CLINICAL INVESTIGATION

30-day mortality following COVID-19 and influenza hospitalization among US veterans aged 65 and older

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Abstract

Background: COVID-19 and influenza are important sources of morbidity and mortality among older adults. Understanding how outcomes differ for older adults hospitalized with either infection is important for improving care. We compared outcomes from infection with COVID-19 and influenza among hospitalized older adults.

Methods: We conducted a retrospective study of 30-day mortality among veterans aged 65+ hospitalized with COVID-19 from March 1, 2020–December 31, 2020 or with influenza A/B from September 1, 2017 to August 31, 2019 in Veterans Affairs Health Care System (VAHCS). COVID-19 infection was determined by a positive PCR test and influenza by tests used in the VA system. Frailty was defined by the claims-based Veterans Affairs Frailty Index (VA-FI). Logistic regressions of mortality on frailty, age, and infection were adjusted for multiple confounders.

Results: A total of 15,474 veterans were admitted with COVID-19 and 7867 with influenza. Mean (SD) ages were 76.1 (7.8) and 75.8 (8.3) years, 97.7% and 97.4% were male, and 66.9% and 76.4% were white in the COVID-19 and influenza cohorts respectively. Crude 30-day mortality (95% CI) was 18.9% (18.3%–19.5%) for COVID-19 and 4.3% (3.8%–4.7%) for influenza.

Combining cohorts, the odds ratio for 30-day mortality from COVID-19 (versus influenza) was 6.61 (5.74–7.65). There was a statistically significant interaction between infection with COVID-19 and frailty, but there was no significant interaction between COVID-19 and age.

Separating cohorts, greater 30-day mortality was significantly associated with older age (p: COVID-19: <0.001, Influenza: <0.001) and for frail compared with robust individuals (p for trend: COVID-19: <0.001, Influenza: <0.001).

Conclusion: Mortality from COVID-19 exceeded that from influenza among hospitalized older adults. However, odds of mortality were higher at every level of frailty among those admitted with influenza compared to COVID-19. Prevention will remain key to reducing mortality from viral illnesses among older adults.

INTRODUCTION

Coronavirus Disease-2019 (COVID-19) and influenza share common features that have prompted comparison.[1,2] Both are respiratory infections that produce pandemics, and are disproportionately lethal among older adults. Despite these similarities, early estimates suggested that COVID-19 has a higher case fatality rate than influenza.[1,2] For the 2017–2018 influenza season, the worst since the 2009 H1N1 pandemic, there were 50,903 deaths among adults over the age of 65 in the United States, comprising 83% of all influenza deaths, with a population mortality rate of 100.1 per 100,000.[3] By comparison, as of August 11, 2021 there were 482,727 deaths from COVID-19 among adults age 65 and older, accounting for nearly 80% of all COVID-19 deaths in the United States, with a mortality rate of 889 per 100,000.[4,5] Direct comparisons of influenza and COVID-19 have been limited by a lack of data on the those infected that may explain observed aggregate differences. As governments move to treat COVID-19 as an endemic infection and loosen preventative measures, such decisions need to be put into context with other common, viral respiratory infections. Focusing on high risk-groups such as older adults will help with planning for preventive services, preparing health care systems for further infections, and prognostication by clinicians.

Of special importance to older populations is the role of physiologic changes associated with aging that led to vulnerability and adverse outcomes. Frailty, the impaired ability to restore homeostasis following a physiologic stressor, such as a viral infection, is an important framework for capturing this vulnerability.[6] Frailty has also been associated with poor outcomes following infection with

Key points

- It has been suggested that COVID-19 and flu are similarly fatal for older adults, although there have been limited data to support this observation
- Among older US Veterans hospitalized with COVID-19 and flu, we report that there is a higher risk of mortality with COVID-19 infection
- Stratifying by an electronic frailty index, we found that older adults who are frail and are hospitalized with either COVID-19 or flu are at the highest risk of mortality

Why does this matter?

COVID-19 has been compared to influenza and public health measures to reduce transmission are being reversed despite high mortality. We show that, accounting for patient characteristics including frailty, COVID-19 has higher mortality than influenza among hospitalized older adults. We also demonstrate that frailty is associated with higher mortality from COVID-19 and influenza and may be a tool for prognostication or to prioritize individuals for vaccination/boosters or treatments.

