Supplementary Appendix

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Supplementary Methods

Before conducting the multivariable data analyses to evaluate the primary hypothesis, multiple imputation was performed (with 10 imputations) for the missing values in covariates (not including COVID-19 outcome variables for 30-day mortality or peak disease severity) using additive regression, bootstrapping, and predictive mean matching, where the outcomes were included when imputing covariates. The imputation method took all aspects of uncertainty of the imputations into account by using bootstrap to approximate the process of drawing predicted values from a full Bayesian predictive distribution (see aregImpute in Hmisc package for the details). Of note, the unknow Eastern Cooperative Oncology Group performance status was not treated as missing, and patients with missing outcomes were excluded in the multivariable data analysis.
To reduce the overall imbalance of the confounding variables among the study groups in the non-randomized study we balanced the distribution of covariates between the three study groups using inverse probability treatment weighting (IPTW) with truncation from a multinomial logistic regression model. The covariates balanced between groups are age (as a continuous variable truncated at 90 years due to HIPAA requirements), biologic sex (female; male), race (non-Hispanic White; Hispanic; non-Hispanic Black; other), smoking status (current or former smoker; never smoker), Eastern Cooperative Oncology Group performance status (ECOG PS 0; 1; ≥2), baseline corticosteroid use (none; ≤10mg/day prednisone dose equivalent [PDE]; >10mg/day PDE), lymphopenia (absolute lymphocyte count [ALC], ≤1000 versus >1000 per μL), modified Charlson Comorbidity Index (mCCI, 0; 1; ≥2; Supplementary Table 1), cancer status (active and progressing versus not active and progressing), cancer type (solid organ tumor; hematologic neoplasm; both), and recent systemic anti-cancer therapy (any of cytotoxic chemotherapy, immunotherapy, targeted therapy, or endocrine therapy in the 3 months prior to COVID-19 diagnosis, or not). We controlled the distribution balance of covariates via the probability weights which were obtained from a multinomial logistic regression model and truncated at the lower and upper 2.5th percentiles (i.e., the extremely small and large weights were bounded at the lower and upper 2.5th percentiles). Finally, we applied the generalized linear model - logistic regression method with clinically and biologically pre-determined significant covariates. After the 10-run analyses, i.e., truncated IPTW and logistic regression analysis were sequentially applied in each of the 10 imputed datasets, the reported adjusted odds ratios (AORs) were the average of the results. In addition, we conducted variable selection using the lasso penalty with the optimal lambda that minimized the cross-validated error, which further verified the pre-determined covariates selected.

The secondary endpoints were the rates of ICU admission/MV among cancer patients vaccinated with two and three doses of mRNA vaccines and those unvaccinated, and who developedCOVID-19, following the same analysis procedure as previously stated (Supplementary Table 4).

Several sensitivity analyses were performed for the primary and secondary endpoints: (i) we considered the truncated IPTW with truncations at the lower and upper 2.5th percentile for comparing the three groups after removing the cases with “possible” vaccination status (Supplementary Table 7), (ii) IPTW with truncation at the lower and upper 1st percentile for comparing the three groups (Supplementary Table 8), (iii) IPTW followed by a multivariable logistic regression with the addition of cancer stage as a covariate (Supplementary Table 9), (iv) IPTW followed by a multivariable logistic regression with cluster-robust standard errors to adjust the estimates for the participating institution (Supplementary Table 10), (v) IPTW and multivariable logistic regression comparing the three study groups diagnosed with COVID-19 from October 2021 to March 2022 only (Supplementary Table 11), (vi) IPTW and multivariable logistic regression limited to patients who received three versus two doses of mRNA vaccines (Supplementary Table 12), and (vii) a multivariable logistic regression where IPTW was not used for balancing covariates distributions (supplementary Table 13).

All data analyses were performed by YS, CH and JW using R 4.0.3 and the R packages Hmisc 4.4.2, MatchIt 4.2.0, ipw 1.0-11, survey 4.0, sandwich 3.0-1, and glmnet 4.1-1.

Supplementary Table 1: Modified Charlson Comorbidity Index (mCCI). The mCCI used in this analysis is based on the original CCI, with the following modifications: 1) cancer diagnosis is omitted, similar to the NCI Comorbidity (Klabunde) Index; 2) peptic ulcer disease and hemiplegia are omitted, as these are not routinely collected in the CCC19 survey. As a result, the score can range from 0 to 22.

