## Natural history of COVID-19: Risk factors for hospitalizations and deaths among >26 million U.S. Medicare beneficiaries

Hector S. Izurieta<sup>1</sup>, David J. Graham<sup>2</sup>, Yixin Jiao<sup>3</sup>, Mao Hu<sup>3</sup>, Yun Lu<sup>1</sup>, Yue Wu<sup>3</sup>, Yoganand Chillarige<sup>3</sup>, Michael Wernecke<sup>3</sup>, Mikhail Menis<sup>1</sup>, Douglas Pratt<sup>1</sup>, Jeffrey Kelman<sup>4</sup>, Richard Forshee<sup>1</sup>.

(1) Center for Biologics Evaluation and Research, Food and Drug Administration, Silver Spring, MD, USA;
(2) Center for Drugs Evaluation and Research, Food and Drug Administration, Silver Spring, MD, USA;
(3) Acumen LLC, Burlingame, CA, USA;
(4) Centers for Medicare & Medicaid Services, Washington, DC, USA

Summary: This observational study quantified the degree of elevated risk of COVID-19 deaths and hospitalizations among elderly Medicare beneficiaries who were older, male, lower-SES, immunocompromised, or had comorbidities. Risk was also substantially higher among nursing home residents and those with ESRD.

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#### ABSTRACT

Background: Evaluate risk factors for severe COVID-19 outcomes among Medicare beneficiaries during the pandemic's early phase.

<u>Methods</u>: Retrospective cohort study covering Medicare fee-for-service (FFS) beneficiaries. We separated out elderly residents in nursing homes (NH) and those with end-stage renal disease (ESRD) from the primary study population of individuals ages  $\geq$ 65. Outcomes included COVID-19 hospital encounters and COVID-19-associated deaths. We estimated adjusted odds ratios (ORs) using logistic regression.

<u>Results:</u> We analyzed 25,333,329 elderly non-NH non-ESRD beneficiaries, 653,966 elderly NH residents, and 292,302 ESRD patients. COVID-related death rates (per 10,000) were much higher among elderly NH residents (275.7) and ESRD patients (60.8) than the primary study population (5.0). Regression-adjusted clinical predictors of death among the primary population included immunocompromised status (OR: 1.43), frailty index conditions such as cognitive impairment (3.16) as well as other comorbidities including congestive heart failure (1.30). Demographics-related risk factors included male sex (1.77), older age (OR: 3.09 for 80-year-old vs. 65-year-old), Medicaid dual-eligibility status (2.17) and racial/ethnic minority. Compared to Whites, ORs were higher for Blacks (2.47), Hispanics (3.11), and Native Americans (5.82). Results for COVID-19 hospital encounters were consistent.

<u>Conclusions</u>: Frailty, comorbidities, and race/ethnicity were strong risk factors of COVID-19 hospitalization and death among the U.S. elderly.

Keywords: COVID-19, risk factors, disease severity, epidemics

#### BACKGROUND

The first 2019 coronavirus case (COVID-19) was reported in China in December, 2019 [1]. From January 21 through February 23, 2020, public health agencies detected 14 U.S. COVID-19 cases, all related to travel from China [2, 3]. Although the first non-travel-related U.S. case was confirmed on February 26 in a California resident who had become ill on February 13, the prior occurrence of three cases in California confirm the cryptic circulation of the virus by early February [2-4]. On March 13, the U.S. declared a national emergency [2]. Shortly thereafter, the U.S. became the country with the highest number of reported cases and deaths worldwide [1]. Given the ongoing pandemic, more evidence on the risk factors associated with COVID-19 and severe COVID-related outcomes is needed for filling our knowledge gap of the disease and on ways to reduce its burden on public health [3].

Multiple analyses in the U.S. and abroad have suggested that race, social disparities, old age, and underlying health conditions were associated with a higher risk for COVID-related severe outcomes, including hospitalizations and deaths [3, 5-12]. The findings highlighted the need for an in-depth investigation. Our objective was to utilize Medicare claims data to evaluate risk factors for COVID-19 hospitalizations and deaths among Medicare beneficiaries. We also sought to investigate the specific interconnected effects between age, socioeconomic conditions, frailty and race to understand their associations with the risk of severe COVID-19 outcomes.

#### **METHODS**

#### **Data Sources**

Medicare is a federally funded health insurance program that provides coverage for people ages  $\geq 65$  years, as well as those with disability and/or end-stage renal disease (ESRD), regardless of age. We used Medicare Part A (hospital inpatient care) and B (outpatient medical care) claims to evaluate beneficiaries' health histories and used claims from the Shared Systems Data (SSD), a database updated daily with

processed claims allowing for rapid outcome detection and near real-time analysis. We obtained beneficiaries' demographics and enrollment information from Centers for Medicare and Medicaid Services (CMS) Enrollment Database (EDB), the Common Medicare Environment (CME), and Master Beneficiary Summary File (MBSF). We used the Minimum Data Set (MDS) to ascertain Medicare beneficiaries' nursing home (NH) residence status, American Community Survey (ACS) data to assess population density, and Area Deprivation Index (ADI) data to assess the socioeconomic deprivation of beneficiaries' place of residence [13].

