COVID-19 Hospital Outcomes in CEC-UW: Investigating Potential Disparities in Vulnerable Populations and Comparing Effects Over Health Systems.

Background:

As of October 2022, nearly 100 million cases of COVID-19 have been recorded and over one million deaths have been attributed to the disease in the United States [1]. In Wisconsin, there have been over 1.8 million COVID-19 cases and more than 15,000 deaths [2].

The COVID-19 pandemic has disproportionately impacted members of several vulnerable populations. Heightened risk for COVID-19 infection and mortality has been documented in racial and ethnic minority groups, including Black, Asian, and Hispanic populations [3-5], individuals living in rural areas [6], and persons with mental health disorders including schizophrenia and depression [7-9]. Various mechanisms have been proposed to explain these health inequities, including adverse health effects of accumulative stress, economic disadvantage, limited access to quality health care, crowded living conditions, and higher risks of occupational viral exposure [10-12].

The COVID EHR Cohort at the University of Wisconsin (CEC-UW) is a retrospective cohort study that extracted and harmonized selected electronic health record data from all COVID-19 patients encountered at 21 U.S. health care systems between February 2020 and January 2022. The inpatient subsample from CEC-UW includes data from 145,944 adults hospitalized with either an ICD-10 COVID-19 diagnosis, a positive PCR test for COVID-19, or both.

The current project uses the CEC-UW inpatient sample to investigate disparities in COVID-19 mortality by race, ethnicity, rural vs. urban residence, and mental health disorders. The CEC-UW has two attributes that make it especially useful for investigating disparities. First, its large sample size affords statistical power for testing group differences. Second, the study includes patients treated in numerous health systems from across the country. This provides the opportunity to identify variation in COVID disparities over sites, potentially an important first step in identifying modifiable explanatory variables accounting for site differences.

UW Health was one of the 21 participating CEC-UW health care systems, contributing 1,703 patients to the hospitalized sample. A secondary aim of the current project is to compare possible disparities in hospital outcomes at UW Health to those observed at the other sites. Accurate descriptive data specific to Wisconsin can enhance targeting individuals at greatest risk and inform the treatment of future COVID patients. Additionally, these comparisons can serve as a ‘report card’ indicating how UW Heath measured up to other large health care systems during the pandemic.

Study Design and Measures:

The COVID EHR Cohort at the University of Wisconsin (CEC-UW; ClinicalTrials.gov: NCT04506528) is a retrospective cohort study established in May 2020 with support from the National Cancer Institute [13]. Participating health systems (Figure 1) provided selected EHR

data from all of their COVID-19 patients across the data collection period (February 1, 2020 to January 31, 2022).

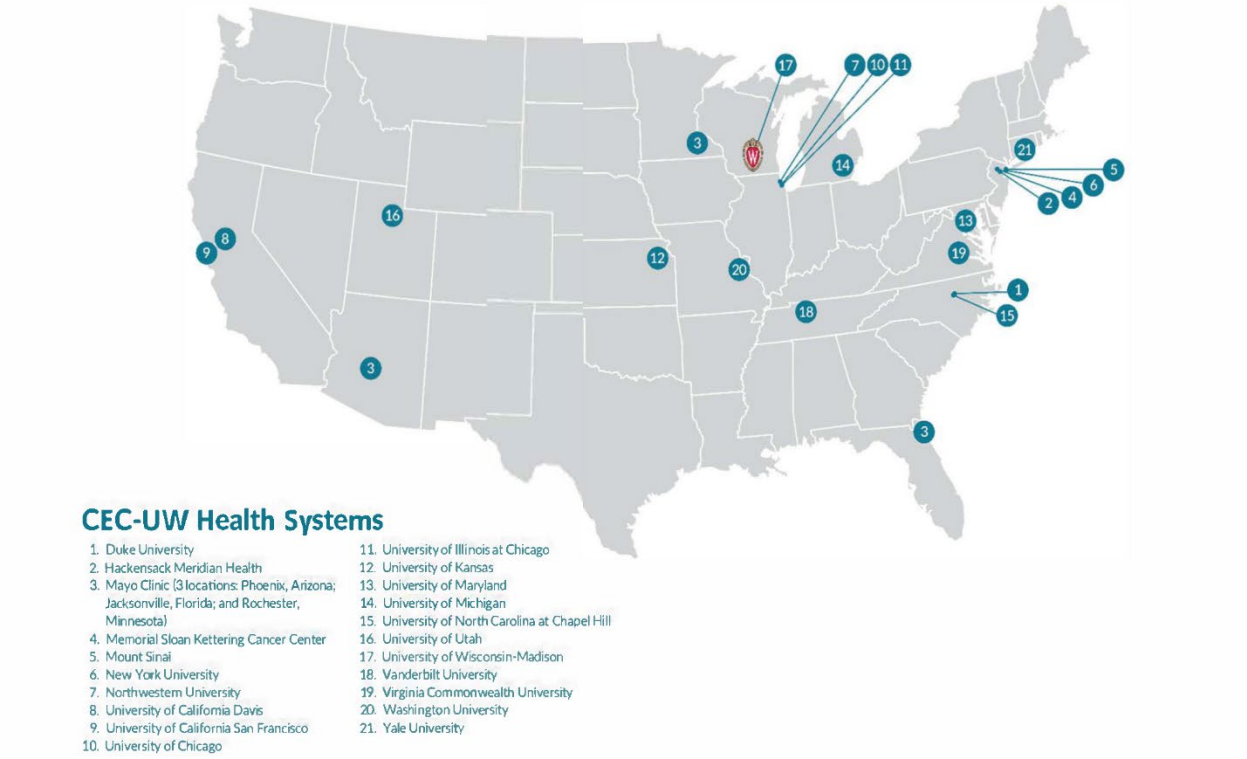

Figure 1. CEC-UW participating health systems. ***Note: the numbers in this figure do not correspond to the system numbers in the reported analytic results.*** Health systems other than UW Health were designated with a random numeric ID for presenting analytic findings.

The analysis sample for the current project consisted of 145,944 patients hospitalized at the 21 health systems with COVID-19 during the study period. Participants in this analysis had to: (1) be age 18 or older, (2) be hospitalized for at least 24 hours, or have died within 24 hours of admission or been transferred to the ICU within 24 hours of admission, (3) have a positive COVID-19 PCR test in a 14-day window from 7 days prior to admission to 7 days following admission or have an ICD-10 COVID-19 diagnosis during their hospitalization, and (4) have had prior contact with the admitting healthcare system. This last criterion increased data availability regarding comorbidities and psychiatric disorder history.

Customized data extraction code was developed by a team of programmers and consultants at UW Health (Madison, WI), Yale New Haven Health (New Haven, CT) and Bluetree Network, Inc. (Madison, WI). Extraction code targeted approximately 250 discrete EHR elements including sociodemographic data and basic health information, pre- and post-COVID-19 ICD-10 diagnoses, clinical encounter data, lab tests and results, and medication information.

Mortality is the primary outcome, reflecting whether the patient died during the index hospitalization or was discharged alive. Data from hospitalized patients with undetermined outcome status at the time of the data extraction were not analyzed.

We investigated racial and ethnic disparities by comparing mortality rates in Black, Asian, and Hispanic patients to those observed in non-Hispanic White (NHW) patients. Patients classified in the remaining racial/ethnic groups extracted from the EHR (American Indian/Alaska Native, Native Hawaiian/Pacific Islander, Other Race Not Specified, More than One Race, Unknown/Not Reported/Missing) were too small, heterogenous, or unequally distributed across sites to permit meaningful analysis.

Rural residence was determined based on Primary Rural/Urban Commuting Area (RUCA) codes [14], which were derive from the patient's 5-digit ZIP code. RUCA codes 1-6 (Metropolitan Area Core to Micropolitan Low Commuting) were classified as 'urban' and codes 7-10 (Small Town Core to Rural Areas) were classified as "rural."

A five-year lookback at EHR ICD-10 diagnoses was used to identify patients with a history of depression (F32, F33, F34.1), anxiety disorder (F41.0 - F43.9) and psychotic disorder (F20 – F29).

Health systems other than UW Health were designated with a unique numeric ID for presenting analytic findings. (These IDs ***do not*** correspond to the numbers used to designate sites in Figure 1.) The same numeric ID was used for a given health system across all analyses.

Statistical Approach:

We used binary logistic generalized linear mixed models (GLMMs [15]) to predict in-hospital mortality from vulnerable population membership, with and without adjustment for other covariates.

The GLMMs included *random intercepts* for the 21 health systems, allowing them to differ with respect to their overall rates of mortality. GLMMs also included *random slope* terms for the vulnerable population variable, allowing health systems to vary with respect to the magnitude of the potential health disparity effects.

Figure 2 illustrates these features, depicting model-predicted mortality rates at each site as a function of race (Black, coded 1 vs. NHW, coded 0) from a model with no other predictor variables. The model produces fixed effects that represent estimates of the overall intercept (the predicted mortality rate when race = 0, in this case representing the mortality in NHW) and the group disparity (the difference between mortality rates in NHW and Black patients, or the slope of the line). The fixed effects are depicted by the black line.

By including a random intercept term, the model allows the health systems to differ from the overall effect with respect to the mortality rate for NHW. This is illustrated by the vertical spread of the predicted lines for individual sites around the fixed effects estimate.

Similarly, including a random slope term allows the magnitude of the difference in mortality between NHW and Black patients vary over sites. This is illustrated by the variation in the slopes of the lines relative to the fixed effect.

The random intercept and slope deviations from the fixed effects are assumed to be normally distributed around a mean of zero. The model produces a significance test for the variance of the intercept deviations and a test for the variance of the slope deviations. For the current project, the test of the variance in random slope for the race/ethnicity effect is most critical – this indicates whether there is statistically significant heterogeneity of the potential disparity effect size over health systems.

The model also produces Empirical Best Linear Unbiased Predictions (EBLUPs) for the magnitude of each site's slope deviation from the fixed effect slope. These site-specific deviations can be plotted to visualize the distribution of random effects and compare UW Health to other health systems. When significant heterogeneity of mortality effects for a vulnerable group were observed or when UW Health appeared to be an outlier, we tested whether the UW Health EBLUP estimate was significantly different from zero (the expected mean effect) and computed the UW Health-specific odds ratio for comparison with the fixed effect OR.

