | 2335 (92.7)         |
| Race/Ethnicity (%)              |                  |                       |                     |
| Non-Hispanic White              | 3782 (75.0)      | 1891 (75.0)           | 1891 (75.0)         |
| Hispanic                        | 176 ( 3.5)       | 88 ( 3.5)             | 88 ( 3.5)           |
| Non-Hispanic Black              | 958 (19.0)       | 479 (19.0)            | 479 (19.0)          |
| Other or Unk                    | 124 ( 2.5)       | 62 ( 2.5)             | 62 ( 2.5)           |
| Ruralitya (%)                   |                  |                       |                     |
| Rural                           | 1536 (30.5)      | 768 (30.5)            | 768 (30.5)          |
| Urban                           | 3482 (69.1)      | 1741 (69.1)           | 1741 (69.1)         |
| Unknown                         | 22 ( 0.4)        | 11 ( 0.4)             | 11 ( 0.4)           |
| Regionb (%)                     |                  |                       |                     |
| North Atlantic                  | 1058 (21.0)      | 529 (21.0)            | 529 (21.0)          |
| Southeast                       | 1214 (24.1)      | 607 (24.1)            | 607 (24.1)          |
| Midwest                         | 1162 (23.1)      | 581 (23.1)            | 581 (23.1)          |
| Continental                     | 672 (13.3)       | 336 (13.3)            | 336 (13.3)          |
| Pacific                         | 934 (18.5)       | 467 (18.5)            | 467 (18.5)          |
| Charlson Score (%)              |                  |                       |                     |
| 0-2                             | 3350 (66.5)      | 1721 (68.3)           | 1629 (64.6)         |
| 3-4                             | 1244 (24.7)      | 602 (23.9)            | 642 (25.5)          |
| 5+                              | 446 ( 8.8)       | 197 ( 7.8)            | 249 ( 9.9)          |
| Vaccine Typec (%)               |                  |                       |                     |
| Moderna                         | -                | -                     | 1388 (55.1)         |
| Pfizer                          | -                | -                     | 1132 (44.9)         |
| Unknown                         | -                | -                     | 0 ( 0.0)            |
| Cancer typed (%)                |                  |                       |                     |
| Prostate                        | 2716 (53.9)      | 1358 (53.9)           | 1358 (53.9)         |
| SCCHN/SCCC/skin                 | 640 (12.7)       | 320 (12.7)            | 320 (12.7)          |
| Leukemia/MDS/MF                 | 336 ( 6.7)       | 168 ( 6.7)            | 168 ( 6.7)          |
| Breast                          | 298 ( 5.9)       | 149 ( 5.9)            | 149 ( 5.9)          |
| Lung                            | 196 ( 3.9)       | 98 ( 3.9)             | 98 ( 3.9)           |
| Urothelial                      | 160 ( 3.2)       | 80 ( 3.2)             | 80 ( 3.2)           |
| Lymphoma                        | 102 ( 2.0)       | 51 ( 2.0)             | 51 ( 2.0)           |
| Multiple myeloma                | 88 ( 1.7)        | 44 ( 1.7)             | 44 ( 1.7)           |
| Colorectal                      | 78 ( 1.5)        | 39 ( 1.5)             | 39 ( 1.5)           |
| Essential thrombocythemia        | 66 ( 1.3)        | 33 ( 1.3)             | 33 ( 1.3)           |
| Polycythemia vera               | 52 ( 1.0)        | 26 ( 1.0)             | 26 ( 1.0)           |
| Other/unknown/lesser | 308 (6.1) | 154 (6.1) | 154 (6.1) |

*Defined based on patient home address.*
*Defined based on VA station at which patient received cancer care.*
*Vaccination type only shown for overall and vaccinated cohort, even though patients in the unvaccinated cohort can be subsequently vaccinated after matching, as those vaccinations are already tabulated in the vaccinated cohort.*
*Cancer type determined by ICD code(s) associated with cancer-directed systemic treatment as detailed in eMethods. Other/unknown/lesser includes cancer of unknown primary, cancer types not included in a predefined category, and cancer types represented by 50 patients or less. CSCC = cutaneous squamous cell carcinoma; MF = myelofibrosis; MDS = myelodysplastic syndrome; SCCHN = squamous cell head and neck cancer.*
eTable 7. Demographic and Clinical Characteristics of Matched Vaccinated and Unvaccinated VA Cancer Patients with Recent Treatment (3-6 Months).