#### **Study Period, Population and Outcomes**

The study begin date was April 1, 2020, since the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) diagnosis code specific for COVID-19 (U07.1) became effective on this date, and COVID-19 coding practices were not standardized prior to then. The population included Medicare beneficiaries continuously enrolled in Medicare Parts A and B Fee-for-Service (FFS) for at least six months prior to study begin date who did not have any COVID-related hospitalizations (ICD-10-CM diagnosis code U07.1 or B97.29) during this period. We stratified beneficiaries into three mutually-exclusive populations: elderly NH, ESRD (including all ages), and the general elderly. We considered beneficiaries as elderly NH resident if they were ages  $\geq$ 65 years at study begin date, resided in a NH anytime in the previous 6 months, and had no records suggesting official discharge. We defined beneficiaries with ESRD as those with at least one dialysis facility claim with no indication of acute kidney injury in the three months prior to study begin date. The primary study population was beneficiaries ages  $\geq$ 65 years not in NH without ESRD (general elderly); a detailed elderly NH residents report will be the subject of a follow-up publication.

Outcomes included COVID-19 hospitalizations, COVID-related deaths, and COVID-related hospitalization complications: intensive care unit/coronary care unit (ICU/CCU) admission, ventilator use, inpatient renal replacement therapy, and inpatient death. We defined incident COVID-19

hospitalizations as those with an inpatient discharge diagnosis of COVID-19 (diagnosis code U07.1) and admission date between April 1, 2020 and May 8, 2020. Additionally, eligible cases must not have had a previous potential COVID-19 hospitalization (with diagnosis code U07.1 or B97.29) in the six months prior to study begin date. We defined COVID-related deaths as deceased patients with a prior COVID-19 discharge diagnosis on a facility claim or at least two professional service claims with COVID-19 diagnosis code within 21 days of the death date. The facility claim or professional service claim immediately preceding the death date must have occurred during the study period of April 1, 2020 to May 8, 2020.

#### Covariates

We assessed demographic and socioeconomic characteristics using enrollment data, chronic conditions using ICD-10-CM diagnosis codes, specific therapies and treatments using the International Classification of Diseases, Tenth Revision, Procedure Coding System (ICD-10-PCS) codes, and Healthcare Common Procedure Coding System (HCPCS) codes on inpatient and outpatient claims (including influenza vaccination) in the 6 months prior to study begin date. We calculated county-level COVID-19 circulation rates among Medicare beneficiaries using COVID-19 diagnoses in any setting. The Area Deprivation Index (ADI) rank, a scale of 1-100 measuring relative socioeconomic disadvantage with higher ADI score indicating higher socioeconomic disadvantage, was assessed using beneficiaries' residence information at the census block group level [13]. We assessed the effects of frailty on COVID-related outcomes using individual clinical conditions and health service utilization from the frailty index, a composite score measuring the probability a person is frail [14, 15], and immunocompromised status using administrative codes indicating presence of immunocompromising conditions or use of immunosuppressive therapies [16].

#### **Statistical Analysis**

We calculated COVID-19 hospitalization and COVID-related death rates among all eligible beneficiaries, and proportions of complications during COVID-19 hospitalization among those who were hospitalized. We summarized proportions of COVID-related deaths and COVID-19 hospitalizations overall and stratified by covariates of interest among the primary study population. We also used multivariate logistic regression models to estimate differences in odds ratios (ORs) and 95% confidence intervals (CIs) of the study outcomes. We modeled continuous variables such as age and ADI rank using natural splines to approximate their non-linear effects, and log-transformed COVID-19 circulation rates and population density to normalize their distribution and allow for easier interpretation of their effects; we included two-way interaction terms of age, Medicare-Medicaid dual-eligibility and race. We also performed analyses where (1) the individual conditions from the frailty index were substituted with a continuous composite score, and (2) an alternative classification of race/ethnicity was used. We derived the alternative race/ethnicity classification using an algorithm combining beneficiaries' last name and residence information, mainly oriented towards the identification of Hispanics and Asian/Pacific Islanders [17, 18].

#### RESULTS

#### **Overall COVID-Related Outcome Summary**

The study analyzed a total of 30,284,193 Medicare FFS-enrolled beneficiaries. Among the three study populations of interest, COVID-19 hospitalization and death rates were the highest among the 653,966 elderly NH residents with 19,637 hospitalizations (300.3 hospitalized cases per 10,000 beneficiaries) and 18,028 deaths (275.7 per 10,000), followed by the 292,302 beneficiaries with ESRD with 4,503 hospitalizations (154.1 per 10,000) and 1,777 deaths (60.8 per 10,000). The primary study population consisted of 25,333,329 beneficiaries. Among this group, 27,961 were hospitalized with COVID-19 (11.0 per 10,000) and 12,613 died with a prior COVID-19 diagnosis (5.0 per 10,000). Among the 27,961 hospitalized with COVID-19, 21.9% were admitted to an ICU/CCU, 16.6% were ventilated, and 26.1%

died at the hospital (Table 1). Of all 12,613 COVID-related deaths, approximately 33.9% did not occur in the hospital and 20.3% were deaths following a hospital discharge, often occurring in hospice or nursing home facilities (Supplementary Table 1).

#### Demographic, Socioeconomic, and Health Status Characteristics

Table 2 summarizes the demographics, socioeconomic status characteristics, and health status of the primary study population. Among them, over half were between the ages of 65 and 74 (55.8%) and over half were female (55.6%). Most were White (85.1%), not dual-eligible for Medicaid (90.6%), and qualified for Medicare due to old age (90.5%). Compared with the overall population, beneficiaries who died with a prior COVID-19 diagnosis were disproportionately older (≥85 years old: 44.5% vs. 12.6%), male (51.5% vs. 44.4%), and non-White (27.6% vs. 14.9%). They were also more likely to be dual-eligible (29.0% vs. 9.4%) and to have qualified for Medicare due to disability (14.1% vs. 9.5%). Beneficiaries hospitalized with COVID-19 had similar demographic and socioeconomic characteristics as those who died. Common pre-existing comorbidities among the study population included hypertension, diabetes, obesity, frailty-related conditions such as musculoskeletal problems, respiratory diseases such as chronic obstructive pulmonary disease (COPD), and cardiovascular diseases such as atrial fibrillation. Prevalence of these conditions was often higher among those who died or were hospitalized with COVID-19 than the overall primary study population. Both COVID-19 deaths and hospitalizations were disproportionately distributed in areas with high COVID-19 circulation rates, high population density, and known early outbreak centers such as New York, New Jersey, Massachusetts, Illinois, and Michigan.