COVID-19 and influenza.[7–11] Understanding outcomes following infection with influenza and COVID-19 among frail older adults is key for risk-stratification and prognostication for older adults, for guiding discussions of goals of care, as well as ultimately improving outcomes.

We sought to address both the severity of COVID-19 in comparison with influenza among those at highest risk from adverse outcomes, as well as the role of frailty in mortality from both of these conditions. We do so by examining 30-day mortality following infection with influenza and COVID-19 among adults aged 65 and older who had been hospitalized in the US Veterans Health Administration (VA) a large, integrated health care system.

METHODS

Cohort selection

We conducted a retrospective analysis of electronic medical record data from the VA. Data were obtained from the VA Corporate Data Warehouse.[12] For the influenza cohort, we included veterans admitted with influenza A or B from September 1, 2017 to August 31, 2019. We considered all available tests in the VA system (Polymerase Chain Reaction (PCR), antigen testing including rapid tests, immunofluorescence [e.g., DFA, EIA, FIA], and viral culture). For the COVID-19 cohort, we considered veterans with a positive PCR test between March 1 and December 31, 2020. Hospitalizations for COVID-19 and influenza were defined as a hospitalization in any VA hospital up to 7 days before or 30 days following a positive virus-specific test. For veterans with multiple positive tests, we used the date of the first positive test. Index date for analysis was the later of date of admission or date of positive test. The sample was restricted to those aged 65 or older at the index date. Veterans who were identified in both the influenza and COVID-19 cohorts were retained only in the influenza cohort to avoid overlap.

Covariates

Demographic covariates included age, sex, race, ethnicity, and region of hospitalization using VA administrative definitions. Clinical and laboratory covariates were month of admission, body mass index, number of systemic inflammatory response syndrome (SIRS) criteria (heart rate >90 beats/min, respiratory rate >20 breaths/min, temperature >38°C or <36°C, and white blood cell count >12,000/mm^3 or <4000/mm^3),[13] maximum systolic blood pressure and squared maximum systolic blood pressure, serum sodium, and serum creatinine. Clinical and laboratory covariates were taken from values closest to the index date in a window extending 3 days before to 3 days after the index date. We used SIRS instead of qSOFA due to lack of accurate data on mentation; SOFA may have a weaker association with mortality from COVID-19 than SIRS.[14]

We considered outpatient medications based on prescription fills in the 12 months prior to admission. Specifically, we extracted data on the use of inhaled and systemic steroids, statins, antiplatelet agents, anticoagulants including injectables, and ACE inhibitors and angiotensin receptor blockers (ARBs). For the influenza cohort, when analyzed separately, we additionally considered influenza specific treatments prescribed by the VA in the 30 days prior to admission (i.e., oseltamivir, zanamivir, and peramivir).

Medication and laboratory records were adjudicated by authors BS and ARO.

Frailty was assessed using the VA Frailty Index (VA-FI) which is based on the accumulation of deficits theory of frailty.[6] The VA-FI is a 31-item frailty index derived from diagnosis and procedure codes in the VA electronic medical record and has been validated for use with or without Medicare claims data (Table SS1).[15,16] According to a standard procedure, items included in the VA-FI cover the domains of multimorbidity, cognitive and mental health, sensory deficits, and physical function.[17] The index is the sum of the number of deficits present divided by number of deficits assessed ($n = 31$), and ranges from zero to one. A VA-FI score of 0–0.1 is robust, >0.1–0.2 pre-frail, >0.2–0.3 mildly frail, >0.3–0.4 moderately frail, and >0.4 severely frail.[15] In regression modeling we stratified frailty into the five categories above, while using it continuously to test for trend.

Outcomes

The primary outcome was all-cause mortality at 30 days. We secondarily considered all-cause in-hospital mortality. Mortality data were sourced from the VA Corporate Data Warehouse.[12]

Statistical analysis

Descriptive statistics were used to summarize the baseline characteristics of the COVID-19 and influenza cohorts.