Characteristic	Original CCI points	Modified CCI points
Myocardial infarct	1	1
Congestive heart failure	1	1
Peripheral vascular disease	1	1
Cerebrovascular disease	1	1
Dementia	1	1
Chronic pulmonary disease	1	1
Connective tissue disease	1	1
Peptic ulcer disease	1	-
Mild liver disease	1	1
Uncomplicated diabetes	1	1
Hemiplegia	2	-
Moderate or severe renal disease	2	2
Diabetes with end organ damage	2	2
Any tumor	2	-
Leukemia	2	-
Lymphoma	2	-
Moderate or severe liver disease	3	3
Metastatic solid tumor	6	-
AIDS	6	6

Supplementary Table 2: Data dictionary used for the analysis
The full CCC19 data dictionary and R code to generate the derived variables is publicly available on GitHub: https://github.com/covidncancer/CCC19_dictionary

Outcome description	Outcome variable name	Outcome values
30-day all-cause mortality (primary outcome measure)	der_dead30	0 = No; 1 = Yes; 99 = Unknown
Ordinal severity of COVID-19	der_ordinal_v1	0 = not hospitalized; 1 = hospitalized; 2 = ICU; 3 = mechanical ventilation; 4 = death within 30 days
Hospitalization (ever)	der_hosp	0 = No; 1 = Yes; 99 = Unknown
ICU or mechanical ventilation (ever)	der_ICU_mv	0 = No; 1 = Yes

Covariate description	Variable name	Possible covariate values
Vaccination status prior to COVID-19 diagnosis[1] (primary stratification variable)	der_vax_count_before	• 0 doses before • 2 mrna doses before, definite • 2 mrna doses before, probable • 2 mrna doses before, possible[2] • 3+ mrna doses before, definite • 3+ mrna doses before, probable • 3+ mrna doses before, possible[2]
Age	der_age_trunc	Integer (ages younger than 18 years are truncated to 18; ages older than 89 years are truncated to 90)
Sex	der_sex	• Male • Female
Race/ethnicity	der_race	• Non-Hispanic White • Hispanic • Non-Hispanic Black • Other
Smoking status	der_smoking2	• Never • Current or Former • Unknown
ECOG performance status	der_ecogcat2	• 0 • 1 • 2+ • Unknown
Baseline steroid use	der_steroids_bl_10	• None • 10 mg prednisone dose-equivalent (PDE) or less per day • More than 10 mg PDE per day • Unknown
Categorical lymphopenia, including whether labs were drawn or not. For this variable, lymphopenia is defined as absolute lymphocyte count <1500/uL	der_lymphopenia	• Not lymphopenic • Lymphopenic • Not drawn/Not available • Unknown
Dichotomized lymphopenia at a threshold of 1000/uL[3]	transformed_alc_v2	• <=1000 • >1000
Modified Charlson comorbidity index[4]	der_ccc19cci_v4	• 0 • 1 • 2+
Cancer active and progressing at the time of COVID-19 diagnosis	der_cancer_prog_bl	0 = No; 1 = Yes; 99 = Unknown
Cancer type	der_cancer_type	• Solid organ tumor • Hematologic neoplasm • Both
Any systemic anti-cancer therapy (cytotoxic chemotherapy, immunotherapy, targeted therapy, and/or endocrine therapy) in the 3 months prior to COVID-19 diagnosis	der_any_systemic_3mo	0 = No; 1 = Yes; 99 = Unknown
Year of COVID-19 diagnosis	dx_year	2020; 2021; 2022
Estimated quarter of COVID-19 diagnosis using the midpoint of the diagnostic interval	der_quarter_mid_dx	Q1 2020; Q2 2020; Q3 2020; Q4 2020; Q1 2021; Q2 2021; Q3 2021; Q4 2021; Q1 2022
Earliest date that COVID-19 could have been diagnosed	meta_lefttime_lb	POSIXlt date, e.g., "2020-01-01 12:00:00 CDT"
Latest date that COVID-19 could have been diagnosed	meta_lefttime_ub	POSIXlt date, e.g., "2020-12-31 12:00:00 CDT"

[1]Due to the phrasing of the vaccination variable "sars_vax" in the CCC19 survey, it is possible that a respondent could misinterpret the variable and report vaccine doses received both before and after the COVID-19 diagnosis. To ameliorate this possibility, additional variables were added specifically asking whether all doses were received before the COVID-19 diagnosis, but these new variables are incompletely

filled. In order to address the uncertainty, vaccination before COVID-19 status is ascertained as “definite”, “probable”, and “possible” based on the timing of the report relative to the diagnosis of COVID-19, as well as whether the additional specific variables are filled.
Definite cases are defined as those for which patients have been directly determined to have received all mRNA vaccines (i.e. 2 or 3 doses, depending on each patient) before COVID-19 diagnosis.
Probable cases are defined among patients who have not been directly determined to have received all mRNA vaccines (i.e. 2 or 3 doses, depending on each patient), based on vaccination status (i.e. 2 or 3 doses of mRNA vaccines), as (1) those for which patients have developed COVID-19 at least 30 days (for 2 doses of mRNA vaccines) or 180 days (for 3 doses of mRNA vaccines) after the first vaccine dose (i.e. 30 and 180 days representing the normal intervals measured since the date of administration of the first dose of a mRNA vaccine, during which a patient is expected to have received the second and third dose of mRNA vaccine, respectively), or (2) which have developed COVID-19 recently (i.e. within the past 8 weeks) in relation to the time at which (a) the patient was reported to the CCC19 registry and (b) was indicated to have already received all mRNA vaccines (i.e. 2 or 3 doses, depending on each patient).
Possible cases are defined among patients who have received 2 or 3 doses of mRNA, but did not meet the defining criteria for definite or probable cases.
[2]Cases assigned this status are flagged for site queries; a sensitivity analysis excluding these categories is also reported.
[3]Numeric absolute lymphocyte count is optionally collected if the category value provided in the survey item *alc_range* is High or Low; after additional transformations to account for outliers and incorrect units, numeric values of 1000/uL or less are assigned to the “<=1000” category; numeric values of greater than 1000/uL and/or categorical *der_lymphopenia* = “Not lymphopenic” are assigned to the “>1000” category.
[4]This integer-based score is calculated using the point system from the original Charlson comorbidity index with modifications as described in **Supplementary Table 1**.