Figure 3 plots the slope EBLUP estimates for each site from the same model as Figure 2. Comparing Figures 2 and 3 illustrates the interpretation of the EBLUP slope estimates. The lowest EBLUP was estimated for System 16 (-.138). This indicates that the slope of the NHW-Black mortality line was more steeply negative at System 16 compared to the overall fixed effect. This can be clearly seen by comparing the dark blue line for System 16 in Figure 2 to the black line for the overall fixed effect. System 2 had the highest EBLUP estimate (.181), indicating that the slope was less negative compared to the fixed effect. The teal line in Figure 2 highlights the slope for System 2 and shows it was nearly flat and most discrepant from the other sites' slopes. The EBLUP for UW Health was in the middle of the distribution and very near zero. This indicates that the slope was very similar to the overall fixed effect estimate. This can be seen by the red line for UW Health in Figure 2 – the slope is nearly parallel with the fixed effect line.

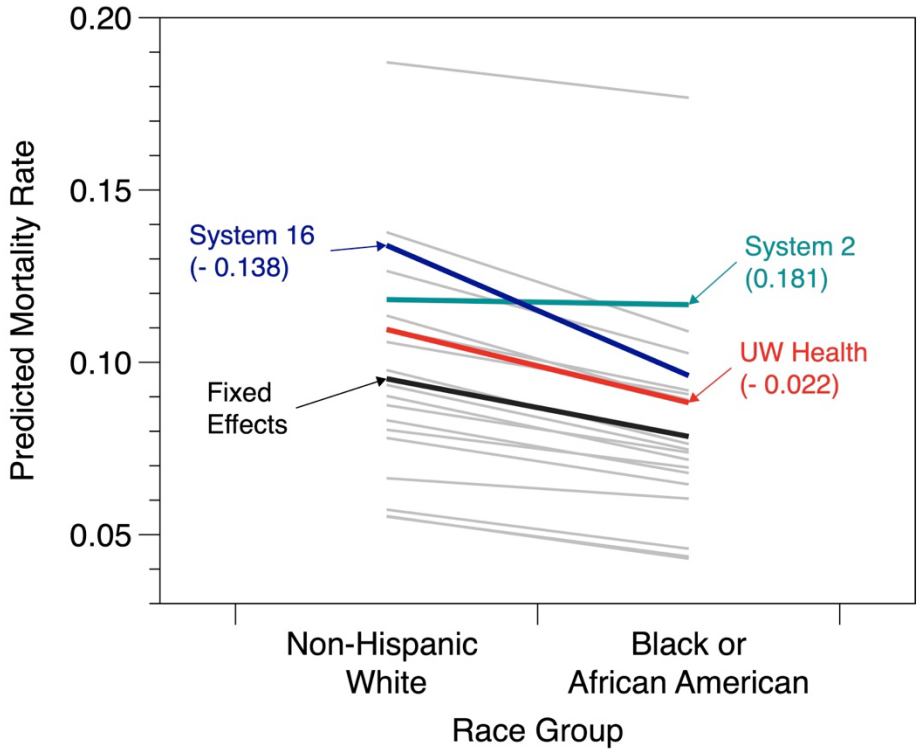

Figure 2. Model-predicted mortality rates from unadjusted model, Black vs. NHW

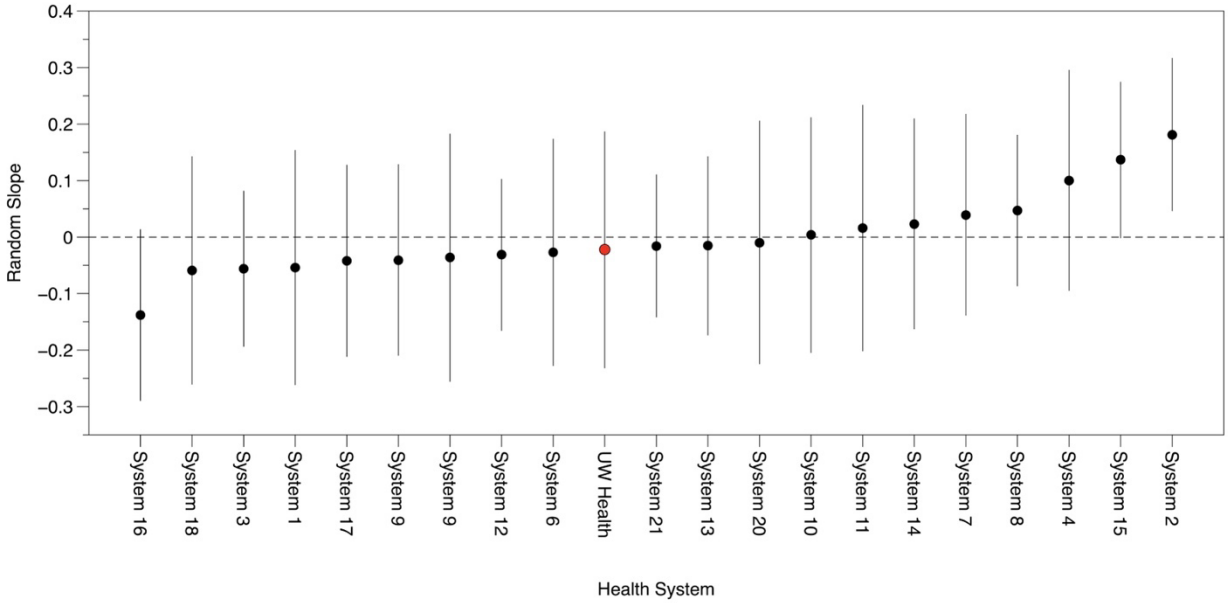

Figure 3. EBLUP slope estimates for unadjusted model, Black vs NHW.

Results:

Table 1 summarizes the total number of patients in analyzed subgroups, the number who died in-hospital within each group, and the observed mortality rate with the associated 95% confidence interval.

Table 1. Number of patients, deaths, and observed mortality rate by subgroup.

Group	Total N	N Died	Mortality Rate (95% CI)
All Inpatients	145,944	13,036	.089 (.087, .091)
Race/Ethnicity			
Non-Hispanic White	78,128	7,005	.090 (.088, .092)
Black	34,663	2,738	.079 (.076, .082)
Asian	3,882	457	.118 (.108, .128)
Hispanic	22,373	2,113	.094 (.091, .098)
Rurality			
Rural Residence	7,050	730	.104 (.097, .111)
Urban Residence	138,791	12,302	.089 (.087, .090)
Psychiatric Disorders			
Depression History	15,924	1,388	.087 (.083, .092)
No Depression History	130,020	11,648	.090 (.088, .091)
Anxiety History	18,723	1,508	.081 (.077, .085)
No Anxiety History	127,221	11,528	.091 (.089, .092)
Psychosis History	2,581	211	.082 (.072, .093)
No Psychosis History	143,363	12,825	.089 (.088, .091)

Black or African American vs. Non-Hispanic Whites. Overall, 7.9% of Black patients died (2,738/34,663) compared to 9.0% of Non-Hispanic White patients (7,005/78,128). GLMM models results are provided in Table 2.

Unadjusted Model. With no adjustment for covariates, the fixed effect was significant, OR = 0.82, 95% CI = 0.76 to 0.89, $p < .001$, indicating that, at the mean of the random slope distribution, Blacks were predicted to have lower odds of dying compared to NHW. The random slope variance for race was not significant, Var = 0.013, *SE* = 0.009, $p = .133$. This indicates that there was not significant heterogeneity over sites with respect to the size of the race effect.

Figure 3 (presented above) shows the distribution of random slope EBLUPs and their associated 95% confidence intervals by health system, sorted by effect size. The overall fixed effect of OR = 0.82 indicates lower odds of mortality among Blacks vs. NHW where the random slope = 0 (dashed reference line). Negative random slopes indicate a smaller site-specific OR compared to this reference fixed effect, in this case indicating a bigger relative advantage for Black vs. NHW patients. Positive random slopes indicated a larger OR and would be associated with a smaller relative advantage for Black patients or potentially a reversed effect. A health system's EBLUP is statistically significant when its 95% interval does not include zero.

Figure 3 shows that there is limited variability over sites in the magnitude of the race effect in this model. Only 1 health system (System 2) had a random slope significantly different from zero. UW Health ranks 10th of 21 systems with a random slope very near zero.

Covariate-Adjusted Model. A comparable model was estimated, this time accounting for several patient characteristics expected to be related to COVID-19 severity, including sex, age, BMI, number of pre-hospitalization SARS-CoV-2 vaccine doses, past 5-year Elixhauser comorbidity index, and Social Deprivation Index based on patient ZIP Code Tabulation Area. As expected, each of the covariates was robustly predictive of in-hospital mortality. After accounting for these effects, the fixed effect for Black vs. NHW was no longer significant, OR = 1.01, 95% CI = 0.94 to 1.09, $p = .723$. The random slope variance for race was not significant:

Var = 0.008, *SE* = 0.007, *p* = .282. This indicates that there was still no significant heterogeneity over sites with respect to the size of the race effect after adjusting for covariates.

Figure 4 shows the random slope EBLUP estimates from this model. Most of the random slope estimates, including UW Health, hover very near zero.

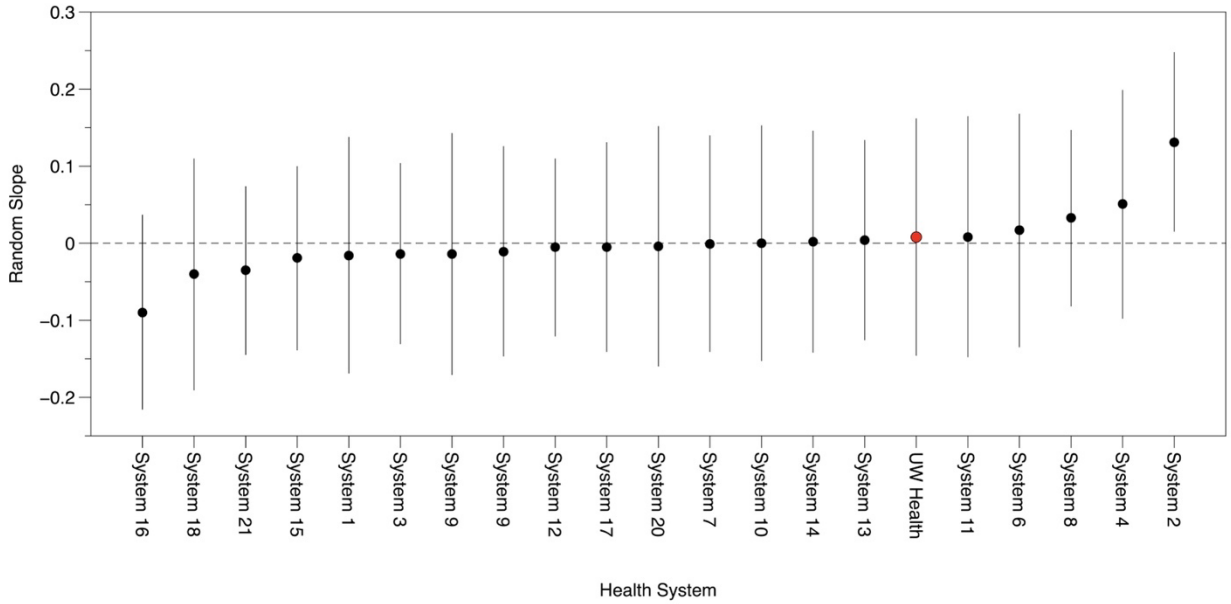

Figure 4. EBLUP estimates for covariate adjusted model, Black vs. NHW

Table 2. Prediction of in-hospital mortality from Black vs. Non-Hispanic White patient race