The primary analysis was the association between hospitalization with COVID-19 as opposed to influenza and 30-day mortality. To draw these comparisons, we combined the 2017–2019 influenza cohort with the 2020 COVID-19 cohort. This was analyzed by cumulative incidence curves with Kaplan–Meier statistics and by multivariable logistic regression adjusted for the covariates above. We also conducted Poisson regression with these covariates and offset for survival time as a sensitivity analysis. We secondarily examined the association

T A B L E 1 Baseline characteristics of veterans aged ≥65 admitted for COVID-19 (N = 15,488, March 1–December 31, 2020) or influenza (N = 7867, September 1, 2017–August 31, 2019) in the Veterans Affairs Health Care System

	COVID-19 (N = 15,474)	Influenza (N = 7867)
Female – N (%)	359 (2.3%)	204 (2.6%)
Age – Mean (SD)	76.1 (7.77)	75.8 (8.28)
Race – N (%)		
White	10,352 (66.9%)	6010 (76.4%)
Black or African American	3943 (25.5%)	1318 (16.8%)
American Indian/Alaska Native	149 (1.0%)	79 (1.0%)
Native Hawaiian/Pacific Islander	124 (0.8%)	56 (0.7%)
Asian	98 (0.6%)	43 (0.5%)
Unknown	808 (5.2%)	361 (4.6%)
Hispanic or Latino Ethnicity – N (%)	1125 (7.3%)	584 (7.4%)
Region – N (%)		
North Atlantic	2925 (18.9%)	1623 (20.6%)
Southeast	3167 (20.5%)	1497 (19.0%)
Midwest	4004 (25.9%)	1739 (22.1%)
Continental	2875 (18.6%)	1121 (14.2%)
Pacific	2503 (16.2%)	1887 (24.0%)
Frailty Index – Mean (SD)	0.213 (0.137)	0.230 (0.130)
Days from Test to Admission – Mean (SD)	1.61 (4.49)	0.71 (4.01)
Charlson Comorbidity Index – Mean (SD)	7.12 (2.94)	7.24 (2.89)
Body Mass Index – Mean (SD)	28.7 (6.6)	28.2 (6.6)
Hypertension – N (%)	13,777 (89.0%)	7087 (90.1%)
Diabetes – N (%)	8694 (56.2%)	4138 (52.6%)
Coronary Artery Disease – N (%)	7070 (45.7%)	4144 (52.7%)
Heart Failure – N (%)	4794 (31.0%)	2972 (37.8%)
Cancer – N (%)	5282 (34.1%)	3071 (39.0%)
Dementia – N (%)	5835 (37.7%)	2721 (34.6%)
SIRS – N (%)		
0	3343 (21.6%)	1193 (15.2%)
1	5212 (33.7%)	2284 (29.0%)
2+	6919 (44.7%)	4390 (55.8%)
Outpatient Medications – N (%)		
ACE-I/ARB	6521 (42.1%)	3809 (48.4%)
Antiplatelet Agent	1560 (10.1%)	935 (11.9%)
Anticoagulation	2864 (18.5%)	1768 (22.5%)
Statin	9473 (61.2%)	5210 (66.2%)
Systemic Steroids	2602 (16.8%)	2267 (28.8%)
Inhaled Steroids	2426 (15.7%)	2276 (28.9%)
Inpatient Medications – N (%)		
Systemic Steroids	8761 (56.6%)	2942 (37.4%)
Remdesivir	6491 (41.9%)	—
Azithromycin	4467 (28.9%)	2213 (28.1%)
Hydroxychloroquine	864 (5.6%)	50 (0.6%)
Anti-Influenza	—	698 (8.9%)

Abbreviations: ACE-I, Angiotensin Converting Enzyme Inhibitor; ARB, Angiotensin Receptor Blocker; SIRS, Systemic Inflammatory Response Syndrome.

between each viral infection and in-hospital mortality using multivariable logistic regression. For these analyses, the 2017–2019 influenza cohort and 2020 COVID-19 cohort were treated separately. All regression models were adjusted for the covariates described above. Regressions with interactions were compared to those without interaction by ANOVA. Kaplan–Meier analyses were stratified by age and by frailty.

Analysis was conducted in R version 4.0.2.[18] IRB approval was obtained from the Boston VA Health Care System. This work was funded by the VA, which did not have a role in study design, analysis, or reporting of results.

