

Multilevel sociodemographic and socioeconomic disparities in COVID-19 outcomes in the  
Central Puget Sound region, 2020-2021

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**Abstract**

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**Background:** Presence of at least one underlying health condition (UHC) is positively associated with severe COVID-19. Although disparities in severe COVID-19 outcomes by race, ethnicity, and socioeconomic position (SEP) are extensively documented, there is little research examining these associations beyond the effect of UHCs. Studies also show regions of lower SEP and higher racial residential segregation (RRS) have greater adverse COVID-19 outcomes, but are limited by their geographic coarseness and ecological nature. Furthermore, relatively few age-stratified studies have been conducted, especially studies focused on young adults, who have had the highest incidence of COVID-19 during much of the pandemic.

**Methods:** We leveraged 2017-2021 electronic health record data from the University of Washington Medicine (UWM) healthcare system and publicly-available neighborhood-level data

to conduct three retrospective cohort studies of UWM patients. First, we used regression modeling to estimate age-stratified (18-39, 40-64, and 65+ years) adjusted risk ratios (aRRs) and risk differences (aRDs) of COVID-19-associated hospitalization by any UHC, among SARS-CoV-2-positive patients. Next, among SARS-CoV-2-positive patients aged 18-39, we used regression modeling to estimate aRRs and aRDs of COVID-19-associated hospitalization by SEP (measured by health insurance status) and race and ethnicity, adjusted for any UHC to examine these associations beyond the effect of UHCs. Finally, in a multilevel analysis, we used generalized estimating equations to estimate aRRs and aRDs of (1) receiving SARS-CoV-2 testing and (2) testing positive by block group-level SEP and RRS (high vs. low disadvantage/segregation), accounting for clustering by residential census block group and adjusted for individual-level SEP (health insurance status) and race and ethnicity. We measured RRS using the divergence index, and group-level SEP using a previously-developed area deprivation index.

**Results:** First, we found that patients with any UHC in all age groups were at significantly increased risk of COVID-19-associated hospitalization, and that the aRR comparing patients with vs. those without UHCs was notably higher for patients aged 40-64 (aRR [95% CI] for 18-39: 4.3 [1.8, 10.0]; 40-64: 12.9 [3.2, 52.5]; 65+: 3.1 [1.2, 8.2]; overall: 5.3 [3.0, 9.6]). Our estimated aRDs increased across age groups (aRD [95% CI] per 1,000 SARS-CoV-2-positive persons for 18-39: 10 [2, 18]; 40-64: 43 [33, 54]; 65+: 84 [51, 116]; overall: 28 [21, 35]). Next, we found that uninsured/publicly insured young adults had a 1.9-fold higher risk of hospitalization (aRR [95% CI]=1.9 [1.0, 3.6]) and 9 additional hospitalizations per 1,000 SARS-CoV-2 positive persons (aRD [95% CI]=9 [-1, 20]) compared to the privately insured. Hispanic or Latine, non-Hispanic (NH) Asian, NH Black, and NH Native Hawaiian or Pacific Islander patients had a 1.5-, 2.7-, 1.4-, and 2.1-fold-higher risk of hospitalization (aRR [95% CI]=1.5 [0.7, 3.1]; 2.7 [1.1, 6.5]; 1.4 [0.6, 3.3]; 2.1 [0.5, 9.1]), respectively, compared to NH White patients.

Finally, we found that patients living in highly disadvantaged neighborhoods were less likely to receive testing (aRR [95% CI] = 0.84 [0.81, 0.87]; aRD [95% CI] = -329 [-404, -254]) and, among those tested, more likely to test positive (aRR [95% CI] = 1.26 [1.16, 1.36]; aRD [95% CI] = 149 [95, 203]) compared to patients in low disadvantage neighborhoods. Patients in highly segregated neighborhoods also were less likely to receive testing (aRR [95% CI] = 0.95 [0.93, 0.98]; aRD [95% CI] = -120 [-184, -55]) and, among those tested, more likely to test positive (aRR [95% CI] = 1.06 [0.99, 1.13]; aRD [95% CI] = 30 [-1, 61]) compared to patients in low segregation neighborhoods, although the latter associations were not statistically significant.

**Conclusions:** We found that individuals with UHCs were at significantly increased risk of COVID-19-associated hospitalization, regardless of age. Furthermore, though they should be interpreted with caution given low precision, our findings suggest the increased risk of COVID-19-associated hospitalization among young adults of color and young adults of lower SEP may be driven by forces other than UHCs, including social determinants of health. These results support the prevention of severe COVID-19 in adults with UHCs in all age groups as an ongoing local public health priority, and underscore the importance of equitable access to vaccines and anti-SARS-CoV-2 therapy for young adults of color and young adults of lower SEP in general, not only for those with UHCs. Finally, our findings support targeted local morbidity and mortality prevention initiatives, including age-group-specific risk communication, and the use of neighborhood measures to inform COVID-19 resource allocation to mitigate disparities.