	Unadjusted			Adjusted		
Fixed Effects	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***
Race						
Non-Hispanic White (REF)	1.00	--	--	1.00	--	--
Black	0.82	0.76, 0.89	< .001	1.01	0.94, 1.09	.723
Sex						
Female (REF)				1.00	--	--
Male				1.49	1.42, 1.56	< .001
Age						
18-29 (REF)				1.00	--	--
30-39				1.51	1.13, 2.03	.006
40-49				2.99	2.29, 3.90	< .001
50-64				6.00	4.67, 7.70	< .001
65-74				10.36	8.08, 13.30	< .001
75-84				14.35	11.18, 18.42	< .001
85+				18.75	14.58, 24.12	< .001
BMI						
Healthy Weight (REF)				1.00	--	--
Underweight				1.17	1.04, 1.32	.009
Overweight				1.15	1.08, 1.22	< .001
Obese				1.40	1.32, 1.49	< .001
Severely Obese				2.02	1.87, 2.19	< .001
Missing or Biologically Implausible				1.87	1.55, 2.26	< .001
Vaccination Status						
0 doses				1.00	--	--
1 dose				0.57	0.50, 0.64	< .001
2 doses				0.56	0.52, 0.61	< .001
3 doses				0.47	0.41, 0.55	< .001
Comorbidity Index				1.020	1.018, 1.023	< .001
Social Deprivation Index				1.001	1.001, 1.002	.001
Random Effects	Var	*SE*	*p*	Var	*SE*	*p*
Intercept (System)	0.108	0.036	.003	0.117	0.039	.003
Slope (Black)	0.013	0.009	.133	0.008	0.007	.232

Asian vs. Non-Hispanic Whites. Overall, 11.8% of Asian patients died (457/3,882) compared to 9.0% of NHW patients (7,005/78,128). GLMM results are provided in Table 3.

Unadjusted Model. With no adjustment for covariates, the fixed effect for race was significant, OR = 1.26, 95% CI = 1.11 to 1.42, $p < .001$. This indicates that, at the mean of the random slopes, Asians had higher odds of dying compared to NHW. The random slope variance was not significant, Var = 0.013, *SE* = 0.023, $p = .582$. This indicates that there was not significant heterogeneity over health systems with respect to the size of the race effect. Random slopes are plotted in Figure 5. In this case, the fixed effect indicates relative increased odds of mortality in Asians vs NHW. Negative random slopes indicate a smaller race gap in mortality and positive slopes indicate an exaggerated group difference compared to the fixed effect estimate. None of the random slopes is different from zero. UW Health ranks in the top third (16th of 21) with respect to effect estimate magnitude, but it is part of a large cluster of sites with random slope estimates very near zero.

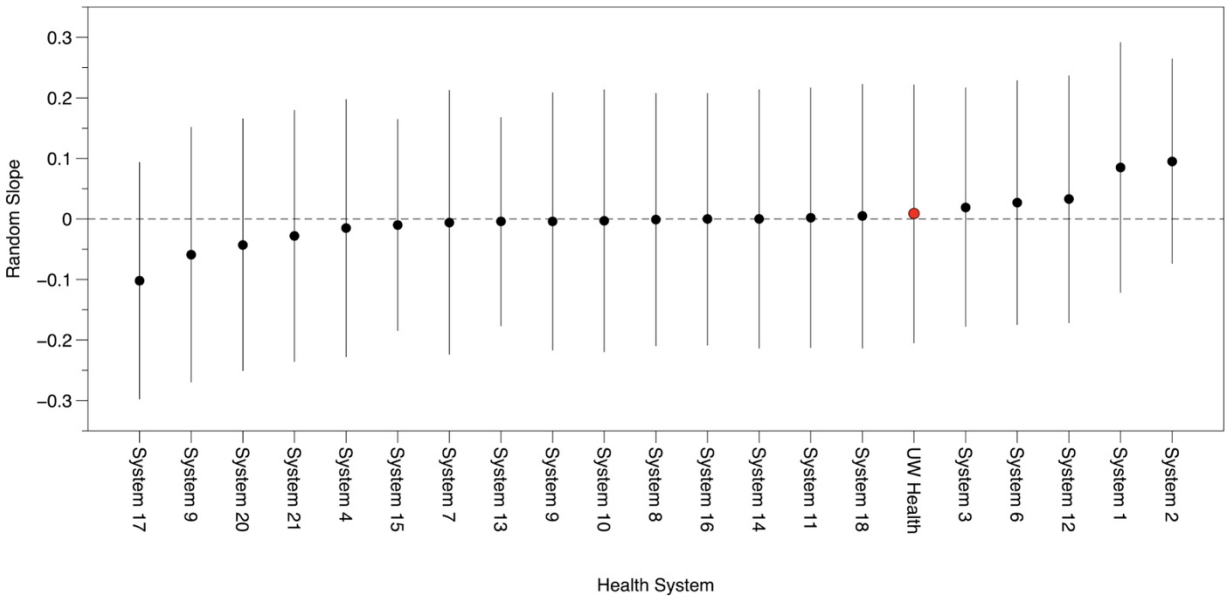

Figure 5. EBLUP estimates for unadjusted model, Asian vs. NH

Covariate-Adjusted Model. After adjusting for covariates, the overall fixed effect was somewhat larger and remained statistically significant, OR = 1.60, 95% CI = 1.34 to 1.92, $p < .001$. Again, the random slope variance was not significant, Var = 0.067, *SE* = 0.050, $p = .180$. This indicates that there was not significant heterogeneity over sites with respect to the size of the race effect.

Random slopes from the covariate-adjusted model are plotted in Figure 6. UW Health ranks 15th of 21 with a random slope estimate very near zero.

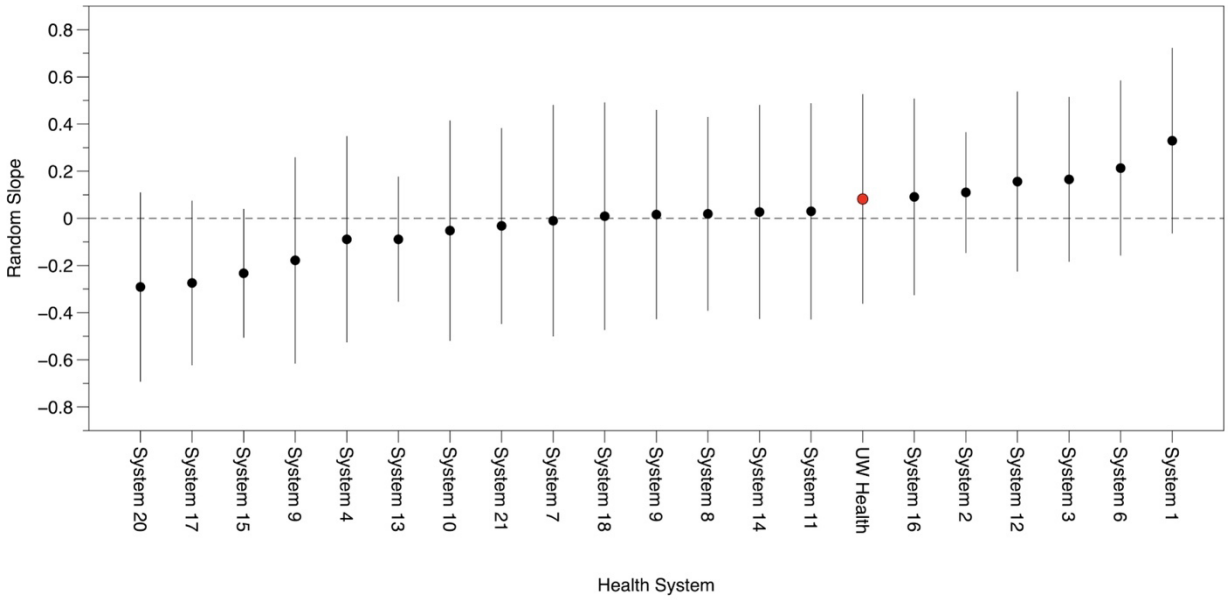

Figure 6. EBLUP estimates for covariate-adjusted model, Asian vs. NH

Table 3. Prediction of in-hospital mortality from Asian vs. Non-Hispanic White patient race

	Unadjusted			Adjusted		
Fixed Effects	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***
Race						
Non-Hispanic White (REF)	1.00	--	--	1.00	--	--
Asian	1.26	1.11, 1.42	< .001	1.60	1.34, 1.92	< .001
Sex						
Female (REF)				1.00	--	--
Male				1.52	1.45, 1.60	< .001
Age						
18-29 (REF)				1.00	--	--
30-39				1.49	1.004, 2.21	.048
40-49				3.27	2.29, 4.67	< .001
50-64				6.54	4.68, 9.14	< .001
65-74				11.28	8.09, 15.74	< .001
75-84				15.24	10.92, 21.26	< .001
85+				20.00	14.31, 27.94	< .001
BMI						
Healthy Weight (REF)				1.00	--	--
Underweight				1.21	1.06, 1.39	.005
Overweight				1.19	1.11, 1.28	< .001
Obese				1.40	1.31, 1.50	< .001
Severely Obese				2.14	1.94, 2.35	< .001
Missing or Biologically Implausible				1.91	1.52, 2.39	< .001
Vaccination Status						
0 doses				1.00	--	--
1 dose				0.47	0.41, 0.56	< .001
2 doses				0.54	0.49, 0.59	< .001
3 doses				0.48	0.40, 0.57	< .001
Comorbidity Index				1.020	1.018, 1.023	< .001
Social Deprivation Index				1.002	1.001, 1.003	< .001
Random Effects	Var	*SE*	*p*	Var	*SE*	*p*
Intercept (System)	0.107	0.037	.004	0.110	0.038	.004
Slope (Asian)	0.013	0.023	.582	0.067	0.050	.180

Hispanic Ethnicity vs Non-Hispanic Whites. Overall, 9.4% of Hispanic patients died (2,113/22,373) compared to 9.0% of Non-Hispanic White patients (7,005/78,128). Results from GLMM analyses are given in Table 4.