Supplementary Table 3: Inclusion and exclusion criteria. Data used in this analysis was downloaded from the CCC19 REDCap registry on 2022-06-02 at 19:56 CT .

Criteria	Difference	Total
Starting number of cases in the CCC19 registry		17,558
Screen failures	-214	17,344
Short form cases[a]	-940	16,404
Passed screening but case never started	-832	15,572
Case started but not completed	-478	15,094
Manual exclusions[b]	-377	14,717
Case started prior to 2022-05-31 23:59 CT	-6	14,711
Cases with a calculable value for der_vax_before	-915	13,796
Require a diagnosis of COVID-19 in 2021or 2022	-10,573	3223
Remove non-mRNA, other, and unknown vaccines	-168	3055
Exclude cases with quality score of 5+	-69	2986
Exclude cases with unknown 30-day all-cause mortality	-3	2983
Require laboratory confirmation of SARS-CoV-2[c]	-49	2934
Missing quarter time	-4	2930
Remove vaccinated after COVID-19, “partially” vaccinated, unknown vaccine timing	-44	2486
Final total		**2486**

[a]Short form cases have limited details and are not used in analyses
[b]Reasons for manual exclusion include identification of duplicated records; non-eligible cases (*in situ* solid malignancies, non-invasive non-melanoma skin cancers, precursor hematologic conditions, and benign hematologic conditions), and false-positive SARS-CoV-2 tests.
[c]Laboratory confirmation includes PCR testing, antigen testing, and serology (antibodies to SARS-CoV-2)

Supplementary Table 4: Standardized mean differences before and after inverse probability treatment weighting (IPTW) of all included variables

Characteristics	SMD (pre-IPTW)	SMD (post-IPTW)
Age	0.179	0.027
Sex	0.041	0.034
Race	0.258	0.058
Smoking status	0.077	0.017
ECOG Performance Status	0.273	0.057
Baseline corticosteroids	0.092	0.023
Lymphopenia <1000/uL	0.103	0.024
Modified Charlson Comorbidity Index	0.081	0.023
Cancer status	0.056	0.005
Cancer type	0.263	0.048
Recent systemic anti-cancer therapy	0.191	0.052

Abbreviations: ECOG: Eastern Cooperative Oncology Group

Supplementary Table 5: Distribution of patients with cancer in each of the three cohorts analyzed (i.e. unvaccinated, 2 and 3 doses of mRNA vaccines) according to the categories of solid and hematological malignancies.

	Unvaccinated (n= 1537)	**2 doses of mRNA vaccines (n=564)**	**3 doses of mRNA vaccines (n=385)**
Type of malignancy			
Breast	282 (18%)	101 (18%)	82 (21%)
GI	211 (14%)	70 (12%)	42 (11%)
Gynecological or GU	305 (20%)	105 (19%)	54 (14%)
Thoracic	160 (10%)	64 (11%)	23 (6%)
Other solid	241 (16%)	59 (10%)	32 (8%)
Myeloid	74 (5%)	28 (5%)	33 (9%)
Lymphoid	260 (17%)	135 (24%)	114 (30%)
Other hematologic	<5 (0%)	<5 (0%)	5 (1%)

Abbreviations: GI: gastrointestinal; GU: genitourinary

Supplementary Table 6: Results of multivariable logistic regression analysis for the primary endpoint of 30-day mortality, and the secondary endpoints of ICU admission and/or MV, and hospitalization.