#### **COVID-19 Hospitalization and Death Risk Factors**

Of the 25,333,329 beneficiaries in the primary study population, 24,367,476 beneficiaries with complete demographic and residence information were included in the logistic regression analysis. In assessing the association of COVID-related death and COVID-19 hospitalization with potential risk factors, the study

found elevated risk of COVID-related outcomes among those who were older, male, dual-eligible for Medicaid, disabled, and those who had specific health-related risk factors (Table 3).

Health-related factors that were associated with higher COVID-related death included being immunocompromised (OR: 1.43, 95% CI: 1.34-1.53), having medical conditions from the frailty index and other chronic conditions. Most conditions from the frailty index were associated with an increased risk of COVID-related death. Among them, cognitive impairment (3.16, 95% CI: 3.02-3.31), pneumonia (1.89, 95% CI: 1.79-2.00), and paranoia (1.66, 95% CI: 1.54-1.80) were highly associated with the outcome. Other comorbidities associated with higher risk included congestive heart failure (1.30, 95% CI: 1.23-1.36), diabetes (1.23, 95% CI: 1.18-1.29), and COPD (1.14, 95% CI: 1.08-1.20). Results for COVID-19 hospitalizations were largely consistent (Table 3).

Consistently for both COVID-related death and COVID-19 hospitalization, being a racial or ethnic minority, dual-eligible and older were generally associated with higher risk, with the magnitude of the difference varying across subgroups (Table 3, Figure 1). Overall, the risk of COVID-related death was higher among beneficiaries who were dual-eligible (2.17, 95% CI: 1.92-2.44). Compared to Whites, Blacks (2.47, 95% CI: 2.17-2.81), Hispanics (3.11, 95% CI: 2.37-4.08), and North American Natives (5.82, 95% CI: 3.25-10.43) had a higher risk of dying with a prior COVID-19 diagnosis. Compared with 65-year-olds, 80-year-olds were at higher risk of dying with COVID-19 (3.09, 95% CI: 2.94-3.25) (Table 3).

Differences in risk between non-Whites and Whites varied depending on beneficiaries' dual-eligibility status. Such differences were greater among non-dual-eligible than dual-eligible beneficiaries for Blacks and Hispanics, whereas the differences were greater among dual-eligible beneficiaries for North American Natives. For example, non-dual-eligible Black beneficiaries' odds of dying with a prior COVID-19 diagnosis were 2.5 times that of their White counterparts (95% CI: 2.21-2.89), whereas dualeligible Black beneficiaries' odds were approximately double that of White dual-eligible beneficiaries (95% CI: 1.74-2.35) (Table 3).

Differences in risk by race and dual-eligibility status were more pronounced among younger than older beneficiaries. For example, compared to Whites of the same age, Hispanics had 4.3 times the odds of dying with COVID-19 at age 65 (95% CI: 2.85-6.59) and 2.5 times the odds at age 80 (95% CI: 2.02-3.08). Compared with non-dual-eligible beneficiaries of the same age, dual-eligible beneficiaries had 2.3 times the odds of dying with COVID-19 at age 65 (95% CI: 1.81-2.80) and 1.8 times the odds at age 80 (95% CI: 1.69-1.98) (Table 4). Trends were similar for COVID-19 hospitalizations (Supplementary Table 2).

Sensitivity analysis results using the alternative race categorization yielded similar results to the primary analysis, where being a minority was generally associated with higher COVID-related outcome risk compared to Whites. Under the alternative race classification, proportion of Hispanics tripled and the differences in risk between Hispanics and non-Hispanic Whites were smaller (Supplementary Table 3, 4, 5). Consistent with the results using individual conditions from the frailty index, our sensitivity analysis results using the frailty index found 58% increased odds of COVID-related death with every additional 10% increase in the probability a person is frail (95% CI: 1.55-1.60) (Supplementary Table 6). When age effects were estimated incorporating the five-year average frailty index of the particular age, the increase in COVID-related outcome risk with advancing age became greater (Supplementary Figure 2).

#### DISCUSSION

In the largest nationwide study on the risk of COVID-19 hospitalization and death among the U.S. elderly, we assessed with high precision the effects of a wide range of potential risk factors, including demographics, frailty, socioeconomic and health status. Our use of a frailty index allowed us to determine that overall frailty, measured using a composite score calculated from a number of health-related conditions was, by itself, highly associated with the risk of COVID-19-associated death and hospitalization (Supplementary Figure 2, Supplementary Table 6). The severity of COVID-19 can be highlighted by our finding that, during this early (April 1 to May 8) pandemic phase, more than a fifth of hospitalized beneficiaries in the primary study population were admitted to the ICU/CCU and over a quarter of those hospitalized died. We also found that among Medicare beneficiaries ages  $\geq$ 65 years, COVID-19 death rates were 55 times and hospitalization rates 27 times higher among NH residents than among the primary study population, highlighting the extremely large risk among NH residents. Rates among beneficiaries with ESRD were also very high (Table 1).

