

EARLY OUTCOMES OF SARS-COV-2 INFECTION IN A LONGITUDINAL PROSPECTIVE COHORT OF VETERANS

CSP #2028

Epidemiology, Immunology, and Clinical Characteristics of COVID-19 (EPIC³) within the Veterans Health Administration



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INTRODUCTION

- More than 770,000 SARS-CoV-2 infections have occurred among users of the Veterans Health Administration (VHA), and more than 23,000 of those infections have resulted in death.¹
- Veterans continue to be hospitalized with COVID-19 despite the development of highly effective COVID-19 vaccines and widespread use in the VHA.²
- The EPIC³ study within the VHA aims to describe the epidemiology and natural history of SARS-CoV-2 among Veterans and to longitudinally characterize host and viral factors associated with severity of infection and the development of immunity.
- **Study objective:** Examine the relationships of demographic characteristics, Charlson Comorbidity Index (CCI), COVID-19 vaccination, and calendar period of enrollment with maximum illness severity, cumulative length of hospitalization, and rehospitalization within 60 days of study entry among Veterans.

METHODS

SAMPLE

- Ongoing, prospective longitudinal cohort study of Veterans ages ≥18
- Eligibility includes Veterans tested for SARS-CoV-2 at 15 Department of Veterans Affairs medical centers between February 2021 and June 18, 2022.
- Study procedures included data collection via questionnaires and biospecimens at in-person or remote visits on days 0, 3, 7, 14, 21, and 28 after enrollment.

EXPOSURES AND OUTCOMES

- Exposure definitions
 - *SARS-CoV-2 positive or negative:* based on the PCR results associated with enrollment eligibility
 - *Fully vaccinated:* received two doses of the Pfizer-BioNTech or Moderna/mRNA-1273 vaccines or one dose of the Johnson and Johnson (Janssen) vaccine at least 14 days prior to enrollment
 - *Charlson Comorbidity Index (CCI):* from two years preceding enrollment
- Outcome definitions calculated over 60 days following study entry
 - *Illness severity:* maximum severity according to four-category VA Severity Index for COVID (mild, moderate, severe, or death)³
 - *Hospitalization duration:* total days spent in hospital
 - *Rehospitalization:* discharged and subsequently readmitted

STATISTICAL ANALYSIS

- Multivariable regression models (unadjusted and adjusted for covariates)
 - Multinomial logistic models for severity
 - Negative binomial models for duration of hospital stay
 - Cox proportional hazards models for rehospitalization

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TABLE 1

ASSOCIATIONS OF SELECTED COVARIATES AND ILLNESS SEVERITY AMONG SARS-COV-2 POSITIVE INPATIENTS

COVARIATE	LEVEL	MODERATE (<i>n</i> = 199)		SEVERE (<i>n</i> = 52)		DEATH (<i>n</i> = 20)	
		ODDS RATIO	95% CI	ODDS RATIO	95% CI	ODDS RATIO	95% CI
Vaccination status	Vaccinated	0.34	(0.12, 0.96)	0.68	(0.20, 2.30)	0.64	(0.14, 2.97)
Age		1.06	(0.77, 1.46)	1.02	(0.70, 1.50)	1.71	(0.98, 2.98)
Sex	Male	4.07	(1.30, 12.81)	1.02	(0.29, 3.53)	—	(0.00, Inf)
Charlson Index (CCI)		1.19	(0.99, 1.44)	1.26	(1.03, 1.54)	1.28	(1.02, 1.62)
Calendar period	June 2021–Nov. 2021	1.93	(0.68, 5.47)	0.88	(0.27, 2.89)	1.47	(0.28, 7.81)
Calendar period	After Nov. 2021	1.94	(0.60, 6.33)	0.74	(0.19, 2.87)	1.77	(0.30, 10.53)

Note: Age estimates are for a change in age of 10 years. Reference levels are: SARS-CoV-2 positive without full vaccination; female; Feb 2021–June 2021 calendar period. Illness severity reference group is mild illness (*n* = 30).

RESULTS

- Our sample included 2,133 participants: 545 inpatients and 1,588 outpatients.
- Inpatients who were SARS-CoV-2+ after vaccination (*n* = 140) were older than unvaccinated SARS-CoV-2+ inpatients (*n* = 161) (median 72.3 years vs. 60.4 years) and had more comorbidities (42% vs. 22% with CCI score ≥ 5).
- In unadjusted analyses, severe illness occurred in 25 (18%) fully vaccinated inpatients, 27 (17%) not fully vaccinated inpatients, and <1% of outpatients.
- Fourteen (10%) of fully vaccinated SARS-CoV-2+ inpatients died from any cause, as did six (4%) of the unvaccinated inpatients.
- Among SARS-CoV-2+ inpatients, a one-step higher CCI was associated with greater odds of severe illness or death relative to mild illness in multivariable analysis adjusted for the covariates shown in Table 1.
- Among all inpatients, a one-step higher CCI was associated with greater risk of hospital days (aIRR = 1.05, 95% CI 1.02–1.08) and hazard of rehospitalization within 60 days (aHR = 1.06, 95% CI 1.0–1.11).

DISCUSSION

- In an ongoing cohort study of SARS-COV-2 infection in U.S. Veterans, fully vaccinated inpatient participants were older and had more comorbidities than inpatients who were not fully vaccinated.
- In exploratory analysis, we did not observe differences in illness severity as a function of calendar periods of enrollment associated with different SARS-CoV-2 variants.
- A greater number of comorbidities was an independent risk factor for more severe illness, more hospital days, and rehospitalization within 60 days, after adjusting for vaccination status, age, sex, and calendar period of enrollment.

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