Unadjusted Model. The overall fixed effect for ethnicity was significant, OR = 0.76, 95% CI = 0.63 to 0.92, p = .005, and indicated that, at the mean random slope, Hispanic patients had lower odds of dying compared to NHW. The random slope variance was significant, Var = 0.140, SE = 0.062, p = .024, indicating the presence of notable heterogeneity over sites with respect to the size of the ethnicity effect.

Figure 7 shows the distribution of random slopes. UW Health ranks 12th of 21 with a slightly positive random slope not significantly different from zero. The site-specific OR estimate for UW Health (0.82) was similar to the fixed effect (0.76).

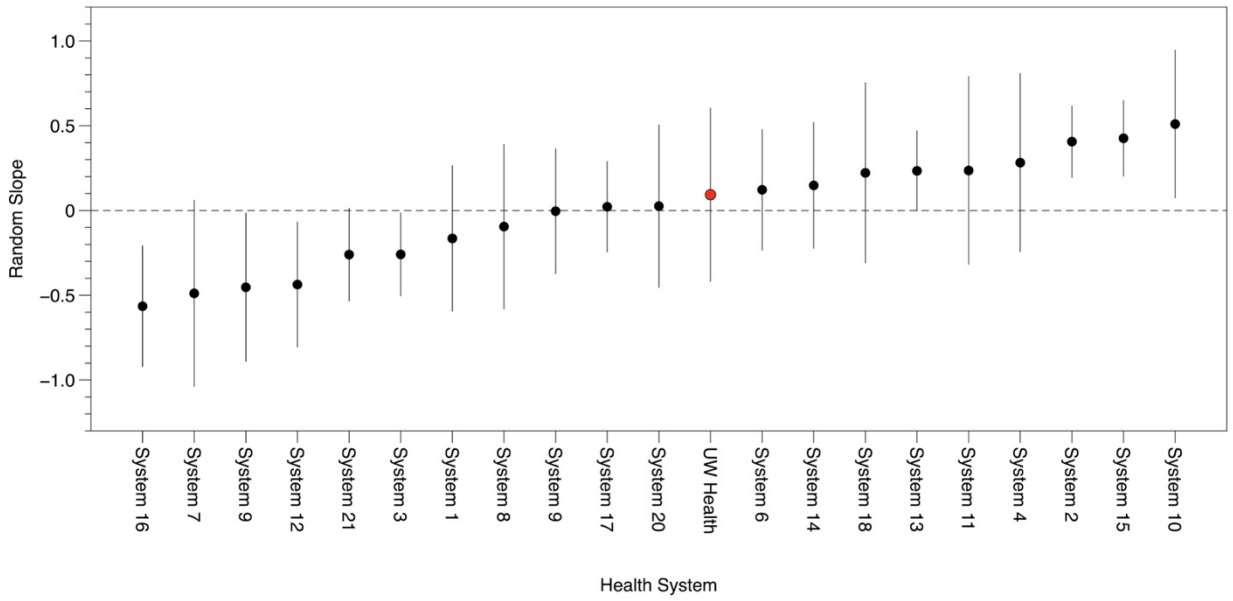

Figure 7. EBLUP estimates from unadjusted model, Hispanic vs. NHW

Covariate-Adjusted Model. After adjusting for covariates, the overall fixed effect was significant and now indicated excess mortality in Hispanic patients vs. NHW patients, OR = 1.20, 95% CI = 1.07 to 1.35, p = .002. The random slope variance was not significant, Var = 0.030, SE = 0.018, p = .097, indicating there was not heterogeneity over sites with respect to the size of the ethnicity effect after adjustment for covariates.

Figure 8 shows the random slope estimates from this model. UW Health ranked 11th of 21 with a random slope effect very near zero.

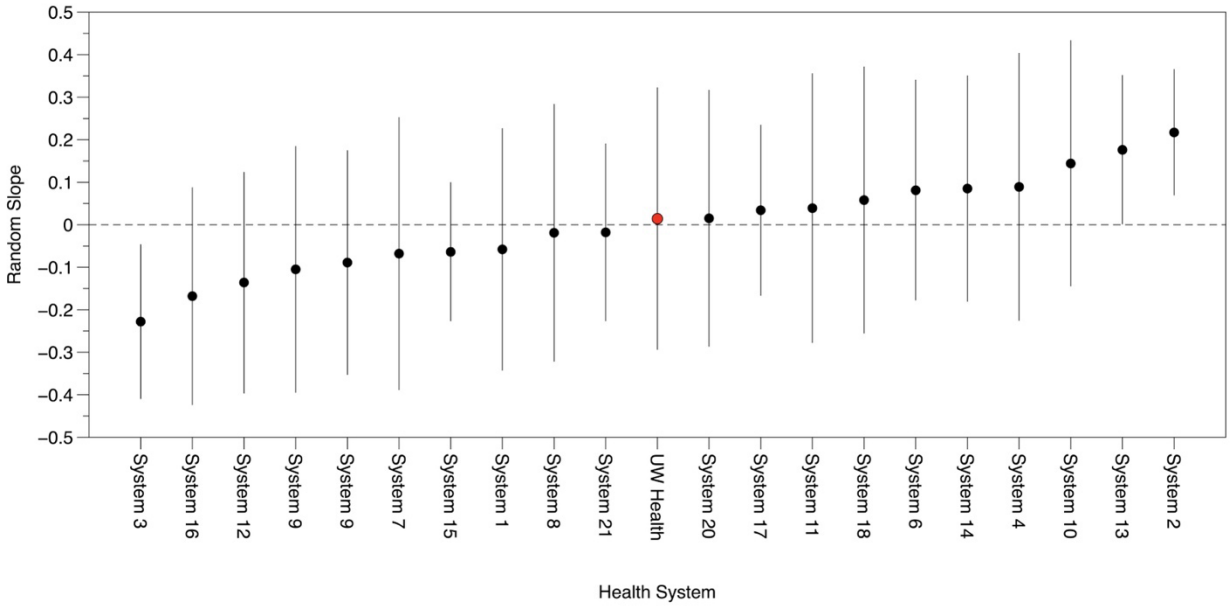

Figure 8. EBLUP estimates from covariate-adjusted model, Hispanic vs. NHW

Table 4. Prediction of in-hospital mortality from Hispanic ethnicity vs. Non-Hispanic White

	Unadjusted			Adjusted		
Fixed Effects	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***
Ethnicity						
Non-Hispanic White (REF)	1.00	--	--	1.00	--	--
Hispanic	0.76	0.63, 0.92	.005	1.20	1.07, 1.35	.002
Sex						
Female (REF)				1.00	--	--
Male				1.55	1.48, 1.63	< .001
Age						
18-29 (REF)				1.00	--	--
30-39				1.67	1.21, 2.31	.002
40-49				3.91	2.92, 5.23	< .001
50-64				8.23	6.24, 10.84	< .001
65-74				14.32	10.87, 18.86	< .001
75-84				19.53	14.82, 25.74	< .001
85+				25.75	19.50, 34.00	< .001
BMI						
Healthy Weight (REF)				1.00	--	--
Underweight				1.23	1.08, 1.40	.001
Overweight				1.18	1.11, 1.25	< .001
Obese				1.42	1.33, 1.51	< .001
Severely Obese				2.20	2.02, 2.40	< .001
Missing or Biologically Implausible				2.21	1.84, 2.66	< .001
Vaccination Status						
0 doses				1.00	--	--
1 dose				0.50	0.43, 0.57	< .001
2 doses				0.51	0.47, 0.56	< .001
3 doses				0.47	0.39, 0.55	< .001
Comorbidity Index				1.020	1.017, 1.022	< .001
Social Deprivation Index				1.003	1.002, 1.004	< .001
Random Effects	Var	*SE*	*p*	Var	*SE*	*p*
Intercept (System)	0.097	0.033	.003	0.097	0.033	.003
Slope (Hispanic)	0.140	0.062	.024	0.030	0.018	.097

Rural vs Urban. Overall, 10.4% of rural-residing patients died (730/7,050) compared to 8.9% of urban-residing patients (12,302/138,791). Results from GLMM analyses are given in Table 5.

Unadjusted Model. The overall fixed effect for rural residence was significant, OR = 1.54, 95% CI = 1.31 to 1.81, $p < .001$, and indicated that, at the mean random slope, rural patients had higher odds of dying compared to urban-residing patients. The random slope variance was not significant, Var = 0.053, *SE* = 0.036, $p = .137$, indicating the absence of significant heterogeneity over sites with respect to the size of the rural disparity effect.

Figure 9 shows the distribution of random slopes. UW Health ranks 20th of 21 with a positive random slope that did not differ significantly from zero ($p = .082$). Accordingly, the site-specific OR point estimate for UW Health (2.02) trended non-significantly larger than fixed effect (1.54).

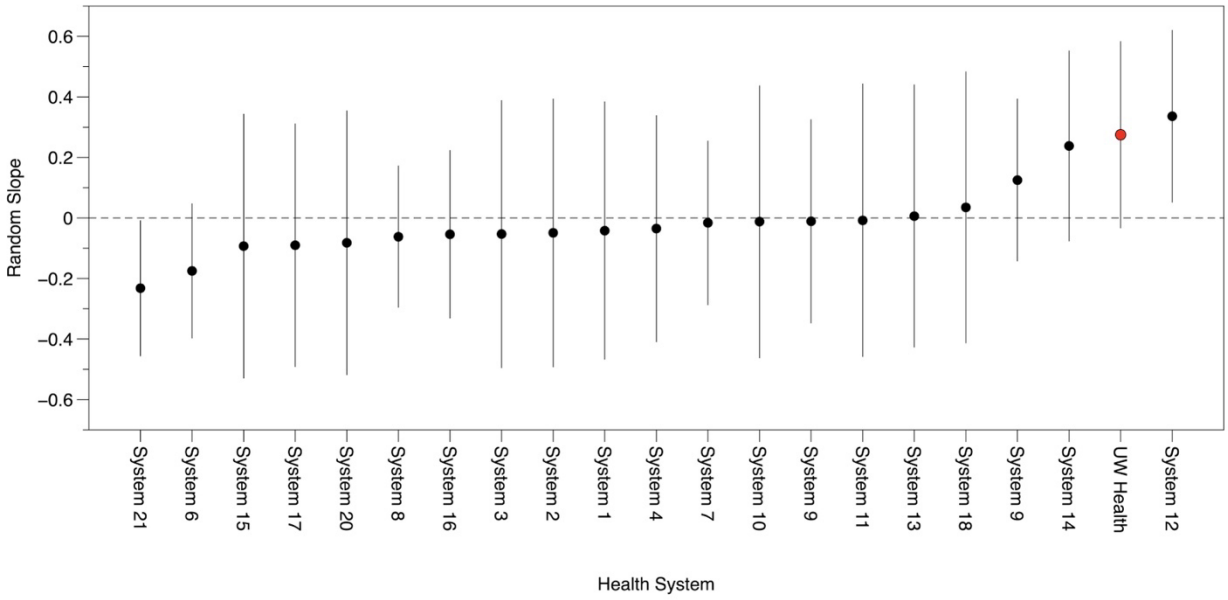

Figure 9. EBLUP estimates from unadjusted model, Rural vs. Urban

Covariate-Adjusted Model. A comparable model was estimated, this time accounting for sex, age, race, ethnicity, BMI, number of pre-hospitalization SARS-CoV-2 vaccine doses, past 5-year Elixhauser comorbidity index, and Social Deprivation Index. Rural residence was associated with increased adjusted odds of death compared to urban residence, OR = 1.44, 95% CI = 1.22 to 1.69, $p < .001$. The random slope variance was not significant, indicating that the rural/urban effect was not heterogeneous across health systems.