Our single-payer fee-for-service Medicare data, which likely constitutes the most representative nationwide sample of U.S. elderly, allowed us to obtain precise, adjusted estimates of COVID-19 risk for almost 100 risk categories, and also allowed us to precisely quantify interactions for age, race and dualeligibility. We found that being immunocompromised (which also includes hematological cancers and solid tumors under treatment), frail (having conditions including but not limited to cognitive impairment, pneumonia, paranoia), having comorbidities such as congestive heart failure, COPD, and diabetes or being male were associated with very high odds of COVID-related death and hospitalization (Table 3). These associations were generally consistent with those described in prior publications, [3, 5-11] despite some differences in the populations investigated and analysis periods. Also, our study accounted for multiple additional conditions and important interactions (Table 3). Of particular interest are our findings of lower risk estimates for hypertension, obesity and asthma than prior studies [3, 5-11]. Our use of adjustments for multiple risks factors may explain the differences found. The lack of association between asthma and risk of COVID-related death in our results requires further evaluation, including an examination of the potential role of asthma treatments.

Our finding that COVID-19 hospitalization and death disproportionately affected Native Americans, Hispanics and Blacks, including but not limited to those sufficiently poor to be eligible for dual Medicare/Medicaid coverage were more granular than comparable results obtained by others [19, 20]. We found that Native Americans had the highest risk estimates, both among dual- and non-dual-eligible, which suggests the need to investigate the possibility of disparities not measured exclusively by income level. We also found that Asians shared the lowest risks with Whites, which also requires further investigation. Interestingly, the risk differences by race and dual-eligibility status became less pronounced among the very old, highlighting the fact that, independently of race or socioeconomic conditions, frailty appeared to play a major role among those ages  $\geq$ 80 years, although other explanations, such as survivor effect, could also be considered.

Our study has several strengths. Using longitudinal data on Medicare beneficiaries' pre-existing health conditions and health services utilization, we defined a wide range of potential COVID-related risk factors among individuals who were unlikely to change insurance affiliation, which allowed us to produce highly precise, adjusted estimates. Additionally, we had granular geographical and demographic information, which allowed us to study risk factors while adjusting for local infection intensity (at the county level) and individual characteristics. Given that Medicare covers the vast majority of U.S. citizens  $\geq 65$  years old, our findings are generalizable to the U.S. elderly and should particularly contribute to the understanding of COVID-19 death risk among all elderly [21]. Reassuringly, our overall hospitalization

rates and our finding that rates of hospitalization and death increased with age were comparable to those obtained by CDC for a slightly larger pandemic period, and with findings from a 12 U.S. states study [19, 20].

Our study had some limitations. The use of administrative claims data to identify COVID-19 cases may result in the inclusion of some non-test-confirmed cases. To minimize the potential misclassification bias, we used inpatient discharge diagnoses for identifying outcomes, which were found to have high accuracy in prior literature [22, 23]. The high attention paid to the COVID-19 pandemic and the seriousness of the events we investigated gives us high confidence that physicians and hospitals were likely to follow CDC's guidelines regarding COVID diagnosis. Although we used the binary Medicaid dual-eligibility status as the proxy for low-income status, this does not provide granular information on people's income level. However, the dual-eligibility status is available for all beneficiaries, highly accurate in identifying low-income individuals, and has been successfully used as poverty surrogate in multiple studies [24-30]. Lastly, our race/ethnicity classification is based on Medicare enrollment data, which under-captures Hispanics and Asians. However, this variable is highly accurate in distinguishing Blacks from Whites, two of the largest racial/ethnic groups in our population. Additionally, our main study results were similar to those of the sensitivity analysis we conducted using an alternative race/ethnicity classification that captured more Hispanics and Asians (Supplementary Table 3) [17]. Our results were, overall, also consistent with prior U.S. studies published on the same topic [3, 5-11].

In conclusion, this large nationwide cohort study among the U.S. elderly confirmed and precisely measured the importance of several risk factors, including particularly NH residence, ESRD status, older age, male sex, racial/ethnic minorities, immunocompromised status, frailty and chronic conditions. Moreover, our study found that social disparities (i.e., socioeconomic factors) were highly associated with an increased risk of COVID-related outcomes, even after adjusting for factors such as age and chronic medical conditions, highlighting the need to consider the interconnected effects of poverty and race/ethnicity in evaluations of COVID-19 risk. Our study demonstrates the benefits of using real-world evidence for the timely evaluation of risk factors for severe disease during pandemics and epidemics, and its potential to contribute to public health decision-making.

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### POTENTIAL CONFLICTS OF INTEREST

None of the authors reported potential conflicts of interest.