RESULTS

Cohort characteristics

The final sample included 15,474 veterans admitted to any VA hospital with a positive COVID-19 test and 7867 admitted with a positive influenza test (Figure SS1). Of the 7867 individuals with influenza, 199 were later admitted to a VA hospital with COVID-19 during the period we considered, but were excluded from our COVID-19 cohort and are not in the reported total. Baseline characteristics are described in Table 1. For the COVID-19 and influenza cohorts respectively, the average age (SD) was 76.1 (7.8) and 75.8 (8.3) years and 97.7% and 97.4% were male. 66.9%, 25.5%, and 7.3% of the COVID-19 cohort were white, black/African-American, and Hispanic respectively, while these proportions were 76.4%, 16.8%, and 7.4% for the influenza cohort. Mean (SD) BMI was 28.7 kg/m^2 (6.6) in the COVID-19 cohort and 28.2 kg/m^2

(6.6) in the influenza cohort. In the COVID-19 cohort 3969 (25.6%) of subjects were robust, 4633 (29.9%) were pre-frail, and 6872 (44.4%) were frail, with 1922 (12.4%) moderately frail and 1600 (10.3%) severely frail. In the influenza cohort, 1474 (18.7%) were robust, 2417 (30.7%) were pre-frail, 3976 (50.5%) were frail, 1190 (15.1%) were moderately frail, and 868 (11.0%) were severely frail.

Overall survival is illustrated in Figure 1, which shows the cumulative incidence of mortality over 30 days for the COVID-19 and influenza cohorts. The proportion who had died by 30 days (95% CI) was 18.9% (18.3%–19.5%) for COVID-19 and 4.3% (3.8%–4.7%) for influenza.

Figure 2 panels A-B shows the results stratified by age for each viral illness. As age increased, the rate and 30-day probability of death likewise increased. For COVID-19 rates were 13.5% (12.7%–14.2%) for those 65–74, 20.3% (19.2%–21.5%) for those 75–84, and 33.1% (31.2%–34.8%) for those aged 85 and older. For influenza rates were 2.9% (2.4%–3.4%), 4.4% (3.5%–5.3%), and 8.2% (6.8%–9.5%), respectively.

There was a similar pattern of increasing mortality with increasing severity of frailty, shown in Figure 2 panels C-D. At each increased level of frailty, the incidence of death increased in both the influenza and COVID-19 cohorts. Comparing non-frail to frail individuals, the absolute risk difference for 30-day mortality (95% CI) was 5.0% (3.7%–6.2%) in the COVID-19 cohort and 2.5% (1.6%–3.4%) in the influenza cohort.

Comparing COVID-19 with influenza

Table 2 summarizes the results of multiple regression analyses of the combined COVID-19 and influenza
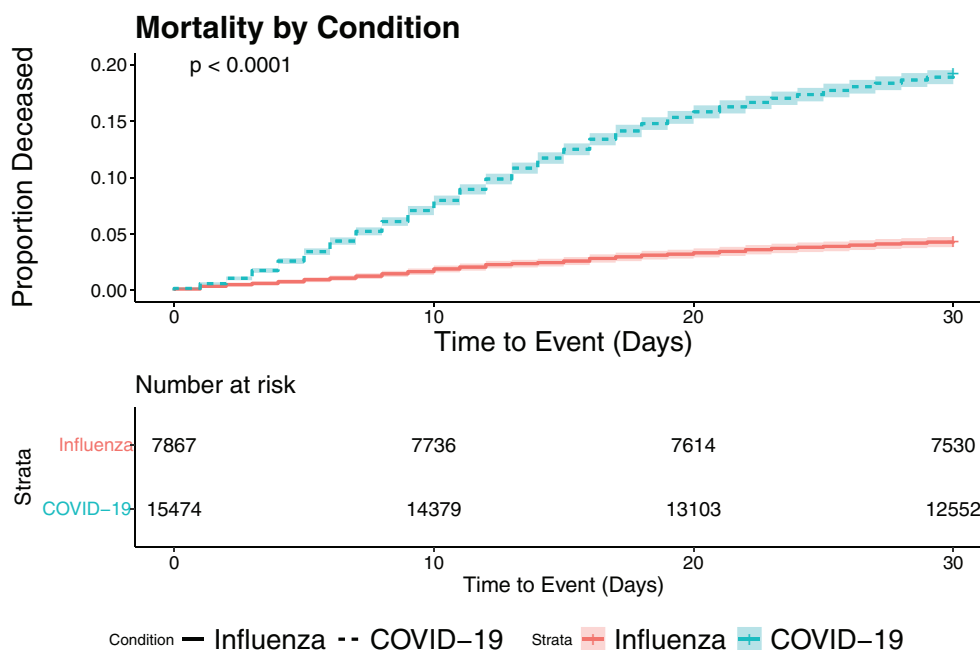