Figure 10 plots the random slopes from the covariate-adjusted model. Again, UW health ranked 20th out of 21, with a random slope effect that was positive but not significantly different from zero ($p = .062$). The site-specific OR estimate for UW Health was 1.94, non-significantly larger than the fixed effect (1.44).

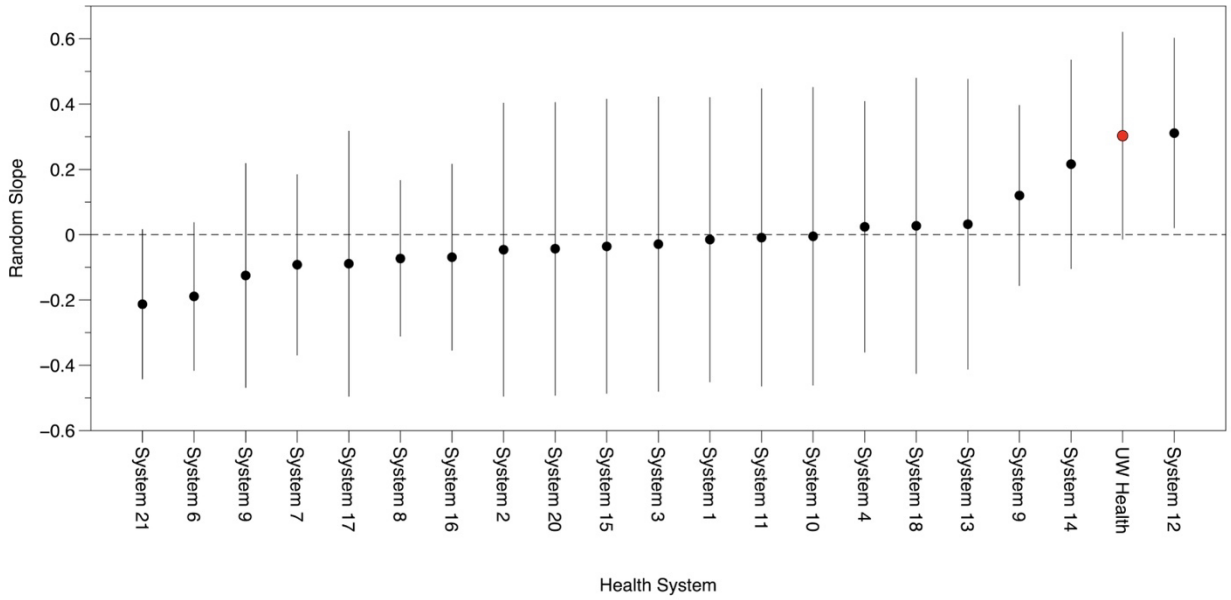

Figure 10. EBLUP estimates from covariate-adjusted model, Rural vs. Urban

Table 5. Prediction of in-hospital mortality from rural vs. urban residence.

	Unadjusted			Adjusted		
Fixed Effects	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***
Rural-Urban						
Urban Residence (REF)	1.00	--	--	1.00	--	--
Rural Residence	1.54	1.31, 1.81	< .001	1.44	1.22, 1.69	< .001
Sex						
Female (REF)				1.00	--	--
Male				1.52	1.46, 1.58	< .001
Age						
18-29 (REF)				1.00	--	--
30-39				1.65	1.29, 2.12	< .001
40-49				3.48	2.78, 4.36	< .001
50-64				7.35	5.95, 9.07	< .001
65-74				12.90	10.45, 15.92	< .001
75-84				17.97	14.55, 22.19	< .001
85+				23.41	18.91, 28.98	< .001
Race						
White (REF)				1.00	--	--
American Indian or Alaska Native				1.99	1.52, 2.59	< .001
Asian				1.55	1.39, 1.72	< .001
Black or African American				1.03	0.97, 1.08	.320
Native Hawaiian or Pacific Islander				1.06	0.76, 1.46	.739
Other Race Not Specified				1.17	1.09, 1.27	< .001
More than One				1.50	1.10, 2.04	.011
Unknown or Missing				1.29	1.11, 1.49	.001
Ethnicity						
Not Hispanic or Latino (REF)				1.00	--	--
Hispanic or Latino				1.15	1.07, 1.23	< .001
Unknown or Missing				1.25	1.09, 1.43	.001
BMI						
Healthy Weight (REF)				1.00	--	--
Underweight				1.14	1.02, 1.26	.017
Overweight				1.17	1.11, 1.23	< .001
Obese				1.41	1.34, 1.49	< .001
Severely Obese				2.10	1.96, 2.26	< .001
Missing or Biologically Implausible				1.89	1.63, 2.19	< .001
Vaccination Status						
0 doses				1.00	--	--
1 dose				0.53	0.47, 0.6	< .001
2 doses				0.54	0.50, 0.58	< .001
3 doses				0.47	0.41, 0.54	< .001
Comorbidity Index				1.019	1.017, 1.021	< .001
Social Deprivation Index				1.002	1.001, 1.002	< .001
Random Effects	Var	*SE*	*p*	Var	*SE*	*p*
Intercept (System)	0.111	0.036	.002	0.101	0.033	.002
Slope (Rural)	0.053	0.036	.137	0.055	0.037	.138

Depression. Overall, 8.7% of patients with a past-5-year history of depression died (1388/15,924) compared to 9.0% of patients without such as history (11,648/130,020). Results from GLMM analyses are given in Table 6.

Unadjusted Model. The overall fixed effect for depression was not significant, OR = 1.03, 95% CI = 0.95 to 1.12, p = 465. The random slope variance was not significant, Var = 0.012, *SE* = 0.011, p = .274, indicating the absence of significant heterogeneity over sites with respect to the size of the depression effect.

Figure 11 shows the distribution of random slopes. UW Health ranks 2nd of 21 with a negative random slope that did not differ significantly from zero (p = .419). The UW Health OR estimate (0.95) was non-significantly lower than the fixed effect OR (1.03).

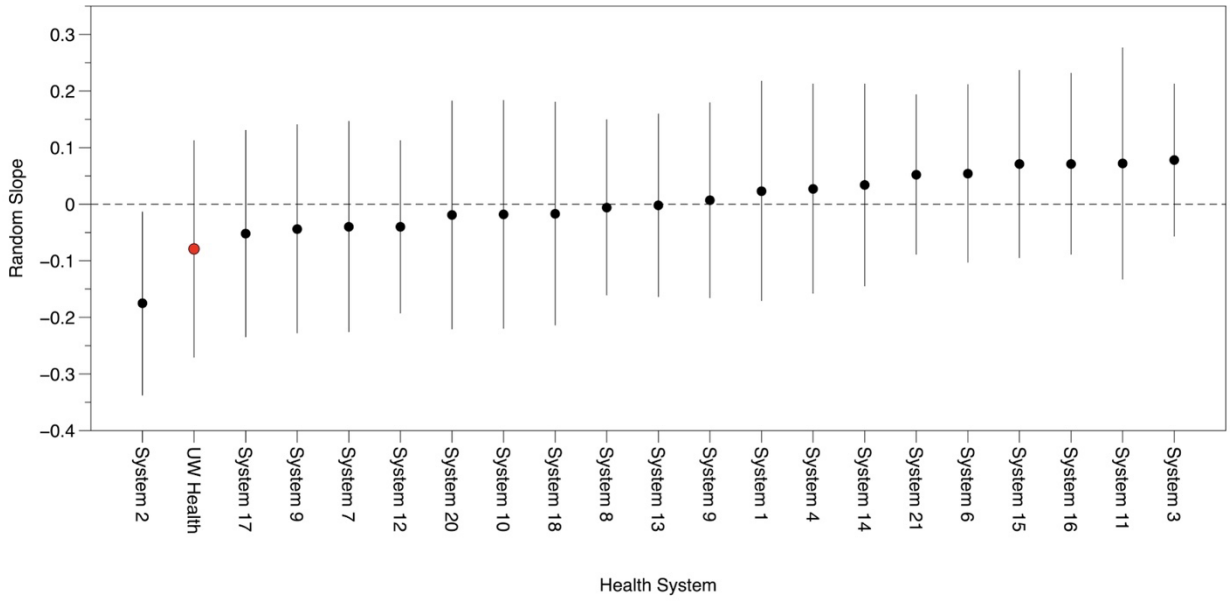

Figure 11. EBLUP estimates from unadjusted model, Depression History vs. No History

Covariate-Adjusted Model. After adjustment for other patient characteristics, depression history remained unrelated to in-hospital mortality, OR = 1.07, 95% CI = 0.996 to 1.14, p = .064. The random slope variance was not significant, *Var* = 0.002, *SE* = 0.007, p = .738, indicating that the magnitude of the depression effect was not heterogeneous across health systems.

Figure 12 plots the random slopes from the covariate-adjusted model. UW Health ranked 3rd out of 21, with a random slope effect that was negative but not significantly different from zero (p = .729). The UW Health adjusted OR estimate (1.05) was non-significantly lower than the fixed effect adjusted OR (1.07).