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### **CORRESPONDING AUTHOR CONTACT INFORMATION**

Address correspondence to: Hector S. Izurieta, MD, MPH, CBER/FDA, 10903 New Hampshire Avenue, Silver Spring, MD 20993; email: <u>Hector.izurieta@fda.hhs.gov</u>

#### ALTERNATE CORRESPONDING AUTHOR CONTACT INFORMATION

Yixin Jiao, MPP, Acumen LLC, 440 1st St NW #900, Washington, DC 20001, email:

yjiao@sphereinstitute.org

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**TABLES AND FIGURES** 

Table 1. Summary of COVID-19 hospitalization rates and proportion of inpatient complications among the primary study

Summary	General El	derly Population	Elderly	NH Population	ESRI	D Population
All Beneficiaries	25	,333,329		653,966	292,302	
Median Age		73		85		65
Sex	#	%	#	%	#	%
Female	14,095,346	55.6%	437,379	66.9%	127,180	43.5%
Male	11,237,983	44.4%	216,587	33.1%	165,122	56.5%
Severe COVID-19 Outcomes	#	<i>Rate<sup>a</sup></i>	#	Rate	#	Rate
COVID-Related Deaths	12,613	5.0	18,028	275.7	1,777	60.8
COVID-19 Hospitalizations	27,961	11.0	19,637	300.3	4,503	154.1
Hospitalization-Related Outcomes	#	% of Hospitalized	#	% of Hospitalized	#	% of Hospitalized
COVID-19 Hospitalizations	27,961	100.0%	19,637	100.0%	4,503	100.0%
ICU/CCU Admission	6,132	21.9%	4,719	24.0%	1,184	26.3%
Ventilator Use/ECMO	4,646	16.6%	2,946	15.0%	842	18.7%
Inpatient Renal Replacement Therapy	985	3.5%	1,529	7.8%	3,744	83.1%
Inpatient Death	7,286	26.1%	6,996	35.6%	1,135	25.2%

population, the elderly NH population, and the ESRD population

Abbreviation: COVID-19, coronavirus disease 2019; ICU, intensive care unit; CCU, coronary care unit; ECMO, extracorporeal membrane oxygenation

Rate per 10,000

# Table 2. Distribution of demographic, socioeconomic, and health status characteristics ofthe primary study population, by COVID-related outcome status

	COVID-Related Outcome					
Covariate	All Beneficiaries	COVID-Related	COVID-19 Hospitalization			
		Deaths				
All	25,333,329	12,613	27,961			
Age Group						
65-69	28.2%	9.8%	16.9%			
70-74	27.6%	13.0%	18.6%			
75-79	19.0%	15.3%	17.4%			
80-84	12.6%	17.5%	16.8%			
>=85	12.6%	44.5%	30.3%			
Sex						
Female	55.6%	48.5%	51.2%			
Male	44.4%	51.5%	48.8%			
Race/Ethnicity						
White	85.1%	72.4%	67.3%			
Black	6.7%	16.0%	20.1%			
Hispanic	1.6%	4.5%	4.9%			
Asian	2.1%	2.6%	2.8%			
North American Native	0.5%	0.9%	0.9%			
Other/Unknown	4.1%	3.6%	4.0%			
Medicaid Dual-Eligibility						
Non-Dual-Eligible	90.6%	71.0%	69.6%			
Dual-Eligible	9.4%	29.0%	30.4%			
ADI Rank Categories						
1-10th	11.8%	21.8%	19.2%			

	CO	VID-Related Outco	me
Covariate	All Beneficiaries	COVID-Related	COVID-19
		Deaths	Hospitalizatio
11-20	12.0%	18.7%	17.6%
21-30	12.4%	12.7%	12.2%
31-40	11.7%	9.1%	9.6%
41-50	11.0%	7.0%	7.4%
51-60	10.0%	5.6%	6.1%
61-70	9.1%	5.0%	5.7%
71-80	8.0%	4.5%	5.0%
81-90	6.6%	4.8%	5.2%
91-100	4.3%	8.0%	9.2%
Missing	3.1%	2.9%	2.9%
ason for Entering Medicare			
Aged in without ESRD	90.5%	85.9%	83.2%
Disabled without ESRD	9.4%	13.8%	16.4%
Aged in with ESRD	0.0%	0.0%	0.0%
Disabled with ESRD	0.0%	0.0%	0.0%
ESRD only	0.1%	0.3%	0.3%
Missing	0.0%	0.0%	0.0%
OVID-19 Circulation Rate by County			
1st Quartile	12.6%	0.9%	1.1%
2nd Quartile	16.0%	2.5%	2.8%
3rd Quartile	23.1%	7.0%	7.1%
4th Quartile	47.3%	88.2%	87.6%
Missing	1.0%	1.5%	1.4%

	COVID-Related Outcome					
Covariate		COVID-Related	COVID-19			
	All Beneficiaries	Deaths	Hospitalization			
[1,10)	2.4%	0.6%	0.6%			
[10,50)	11.7%	3.0%	3.2%			
[50,100)	10.5%	3.1%	3.4%			
[100,500)	31.1%	13.0%	13.1%			
[500,1000)	12.5%	9.5%	9.5%			
[1000+)	30.7%	69.4%	68.7%			
Missing	1.0%	1.5%	1.4%			
tate of Residence <sup>b</sup>						
СА	8.9%	3.1%	3.4%			
СТ	1.0%	2.8%	3.1%			
FL	6.9%	2.8%	2.7%			
IL CONTRACT	4.3%	5.5%	6.1%			
IN	2.2%	1.7%	1.7%			
МА	2.6%	7.7%	7.3%			
MD	2.5%	3.6%	3.3%			
ME	0.5%	0.1%	0.1%			
MI	2.8%	5.4%	6.0%			
NJ	3.0%	13.8%	11.4%			
NY	5.2%	26.5%	27.0%			
PA	4.0%	4.8%	4.7%			
Vaccination Status						
FLUAD Vaccine	7.1%	6.9%	6.5%			
Fluzone High Dose Vaccine	22.8%	20.9%	20.8%			
Other Influenza Vaccine or Administration Code	40.9%	42.9%	41.9%			