Characteristics	30-day mortality Multivariable AOR (95% CI) (n=2486)	ICU admission and/or MV Multivariable AOR (95% CI) (n=2418)	Hospitalization Multivariable AOR (95%CI) (n=2476)
Vaccination Status (ref = Unvaccinated)			
Two doses of mRNA vaccines	0.62 (0.44-0.88)	0.60 (0.45-0.82)	0.60 (0.48-0.75)
Three doses of mRNA vaccines	0.20 (0.11-0.36)	0.37 (0.24-0.58)	0.35 (0.26-0.46)
Age (per 10 years increase)	1.48 (1.30-1.68)	1.20 (1.09-1.33)	1.34 (1.24-1.45)
Sex (ref = Female)			
Male	1.33 (0.98-1.80)	1.36 (1.05-1.76)	1.20 (0.99-1.45)
Cancer status active and progressing (ref = not active and progressing)			
Active and progressing	4.85 (3.40-6.93)	1.55 (1.11-2.18)	2.15 (1.60-2.88)
Modified Charlson Comorbidity Index (ref = 0)			
1	1.16 (0.78-1.71)	1.13 (0.81-1.57)	1.60 (1.26-2.02)
≥2	1.20 (0.83-1.73)	1.36 (0.99-1.86)	2.45 (1.91-3.15)
ECOG Performance Status (ref = 0)			
1	1.59 (0.97-2.59)	1.59 (1.11-2.28)	1.45 (1.14-1.83)
≥2	3.86 (2.35-6.35)	2.29 (1.48-3.53)	3.31 (2.35-4.67)
Unknown or missing	1.92 (1.17-3.14)	1.65 (1.13-2.41)	1.71 (1.33-2.20)
Baseline corticosteroids (ref = none)			
≤ 10mg/day PDE	1.91 (1.12-3.25)	1.58 (0.97-2.56)	1.36 (0.92-2.01)
> 10mg/day PDE	1.17 (0.70-1.96)	1.18 (0.76-1.86)	1.51 (1.06-2.14)
Lymphopenia <1000/uL (ref = ≥1000/uL)			
Yes	1.33 (0.97-1.82)	1.65 (1.25-2.17)	1.67 (1.34-2.09)
Cancer type (ref = Solid)			
Hematologic	1.22 (0.84-1.78)	1.82 (1.35-2.44)	1.72 (1.37-2.17)
Both	1.30 (0.65-2.60)	1.83 (1.05-3.21)	1.46 (0.90-2.38)
Race (ref = non-Hispanic White)			
Non-Hispanic Black	1.10 (0.75-1.63)	1.36 (0.98-1.90)	1.47 (1.12-1.92)
Hispanic	1.27 (0.76-2.14)	1.61 (1.06-2.44)	1.33 (0.95-1.88)
Other	0.77 (0.44-1.36)	1.34 (0.87-2.08)	1.06 (0.76-1.47)
Smoking status (ref = non-smoker)			
Current or former smoker	1.01 (0.74-1.38)	1.20 (0.92-1.55)	1.16 (0.96-1.40)
Recent systemic anti-cancer therapy (ref = No)			
Yes	1.04 (0.74-1.44)	0.93 (0.71-1.24)	1.08 (0.88-1.34)

Abbreviations: AOR: Adjusted Odds Ratio, CI: confidence interval; ECOG: Eastern Cooperative Oncology Group; PDE: prednisone dose equivalent; ref: reference.

Supplementary Table 7: Results of the sensitivity analysis using a multivariable logistic regression model with IPTW truncated at the lower and upper 2.5th percentiles, after removing cases with "possible" vaccination status, for the primary endpoint of 30-day mortality and the secondary endpoints of ICU admission and/or MV, and hospitalization.

Characteristics	30-day mortality Multivariable AOR (95% CI) (n=2365)	ICU admission and/or MV Multivariable AOR (95% CI) (n=2298)	Hospitalization Multivariable AOR (95%CI) (n=2355)
Vaccination Status (ref = Unvaccinated)			
Two doses of mRNA vaccines	0.59 (0.40-0.87)	0.60 (0.44-0.83)	0.58 (0.47-0.73)
Three doses of mRNA vaccines	0.20 (0.11-0.37)	0.39 (0.25-0.61)	0.34 (0.25-0.45)
Age (per 10 years increase)	1.47 (1.29-1.67)	1.20 (1.08-1.34)	1.35 (1.24-1.46)
Sex (ref = Female)			
Male	1.35 (0.99-1.84)	1.37 (1.05-1.78)	1.20 (0.99-1.47)
Cancer status active and progressing (ref = not active and progressing)			
Active and progressing	4.89 (3.42-6.99)	1.62 (1.15-2.29)	2.14 (1.59-2.88)
Modified Charlson Comorbidity Index (ref = 0)			
1	1.15 (0.78-1.72)	1.13 (0.80-1.59)	1.49 (1.17-1.89)
≥2	1.13 (0.78-1.65)	1.44 (1.04-1.99)	2.37 (1.83-3.06)
ECOG Performance Status (ref = 0)			
1	1.58 (0.96-2.60)	1.51 (1.05-2.17)	1.49 (1.17-1.89)
≥2	3.90 (2.36-6.46)	2.02 (1.30-3.15)	3.41 (2.40-4.83)
Unknown or missing	1.85 (1.12-3.07)	1.53 (1.04-2.27)	1.80 (1.39-2.34)
Baseline corticosteroids (ref = none)			
≤ 10mg/day PDE	1.83 (1.06-3.17)	1.53 (0.93-2.52)	1.36 (0.92-2.02)
> 10mg/day PDE	1.24 (0.74-2.07)	1.27 (0.81-1.99)	1.44 (1.01-2.04)
Lymphopenia <1000/uL (ref = ≥1000/uL)			
Yes	1.43 (1.04-1.97)	1.71 (1.29-2.28)	1.64 (1.31-2.05)
Cancer type (ref = Solid)			
Hematologic	1.21 (0.83-1.78)	1.80 (1.33-2.44)	1.75 (1.38-2.22)
Both	1.17 (0.56-2.41)	1.88 (1.07-3.30)	1.63 (0.99-2.67)
Race (ref = non-Hispanic White)			
Non-Hispanic Black	1.17 (0.79-1.74)	1.38 (0.98-1.95)	1.55 (1.17-2.05)
Hispanic	1.27 (0.75-2.16)	1.58 (1.03-2.42)	1.39 (0.98-1.96)
Other	0.84 (0.47-1.49)	1.45 (0.93-2.25)	1.05 (0.75-1.47)
Smoking status (ref = non-smoker)			
Current or former smoker	1.06 (0.77-1.46)	1.22 (0.93-1.59)	1.19 (0.98-1.44)
Recent systemic anti-cancer therapy (ref = No)			
Yes	1.00 (0.71-1.40)	0.96 (0.72-1.28)	1.14 (0.92-1.41)

Abbreviations: AOR: Adjusted Odds Ratio, CI: confidence interval; ECOG: Eastern Cooperative Oncology Group; PDE: prednisone dose equivalent; ref: reference.