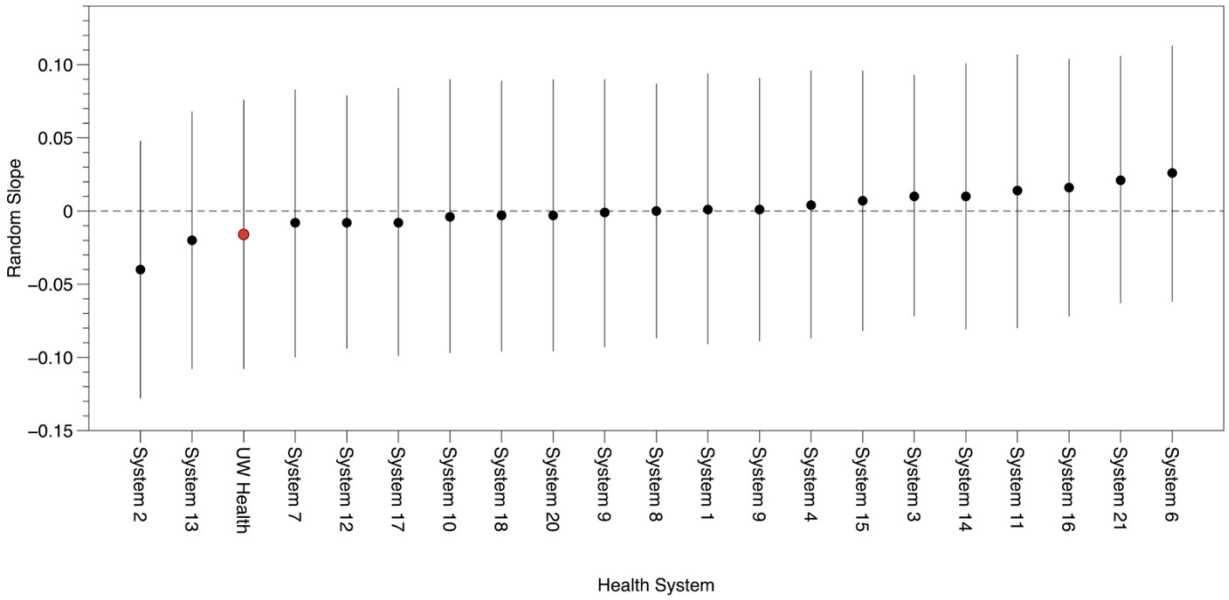

Figure 12. EBLUP estimates from covariate-adjusted model, Depression History vs. No History

Table 6. Prediction of in-hospital mortality from Past 5-Year History of Depression.

	Unadjusted			Adjusted		
Fixed Effects	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***
Mental Disorder History						
No History (REF)	1.00	--	--	1.00	--	--
ICD-10 Depression	1.03	0.95, 1.12	.465	1.07	1.00, 1.14	.064
Sex						
Female (REF)				1.00	--	--
Male				1.53	1.47, 1.59	< .001
Age						
18-29 (REF)				1.00	--	--
30-39				1.65	1.29, 2.12	< .001
40-49				3.48	2.78, 4.35	< .001
50-64				7.36	5.96, 9.09	< .001
65-74				12.93	10.47, 15.96	< .001
75-84				18.04	14.61, 22.29	< .001
85+				23.48	18.97, 29.06	< .001
Race						
White (REF)				1.00	--	--
American Indian or Alaska Native				2.02	1.55, 2.63	< .001
Asian				1.54	1.38, 1.71	< .001
Black or African American				1.02	0.96, 1.07	.580
Native Hawaiian or Pacific Islander				1.05	0.76, 1.45	.771
Other Race Not Specified				1.17	1.08, 1.26	< .001
More than One				1.49	1.09, 2.03	.012
Unknown or Missing				1.29	1.11, 1.49	.001
Ethnicity						
Not Hispanic or Latino (REF)				1.00	--	--
Hispanic or Latino				1.14	1.06, 1.23	< .001
Unknown or Missing				1.25	1.1, 1.43	.001
BMI						
Healthy Weight (REF)				1.00	--	--
Underweight				1.13	1.02, 1.26	.018
Overweight				1.17	1.11, 1.23	< .001
Obese				1.41	1.34, 1.49	< .001
Severely Obese				2.11	1.96, 2.26	< .001
Missing or Biologically Implausible				1.89	1.63, 2.19	< .001
Vaccination Status						
0 doses				1.00	--	--
1 dose				0.53	0.47, 0.59	< .001
2 doses				0.53	0.49, 0.57	< .001
3 doses				0.47	0.41, 0.54	< .001
Comorbidity Index				1.019	1.017, 1.021	< .001
Social Deprivation Index				1.019	1.017, 1.021	< .001
Random Effects	Var	*SE*	*p*	Var	*SE*	*p*
Intercept (System)	0.110	0.036	.002	0.104	0.034	.002
Slope (Depression)	0.012	0.011	.274	0.002	0.007	.738

Anxiety. Overall, 8.1% of patients with a past-5-year history of anxiety disorder died (1508/18,723) compared to 9.1% of patients without such as history (11,528/127,221). Results from GLMM analyses are given in Table 7.

Unadjusted Model. A model including a random slope term produced errors indicating that the variation over sites in the magnitude of the anxiety-mortality association was effectively zero and could not be modeled accurately. Accordingly, the model was re-specified assuming only a random intercept term. Anxiety disorder history was associated with decreased odds of mortality, OR = 0.94, 95% CI = 0.89 to 0.99, p = .029.

Covariate-Adjusted Model. The covariate-adjusted model again produced errors indicating that a random slope term could not be estimated. Therefore, an adjusted model with only a random intercept term was estimated. Findings indicated that adjusted odds of mortality did not differ in patients with and without a history of anxiety disorder, OR = 0.99, 95% CI = 0.93 to 1.05, p =.625.

Table 7. Prediction of in-hospital mortality from Past 5-Year History of Anxiety.

	Unadjusted			Adjusted		
Fixed Effects	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***
Mental Disorder History						
No History (REF)	1.00	--	--	1.00	--	--
ICD-10 Anxiety	0.94	0.89, 0.99	.029	0.99	0.93, 1.05	.625
Sex						
Female (REF)				1.00	--	--
Male				1.52	1.46, 1.58	< .001
Age						
18-29 (REF)				1.00	--	--
30-39				1.65	1.29, 2.12	< .001
40-49				3.48	2.78, 4.36	< .001
50-64				7.36	5.96, 9.09	< .001
65-74				12.92	10.46, 15.95	< .001
75-84				18.01	14.58, 22.24	< .001
85+				23.40	18.91, 28.97	< .001
Race						
White (REF)				1.00	--	--
American Indian or Alaska Native				2.01	1.55, 2.62	< .001
Asian				1.53	1.38, 1.71	< .001
Black or African American				1.01	0.96, 1.07	.661
Native Hawaiian or Pacific Islander				1.05	0.76, 1.45	.784
Other Race Not Specified				1.17	1.08, 1.26	< .001
More than One				1.49	1.09, 2.03	.012
Unknown or Missing				1.29	1.11, 1.49	.001
Ethnicity						
Not Hispanic or Latino (REF)				1.00	--	--
Hispanic or Latino				1.14	1.06, 1.23	< .001
Unknown or Missing				1.25	1.09, 1.43	.001
BMI						
Healthy Weight (REF)				1.00	--	--
Underweight				1.13	1.02, 1.26	.018
Overweight				1.17	1.11, 1.23	< .001
Obese				1.41	1.34, 1.49	< .001
Severely Obese				2.11	1.96, 2.26	< .001
Missing or Biologically Implausible				1.89	1.63, 2.19	< .001
Vaccination Status						
0 doses				1.00	--	--
1 dose				0.53	0.47, 0.60	< .001
2 doses				0.53	0.50, 0.58	< .001
3 doses				0.47	0.41, 0.54	< .001
Comorbidity Index				1.019	1.017, 1.021	< .001
Social Deprivation Index				1.002	1.001, 1.003	< .001
Random Effects	Var	*SE*	*p*	Var	*SE*	*p*
Intercept (System)	0.110	0.036	.002	0.103	0.034	.002
Slope (Anxiety)	--	--	--	--	--	--

Psychotic Disorders. Overall, 8.2% of patients with a past-5-year history of psychotic disorder died (211/2,581) compared to 8.9% of patients without such as history (12,825/127,221). Results from GLMM analyses are given in Table 8.

Unadjusted Model. The overall fixed effect for psychotic disorder history was not significant, OR = 0.90, 95% CI = 0.76 to 1.07, p = .241. The random slope variance was not significant, Var = 0.031, SE = 0.047, p = .664, indicating the absence of significant heterogeneity over sites with respect to the size of the psychosis history effect.

Figure 13 shows the distribution of random slopes. UW Health ranks 11th of 21 with a random slope very close to zero (p = .986).

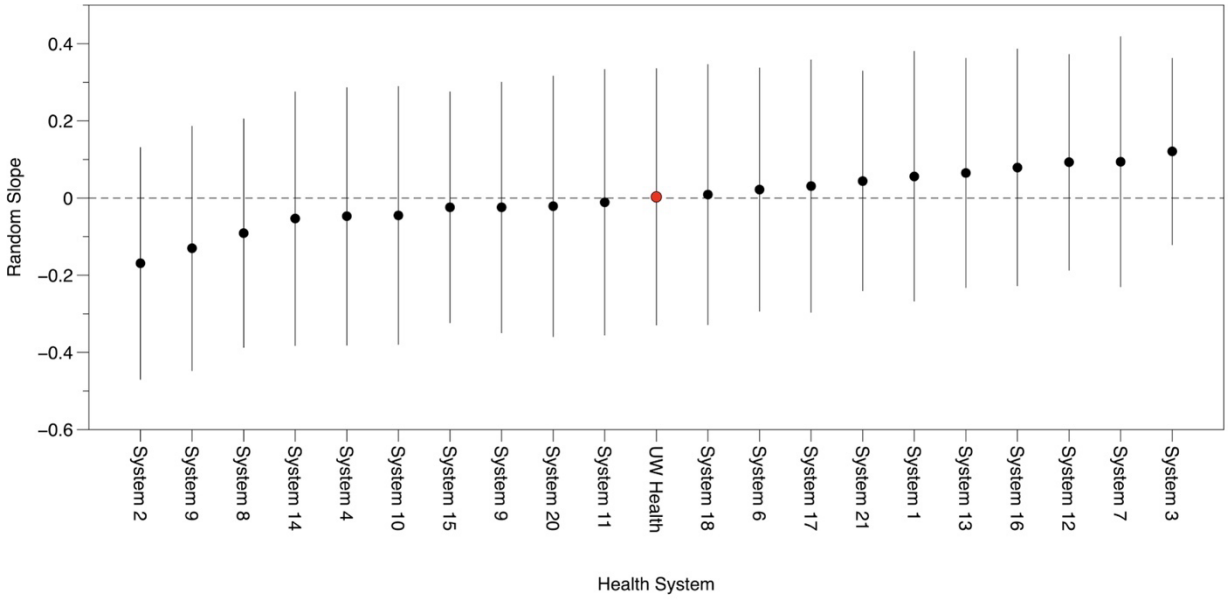

Figure 13. EBLUP estimates from unadjusted model, Psychotic Disorder History vs. No History

Covariate-Adjusted Model. A covariate-adjusted model specifying a random slope term produced errors indicating that the variation over sites in the magnitude of the anxiety-mortality association was effectively zero and could not be modeled accurately. Therefore, the model was re-specified assuming only an random intercept term. Findings indicated that adjusted odds of mortality did not differ in patients with and without a history of psychotic disorder, OR = 1.06, 95% CI = 0.91 to 1.23, p =.447.