FIGURE 1 Cumulative incidence curves of 30-day survival by condition among veterans aged ≥65 admitted for COVID-19 (March 1–December 31, 2020) or influenza (September 1, 2017–August 31, 2019) in the Veterans Affairs Health Care System
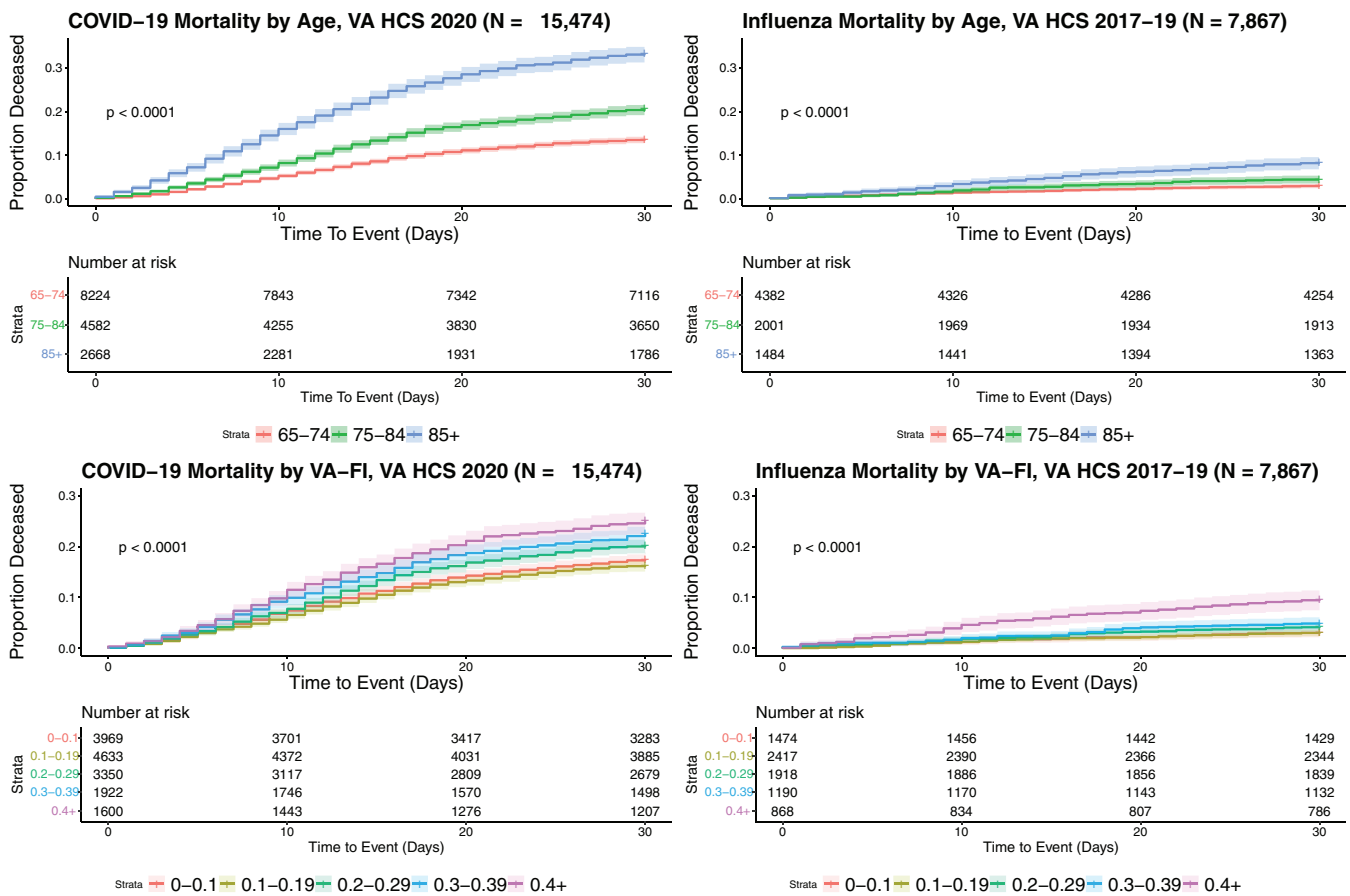
FIGURE 2 Panels A, B, C, D. Cumulative Incidence curves of 30-day survival by age (Panels A and B) or frailty level (Panels C and D) among veterans aged ≥65 admitted for (A and C) COVID-19 (March 1–December 31, 2020) or (B and D) influenza (September 1, 2017–August 31, 2019) in the Veterans Affairs Health Care System. VA-FI, Veterans Affairs Frailty Index