Supplementary Table 8: Results of the sensitivity analysis using a multivariable logistic regression model with IPTW truncated at the lower and upper 1st percentiles, for the primary endpoint of 30-day mortality and the secondary endpoints of ICU admission and/or MV, and hospitalization.

Characteristics	30-day mortality Multivariable AOR (95% CI) (n=2486)	ICU admission and/or MV Multivariable AOR (95% CI) (n=2418)	Hospitalization Multivariable AOR (95%CI) (n=2476)
Vaccination Status (ref = Unvaccinated)			
Two doses of mRNA vaccines	0.62 (0.43-0.88)	0.60 (0.44-0.81)	0.60 (0.48-0.75)
Three doses of mRNA vaccines	0.18 (0.10-0.34)	0.37 (0.23-0.59)	0.33 (0.25-0.45)
Age (per 10 years increase)	1.48 (1.31-1.69)	1.20 (1.08-1.33)	1.34 (1.24-1.45)
Sex (ref = Female)			
Male	1.32 (0.98-1.80)	1.35 (1.04-1.76)	1.20 (0.99-1.46)
Cancer status active and progressing (ref = not active and progressing)			
Active and progressing	4.86 (3.40-6.94)	1.56 (1.11-2.21)	2.16 (1.60-2.92)
Modified Charlson Comorbidity Index (ref = 0)			
1	1.14 (0.77-1.69)	1.12 (0.80-1.56)	1.62 (1.28-2.05)
≥2	1.19 (0.82-1.71)	1.36 (0.99-1.87)	2.47 (1.91-3.18)
ECOG Performance Status (ref = 0)			
1	1.57 (0.96-2.57)	1.58 (1.10-2.26)	1.44 (1.14-1.83)
≥2	3.82 (2.32-6.30)	2.28 (1.48-3.53)	3.28 (2.32-4.64)
Unknown or missing	1.89 (1.15-3.10)	1.67 (1.13-2.46)	1.69 (1.31-2.18)
Baseline corticosteroids (ref = none)			
≤ 10mg/day PDE	1.96 (1.14-3.36)	1.60 (0.98-2.61)	1.38 (0.93-2.04)
> 10mg/day PDE	1.17 (0.70-1.96)	1.18 (0.75-1.85)	1.51 (1.06-2.14)
Lymphopenia <1000/uL (ref = ≥1000/uL)			
Yes	1.33 (0.97-1.82)	1.66 (1.26-2.19)	1.66 (1.33-2.08)
Cancer type (ref = Solid)			
Hematologic	1.23 (0.84-1.79)	1.85 (1.37-2.49)	1.73 (1.37-2.18)
Both	1.34 (0.66-2.70)	1.86 (1.06-3.28)	1.47 (0.90-2.40)
Race (ref = non-Hispanic White)			
Non-Hispanic Black	1.09 (0.74-1.61)	1.33 (0.95-1.86)	1.42 (1.08-1.87)
Hispanic	1.27 (0.76-2.12)	1.60 (1.05-2.42)	1.33 (0.94-1.88)
Other	0.77 (0.44-1.35)	1.37 (0.87-2.15)	1.04 (0.75-1.44)
Smoking status (ref = non-smoker)			
Current or former smoker	1.02 (0.74-1.39)	1.21 (0.93-1.57)	1.15 (0.95-1.40)
Recent systemic anti-cancer therapy (ref = No)			
Yes	1.04 (0.75-1.45)	0.95 (0.71-1.26)	1.09 (0.88-1.35)

Abbreviations: AOR: Adjusted Odds Ratio, CI: confidence interval; ECOG: Eastern Cooperative Oncology Group; PDE: prednisone dose equivalent; ref: reference.

Supplementary Table 9: Results of multivariable binary logistic regression analysis using IPTW for comparing three study groups diagnosed with COVID-19, where cancer stage was included in the models for the primary endpoint of 30-day mortality, and the secondary endpoints of ICU admission and/or MV, and hospitalization.