Table 8. Prediction of in-hospital mortality from Past 5-Year History of Psychotic Disorder.

	Unadjusted			Adjusted		
Fixed Effects	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***
Mental Disorder History						
No History (REF)	1.00	--	--	1.00	--	--
ICD-10 Psychotic Disorder	0.90	0.76, 1.07	.241	1.06	0.91, 1.23	.447
Sex						
Female (REF)				1.00	--	--
Male				1.52	1.46, 1.58	< .001
Age						
18-29 (REF)				1.00	--	--
30-39				1.65	1.29, 2.12	< .001
40-49				3.48	2.78, 4.36	< .001
50-64				7.37	5.97, 9.10	< .001
65-74				12.93	10.48, 15.97	< .001
75-84				18.04	14.60, 22.28	< .001
85+				23.46	18.95, 29.03	< .001
Race						
White (REF)				1.00	--	--
American Indian or Alaska Native				2.02	1.55, 2.63	< .001
Asian				1.53	1.38, 1.71	< .001
Black or African American				1.01	0.96, 1.07	.648
Native Hawaiian or Pacific Islander				1.05	0.76, 1.45	.779
Other Race Not Specified				1.17	1.08, 1.26	< .001
More than One				1.49	1.09, 2.03	.012
Unknown or Missing				1.29	1.11, 1.49	.001
Ethnicity						
Not Hispanic or Latino (REF)				1.00	--	--
Hispanic or Latino				1.14	1.06, 1.23	< .001
Unknown or Missing				1.25	1.10, 1.43	.001
BMI						
Healthy Weight (REF)				1.00	--	--
Underweight				1.13	1.02, 1.26	.018
Overweight				1.17	1.11, 1.23	< .001
Obese				1.41	1.34, 1.49	< .001
Severely Obese				2.11	1.96, 2.26	< .001
Missing or Biologically Implausible				1.89	1.63, 2.19	< .001
Vaccination Status						
0 doses				1.00	--	--
1 dose				0.53	0.47, 0.60	< .001
2 doses				0.53	0.50, 0.57	< .001
3 doses				0.47	0.41, 0.54	< .001
Comorbidity Index				1.019	1.017, 1.021	< .001
Social Deprivation Index				1.002	1.001, 1.003	< .001
Random Effects	Var	*SE*	*p*	Var	*SE*	*p*
Intercept (System)	0.110	0.036	.002	0.103	0.034	.002
Slope (Psychotic Disorder)	0.031	0.047	.664	--	--	--

Overview and Conclusions:

Table 9 summarizes key findings across the series of analyses.

Table 9. Overview of Key Findings

	Fixed Effect Significant?	Fixed Effect OR > 1.0?	Random Slope Variance Significant?	Fixed Effect Odds Ratio	UW Health Model-Predicted Odds Ratio	UW Health Ranking[a]	UW Health Random Slope *p*-value
Unadjusted Models							
Race							
Black vs. NHW	✓	×	×	0.82	0.81	10th	.835
Asian vs. NHW	✓	✓	×	1.26	1.27	16th	.937
Ethnicity							
Hispanic vs. NHW	✓	×	✓	0.76	0.82	12th	.723
Rurality							
Rural vs. Urban Residence	✓	✓	×	1.54	2.02	20th	.082
Psychiatric Disorders							
Depression vs. No History	×	✓	×	1.03	0.95	2nd	.419
Anxiety vs, No History	✓	×	×	0.94	0.94	--	--
Psychosis vs. No History	×	×	×	0.90	0.90	11th	.986
Covariate-Adjusted Models							
Race							
Black vs. NHW	×	×	×	1.01	1.02	16th	.577
Asian vs. NHW	✓	✓	×	1.60	1.74	15th	.716
Ethnicity							
Hispanic vs. NHW	✓	✓	×	1.20	1.22	11th	.929
Rurality							
Rural vs. Urban Residence	✓	✓	×	1.44	1.94	20th	.062
Psychiatric Disorders							
Depression vs. No History	×	✓	×	1.07	1.05	3rd	.729
Anxiety vs, No History	×	×	×	0.99	0.99	--	--
Psychosis vs. No History	×	✓	×	1.06	1.06	--	--

[a]Rank out of 21 health systems relative to the site with respect to the magnitude of random slope effect. When the overall fixed effect is disadvantageous to minority group, lower rank indicates better performance than the average site (smaller race/ethnicity effect). When the overall fixed effect does not indicate a disparity, middle ranks are better (as these indicate consistency with the overall lack of effect whereas outliers may indicate presence of group disparities in outcome in one direction or the other).
NHW = Non-Hispanic White

Is membership in vulnerable groups associated with disparate mortality outcomes in the hospitalized CEC-UW sample?

There was evidence for increased adjusted odds of mortality in Asians and Hispanic patients compared to non-Hispanic Whites, and in rural-residing patients compared to urban dwellers. Black patients and those with a history of psychiatric disorders were not found to experience differential mortality relative to comparison groups (NHW and those without a psychiatric disorder history, respectively).

Does the magnitude of associations between membership in vulnerable groups and mortality differ across CEC-UW health systems?

In general, no – there was evidence of significant variance in random slopes for only one model. The mortality burden of Hispanic patients varied across health systems without covariate adjustment, but this was no longer observed in the adjusted analyses. The overall fixed effect in this model indicated that mortality was lower in Hispanic patients vs. NHW. To investigate possible explanations for the site differences, a series of models were performed in which each covariate was entered singly. Figure 14 depicts the percentage reduction in random slope variance relative to the unadjusted model for each covariate. The dashed line represents the reduction in random slope variance observed in the fully adjusted model. Adjusting for age alone nearly accounted for all the variance reduction observed in the fully adjusted model. The Hispanic random slope variance remained statistically significant in each of these single-covariate models except for the age-adjusted model. Thus, the data suggest differences in the age structure of Hispanic vs. NHW populations across health care systems are likely to account for heterogeneity of observed ethnicity-mortality associations.

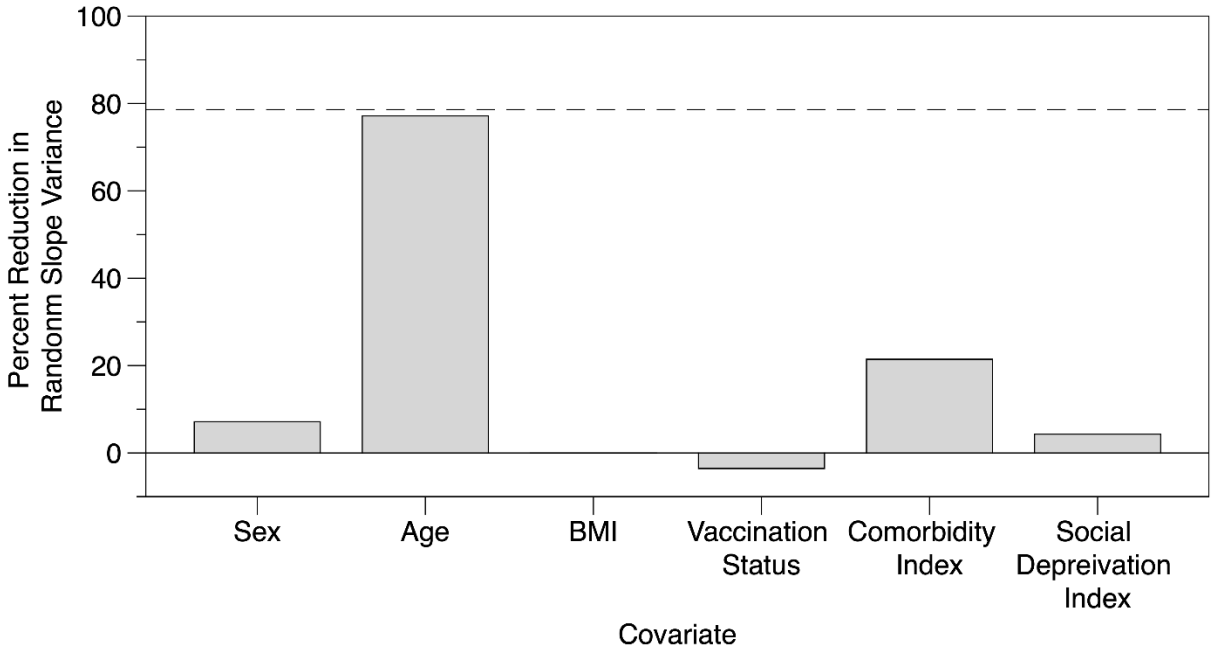

Figure 14. Percent reduction in Hispanic vs. NHW random slope variance observed when each covariate entered singly. Dashed line = variance reduction observed in fully adjusted model including all covariates.

Figure 15 depicts the mean ages of NHW and Hispanic patients at each health system. Figure 16 shows the corresponding effect sizes and 95% CIs for age comparisons across these groups. In both figures, the health systems are sorted according to the size of Hispanic random slope deviation in the unadjusted models (cf. Figure 7).Variation in the magnitude of the Hispanic vs. NHW morality slope clearly corresponds with relative age differences across participating health systems.