cohorts. In each of the models considered, COVID-19 increased the odds or rate of mortality above those of influenza. The odds ratio (95% CI) was 6.61 (5.74–7.65) for 30-day mortality and 12.44 (10.12–15.47) for in-hospital mortality. The association between frailty and 30-day mortality was statistically significant for moderate and severe frailty. Interaction between COVID-19 infection and frailty index was statistically significant only in the Poisson regression for 30-day mortality ($p = 0.018$), but the interaction between COVID-19 and age did not reach statistical significance at $p < 0.05$ in any regression. For in-hospital mortality, pre-frailty and severe frailty had statistically significant associations.

Frailty and infection-specific outcomes

Results of analyzing the COVID-19 and influenza cohorts separately are presented in logistic and Poisson regression of 30-day mortality are presented in Table 3 and Table S2. For COVID-19, the multivariable adjusted odds ratios for 30-day mortality by frailty rose

with greater severity of frailty and were similar to the rate ratios from Poisson regression. For the influenza cohort, the multivariable odds ratios for mild, moderate, and severe frailty, compared to robust individuals, were greater than in the COVID-19 cohort. Poisson regression of 30-day mortality in the influenza cohort, again, yielded broadly similar results as the logistic regression models. Odds and rate ratios for 30-day mortality for the pre-frail versus robust individuals was not statistically significant in the COVID-19 cohort nor the influenza cohort. The trend of greater odds ratios for mortality with greater 30-day mortality was supported with the treatment of frailty continuously, with p for trend <0.001 in all regressions.

Results for in-hospital mortality are summarized in Table 3. Adjusted odds ratios for in-hospital mortality from COVID-19 by degree of frailty were non-significant with the exception of pre-frailty. For influenza, odds ratios were also non-significant with the exception of severe frailty. However, p for the trend of greater frailty associated with greater odds of in-hospital mortality was <0.05 for both COVID-19 and influenza.

TABLE 2 Adjusted associations of infection with COVID-19 versus influenza with mortality among veterans aged ≥65 admitted in the Veterans Affairs Health Care System for COVID-19 (March 1–December 31, 2020), for influenza (September 1, 2017–August 31, 2019)

Logistic regression			
30-day mortality	**Odds ratio**	**95% CI**	**p-value**
Age	1.06	1.06–1.07	< 0.001
COVID-19	8.13	6.87–9.66	< 0.001
Robust	1.00	Reference	—
Pre-frailty	0.89	0.78–1.02	0.107
Mild frailty	1.09	0.95–1.26	0.219
Moderate frailty	1.19	1.01–1.4	0.038
Severe frailty	1.47	1.24–1.74	< 0.001
In-hospital mortality	**Odds ratio**	**95% CI**	**p-value**
Age	1.05	1.05–1.06	<0.001
COVID-19	17.31	13.71–22.06	<0.001
Robust	1.00	Reference	—
Pre-frailty	0.84	0.72–0.97	0.019
Mild frailty	0.97	0.83–1.14	0.697
Moderate frailty	1.04	0.86–1.25	0.707
Severe frailty	1.18	0.97–1.43	0.102
Poisson regression			
30-day mortality	**Rate ratio**	**95% CI**	**p-value**
Age	1.06	1.05–1.06	<0.001
COVID-19	7.15	6.11–8.4	<0.001
Robust	1.00	Reference	—
Pre-Frailty	0.90	0.8–1.02	0.101
Mild Frailty	1.07	0.94–1.21	0.312
Moderate Frailty	1.15	1.00–1.33	0.049
Severe Frailty	1.37	1.18–1.58	<0.001