Characteristics	**30-day mortality Multivariable AOR (95% CI) (n=2486)**	**ICU admission and/or MV Multivariable AOR (95% CI) (n=2418)**	**Hospitalization Multivariable AOR (95%CI) (n=2476)**
Vaccination Status (ref = Unvaccinated)			
Two doses of mRNA vaccines	0.62 (0.43-0.88)	0.60 (0.44-0.81)	0.60 (0.48-0.74)
Three doses of mRNA vaccines	0.19 (0.10-0.36)	0.37 (0.24-0.58)	0.35 (0.26-0.46)
Age (per 10 years increase)	1.49 (1.31-1.69)	1.20 (1.09-1.33)	1.34 (1.24-1.45)
Sex (ref = Female)			
Male	1.34 (0.99-1.81)	1.36 (1.05-1.77)	1.19 (0.98-1.44)
Cancer status active and progressing (ref = not active and progressing)			
Active and progressing	4.93 (3.46-7.02)	1.60 (1.12-2.27)	2.16 (1.61-2.89)
Cancer stage (ref = Localized disease)			
Disseminated	1.22 (0.82-1.79)	1.03 (0.74-1.42)	1.24 (0.97-1.58)
Unknown	1.08 (0.67-1.74)	1.47 (1.01-2.16)	1.19 (0.89-1.61)
Modified Charlson Comorbidity Index (ref = 0)			
1	1.14 (0.77-1.68)	1.13 (0.81-1.57)	1.59 (1.26-2.01)
≥2	1.20 (0.83-1.73)	1.37 (1.00-1.89)	2.48 (1.92-3.19)
ECOG Performance Status (ref = 0)			
1	1.54 (0.94-2.53)	1.59 (1.11-2.28)	1.44 (1.14-1.82)
≥2	3.69 (2.22-6.13)	2.20 (1.42-3.41)	3.16 (2.24-4.46)
Unknown or missing	1.91 (1.16-3.13)	1.55 (1.06-2.28)	1.67 (1.30-2.15)
Baseline corticosteroids (ref = none)			
≤ 10mg/day PDE	1.83 (1.05-3.19)	1.49 (0.93-2.38)	1.32 (0.90-1.93)
> 10mg/day PDE	1.12 (0.66-1.89)	1.17 (0.73-1.86)	1.45 (1.02-2.07)
Lymphopenia <1000/uL (ref = ≥1000/uL)			
Yes	1.30 (0.94-1.80)	1.57 (1.20-2.07)	1.64 (1.29-2.08)
Cancer type (ref = Solid)			
Hematologic	1.16 (0.76-1.75)	1.78 (1.29-2.45)	1.56 (1.21-2.00)
Both	1.26 (0.63-2.51)	1.79 (1.01-3.17)	1.39 (0.85-2.28)
Race (ref = non-Hispanic White)			
Non-Hispanic Black	1.29 (0.77-2.16)	1.65 (1.08-2.50)	1.30 (0.93-1.83)
Hispanic	1.11 (0.75-1.64)	1.37 (0.98-1.91)	1.48 (1.14-1.93)
Other	0.75 (0.42-1.33)	1.36 (0.88-2.11)	1.07 (0.76-1.51)
Smoking status (ref = non-smoker)			
Current or former smoker	1.04 (0.76-1.44)	1.22 (0.94-1.59)	1.18 (0.98-1.43)
Recent systemic anti-cancer therapy (ref = No)			
Yes	1.02 (0.73-1.43)	0.98 (0.74-1.30)	1.07 (0.86-1.32)

Abbreviations: AOR: Adjusted Odds Ratio, CI: confidence interval; ECOG: Eastern Cooperative Oncology Group; PDE: prednisone dose equivalent; ref: reference.

Supplementary Table 10: Results of multivariable binary logistic regression analysis using IPTW truncated at the lower and upper 2.5th percentiles for comparing three study groups diagnosed with COVID-19, where cluster-robust standard errors were implemented to adjust the estimates for the participating institution (sensitivity analysis).