| Baseline Covariates                      | Overall (N=15260) | Unvaccinated (N=7630) | Vaccinated (N=7630) |
|-----------------------------------------|-------------------|-----------------------|---------------------|
| Age (median [IQR])                      | 73.67 [69.40, 78.67] | 73.25 [68.60, 78.10]  | 74.03 [70.14, 79.30] |
| Age (%)                                 |                   |                       |                     |
| <50                                     | 269 ( 1.8)        | 177 ( 2.3)            | 92 ( 1.2)           |
| 50-59                                   | 715 ( 4.7)        | 425 ( 5.6)            | 290 ( 3.8)          |
| 60-69                                   | 3102 (20.3)       | 1615 (21.2)           | 1487 (19.5)         |
| 70-79                                   | 7867 (51.6)       | 3878 (50.8)           | 3989 (52.3)         |
| >=80                                    | 3307 (21.7)       | 1535 (20.1)           | 1772 (23.2)         |
| Gender = M (%)                          | 14235 (93.3)      | 7091 (92.9)           | 7144 (93.6)         |
| Race/Ethnicity (%)                      |                   |                       |                     |
| Non-Hispanic White                      | 10678 (70.0)      | 5339 (70.0)           | 5339 (70.0)         |
| Hispanic                                | 624 ( 4.1)        | 312 ( 4.1)            | 312 ( 4.1)          |
| Non-Hispanic Black                      | 3362 (22.0)       | 1681 (22.0)           | 1681 (22.0)         |
| Other or Unk                            | 596 ( 3.9)        | 298 ( 3.9)            | 298 ( 3.9)          |
| Ruralitya (%)                           |                   |                       |                     |
| Rural                                   | 4966 ( 32.5)      | 2483 ( 32.5)          | 2483 ( 32.5)        |
| Urban                                   | 10238 (67.1)      | 5119 (67.1)           | 5119 (67.1)         |
| Unknown                                 | 56 ( 0.4)         | 28 ( 0.4)             | 28 ( 0.4)           |
| Regionb (%)                             |                   |                       |                     |
| North Atlantic                          | 3388 (22.2)       | 1694 (22.2)           | 1694 (22.2)         |
| Southeast                               | 3610 (23.7)       | 1805 (23.7)           | 1805 (23.7)         |
| Midwest                                 | 3662 (24.0)       | 1831 (24.0)           | 1831 (24.0)         |
| Continental                             | 2114 (13.9)       | 1057 (13.9)           | 1057 (13.9)         |
| Pacific                                 | 2486 (16.3)       | 1243 (16.3)           | 1243 (16.3)         |
| Charlson Score (%)                      |                   |                       |                     |
| 0-2                                     | 9418 (61.7)       | 4861 (63.7)           | 4557 (59.7)         |
| 3-4                                     | 4324 (28.3)       | 2065 (27.1)           | 2259 (29.6)         |
| 5+                                      | 1518 ( 9.9)       | 704 ( 9.2)            | 814 (10.7)          |
| Vaccine Typec (%)                       |                   |                       |                     |
| Moderna                                 | -                 | -                     | 4207 (55.1)         |
| Pfizer                                  | -                 | -                     | 3421 (44.8)         |
| Unknown                                 | -                 | -                     | 2 ( 0.0)            |
| Cancer typed (%)                        |                   |                       |                     |
| Prostate                                | 8372 (54.9)       | 4186 (54.9)           | 4186 (54.9)         |
| SCCHN/CSCC/skin                        | 1638 (10.7)       | 819 (10.7)            | 819 (10.7)          |
| Leukemia/MDS/MF                         | 1106 ( 7.2)       | 553 ( 7.2)            | 553 ( 7.2)          |
| Breast                                  | 798 ( 5.2)        | 399 ( 5.2)            | 399 ( 5.2)          |
| Urothelial                              | 492 ( 3.2)        | 246 ( 3.2)            | 246 ( 3.2)          |
| Lung                                    | 460 ( 3.0)        | 230 ( 3.0)            | 230 ( 3.0)          |
| Colorectal                              | 324 ( 2.1)        | 162 ( 2.1)            | 162 ( 2.1)          |
| Lymphoma                                | 300 ( 2.0)        | 150 ( 2.0)            | 150 ( 2.0)          |
| Essential thrombocythemia               | 294 ( 1.9)        | 147 ( 1.9)            | 147 ( 1.9)          |
| Multiple myeloma                        | 210 ( 1.4)        | 105 ( 1.4)            | 105 ( 1.4)          |
| Polycythemia vera                       | 182 ( 1.2)        | 91 ( 1.2)             | 91 ( 1.2)           |
| Cancer Type          | Count (%)   | Count (%)   | Count (%)   |
|---------------------|-------------|-------------|-------------|
| HCC                 | 180 (1.2)   | 90 (1.2)    | 90 (1.2)    |
| Neuroendocrine      | 98 (0.6)    | 49 (0.6)    | 49 (0.6)    |
| Melanoma            | 96 (0.6)    | 48 (0.6)    | 48 (0.6)    |
| Esophagus/gastric   | 88 (0.6)    | 44 (0.6)    | 44 (0.6)    |
| RCC                 | 70 (0.5)    | 35 (0.5)    | 35 (0.5)    |
| Other/unknown/lesser| 552 (3.6)   | 276 (3.6)   | 276 (3.6)   |

- Defined based on patient home address.
- Defined based on VA station at which patient received cancer care.
- Vaccination type only shown for overall and vaccinated cohort, even though patients in the unvaccinated cohort can be subsequently vaccinated after matching, as those vaccinations are already tabulated in the vaccinated cohort.
- Cancer type determined by ICD code(s) associated with cancer-directed systemic treatment as detailed in eMethods. Other/unknown/lesser includes cancer of unknown primary, cancer types not included in a predefined category, and cancer types represented by 50 patients or less. CSCC = cutaneous squamous cell carcinoma; HCC = hepatocellular carcinoma; MF = myelofibrosis; MDS = myelodysplastic syndrome; RCC = renal cell carcinoma; SCCHN = squamous cell head and neck cancer.
eTable 8. Demographic and Clinical Characteristics of Matched Vaccinated and Unvaccinated VA Cancer Patients with Current Treatment (<3 Months).

| Baseline Covariates                           | Overall (N=34508) | Unvaccinated (N=17254) | Vaccinated (N=17254) |
|-----------------------------------------------|-------------------|------------------------|----------------------|
| **Age (median [IQR])**                        | 73.68 [69.37, 78.43] | 73.32 [68.59, 77.76] | 74.08 [70.13, 79.06] |
| **Age (%)**                                   |                   |                        |                      |
| <50                                           | 548 (1.6)         | 346 (2.0)              | 202 (1.2)            |
| 50-59                                         | 1728 (5.0)        | 995 (5.8)              | 733 (4.2)            |
| 60-69                                         | 7045 (20.4)       | 3766 (21.8)            | 3279 (19.0)          |
| 70-79                                         | 18159 (52.6)      | 8935 (51.8)            | 9224 (53.5)          |
| >=80                                          | 7028 (20.4)       | 3212 (18.6)            | 3816 (22.1)          |
| **Gender = M (%)**                            | 32731 (94.9)      | 16293 (94.4)           | 16438 (95.3)         |
| **Race/Ethnicity (%)**                        |                   |                        |                      |
| Non-Hispanic White                            | 24204 (70.1)      | 12102 (70.1)           | 12102 (70.1)         |
| Hispanic                                      | 1460 (4.2)        | 730 (4.2)              | 730 (4.2)            |
| Non-Hispanic Black                            | 7466 (21.6)       | 3733 (21.6)            | 3733 (21.6)          |
| Other or Unk                                  | 1378 (4.0)        | 689 (4.0)              | 689 (4.0)            |
| **Ruralitya (%)**                             |                   |                        |                      |
| Rural                                         | 10226 (29.6)      | 5113 (29.6)            | 5113 (29.6)          |
| Urban                                         | 24128 (69.9)      | 12064 (69.9)           | 12064 (69.9)         |
| Unknown                                       | 154 (0.4)         | 77 (0.4)               | 77 (0.4)             |
| **Regionb (%)**                               |                   |                        |                      |
| North Atlantic                                | 7996 (23.2)       | 3998 (23.2)            | 3998 (23.2)          |
| Southeast                                     | 7546 (21.9)       | 3773 (21.9)            | 3773 (21.9)          |
| Midwest                                       | 8666 (25.1)       | 4333 (25.1)            | 4333 (25.1)          |
| Continental                                   | 4464 (12.9)       | 2232 (12.9)            | 2232 (12.9)          |
| Pacific                                       | 5836 (16.9)       | 2918 (16.9)            | 2918 (16.9)          |
| **Charlson Score (%)**                        |                   |                        |                      |
| 0-2                                           | 19573 (56.7)      | 10182 (59.0)           | 9391 (54.4)          |
| 3-4                                           | 10769 (31.2)      | 5199 (30.1)            | 5570 (32.3)          |
| 5+                                            | 4166 (12.1)       | 1873 (10.9)            | 2293 (13.3)          |
| **Vaccine Typec (%)**                         |                   |                        |                      |
| Modern                                       | -                 | -                      | 9214 (53.4)          |
| Pfizer                                        | -                 | -                      | 8032 (46.6)          |
| Unknown                                       | -                 | -                      | 8 (0.0)              |
| **Systemic therapy receivedd**                |                   |                        |                      |
| Current chemotherapy-Containing (<3 Months)   | 8452 (24.5)       | 4226 (24.5)            | 4226 (24.5)          |
| Current immunotherapy (<3 Months)             | 1958 (5.7)        | 979 (5.7)              | 979 (5.7)            |
| Current targeted (<3 Months)                  | 8584 (24.9)       | 4292 (24.9)            | 4292 (24.9)          |
| Current endocrine (<3 Months)                 | 15514 (45.0)      | 7757 (45.0)            | 7757 (45.0)          |
| **Cancer typee (%)**                          |                   |                        |                      |
| Prostate                                      | 15402 (44.6)      | 7701 (44.6)            | 7701 (44.6)          |
| Leukemia/MDS/MF                               | 3354 (9.7)        | 1677 (9.7)             | 1677 (9.7)           |
| Multiple myeloma                              | 2818 (8.2)        | 1409 (8.2)             | 1409 (8.2)           |