	COVID-Related Outcome					
Covariate		<b>COVID-Related</b>	COVID-19			
	All Beneficiaries	Deaths	Hospitalization			
Presence of Medical Conditions						
Diabetes	23.5%	41.6%	42.8%			
Obesity	15.9%	18.0%	21.4%			
Hypertension	58.3%	78.7%	77.3%			
Hospitalized Stroke/TIA	0.3%	1.5%	1.2%			
Coronary Revascularization	0.5%	0.9%	0.8%			
Atrial Fibrillation	11.4%	24.7%	20.4%			
Congestive Heart Failure	8.0%	28.2%	22.6%			
Hospitalized AMI	0.4%	1.7%	1.2%			
Other Cerebrovascular Disease	6.4%	14.8%	13.2%			
Chronic Obstructive Pulmonary Disease	9.4%	20.5%	18.5%			
(COPD)						
Asthma without COPD	3.8%	3.8%	4.9%			
Interstitial Lung Disease	1.3%	3.3%	2.5%			
Hypersensitivity Pneumonitis	0.2%	0.4%	0.3%			
Bronchiectasis	0.7%	1.4%	1.3%			
Chronic Liver Disease	2.3%	3.3%	3.7%			
Neurological/Neurodevelopmental Conditions	4.5%	16.6%	14.4%			
Frailty Index						
[0-0.2)	85.2%	37.0%	52.4%			
[0.2-0.4)	11.3%	31.3%	26.8%			
[0.4-0.6)	2.7%	19.4%	13.4%			
[0.6-0.8)	0.7%	10.1%	6.3%			
[0.8-1)	0.1%	2.1%	1.2%			

	COVID-Related Outcome					
Covariate		COVID-Related	COVID-19			
	All Beneficiaries	Deaths	Hospitalization			
Frailty Conditions						
Impaired Mobility	0.2%	2.4%	1.8%			
Depression	11.8%	27.2%	24.2%			
Parkinson's Disease	1.2%	4.9%	3.7%			
Arthritis	22.3%	32.9%	32.0%			
Cognitive Impairment	4.8%	37.6%	25.6%			
Paranoia	0.7%	6.9%	5.9%			
Chronic Skin Ulcer	2.1%	11.2%	8.4%			
Skin and Soft Tissue Infection	4.3%	11.2%	9.7%			
Mycoses	9.9%	37.7%	31.6%			
Gout	3.7%	7.3%	6.6%			
Falls	3.0%	13.6%	10.6%			
Musculoskeletal Problems	39.9%	53.0%	51.8%			
Urinary Tract Infection	8.9%	25.8%	21.7%			
Pneumonia	3.0%	17.6%	14.5%			
Charlson>0	32.6%	59.1%	56.8%			
Hospital Admission in Past 6 Months	7.7%	32.6%	28.1%			
Immunocompromised Status						
Immunocompromised	3.4%	8.1%	6.9%			
Non-Immunocompromised	96.6%	91.9%	93.1%			

Abbreviation: COVID-19, coronavirus disease 2019; ADI, Area Deprivation Index; ESRD, end-stage renal disease;

FLUAD, standard-dose, inactivated influenza (flu) vaccine; Fluzone High Dose, high-dose inactivated influenza

(flu) vaccine

Population density measured as number of persons per square mile

States with the highest proportion of COVID-related deaths and COVID-19 hospitalizations displayed

## Table 3. Logistic regression model results assessing potential risk factors for COVID-19

Constitutes	COVID-Related Death		COVID-19 Hospitalization	
Covariates	Odds Ratio	95% CI	Odds Ratio	95% CI
Sex (Reference: Female)				
Male	1.77	(1.71, 1.84)	1.48	(1.45, 1.52)
Reason for entering Medicare (Reference: Not Ag	ed into Medica	re)		
A god into Modigara	0.72	(0.68, 0.76)	0.74	(0.72, 0.77)
	0.72	(0.08, 0.70)	0.74	(0.72, 0.77)
ADI National Rank (Reference: ADI=1)				
ADI=50	0.97	(0.91, 1.03)	1.08	(1.04, 1.12)
ADI=100	1.09	(1.00, 1.18)	1.23	(1.16, 1.29)
Logged COVID-19 Circulation Rate by 100,000 <sup>a</sup>	10			
Circulation Rate (Change by 2x)	1.98	(1.94, 2.01)	1.94	(1.92, 1.96)
Logged Population Density by County <sup>b</sup>				
Population Density (Change by 2x)	1.00	(0.99, 1.01)	1.02	(1.01, 1.03)
Vaccination (Reference: Non-Vaccinated)				
FLUAD Vaccine	1.04	(0.96, 1.11)	1.01	(0.96, 1.06)
Fluzone High Dose Vaccine	0.91	(0.87, 0.95)	0.95	(0.92, 0.98)
Other Influenza Vaccine or Vaccine	1.05	(1.00, 1.10)	1.05	(1 01 1 00)
Administration	1.05	(1.00, 1.10)	1.05	(1.01, 1.09)
Presence of Medical Conditions <sup>c</sup>				
Hypertension	1.02	(0.97, 1.07)	1.13	(1.09, 1.16)
Obesity	1.10	(1.05, 1.16)	1.16	(1.13, 1.20)
Diabetes	1.23	(1.18, 1.29)	1.28	(1.24, 1.32)
Hospitalized Stroke/TIA	1.07	(0.91, 1.25)	0.94	(0.84, 1.06)
Coronary Revascularization	1.03	(0.85, 1.26)	0.86	(0.74, 1.00)
Atrial Fibrillation	0.97	(0.92, 1.01)	0.98	(0.95, 1.01)