Note: Results are adjusted for sex, race, ethnicity, region, body mass index, month of admission, vital signs, laboratory values, and outpatient medications.

DISCUSSION

Leveraging data from an extensive electronic medical record of veterans hospitalized throughout the United States, we demonstrate that after accounting for patient characteristics, Veterans aged 65 and older had greater odds of mortality at 30-days following infection with COVID-19 than with influenza. This pattern remained at advanced ages and for older adults with frailty who are more vulnerable to adverse outcomes from either infection. This work provides evidence supporting prior clinical experience and population-level data that COVID-19 is a deadlier illness than influenza. We account for differing patient characteristics in ways that some prior work did not.[19,20] High case fatality rates were observed in the SARS-CoV-1 and MERS-CoV epidemics, and this may be a feature of novel coronaviridae.[21–23]

Our results are similar to work earlier in the pandemic looking at admissions of all ages in the VA system that also noted higher 60-day mortality between veterans admitted for COVID-19 (18.6%) or for influenza (5.3%).[24] Administrative data on patients of all ages throughout France reported similar differences in inpatient mortality between COVID-19 and influenza using diagnosis codes rather than laboratory confirmation of infection: 16.9% admissions for COVID-19 ended in patient death versus 5.8% admissions for influenza.[20] We add to this by looking over a longer period of the COVID-19 epidemic in the United States and by focusing on older adults in particular, who are at the greatest risk for poor outcomes from both infections.[20]

Frailty and outcomes from infection

Importantly in this investigation of older adults, we accounted for aging physiology using a validated frailty index. Two large prospective studies of COVID-19 admissions, COPE in the UK and Italy ($N = 1564$) and CO-FRAIL in Brazil ($N = 2463$) both found large, significant associations between the Clinical Frailty Scale and mortality from COVID-19.[7,25] The Clinical Frailty Scale primarily relies on functional assessment, while deficit accumulation frailty indices like the VA-FI also incorporate cognition and multimorbidity.[26] Meta-analyses have likewise found associations between frailty and mortality from COVID-19.[27,28] By contrast, there is little available data on outcomes for frail older adults with influenza.[11]

More generally, aging physiology, especially frailty, plays an important role in infectious diseases among older adults, leading to greater susceptibility to infection.[29] Further, infections have important implications for outcomes relevant to older adults, including physical function and cognition.[29] Aging physiology, including frailty, should be incorporated as a covariate or as an outcome in future studies of medical problems among older adults. This is important for understanding the role of the aging process in health outcomes and the potential use of frailty as a prognostic tool.[25] Clinically, frailty can be used to risk-stratify older adults early in the course of their illness, identifying those at higher risk who may benefit from greater prevention and treatment strategies such as monoclonal antibodies or oral medications

TABLE 3 Adjusted odds ratios for 30-day and in-hospital mortality by frailty among veterans aged ≥65 admitted in the Veterans Affairs Health Care System for COVID-19 (March 1–December 31, 2020), for influenza (September 1, 2017–August 31, 2019)

	COVID-19			Influenza		
	Odds ratio	95% CI	*p* for trend	Odds ratio	95% CI	*p* for trend
30-day mortality						
Robust	1	Reference	<0.001	1	Reference	<0.001
Pre-Frailty	0.90	0.78–1.04		1.04	0.65–1.69	
Mild Frailty	1.06	0.91–1.24		1.69	1.07–2.73	
Moderate Frailty	1.18	0.99–1.41		1.75	1.06–2.94	
Severe Frailty	1.33	1.10–1.60		3.23	1.96–5.40	
In-hospital mortality						
Robust	1	Reference	0.151	1	Reference	<0.001
Pre-Frailty	0.84	0.72–0.98		0.83	0.40–1.73	
Mild Frailty	0.94	0.79–1.11		1.82	0.93–3.66	
Moderate Frailty	1.04	0.86–1.26		1.69	0.77–3.70	
Severe Frailty	1.10	0.90–1.35		2.94	1.39–6.35	