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| Cancer Type                  | Vaccinated n (%) | Unvaccinated n (%) | Matched n (%) |
|-----------------------------|------------------|-------------------|---------------|
| Lung                        | 2538 (7.4)       | 1269 (7.4)        | 1269 (7.4)    |
| SCCHN/CSCC/skin             | 2518 (7.3)       | 1259 (7.3)        | 1259 (7.3)    |
| Breast                      | 1228 (3.6)       | 614 (3.6)         | 614 (3.6)     |
| Colorectal                  | 992 (2.9)        | 496 (2.9)         | 496 (2.9)     |
| Lymphoma                    | 970 (2.8)        | 485 (2.8)         | 485 (2.8)     |
| Urothelial                  | 896 (2.6)        | 448 (2.6)         | 448 (2.6)     |
| Essential thrombocythemia   | 532 (1.5)        | 266 (1.5)         | 266 (1.5)     |
| HCC                         | 408 (1.2)        | 204 (1.2)         | 204 (1.2)     |
| Polycythemia vera           | 382 (1.1)        | 191 (1.1)         | 191 (1.1)     |
| RCC                         | 344 (1.0)        | 172 (1.0)         | 172 (1.0)     |
| Esophagus/gastric           | 342 (1.0)        | 171 (1.0)         | 171 (1.0)     |
| Melanoma                    | 318 (0.9)        | 159 (0.9)         | 159 (0.9)     |
| Neuroendocrine              | 266 (0.8)        | 133 (0.8)         | 133 (0.8)     |
| Other GI                    | 236 (0.7)        | 118 (0.7)         | 118 (0.7)     |
| Gyn                         | 54 (0.2)         | 27 (0.2)          | 27 (0.2)      |
| Other/unknown/lesser        | 910 (2.6)        | 455 (2.6)         | 455 (2.6)     |

a Defined based on patient home address.

b Defined based on VA station at which patient received cancer care.

c Vaccination type only shown for overall and vaccinated cohort, even though patients in the unvaccinated cohort can be subsequently vaccinated after matching, as those vaccinations are already tabulated in the vaccinated cohort.

d Systemic therapy received prior to vaccination (if in the vaccinated cohort) or prior to entry date (if in the unvaccinated cohort) with timing determined by the last dose of systemic therapy received. Different treatment types defined as detailed in eMethods.

e Cancer type determined by ICD code(s) associated with cancer-directed systemic treatment as detailed in eMethods. Other/unknown/lesser includes cancer of unknown primary, cancer types not included in a predefined category, and cancer types represented by 50 patients or less. SCCHN = cutaneous squamous cell carcinoma; Gyn = gynecologic malignancy; HCC = hepatocellular carcinoma; MF = myelofibrosis; MDS = myelodysplastic syndrome; Other GI = anal/biliary/GIST/pancreas/small intestine; RCC = renal cell carcinoma; SCCHN = squamous cell head and neck cancer.
**eTable 9. Demographic and Clinical Characteristics of Matched Vaccinated and Unvaccinated VA Cancer Patients with Treatment After Vaccination.**