## hospitalization and COVID-related death in the primary study population

Coverietes	COVID-Re	lated Death	COVID-19 Hospitalization	
Covariates	<b>Odds Ratio</b>	95% CI	<b>Odds Ratio</b>	95% CI
Congestive Heart Failure	1.30	(1.23, 1.36)	1.15	(1.11, 1.19)
Hospitalized AMI	0.99	(0.85, 1.16)	0.89	(0.79, 1.00)
Other Cerebrovascular Disease	0.90	(0.85, 0.95)	0.91	(0.87, 0.94)
COPD	1.14	(1.08, 1.20)	1.10	(1.06, 1.14)
Asthma without COPD	0.93	(0.85, 1.03)	1.06	(1.00, 1.13)
Interstitial Lung Disease	1.08	(0.97, 1.20)	0.95	(0.88, 1.03)
Hypersensitivity Pneumonitis	1.11	(0.83, 1.48)	1.00	(0.81, 1.25)
Bronchiectasis	0.85	(0.73, 1.00)	0.89	(0.80, 0.99)
Chronic Liver Disease	1.07	(0.97, 1.19)	1.07	(1.00, 1.14)
Neurological/Neurodevelopmental Conditions	1.08	(1.02, 1.14)	1.14	(1.10, 1.19)
Frailty Conditions	NO			
Impaired Mobility	1.45	(1.29, 1.65)	1.40	(1.27, 1.54)
Depression	1.32	(1.26, 1.38)	1.26	(1.22, 1.30)
Parkinson's Disease	1.27	(1.17, 1.39)	1.23	(1.15, 1.32)
Arthritis	0.97	(0.93, 1.01)	0.99	(0.97, 1.02)
Cognitive Impairment	3.16	(3.02, 3.31)	2.24	(2.16, 2.32)
Paranoia	1.66	(1.54, 1.80)	1.63	(1.54, 1.73)
Chronic Skin Ulcer	1.12	(1.05, 1.20)	1.06	(1.01, 1.11)
Skin and Soft Tissue Infection	1.13	(1.06, 1.20)	1.12	(1.07, 1.17)
Mycoses	1.57	(1.51, 1.64)	1.47	(1.43, 1.51)
Gout	1.06	(0.99, 1.14)	1.02	(0.97, 1.07)
Falls	1.37	(1.30, 1.46)	1.36	(1.31, 1.42)
Musculoskeletal Problems	0.96	(0.92, 1.00)	1.01	(0.98, 1.03)
Urinary Tract Infection	1.22	(1.17, 1.28)	1.19	(1.15, 1.23)
Pneumonia	1.89	(1.79, 2.00)	1.94	(1.86, 2.02)

	COVID-Related Death		COVID-19 Hospitalization			
Covariates	Odds Ratio	95% CI	Odds Ratio	95% CI		
	Ouus Katio	<b>J</b> J /0 CI	Ouus Katio	<b>75</b> /0 CI		
Charlson Score>0	1.08	(1.03, 1.14)	1.09	(1.06, 1.13)		
Hospital Admission in Past 6 Months	1.43	(1.35, 1.51)	1.55	(1.49, 1.61)		
Immunocompromised Status (Reference: Non-Im	on-Immunocompromised)					
Immunocompromised	1.43	(1.34, 1.53)	1.24	(1.18, 1.30)		
Estimated Overall Interaction Effects of Age, Dua	al-Eligibility, aı	nd Race <sup>d</sup>				
80 Years Old vs. 65 Years Old				•		
80 Years Old vs. 65 Years Old	3.09	(2.94, 3.25)	1.74	(1.68, 1.80)		
Dual-Eligible vs. Non-Dual-Eligible						
Dual-Eligible vs. Non-Dual-Eligible	2.17	(1.92, 2.44)	2.23	(2.08, 2.39)		
Non-Whites vs. Whites						
	NO	·				
Black	2.47	(2.17, 2.81)	2.81	(2.62, 3.02)		
Hispanic	3.11	(2.37, 4.08)	3.31	(2.83, 3.87)		
North American Native	5.82	(3.25, 10.43)	4.22	(2.90, 6.16)		
Asian	1.32	(0.93, 1.87)	1.50	(1.23, 1.82)		
Other/Unknown	1.19	(0.95, 1.50)	1.16	(1.01, 1.32)		
Effects of Being Dual-Eligible, by Race						
White (Dual vs. Non-Dual)	2.25	(1.97, 2.55)	2.35	(2.18, 2.54)		
Black	1.79	(1.54, 2.09)	1.60	(1.46, 1.74)		
Hispanic	1.46	(1.14, 1.87)	1.34	(1.16, 1.54)		
North American Native	3.09	(1.75, 5.46)	2.44	(1.66, 3.59)		
Asian	1.28	(0.90, 1.82)	1.12	(0.91, 1.37)		
Other/Unknown	2.00	(1.52, 2.63)	2.15	(1.83, 2.53)		
Non-Whites vs. Whites, Non-Dual-Eligible						
Black	2.53	(2.21, 2.89)	2.92	(2.71, 3.14)		
Hispanic	3.23	(2.44, 4.29)	3.49	(2.96, 4.10)		

Covariates	COVID-Re	elated Death	COVID-19 Hospitalization	
	Odds Ratio	95% CI	Odds Ratio	95% CI
North American Native	5.65	(3.09, 10.32)	4.21	(2.85, 6.21)
Asian	1.39	(0.98, 1.99)	1.60	(1.31, 1.97)
Other/Unknown	1.21	(0.95, 1.53)	1.17	(1.01, 1.34)
Non-Whites vs. Whites, Dual-Eligible				
Black	2.02	(1.74, 2.35)	1.98	(1.81, 2.16)
Hispanic	2.10	(1.64, 2.69)	1.99	(1.72, 2.29)
North American Native	7.77	(4.39, 13.75)	4.37	(2.97, 6.43)
Asian	0.80	(0.56, 1.13)	0.76	(0.62, 0.94)
Other/Unknown	1.08	(0.82, 1.41)	1.07	(0.91, 1.25)