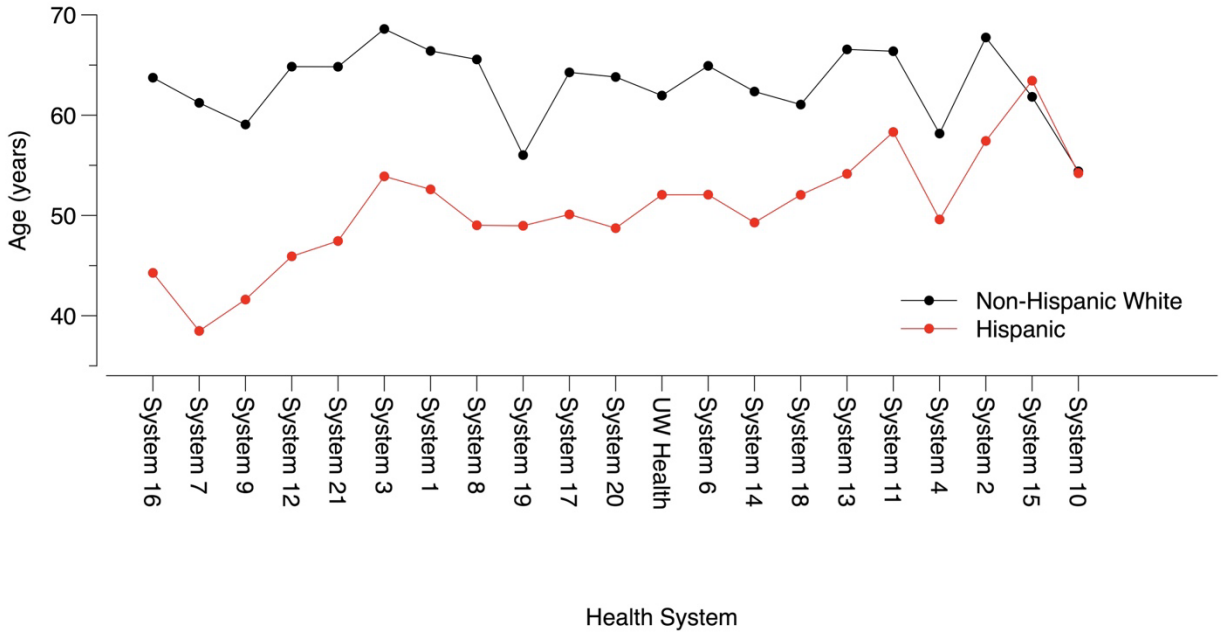

Figure 15. Mean ages of Hispanic and NHW patients by health care system. Systems are sorted from lowest to highest random slope from the unadjusted Hispanic vs. NHW analysis.

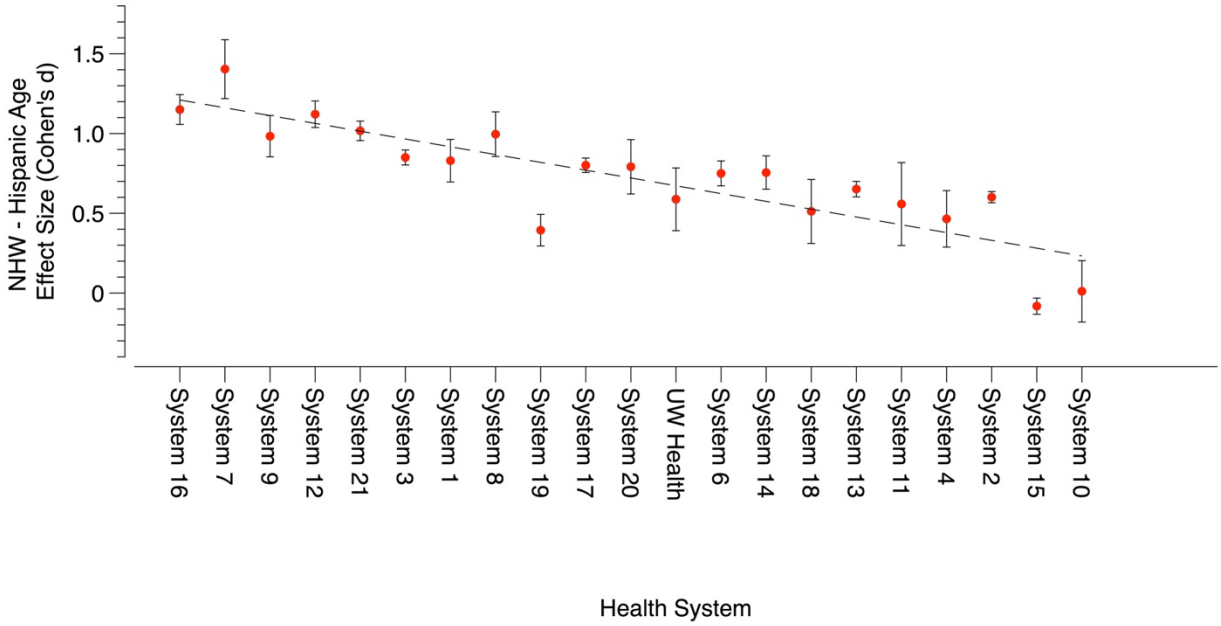

Figure 16. NHW - Hispanic age difference effect sizes and 95% CIs by health system. Systems are sorted from lowest to highest random slope from the unadjusted Hispanic vs. NHW analysis.

How does UW Health compare to other health systems with respect to disparities in mortality among COVID-19 inpatients?

In nearly all models, random slope variances were not statistically significant, indicating negligible variability across sites in the size of group differences. The ranking of UW Health in the distribution of random slope deviations varied substantially across models (Table 9) and it

sometimes appeared to be an outlier on this basis. However, the ranks *per se* may not be highly meaningful because they can be based upon very small effects, especially when slopes are statistically homogeneous. In no case did UW Health have an EBLUP estimate that was significantly different from zero. Thus, the bulk of the evidence indicates that mortality outcomes for vulnerable COVID-19 patients at UW Health were equivalent to those at most other health systems in the CEC-UW study.

Using liberal criteria to look for trouble areas, it is notable that the rural vs. urban random slope was marginally significant (*p*s < .10) at UW Health in unadjusted and adjusted models. Of the 1,703 patients admitted at UW Health, 228 (13.4%) were classified as rural residents. Mortality in UW Health rural patients was 18.9% (43/228), substantially higher than the mortality rate observed in UW Health urban patients (8.7%, 128/1475) and in rural patients in the full sample (10.4%; Table 1). The source of these differences requires further investigation. Because effects were comparable across unadjusted and adjusted models, the covariates examined here cannot explain why mortality among rural patients trends higher at UW Health.

We explored whether the prevalence of rural patients might be related to the size of rural-urban mortality differences across health systems. Figure 17 depicts the percentage of hospitalized patients in each health system classified as rural residing. Health systems are sorted from lowest (left) to highest in terms of the size of rural random slope deviation in the adjusted model (cf. Figure 10). The middle of the random slope distribution comprises health systems that admitted very few rural patients. Systems treating notable percentages of rural patients clustered at the ends of the distribution of random effects. Thus, trends toward disparate mortality outcomes over site were not a simple function of rural patient prevalence – systems that commonly treated rural patients differed substantially from one another in random slopes. Closer scrutiny of the differences between these clusters of more rural-serving health systems might generate clues about how to optimize care for rural-residing COVID-19 inpatients.

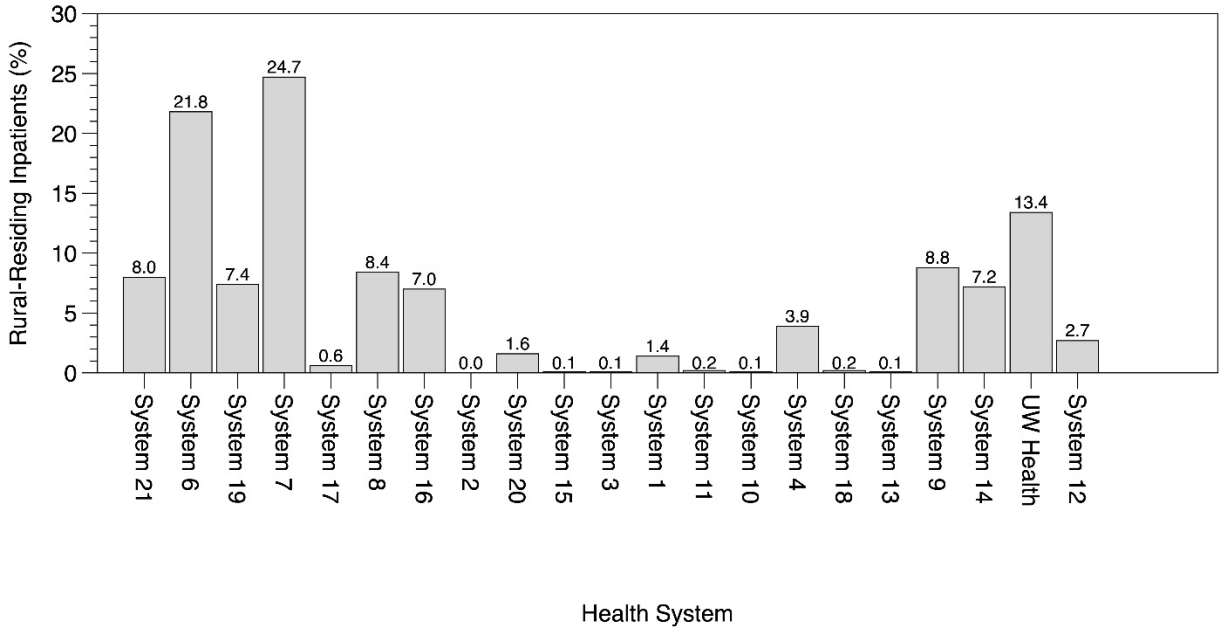

Figure 16. Percentage of inpatients classified as rural by health system. Systems are sorted from lowest to highest random slope from the adjusted rural vs. urban analysis.

Limitations:

Several limitations should be acknowledged. Although the overall sample size was large, we were not able to test for potential disparities experienced by all the racial minority groups represented in the sample. This is because some subgroups were too small (e.g., American Indian/Alaska Native *N* = 546, 0.4%; Native Hawaiian or Other Pacific Islander *N* = 588, 0.4%) or too unevenly represented across health systems for meaningful GLMMs to be estimated. Other patients were classified into racial categories that were too heterogenous (e.g., More than One Race, Other Race Not Specified) to permit informative analyses or were missing race information in the EHR.

Diagnoses of depression and psychosis are included in the calculation of the Elixhauser comorbidity index. Thus, including the Elixhauser as a covariate in adjusted models for these conditions may complicate interpretation of the findings. In principle, this could be investigated by computing customized comorbidity indices for specific models that omit the focal psychiatric conditions. This strategy was not pursued in the current project because neither unadjusted or adjusted models indicated elevated odds of mortality in patients with depression or psychosis.

The current analyses were limited to predicting in-hospital mortality from group membership. A wider array of hospital outcomes (e.g., intubation, ICU admission, length of stay) could be tested. The present analyses were limited to the inpatient subsample of CEC-UW. The full cohort includes data on approximately 1.6 million individuals with COVID-19. Further analyses could use this larger data set to test for disparities in other outcomes (e.g., hospital admission).

Finally, COVID-19 has been a dynamic, protean event and there is evidence that the relative magnitudes of COVID-19 disparities have changed substantially over the course of the pandemic [6,16]. The CEC-UW data were collected over a full two years of the pandemic, providing the opportunity to identify possible variation in disparities over time. Future analyses should test for potential variation of COVID-19 related disparities over both time and health systems.

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