| Baseline Covariates | Overall (N=3496) | Unvaccinated (N=1748) | Vaccinated (N=1748) |
|---------------------|------------------|-----------------------|---------------------|
| Age (median [IQR])  | 73.55 [69.41, 77.87] | 72.71 [68.00, 76.26] | 74.33 [70.58, 79.42] |
| Age (%)             |                  |                       |                     |
| <50                 | 41 ( 1.2)        | 31 ( 1.8)             | 10 ( 0.6)           |
| 50-59               | 151 ( 4.3)       | 100 ( 5.7)            | 51 ( 2.9)           |
| 60-69               | 755 (21.6)       | 423 (24.2)            | 332 (19.0)          |
| 70-79               | 1888 (54.0)      | 947 (54.2)            | 941 (53.8)          |
| >=80                | 661 (18.9)       | 247 (14.1)            | 414 (23.7)          |
| Gender = M (%)      | 3398 (97.2)      | 1694 (96.9)           | 1704 (97.5)         |
| Race/Ethnicity (%)  |                  |                       |                     |
| Non-Hispanic White  | 2738 (78.3)      | 1369 (78.3)           | 1369 (78.3)         |
| Hispanic            | 104 ( 3.0)       | 52 ( 3.0)             | 52 ( 3.0)           |
| Non-Hispanic Black  | 548 (15.7)       | 274 (15.7)            | 274 (15.7)          |
| Other or Unk        | 106 ( 3.0)       | 53 ( 3.0)             | 53 ( 3.0)           |
| Ruralitya (%)       |                  |                       |                     |
| Rural               | 1012 (28.9)      | 506 (28.9)            | 506 (28.9)          |
| Urban               | 2474 (70.8)      | 1237 (70.8)           | 1237 (70.8)         |
| Unknown             | 10 ( 0.3)        | 5 ( 0.3)              | 5 ( 0.3)            |
| Regionb (%)         |                  |                       |                     |
| North Atlantic      | 792 (22.7)       | 396 (22.7)            | 396 (22.7)          |
| Southeast           | 776 (22.2)       | 388 (22.2)            | 388 (22.2)          |
| Midwest             | 924 (26.4)       | 462 (26.4)            | 462 (26.4)          |
| Continental         | 450 (12.9)       | 225 (12.9)            | 225 (12.9)          |
| Pacific             | 554 (15.8)       | 277 (15.8)            | 277 (15.8)          |
| Charlson Score (%)  |                  |                       |                     |
| 0-2                 | 2523 (72.2)      | 1299 (74.3)           | 1224 (70.0)         |
| 3-4                 | 745 (21.3)       | 342 (19.6)            | 403 (23.1)          |
| 5+                  | 228 ( 6.5)       | 107 ( 6.1)            | 121 ( 6.9)          |
| Vaccine Typec (%)   |                  |                       |                     |
| Moderna             | -                 | -                     | 907 (51.9)          |
| Pfizer              | -                 | -                     | 841 (48.1)          |
| Unknown             | -                 | -                     | 0 ( 0.0)            |
| Cancer typee (%)    |                  |                       |                     |
| Prostate            | 1358 (38.8)      | 679 (38.8)            | 679 (38.8)          |
| SCCHN/CSCC/skin     | 514 (14.7)       | 257 (14.7)            | 257 (14.7)          |
| Lung                | 498 (14.2)       | 249 (14.2)            | 249 (14.2)          |
| Urothelial          | 208 ( 5.9)       | 104 ( 5.9)            | 104 ( 5.9)          |
| Leukemia/MDS/MF     | 190 ( 5.4)       | 95 ( 5.4)             | 95 ( 5.4)           |
| Lymphoma            | 132 ( 3.8)       | 66 ( 3.8)             | 66 ( 3.8)           |
| HCC                 | 112 ( 3.2)       | 56 ( 3.2)             | 56 ( 3.2)           |
| Multiple myeloma    | 96 ( 2.7)        | 48 ( 2.7)             | 48 ( 2.7)           |
| Colorectal          | 72 ( 2.1)        | 36 ( 2.1)             | 36 ( 2.1)           |
| Esophagus/gastric   | 60 ( 1.7)        | 30 ( 1.7)             | 30 ( 1.7)           |
| Other/unknown/lesser| 256 ( 7.3)       | 128 ( 7.3)            | 128 ( 7.3)          |
a Defined based on patient home address.
b Defined based on VA station at which patient received cancer care.
c Vaccination type only shown for overall and vaccinated cohort, even though patients in the unvaccinated cohort can be subsequently vaccinated after matching, as those vaccinations are already tabulated in the vaccinated cohort.
d Systemic therapy received prior to vaccination (if in the vaccinated cohort) or prior to entry date (if in the unvaccinated cohort) with timing determined by the last dose of systemic therapy received. Different treatment types defined as detailed in eMethods.
e Cancer type determined by ICD code(s) associated with cancer-directed systemic treatment as detailed in eMethods. Other/unknown/lesser includes cancer of unknown primary, cancer types not included in a predefined category, and cancer types represented by 50 patients or less. CSCC = cutaneous squamous cell carcinoma; HCC = hepatocellular carcinoma; MF = myelofibrosis; MDS = myelodysplastic syndrome; SCCHN = squamous cell head and neck cancer.
eTable 10. Demographic and Clinical Characteristics of Matched Vaccinated and Unvaccinated VA Cancer Patients on Current Chemotherapy-containing Treatment (<3 Months).