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## CHAPTER 1. Introduction

Coronavirus disease 2019 (COVID-19) - the disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) - has had an unparalleled global impact.<sup>1</sup> Since December 2019, the COVID-19 pandemic has led to over 762 million confirmed cases and over 6 million confirmed deaths around the world.<sup>1</sup> In terms of absolute morbidity and mortality, the United States (US) has the highest numbers of COVID-19 cases and deaths by country, area, or territory reported to the World Health Organization,<sup>1</sup> with over 104 million cases and over 1 million deaths as of April 2023.<sup>2</sup>

SARS-CoV-2 is a positive-sense single-stranded RNA virus that enters the body primarily through the upper respiratory tract and facial mucous membranes.<sup>3</sup> In order to invade human host cells, the viral surface spike glycoprotein binds to the angiotensin-converting enzyme 2 (ACE2) receptor on the host cell membrane, facilitating internalization of the viral particle through endocytosis.<sup>3,4</sup> The spectrum of COVID-19 clinical severity is wide, ranging from asymptomatic to fatal.<sup>5</sup> Most people with COVID-19 (about 80% by some estimates<sup>6</sup>) experience only mild illness and recover without requiring hospitalization.<sup>5</sup> Severe or critical disease - the pathophysiology of which likely involves dysregulated homeostatic systems and immune response related to ACE2<sup>3,7,8</sup> - includes pneumonia, respiratory failure, and cardiovascular, thromboembolic, and inflammatory complications, and requires hospitalization or intensive care.<sup>5</sup>

Individuals of all ages and any health status - including healthy young adults - may experience severe or life-threatening COVID-19 disease.<sup>9</sup> Those at higher risk of developing severe outcomes include adults aged 65 years and older and people with certain underlying health conditions (UHCs).<sup>10-26</sup> The US Centers for Disease Control and Prevention categorizes these UHCs by the level of evidence supporting an increased risk of severe COVID-19.<sup>26</sup> For

example, the elevated risks of severe disease associated with comorbidities such as cancer, cerebrovascular disease, chronic kidney disease, chronic obstructive pulmonary disease, diabetes mellitus types 1 and 2, and heart conditions are supported by meta-analyses or systematic reviews (the highest level of evidence).<sup>26</sup>

In the US, severe COVID-19 has disproportionately impacted people of color (POC).<sup>27</sup>

Compared to non-Hispanic (NH) White individuals, POC have experienced a disproportionate burden of COVID-19-associated emergency department visits, hospitalizations, and deaths,<sup>28-34</sup> as well as a higher incidence of SARS-CoV-2 infections.<sup>31,35-38</sup> In addition, severe COVID-19 has disproportionately impacted people of lower socioeconomic position (SEP), including people with lower incomes, people without a high school education, uninsured or publicly-insured individuals, people experiencing homelessness, and incarcerated individuals.<sup>39-43</sup>

These racial, ethnic, and socioeconomic disparities in severe COVID-19 are frequently attributed to higher rates of UHCs among POC<sup>44-47</sup> and people of lower SEP.<sup>47,48</sup> However, this emphasis on UHCs may minimize the significance of social determinants of health (SDOH)<sup>49</sup> - including experienced racism, limited healthcare access and utilization, living in higher density and multigenerational households, and inequities in education, employment, income, and wealth - that have long prevented POC and people of lower SEP from having fair opportunities for health in the US.<sup>50-53</sup> Residential environment is another important SDOH,<sup>54</sup> and two otherwise identical individuals may experience different risks of SARS-CoV-2 exposure,<sup>55</sup> access to COVID-19 information,<sup>56</sup> and access to SARS-CoV-2 testing<sup>57</sup> depending on the neighborhood in which they live. Numerous ecological studies (most of which were conducted at the county, ZIP code, or ZCTA level) show adverse COVID-19 outcomes are greater in regions of lower SEP<sup>57-68</sup> and regions of higher racial residential segregation (RRS)<sup>69-74</sup> - the physical separation of racial and ethnic groups in a residential context and a metric of structural racism commonly used in quantitative health research.<sup>75-77</sup>