Note: Results are adjusted for age, sex, race, ethnicity, region, body mass index, vital signs, laboratory values, and outpatient medications including anti-influenza medications (influenza results only).
Abbreviations: FI, Frailty Index.

following exposure, as well as earlier discussion of goals of care and treatment plans.[30] Further, the VA-FI and other claims-based FIs can be automated, allowing for population-based assessment.[31,32]

Strengths and limitations

This study has several strengths. We use data from a large, nationwide health care system that provides both statistical power and representation from diverse regions. Subjects in the study also have equitable access to health care provided through the VAHCS, reducing a possible source of variation. We identified cases based on diagnostic test results rather than diagnosis codes, which permits more certainty about infectious diagnoses and captures severe cases that may manifest as bacterial superinfection. We are also able to account for aspects of pre-hospital care and health through the health record, including comorbidities and medications, though the possibility of relevant, unmeasured variables cannot be eliminated.

There are also important limitations to this study. The population of the VA health care system is not the same as the United States population at-large, particularly that it is predominantly male, which may limit generalizability. Information on comorbidities was limited to data from the VA system and may miss diagnoses among veterans who also seek care outside the VA. This may

misclassify some individuals in our dataset as less frail than they truly are and may explain the odds ratios for pre-frailty that are less than one. Likewise, some fraction of patients admitted with acute coronary syndromes or stroke during the influenza seasons considered may have had influenza but not been tested and be missing from our cohort. Further, the influenza cohorts experienced care under normal health care conditions while those with COVID-19 were treated during a pandemic that strained the resources of all health systems. This may lead to differences in presentation and care not captured in the available data. Influenza also had effective vaccines and treatment available that may have reduced morbidity and mortality even among hospitalized frail older adults, while there were far more limited options for the care of people with COVID-19 during the period studied. It was not possible to reliably determine who in the VA system has not been vaccinated for influenza. Finally, the deployment of vaccines and the spread of the Delta and Omicron variants of COVID-19 may change the relationship between frailty and hospital outcomes.

CONCLUSION

In a cohort of Veterans aged 65 and older admitted to VA hospitals, we found that mortality from COVID-19 is greater than for influenza after adjusting for a wide array of confounders. Further, we find that frail older adults

carry the highest burden of mortality with either infection. Prevention through vaccination, masking, and social distancing remain key to reducing mortality. Our findings illustrate that the lifting of measures such as universal masking may put people with significant health problems at high risk for mortality; such individuals made up more than 10% of our sample. Vaccination for COVID-19 and influenza should be given great priority given their associated high mortality and transmissibility, and their effectiveness in frail individuals should be specifically assessed. Similarly, new COVID-19 treatments such as nirmatrelvir/ritonavir and tixagevimab/ cilgavimab need to be evaluated in frail individuals and allocated accordingly. With the potential for a season with both COVID-19 and influenza cases, health care providers should seek to differentiate these viral infections both for infection control purposes and to guide prognostication and shared decision-making with patients and their health care proxies. In future work studying outcomes among older adults, frailty should continue to be incorporated into assessments and analyses.

AUTHOR CONTRIBUTIONS

Benjamin Seligman and Ariela R. Orkaby designed the study with input from David R. Gagnon. Brian Charest developed the cohort, Brian Charest and Benjamin Seligman conducted the analysis. Benjamin Seligman drafted the manuscript. All authors reviewed and revised the manuscript.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to report.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

Figure S1. CONSORT diagrams for the creation of (A) COVID-19 and (B) influenza cohorts in the Veterans Affairs Health Care System.

Table S1. Items in the VA Frailty Index.

Table S2. Poisson regression results for 30-day mortality among veterans aged ≥65 admitted in the Veterans Affairs Health Care System for COVID-19 (March 1–December 31, 2020) or for influenza (September 1, 2017–August 31, 2019).