| Baseline Covariates | Overall (N=8452) | Unvaccinated (N=4226) | Vaccinated (N=4226) |
|---------------------|------------------|-----------------------|---------------------|
| Age (median [IQR])  | 72.88 [67.92, 76.49] | 72.26 [66.80, 75.64] | 73.35 [68.90, 77.34] |
| Age (%)             |                  |                       |                     |
| <50                 | 169 (2.0)        | 106 (2.5)             | 63 (1.5)            |
| 50-59               | 520 (6.2)        | 314 (7.4)             | 206 (4.9)           |
| 60-69               | 2019 (23.9)      | 1094 (25.9)           | 925 (21.9)          |
| 70-79               | 4555 (53.9)      | 2227 (52.7)           | 2328 (55.1)         |
| >=80                | 1189 (14.1)      | 485 (11.5)            | 704 (16.7)          |
| Gender = M (%)      | 8048 (95.2)      | 3996 (94.6)           | 4052 (95.9)         |
| Race/Ethnicity (%)  |                  |                       |                     |
| Non-Hispanic White  | 6702 (79.3)      | 3351 (79.3)           | 3351 (79.3)         |
| Hispanic            | 248 (2.9)        | 124 (2.9)             | 124 (2.9)           |
| Non-Hispanic Black  | 1272 (15.0)      | 636 (15.0)            | 636 (15.0)          |
| Other or Unk        | 230 (2.7)        | 115 (2.7)             | 115 (2.7)           |
| Rurality (%)        |                  |                       |                     |
| Rural               | 2480 (29.3)      | 1240 (29.3)           | 1240 (29.3)         |
| Urban               | 5966 (70.6)      | 2983 (70.6)           | 2983 (70.6)         |
| Unknown             | 6 (0.1)          | 3 (0.1)               | 3 (0.1)             |
| Region (%)          |                  |                       |                     |
| North Atlantic      | 2010 (23.8)      | 1005 (23.8)           | 1005 (23.8)         |
| Southeast           | 1740 (20.6)      | 870 (20.6)            | 870 (20.6)          |
| Midwest             | 2236 (26.5)      | 1118 (26.5)           | 1118 (26.5)         |
| Continental         | 1040 (12.3)      | 520 (12.3)            | 520 (12.3)          |
| Pacific             | 1426 (16.9)      | 713 (16.9)            | 713 (16.9)          |
| Charlson Score (%)  |                  |                       |                     |
| 0-2                 | 4595 (54.4)      | 2395 (56.7)           | 2200 (52.1)         |
| 3-4                 | 2722 (32.2)      | 1307 (30.9)           | 1415 (33.5)         |
| 5+                  | 1135 (13.4)      | 524 (12.4)            | 611 (14.5)          |
| Vaccine Type (%)    |                  |                       |                     |
| Moderna             | -                 | -                     | 2102 (49.7)         |
| Pfizer              | -                 | -                     | 2122 (50.2)         |
| Unknown             | -                 | -                     | 2 (0.0)             |
| Cancer type (%)     |                  |                       |                     |
| Lung                | 1298 (15.4)      | 649 (15.4)            | 649 (15.4)          |
| SCCHN/CSCC/skin     | 1272 (15.0)      | 636 (15.0)            | 636 (15.0)          |
| Prostate            | 996 (11.8)       | 498 (11.8)            | 498 (11.8)          |
| Colorectal          | 898 (10.6)       | 449 (10.6)            | 449 (10.6)          |
| Urothelial          | 748 (8.8)        | 374 (8.8)             | 374 (8.8)           |
| Essential thrombocytethemia | 524 (6.2) | 262 (6.2)             | 262 (6.2)           |
| Leukemia/MDS/MF     | 424 (5.0)        | 212 (5.0)             | 212 (5.0)           |
| Lymphoma            | 364 (4.3)        | 182 (4.3)             | 182 (4.3)           |
| Polycythemia vera   | 344 (4.1)        | 172 (4.1)             | 172 (4.1)           |
| Other GI            | 226 (2.7)        | 113 (2.7)             | 113 (2.7)           |
| Cancer Type                | Unvaccinated | Vaccinated | Vaccinated Cohort |
|---------------------------|--------------|------------|------------------|
| Esophagus/gastric         | 216 (2.6)    | 108 (2.6)  | 108 (2.6)        |
| HCC                       | 188 (2.2)    | 94 (2.2)   | 94 (2.2)         |
| Multiple myeloma          | 124 (1.5)    | 62 (1.5)   | 62 (1.5)         |
| Breast                    | 86 (1.0)     | 43 (1.0)   | 43 (1.0)         |
| Neuroendocrine            | 82 (1.0)     | 41 (1.0)   | 41 (1.0)         |
| Melanoma                  | 56 (0.7)     | 28 (0.7)   | 28 (0.7)         |
| Other/unknown/lesser      | 606 (7.2)    | 303 (7.2)  | 303 (7.2)        |

*a Defined based on patient home address.  
b Defined based on VA station at which patient received cancer care.  
c Vaccination type only shown for overall and vaccinated cohort, even though patients in the unvaccinated cohort can be subsequently vaccinated after matching, as those vaccinations are already tabulated in the vaccinated cohort.  
d Cancer type determined by ICD code(s) associated with cancer-directed systemic treatment as detailed in eMethods. Other/unknown/lesser includes cancer of unknown primary, cancer types not included in a predefined category, and cancer types represented by 50 patients or less. CSCC = cutaneous squamous cell carcinoma; HCC = hepatocellular carcinoma; MF = myelofibrosis; MDS = myelodysplastic syndrome; SCCHN = squamous cell head and neck cancer.
eTable 11. Demographic and Clinical Characteristics of Matched Vaccinated and Unvaccinated VA Cancer Patients on Current Targeted Treatment (<3 Months).

| Baseline Covariates | Overall (N=8584) | Unvaccinated (N=4292) | Vaccinated (N=4292) |
|---------------------|------------------|-----------------------|---------------------|
| Age (median [IQR])  | 73.37 [68.86, 77.31] | 72.97 [67.92, 76.48] | 73.79 [69.66, 78.08] |
| Age (%)             |                  |                       |                     |
| <50                 | 197 (2.3)        | 128 (3.0)             | 69 (1.6)            |
| 50-59               | 555 (6.5)        | 325 (7.6)             | 230 (5.4)           |
| 60-69               | 1736 (20.2)      | 899 (20.9)            | 837 (19.5)          |
| 70-79               | 4670 (54.4)      | 2319 (54.0)           | 2351 (54.8)         |
| >=80                | 1426 (16.6)      | 621 (14.5)            | 805 (18.8)          |
| Gender = M (%)      |                  |                       |                     |
| Race/Ethnicity (%)  |                  |                       |                     |
| Non-Hispanic White  | 6572 (76.6)      | 3286 (76.6)           | 3286 (76.6)         |
| Hispanic            | 278 (3.2)        | 139 (3.2)             | 139 (3.2)           |
| Non-Hispanic Black  | 1442 (16.8)      | 721 (16.8)            | 721 (16.8)          |
| Other or Unk        | 292 (3.4)        | 146 (3.4)             | 146 (3.4)           |
| Rurality (%)        |                  |                       |                     |
| Rural               | 2640 (30.8)      | 1320 (30.8)           | 1320 (30.8)         |
| Urban               | 5922 (69.0)      | 2961 (69.0)           | 2961 (69.0)         |
| Unknown             | 22 (0.3)         | 11 (0.3)              | 11 (0.3)            |
| Region (%)          |                  |                       |                     |
| North Atlantic      | 1856 (21.6)      | 928 (21.6)            | 928 (21.6)          |
| Southeast           | 1852 (21.6)      | 926 (21.6)            | 926 (21.6)          |
| Midwest             | 2140 (24.9)      | 1070 (24.9)           | 1070 (24.9)         |
| Continental         | 1234 (14.4)      | 617 (14.4)            | 617 (14.4)          |
| Pacific             | 1502 (17.5)      | 751 (17.5)            | 751 (17.5)          |
| Charlson Score (%)  |                  |                       |                     |
| 0-2                 | 5297 (61.7)      | 2764 (64.4)           | 2533 (59.0)         |
| 3-4                 | 2392 (27.9)      | 1151 (26.8)           | 1241 (28.9)         |
| 5+                  | 895 (10.4)       | 377 (8.8)             | 518 (12.1)          |
| Vaccine Type (%)    |                  |                       |                     |
| Moderna             | -                 | -                     | 2320 (54.1)         |
| Pfizer              | -                 | -                     | 1970 (45.9)         |
| Unknown             | -                 | -                     | 2 (0.0)             |
| Cancer type (%)     |                  |                       |                     |
| Leukemia/MDS/MF     | 2926 (34.1)      | 1463 (34.1)           | 1463 (34.1)         |
| Multiple myeloma    | 2690 (31.3)      | 1345 (31.3)           | 1345 (31.3)         |
| SCCHN/CSCC/skin     | 1020 (11.9)      | 510 (11.9)            | 510 (11.9)          |
| Lymphoma            | 594 (6.9)        | 297 (6.9)             | 297 (6.9)           |
| Prostate            | 212 (2.5)        | 106 (2.5)             | 106 (2.5)           |
| RCC                 | 170 (2.0)        | 85 (2.0)              | 85 (2.0)            |
| Lung                | 158 (1.8)        | 79 (1.8)              | 79 (1.8)            |
| Esophagus/gastric   | 104 (1.2)        | 52 (1.2)              | 52 (1.2)            |
| Colorectal          | 84 (1.0)         | 42 (1.0)              | 42 (1.0)            |
| Breast              | 82 (1.0)         | 41 (1.0)              | 41 (1.0)            |
| HCC                 | 76 (0.9)         | 38 (0.9)              | 38 (0.9)            |
| Cancer Type          | Vaccinated Cohort | Unvaccinated Cohort | Matched Cohort |
|---------------------|-------------------|---------------------|----------------|
| Neuroendocrine      | 54 (0.6)          | 27 (0.6)            | 27 (0.6)       |
| Other/unknown/lesser| 414 (4.8)         | 207 (4.8)           | 207 (4.8)      |