Abbreviation: COVID-19, coronavirus disease 2019; CI, confidence interval; ADI, area deprivation index; FLUAD, standard-dose, inactivated influenza (flu) vaccine; Fluzone High Dose, high-dose inactivated influenza (flu) vaccine; TIA, transient ischemic attack; AMI, acute myocardial infarction; COPD, chronic obstructive pulmonary disease

County-level circulation rate log-transformed using a base of 2, where the OR is interpreted as the estimated odds ratio of doubling the circulation rate

County-level population density log-transformed using a base of 2, where the OR is interpreted as the estimated odds ratio of doubling the circulation rate

Odds ratios obtained from logistic regression models. For the odds ratio for the COPD and asthma without COPD groups, the reference group is people with no COPD or asthma

Interaction effects estimated at median age of the cohort (73 years old), except for the effects of age

Covorietes	At	Age 65	At Age 80	
Covariates	Odds Ratio	95% CI	<b>Odds Ratio</b>	95% CI
Dual-Eligible vs. Non-Dual-Eligible				
Dual-Eligible vs. Non-Dual-Eligible	2.25	(1.81, 2.80)	1.82	(1.69, 1.98)
Non-Whites vs. Whites				•
Black	2.20	(1.68, 2.88)	2.04	(1.87, 2.23)
Hispanic	4.33	(2.85, 6.59)	2.49	(2.02, 3.08)
North American Native	7.45	(2.52, 22.03)	4.11	(2.64, 6.39)
Asian	1.13	(0.52, 2.47)	1.29	(1.02, 1.63)
Other/Unknown	0.98	(0.54, 1.80)	1.20	(1.00, 1.45)
Effects of Being Dual-Eligible, by Race				
White	2.34	(1.85, 2.96)	1.89	(1.74, 2.06)
Black	1.87	(1.44, 2.43)	1.51	(1.36, 1.69)
Hispanic	1.52	(1.02, 2.26)	1.23	(1.05, 1.44)
North American Native	3.21	(1.13, 9.12)	2.60	(1.67, 4.05)
Asian	1.33	(0.61, 2.94)	1.08	(0.88, 1.33)
Other/Unknown	2.08	(1.11, 3.91)	1.69	(1.40, 2.04)
Non-Whites vs. Whites, Non-Dual-Eligible				
Black	2.25	(1.70, 2.97)	2.09	(1.90, 2.29)
Hispanic	4.51	(2.93, 6.95)	2.60	(2.08, 3.25)
North American Native	7.23	(2.40, 21.73)	3.99	(2.50, 6.35)
Asian	1.19	(0.55, 2.61)	1.36	(1.06, 1.75)
Other/Unknown	0.99	(0.54, 1.82)	1.21	(1.00, 1.48)
Non-Whites vs. Whites, Dual-Eligible				
Black	1.80	(1.38, 2.34)	1.67	(1.50, 1.86)

# Table 4. Estimated odds ratio of COVID-related death by dual-eligibility status and race atage 65 and 80 in the primary study population

Coverietes	At Age 65		At A	Age 80
Covariates	Odds Ratio	95% CI	Odds Ratio	95% CI
Hispanic	2.93	(1.97, 4.36)	1.69	(1.44, 1.98)
North American Native	9.94	(3.50, 28.21)	5.48	(3.52, 8.54)
Asian	0.68	(0.31, 1.50)	0.78	(0.63, 0.95)
Other/Unknown	0.89	(0.47, 1.66)	1.08	(0.90, 1.31)
Comparing to White, Non-Dual-Eligible				
Beneficiaries		(		
White, Dual-Eligible	2.34	(1.85, 2.96)	1.89	(1.74, 2.06)
Black, Non-Dual-Eligible	2.25	(1.70, 2.97)	2.09	(1.90, 2.29)
Black, Dual-Eligible	4.20	(3.23, 5.46)	3.16	(2.83, 3.52)
Hispanic, Non-Dual-Eligible	4.51	(2.93, 6.95)	2.60	(2.08, 3.25)
Hispanic, Dual-Eligible	6.85	(4.61, 10.18)	3.19	(2.72, 3.75)
North American Native, Non-Dual-Eligible	7.23	(2.40, 21.73)	3.99	(2.50, 6.35)
North American Native, Dual-Eligible	23.22	(8.18, 65.91)	10.38	(6.66, 16.16)
Asian, Non-Dual-Eligible	1.19	(0.55, 2.61)	1.36	(1.06, 1.75)
Asian, Dual-Eligible	1.59	(0.72, 3.51)	1.47	(1.19, 1.80)
Other/Unknown, Non-Dual-Eligible	0.99	(0.54, 1.82)	1.21	(1.00, 1.48)
Other/Unknown, Dual-Eligible	2.07	(1.10, 3.88)	2.05	(1.70, 2.48)

Abbreviation: COVID-19, coronavirus disease 2019; CI, confidence interval

Figure 1. Odds ratio of COVID-related death and COVID-19 hospitalization for beneficiaries with different dual-eligibility status, race, and age in the primary study us population (elderly Medicare beneficiaries without ESRD not in nursing home)