Characteristics	30-day mortality Multivariable AOR (95% CI) (n=2486)	ICU admission and/or MV Multivariable AOR (95% CI) (n=2418)	Hospitalization Multivariable AOR (95%CI) (n=2476)
Vaccination Status (ref = Unvaccinated)			
Two doses of mRNA vaccines	0.62 (0.46-0.84)	0.60 (0.44-0.84)	0.60 (0.46-0.78)
Three doses of mRNA vaccines	0.20 (0.12-0.33)	0.37 (0.24-0.56)	0.35 (0.24-0.49)
Age (per 10 years increase)	1.48 (1.27-1.72)	1.20 (1.07-1.35)	1.34 (1.23-1.46)
Sex (ref = Female)			
Male	1.33 (1.04-1.70)	1.36 (0.99-1.86)	1.20 (1.04-1.39)
Cancer status active and progressing (ref = not active and progressing)			
Active and progressing	4.85 (3.22-7.30)	1.55 (1.09-2.22)	2.15 (1.55-2.98)
Modified Charlson Comorbidity Index (ref = 0)			
1	1.16 (0.90-1.49)	1.13 (0.84-1.52)	1.60 (1.23-2.08)
≥2	1.20 (0.89-1.62)	1.36 (1.03-1.78)	2.45 (1.92-3.13)
ECOG Performance Status (ref = 0)			
1	1.59 (0.82-3.09)	1.59 (1.03-2.44)	1.45 (1.13-1.84)
≥2	3.86 (2.25-6.64)	2.29 (1.37-3.83)	3.31 (2.21-4.96)
Unknown or missing	1.92 (0.90-4.06)	1.65 (1.01-2.68)	1.71 (1.20-2.45)
Baseline corticosteroids (ref = none)			
≤ 10mg/day PDE	1.91 (1.22-2.98)	1.58 (0.93-2.67)	1.36 (0.93-1.99)
> 10mg/day PDE	1.17 (0.73-1.88)	1.18 (0.86-1.64)	1.51 (1.04-2.19)
Lymphopenia <1000/uL (ref = ≥1000/uL)			
Yes	1.33 (1.00-1.76)	1.65 (1.30-2.09)	1.67 (1.28-2.18)
Cancer type (ref = Solid)			
Hematologic	1.22 (0.85-1.77)	1.82 (1.43-2.31)	1.72 (1.24-2.38)
Both	1.30 (0.71-2.38)	1.83 (1.02-3.30)	1.46 (0.99-2.16)
Race (ref = non-Hispanic White)			
Non-Hispanic Black	1.10 (0.70-1.73)	1.36 (0.98-1.90)	1.47 (1.17-1.85)
Hispanic	1.27 (0.79-2.05)	1.61 (0.97-2.67)	1.33 (0.83-2.14)
Other	0.77 (0.43-1.40)	1.34 (0.88-2.06)	1.06 (0.73-1.53)
Smoking status (ref = non-smoker)			
Current or former smoker	1.01 (0.79-1.30)	1.20 (0.94-1.52)	1.16 (0.97-1.38)
Recent systemic anti-cancer therapy (ref = No)			
Yes	1.04 (0.74-1.45)	0.93 (0.73-1.20)	1.08 (0.86-1.36)

Abbreviations: AOR: Adjusted Odds Ratio, CI: confidence interval; ECOG: Eastern Cooperative Oncology Group; PDE: prednisone dose equivalent; ref: reference.

Supplementary Table 11: Results of multivariable binary logistic regression analysis using IPTW for comparing three study groups diagnosed with COVID-19 from October 2021 to March 2022 only, for the primary endpoint of 30-day mortality, and the secondary endpoints of ICU admission and/or MV, and hospitalization (sensitivity analysis).

Characteristics	**30-day mortality Multivariable AOR (95% CI) (n=1007)**	**ICU admission and/or MV Multivariable AOR (95% CI) (n=999)**	**Hospitalization Multivariable AOR (95%CI) (n=1007)**
Vaccination Status (ref = Unvaccinated)			
Two doses of mRNA vaccines	0.63 (0.33-1.22)	0.73 (0.42-1.27)	0.62 (0.43-0.92)
Three doses of mRNA vaccines	0.37 (0.17-0.81)	0.57 (0.31-1.04)	0.45 (0.31-0.67)
Age (per 10 years increase)	1.51 (1.20-1.90)	1.30 (1.09-1.55)	1.53 (1.34-1.74)
Sex (ref = Female)			
Male	1.64 (0.91-2.94)	1.24 (0.76-2.01)	1.04 (0.77-1.41)
Cancer status active and progressing (ref = not active and progressing)			
Active and progressing	4.53 (2.29-8.95)	1.76 (0.97-3.20)	1.88 (1.25-2.83)
ECOG Performance Status (ref = 0)			
1	0.91 (0.36-2.29)	1.89 (0.93-3.85)	1.85 (1.29-2.66)
≥2	2.77 (1.11-6.87)	3.91 (1.83-8.35)	3.35 (2.02-5.57)
Unknown or missing	1.24 (0.43-3.52)	2.84 (1.29-6.23)	1.75 (1.15-2.66)

Abbreviations: AOR: Adjusted Odds Ratio, CI: confidence interval; ECOG: Eastern Cooperative Oncology Group; ref: reference.

Supplementary Table 12: Results of multivariable binary logistic regression analysis using IPTW truncated at the lower and upper 2.5th percentiles for comparing three study groups diagnosed with COVID-19, where only patients who received 3 doses or 2 doses were included and compared (sensitivity analysis).

Characteristics	30-day mortality Multivariable AOR (95% CI) (n=949)	ICU admission and/or MV Multivariable AOR (95% CI) (n=943)	Hospitalization Multivariable AOR (95%CI) (n=949)
Vaccination Status (ref = Two doses of mRNA vaccines)			
Three doses of mRNA vaccines	0.38 (0.20-0.71)	0.63 (0.39-1.03)	0.58 (0.43-0.79)
Age (per 10 years increase)	1.20 (0.96-1.50)	1.25 (1.02-1.53)	1.38 (1.21-1.58)
Sex (ref = Female)			
Male	2.08 (1.20-3.61)	1.65 (1.04-2.62)	1.25 (0.92-1.69)
Cancer status active and progressing (ref = not active and progressing)			
Active and progressing	4.02 (2.11-7.67)	1.76 (0.96-3.25)	2.23 (1.42-3.51)
Modified Charlson Comorbidity Index (ref = 0)			
1	2.14 (1.02-4.48)	1.50 (0.84-2.66)	1.71 (1.17-2.48)
≥2	2.55 (1.31-4.96)	1.61 (0.91-2.86)	2.95 (2.01-4.34)
ECOG Performance Status (ref = 0)			
1	1.27 (0.49-3.32)	1.78 (0.92-3.46)	1.96 (1.35-2.85)
≥2	4.06 (1.61-10.26)	2.52 (1.18-5.39)	3.73 (2.29-6.08)
Unknown or missing	1.79 (0.70-4.61)	1.53 (0.71-3.30)	1.53 (1.00-2.35)

Abbreviations: AOR: Adjusted Odds Ratio, CI: confidence interval; ECOG: Eastern Cooperative Oncology Group; PDE: prednisone dose equivalent; ref: reference.