a Defined based on patient home address.
b Defined based on VA station at which patient received cancer care.
c Vaccination type only shown for overall and vaccinated cohort, even though patients in the unvaccinated cohort can be subsequently vaccinated after matching, as those vaccinations are already tabulated in the vaccinated cohort.
d Cancer type determined by ICD code(s) associated with cancer-directed systemic treatment as detailed in eMethods. Other/unknown/lesser includes cancer of unknown primary, cancer types not included in a predefined category, and cancer types represented by 50 patients or less. CSCC = cutaneous squamous cell carcinoma; HCC = hepatocellular carcinoma; MF = myelofibrosis; MDS = myelodysplastic syndrome; RCC = renal cell carcinoma; SCCHN = squamous cell head and neck cancer.
eTable 12. Demographic and Clinical Characteristics of Matched Vaccinated and Unvaccinated VA Cancer Patients on Current Endocrine Treatment (<3 Months).

| Baseline Covariates       | Overall (N=15514) | Unvaccinated (N=7757) | Vaccinated (N=7757) |
|---------------------------|-------------------|-----------------------|---------------------|
| Age (median [IQR])        | 74.53 [70.71, 80.80] | 74.22 [70.28, 80.43] | 74.92 [71.18, 81.25] |
| Age (%)                   |                   |                       |                     |
| <50                       | 166 ( 1.1)        | 102 ( 1.3)            | 64 ( 0.8)           |
| 50-59                     | 559 ( 3.6)        | 304 ( 3.9)            | 255 ( 3.3)          |
| 60-69                     | 2705 (17.4)       | 1450 (18.7)           | 1255 (16.2)         |
| 70-79                     | 7893 (50.9)       | 3883 (50.1)           | 4010 (51.7)         |
| >=80                      | 4191 (27.0)       | 2018 (26.0)           | 2173 (28.0)         |
| Gender = M (%)            | 14540 (93.7)      | 7260 (93.6)           | 7280 (93.9)         |
| Race/Ethnicity (%)        |                   |                       |                     |
| Non-Hispanic White        | 9406 (60.6)       | 4703 (60.6)           | 4703 (60.6)         |
| Hispanic                  | 866 ( 5.6)        | 433 ( 5.6)            | 433 ( 5.6)          |
| Non-Hispanic Black        | 4418 (28.5)       | 2209 (28.5)           | 2209 (28.5)         |
| Other or Unk              | 824 ( 5.3)        | 412 ( 5.3)            | 412 ( 5.3)          |
| Ruralitya (%)             |                   |                       |                     |
| Rural                     | 4584 (29.5)       | 2292 (29.5)           | 2292 (29.5)         |
| Urban                     | 10808 (69.7)      | 5404 (69.7)           | 5404 (69.7)         |
| Unknown                   | 122 ( 0.8)        | 61 ( 0.8)             | 61 ( 0.8)           |
| Regionb (%)               |                   |                       |                     |
| North Atlantic            | 3672 (23.7)       | 1836 (23.7)           | 1836 (23.7)         |
| Southeast                 | 3534 (22.8)       | 1767 (22.8)           | 1767 (22.8)         |
| Midwest                   | 3786 (24.4)       | 1893 (24.4)           | 1893 (24.4)         |
| Continental               | 1906 (12.3)       | 953 (12.3)            | 953 (12.3)          |
| Pacific                   | 2616 (16.9)       | 1308 (16.9)           | 1308 (16.9)         |
| Charlson Score (%)        |                   |                       |                     |
| 0-2                       | 9134 (58.9)       | 4732 (61.0)           | 4402 (56.7)         |
| 3-4                       | 4748 (30.6)       | 2288 (29.5)           | 2460 (31.7)         |
| 5+                        | 1632 (10.5)       | 737 ( 9.5)            | 895 (11.5)          |
| Vaccine Typec (%)         |                   |                       |                     |
| Moderna                   | -                  | -                     | 4331 (55.8)         |
| Pfizer                    | -                  | -                     | 3423 (44.1)         |
| Unknown                   | -                  | -                     | 3 ( 0.0)            |
| Cancer typed (%)          |                   |                       |                     |
| Prostate                  | 14180 (91.4)      | 7090 (91.4)           | 7090 (91.4)         |
| Breast                    | 1060 ( 6.8)       | 530 ( 6.8)            | 530 ( 6.8)          |
| Neuroendocrine            | 130 ( 0.8)        | 65 ( 0.8)             | 65 ( 0.8)           |
| Other/unknown/lesser      | 144 ( 0.9)        | 72 ( 0.9)             | 72 ( 0.9)           |

a Defined based on patient home address.
b Defined based on VA station at which patient received cancer care.
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c Vaccination type only shown for overall and vaccinated cohort, even though patients in the unvaccinated cohort can be subsequently vaccinated after matching, as those vaccinations are already tabulated in the vaccinated cohort.

d Cancer type determined by ICD code(s) associated with cancer-directed systemic treatment as detailed in eMethods. Other/unknown/lesser includes cancer of unknown primary, cancer types not included in a predefined category, and cancer types represented by 50 patients or less.
### eTable 13. Cancer-directed Systemic Therapies by Treatment Type.

| Treatment                  | Type            |
|----------------------------|-----------------|
| abemaciclib                | Targeted therapy|
| abiraterone                | Endocrine therapy|
| abvd                       | Chemotherapy    |
| abve                       | Chemotherapy    |
| abve-pc                    | Chemotherapy    |
| ac                         | Chemotherapy    |
| ac-t                       | Chemotherapy    |
| acalectinib                | Targeted therapy|
| ade                        | Chemotherapy    |
| ado trastuzumab            | Targeted therapy|
| afatinib                   | Targeted therapy|
| aldesleukin                | Immunotherapy   |
| alectinib                  | Targeted therapy|
| alemtuzumab                | Targeted therapy|
| aminolevulinic             | Targeted therapy|
| anastrozole                | Endocrine therapy|
| apalutamide                | Endocrine therapy|
| arsenic                    | Chemotherapy    |
| asparaginase erwinia chrysanthemi | Chemotherapy  |
| atezolizumab               | Immunotherapy   |
| avelumab                   | Immunotherapy   |
| axicabtagene               | Targeted therapy|
| axitinib                   | Targeted therapy|
| azacitidine                | Chemotherapy    |
| beacopp                    | Chemotherapy    |
| belinostat                 | Targeted therapy|
| bendamustine               | Chemotherapy    |
| bce                         | Chemotherapy    |
| bevacizumab                | Targeted therapy|
| bexarotene                 | Targeted therapy|
| bicalutamide               | Endocrine therapy|
| binimetinib                | Targeted therapy|
| bleomycin                  | Chemotherapy    |
| blinatumomab               | Immunotherapy   |
| bortezomib                 | Targeted therapy|
| bosutinib                  | Targeted therapy|
| brentuximab                | Targeted therapy|
| brigatinib                 | Targeted therapy|
| bumel                      | Chemotherapy    |
| Treatment                  | Category        |
|---------------------------|----------------|
| busulfan                  | Chemotherapy    |
| cabazitaxel               | Chemotherapy    |
| cabozantinib              | Targeted therapy|
| caf                       | Chemotherapy    |
| calaspargase              | Chemotherapy    |
| capecitabine              | Chemotherapy    |
| caplacizumab              | Targeted therapy|
| capox                     | Chemotherapy    |
| carboplatin               | Chemotherapy    |
| carboplatin-taxol         | Chemotherapy    |
| carfilzomib               | Targeted therapy|
| carmustine                | Chemotherapy    |
| cem                       | Chemotherapy    |
| cemiplimab                | Immunotherapy   |
| ceritinib                 | Targeted therapy|
| cetuximab                 | Targeted therapy|
| cev                       | Chemotherapy    |
| chlorambucil              | Chemotherapy    |
| chlorambucil-prednisone   | Chemotherapy    |
| chop                      | Chemotherapy    |
| cisplatin                 | Chemotherapy    |
| cladribine                | Chemotherapy    |
| clofarabine               | Chemotherapy    |
| cmf                       | Chemotherapy    |
| cobimetinib               | Targeted therapy|
| copanlisib                | Targeted therapy|
| copdac                    | Chemotherapy    |
| copp                      | Chemotherapy    |
| copp-abv                  | Chemotherapy    |
| crizotinib                | Targeted therapy|
| cvp                       | Chemotherapy    |
| cyclophosphamide          | Chemotherapy    |
| cytarabine                | Chemotherapy    |
| cytarabine                | Chemotherapy    |
| dabrafenib                | Targeted therapy|
| dacarbazine               | Chemotherapy    |
| dacomitinib               | Targeted therapy|
| dactinomycin              | Chemotherapy    |
| daratumumab               | Targeted therapy|
| dasatinib                 | Targeted therapy|
| daunorubicin              | Chemotherapy    |
| Drug Name                        | Therapy Type  |
|---------------------------------|---------------|
| daunorubicin cytarabine         | Chemotherapy  |
| decitabine                      | Chemotherapy  |
| degarelix                       | Endocrine therapy |
| denileukin                      | Targeted therapy |
| dinutuximab                     | Targeted therapy |
| docetaxel                       | Chemotherapy  |
| doxorubicin                     | Chemotherapy  |
| doxorubicin lipo                | Chemotherapy  |
| durvalumab                      | Immunotherapy |
| duvelisib                       | Targeted therapy |
| elotuzumab                      | Targeted therapy |
| emapalumab                      | Targeted therapy |
| enasidenib                      | Targeted therapy |
| encorafenib                     | Targeted therapy |
| enzalutamide                    | Endocrine therapy |
| epirubicin                      | Chemotherapy  |
| epoch                           | Chemotherapy  |
| erdafitinib                     | Targeted therapy |
| eribulin                        | Chemotherapy  |
| erlotinib                       | Targeted therapy |
| etoposide                       | Chemotherapy  |
| etoposide                       | Chemotherapy  |
| everolimus                      | Targeted therapy |
| exemestane                      | Endocrine therapy |
| fec                             | Chemotherapy  |
| fludarabine                     | Chemotherapy  |
| fluorouracil inj                | Chemotherapy  |
| fluorouracil top                | Chemotherapy  |
| flutamide                       | Endocrine therapy |
| folfiri                         | Chemotherapy  |
| folfiri-bevacizumab             | Chemotherapy  |
| folfiri-cetuximab               | Chemotherapy  |
| folfirinox                      | Chemotherapy  |
| folfox                           | Chemotherapy  |
| fostamatinib                    | Targeted therapy |
| fu-lv                           | Chemotherapy  |
| fulvestrant                     | Endocrine therapy |
| gefitinib                       | Targeted therapy |
| gemcitabine                     | Chemotherapy  |
| gemcitabine-cisplatin           | Chemotherapy  |
| gemcitabine-oxaliplatin         | Chemotherapy  |
| gemtuzumab                      | Targeted therapy |
| Chemical Name       | Therapy Type          |
|---------------------|-----------------------|
| gilteritinib        | Targeted therapy      |
| glasdegib           | Targeted therapy      |
| goserelin           | Endocrine therapy     |
| hvp                 | Chemotherapy          |