Supplementary Table 13: Results of multivariable logistic regression analysis for comparing three study groups diagnosed with COVID-19, where IPTW was not used for balancing covariates distributions, for the primary and secondary endpoints.

Characteristics	30-day mortality Multivariable AOR (95% CI) (n=2486)	ICU admission and/or MV Multivariable AOR (95% CI) (n=2418)	Hospitalization Multivariable AOR (95%CI) (n=2476)
Vaccination Status (ref = Unvaccinated)			
Two doses of mRNA vaccines	0.60 (0.42-0.85)	0.61 (0.45-0.83)	0.61 (0.49-0.75)
Three doses of mRNA vaccines	0.25 (0.14-0.44)	0.42 (0.28-0.63)	0.37 (0.28-0.48)
Age (per 10 years increase)	1.43 (1.27-1.62)	1.21 (1.09-1.34)	1.33 (1.23-1.43)
Sex (ref = Female)			
Male	1.37 (1.03-1.84)	1.36 (1.06-1.74)	1.19 (0.99-1.43)
Cancer status active and progressing (ref = not active and progressing)			
Active and progressing	4.64 (3.30-6.51)	1.54 (1.11-2.13)	2.04 (1.54-2.70)
Modified Charlson Comorbidity Index (ref = 0)			
1	1.26 (0.86-1.83)	1.24 (0.90-1.72)	1.63 (1.30-2.03)
≥2	1.38 (0.97-1.97)	1.47 (1.08-1.99)	2.48 (1.95-3.16)
ECOG Performance Status (ref = 0)			
1	1.70 (1.06-2.73)	1.61 (1.14-2.28)	1.42 (1.13-1.79)
≥2	4.16 (2.58-6.71)	2.32 (1.54-3.51)	3.36 (2.42-4.66)
Unknown or missing	1.93 (1.19-3.13)	1.63 (1.12-2.35)	1.73 (1.36-2.22)
Baseline corticosteroids (ref = none)			
≤ 10mg/day PDE	1.66 (0.99-2.79)	1.41 (0.89-2.23)	1.26 (0.87-1.83)
> 10mg/day PDE	1.08 (0.66-1.75)	1.17 (0.76-1.79)	1.49 (1.06-2.09)
Lymphopenia <1000/uL (ref = ≥1000/uL)			
Yes	1.40 (1.03-1.89)	1.68 (1.29-2.18)	1.63 (1.31-2.04)
Cancer type (ref = Solid)			
Hematologic	1.14 (0.79-1.63)	1.74 (1.31-2.31)	1.77 (1.41-2.21)
Both	1.43 (0.73-2.82)	2.00 (1.16-3.44)	1.59 (1.01-2.50)
Race (ref = non-Hispanic White)			
Non-Hispanic Black	1.06 (0.72-1.56)	1.35 (0.97-1.88)	1.48 (1.15-1.92)
Hispanic	1.16 (0.70-1.91)	1.60 (1.07-2.39)	1.40 (1.00-1.96)
Other	0.80 (0.46-1.40)	1.31 (0.86-1.99)	1.06 (0.77-1.47)
Smoking status (ref = non-smoker)			
Current or former smoker	0.96 (0.71-1.31)	1.11 (0.86-1.43)	1.16 (0.96-1.39)
Recent systemic anti-cancer therapy (ref = No)			
Yes	1.06 (0.77-1.46)	0.92 (0.70-1.20)	1.11 (0.91-1.36)

Abbreviations: AOR: Adjusted Odds Ratio, CI: confidence interval; ECOG: Eastern Cooperative Oncology Group; PDE: prednisone dose equivalent; ref: reference.

Supplementary Table 14: Non-adjusted odds ratios and associated p-values for vaccination status subgroups in relation to primary endpoint of 30-day mortality and the secondary endpoints of ICU/MV and hospitalization.

Vaccination Status (ref = Unvaccinated)	**30-day mortality**		**ICU admission and/or MV**		**Hospitalization**	
	OR (95%CI)	p-value	OR (95%CI)	p-value	OR (95%CI)	p-value
Two doses of mRNA vaccines	0.77 (0.56-1.06)	0.11	0.70 (0.52-0.93)	0.015	0.76 (0.63-0.92)	0.0062
Three doses of mRNA vaccines	0.33 (0.20-0.55)	< 0.0001	0.47 (0.32-0.69)	< 0.0001	0.46 (0.37-0.58)	< 0.0001

Abbreviations: OR: Odds Ratio, CI: confidence interval; ref: reference.