| hydroxyurea         | Chemotherapy          |
| hyper-cvad          | Chemotherapy          |
| ibrutinomab         | Targeted therapy      |
| ibrutinib           | Targeted therapy      |
| ice                 | Chemotherapy          |
| idarubicin          | Chemotherapy          |
| idelalisib          | Targeted therapy      |
| ifosfamide          | Chemotherapy          |
| imatinib            | Targeted therapy      |
| imiquimod           | Targeted therapy      |
| inotuzumab          | Targeted therapy      |
| interferon alfa     | Immunotherapy         |
| interferon alfa-2b  | Immunotherapy         |
| iobenguane i 131    | Targeted therapy      |
| ipilimumab          | Immunotherapy         |
| irinotecan          | Chemotherapy          |
| irinotecan liposome  | Chemotherapy          |
| ivosidenib          | Targeted therapy      |
| ixabepilone         | Chemotherapy          |
| ixazomib            | Targeted therapy      |
| jeb                 | Chemotherapy          |
| lanreotide          | Endocrine therapy     |
| lapatinib           | Targeted therapy      |
| laronatatinib       | Targeted therapy      |
| lenalidomide        | Targeted therapy      |
| lenvatinib          | Targeted therapy      |
| letrozole           | Endocrine therapy     |
| leuprolide          | Endocrine therapy     |
| lomustine           | Chemotherapy          |
| lorlatinib          | Targeted therapy      |
| lu 177-dotatate     | Targeted therapy      |
| lutetium lu 177-dotatate | Targeted therapy     |
| mechlorethamine     | Chemotherapy          |
| melphalan           | Chemotherapy          |
| melphalan           | Chemotherapy          |
| mercaptopurine      | Chemotherapy          |
| methotrexate        | Chemotherapy          |
| midostaurin         | Targeted therapy      |
| Drug                  | Therapy Type         |
|----------------------|----------------------|
| mitomycin c          | Chemotherapy         |
| mitoxantrone         | Chemotherapy         |
| mogamulizumab        | Targeted therapy     |
| moxetumomab          | Targeted therapy     |
| mvac                 | Chemotherapy         |
| necitumumab          | Targeted therapy     |
| nelarabine           | Chemotherapy         |
| neratinib            | Targeted therapy     |
| nilotinib            | Targeted therapy     |
| nilutamide           | Endocrine therapy    |
| niraparib            | Targeted therapy     |
| nivolumab            | Immunotherapy        |
| obinutuzumab         | Targeted therapy     |
| oepa                 | Chemotherapy         |
| ofatumumab           | Targeted therapy     |
| of                           | Chemotherapy         |
| olaparib             | Targeted therapy     |
| olaratumab           | Targeted therapy     |
| omacetaxine          | Targeted therapy     |
| oppa                 | Chemotherapy         |
| osimertinib          | Targeted therapy     |
| oxaliplatin          | Chemotherapy         |
| paclitaxel           | Chemotherapy         |
| paclitaxel nab       | Chemotherapy         |
| pad                  | Chemotherapy         |
| palbociclib          | Targeted therapy     |
| panitumumab          | Targeted therapy     |
| panobinostat         | Targeted therapy     |
| pazopanib            | Targeted therapy     |
| pcv                  | Chemotherapy         |
| peb                  | Chemotherapy         |
| pegaspargase         | Chemotherapy         |
| peginterferon alfa   | Immunotherapy        |
| pembrolizumab        | Immunotherapy        |
| pemetrexed           | Chemotherapy         |
| pertuzumab           | Targeted therapy     |
| pomalidomide         | Targeted therapy     |
| ponatinib            | Targeted therapy     |
| pralatrexate         | Chemotherapy         |
| procarbazine         | Chemotherapy         |
| r-chop               | Chemotherapy         |
| r-cvp                | Chemotherapy         |
| Drug Name                        | Therapy Type       |
|---------------------------------|--------------------|
| r-epoch                         | Chemotherapy       |
| r-ice                           | Chemotherapy       |
| radium 223                      | Targeted therapy   |
| raloxifene                      | Endocrine therapy  |
| ramucirumab                     | Targeted therapy   |
| ravulizumab                     | Targeted therapy   |
| regorafenib                     | Targeted therapy   |
| ribociclib                      | Targeted therapy   |
| rituximab                       | Targeted therapy   |
| rituximab and hyaluronidase     | Targeted therapy   |
| romidepsin                      | Targeted therapy   |
| rucaparib                       | Targeted therapy   |
| ruxolitinib                     | Targeted therapy   |
| siltuximab                      | Targeted therapy   |
| sipuleucel                      | Immunotherapy      |
| sonidegib                       | Targeted therapy   |
| sorafenib                       | Targeted therapy   |
| stanford v                      | Chemotherapy       |
| sunitinib                       | Targeted therapy   |
| tac                             | Chemotherapy       |
| tagraxofusp                     | Targeted therapy   |
| talazoparib                     | Targeted therapy   |
| talimogene                      | Immunotherapy      |
| tamoxifen                       | Endocrine therapy  |
| temozolomide                    | Chemotherapy       |
| temsirolimus                    | Targeted therapy   |
| thalidomide                     | Targeted therapy   |
| thioguanine                     | Chemotherapy       |
| thiotepa                        | Chemotherapy       |
| tisagenlecleucel                | Immunotherapy      |
| topotecan                       | Chemotherapy       |
| toremifene                      | Endocrine therapy  |
| tpf                             | Chemotherapy       |
| trabectedin                     | Chemotherapy       |
| trametinib                      | Targeted therapy   |
| trastuzumab                     | Targeted therapy   |
| trastuzumab and hyaluronidase-   | Targeted therapy   |
| oxyk                            |                   |
| trifluridine and tipiracil      | Chemotherapy       |
| hydrochloride                   | Chemotherapy       |
| vac                             | Chemotherapy       |
| valrubicin                      | Chemotherapy       |

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| Name         | Type            |
|--------------|-----------------|
| vamp         | Chemotherapy    |
| vandetanib   | Targeted therapy|
| veip         | Chemotherapy    |
| vemurafenib  | Targeted therapy|
| venetoclax   | Targeted therapy|
| vinblastine  | Chemotherapy    |
| vincristine  | Chemotherapy    |
| vincristine  | Chemotherapy    |
| vinorelbine  | Chemotherapy    |
| vip          | Chemotherapy    |
| vismodegib   | Targeted therapy|
| vorinostat   | Targeted therapy|
| xeliri       | Chemotherapy    |
| xelox        | Chemotherapy    |
| ziv aflibercept | Targeted therapy |