Patterns of adverse COVID-19 outcomes, including severe disease, have also differed by age group in the US.<sup>2,78-81</sup> Young adults under age 40 have represented a substantial proportion of COVID-19-associated hospitalizations<sup>82</sup> and have had the highest incidence of COVID-19 cases during much of the pandemic.<sup>2</sup> Furthermore, as with POC and people of lower SEP, young adults are more likely to experience lack of health insurance and limited healthcare access and utilization,<sup>83</sup> potentially increasing their risk of severe COVID-19. Nevertheless, COVID-19 messaging has focused primarily on threats to older individuals, raising concerns that younger people might incorrectly assume they are less likely to contract SARS-CoV-2 and/or they are not susceptible to severe disease.<sup>84,85</sup>

These national trends have also been observed in Washington (WA) State. The first laboratory-confirmed case of COVID-19 in the US was reported in WA State in January 2020.<sup>86</sup> As of April 2023, over 1 million confirmed and probable COVID-19 cases have been reported in WA State, with the majority (about 55%) occurring in the Central Puget Sound region<sup>87</sup> (which includes the Seattle metropolitan area and comprises 56% of the state's population<sup>88</sup>). As they have across the US, young adults under age 40 in WA State have made up a notable percentage of COVID-19-associated hospitalizations<sup>89</sup> and have had the highest incidence of COVID-19 cases throughout much of the pandemic.<sup>87</sup> POC in WA State have experienced a disproportionate burden of adverse COVID-19 outcomes, with the highest age-adjusted case, hospitalization, and death rates in the state among NH Native Hawaiian or Pacific Islander and NH American Indian or Alaska Native populations.<sup>90</sup> In addition, a 2020 ecological study of the Seattle, King County, WA State region found SARS-CoV-2 testing rates were lower and test positivity rates were higher in census tracts with higher proportions of POC and lower group-level SEP.<sup>91</sup>

Unfortunately, both nationally and in WA State, there is relatively limited research examining the associations between UHCs, race, ethnicity, and SEP and severe COVID-19 outcomes stratified by age group<sup>19-25</sup> - and particularly studies focused on young adult populations - which would

inform targeted public health action including risk communication, collaboration with community partners, and prioritization of vaccination and anti-SARS-CoV-2 therapy. Specifically, research focused on differences in severe COVID-19 outcomes between racial, ethnic, and socioeconomic groups beyond the effect of UHCs is needed to better understand the role of SDOH.<sup>92-96</sup> Existing studies of group-level effects are generally limited by their ecological nature and geographic coarseness, and multilevel studies<sup>42,97-102</sup> at finer geographic scales would strengthen understanding of neighborhood-level characteristics as risk factors for COVID-19 outcomes such as SARS-CoV-2 testing and infection, which would help public health agencies deliver optimal community-based interventions.

This dissertation leveraged electronic health record data from the University of Washington Medicine (UWM) healthcare system - the largest academic medical system in the Central Puget Sound region - as well as publicly-available neighborhood-level data from the Neighborhood Atlas<sup>103,104</sup> and from the 2020 decennial census<sup>105</sup> to address the research limitations described above in three retrospective cohort studies of UWM patients. First, we examined the association between any UHC and COVID-19-associated hospitalization, overall and stratified by age group (Chapter 2). Next, we examined the associations between race and ethnicity, SEP, and COVID-19-associated hospitalization, above and beyond the effect of any diagnosed UHC, among patients aged 18-39 (Chapter 3). Finally, in a multilevel study, we examined the associations between census block group-level SEP and RRS and (1) receiving SARS-CoV-2 testing and (2) testing positive, independent of individual-level characteristics including SEP and race and ethnicity (Chapter 4). We conclude with a summary of our findings and a discussion of their implications for local public health action and future research (Chapter 5).

## **CHAPTER 2. Association between any underlying health condition and COVID-19-associated hospitalization by age group**

### **ABSTRACT**

**Background:** Presence of at least one underlying health condition (UHC) is positively associated with severe COVID-19, but there is limited research examining this association by age group, particularly among young adults.

**Methods:** We examined age-stratified associations between any UHC and COVID-19-associated hospitalization using a retrospective cohort study of electronic health record data from the University of Washington Medicine healthcare system for adult patients with a positive SARS-CoV-2 test from February 29, 2020, to March 13, 2021. Any UHC was defined as documented diagnosis of at least one UHC identified by the CDC as a potential risk factor for severe COVID-19. Adjusting for sex, age, race and ethnicity, and health insurance, we estimated risk ratios (aRRs) and risk differences (aRDs), overall and by age group (18-39, 40-64, and 65+ years).

**Results:** Among patients aged 18-39 (N=3,249), 40-64 (N=2,840), 65+ years (N=1,363), and overall (N=7,452), 57.5%, 79.4%, 89.4%, and 71.7% had at least one UHC, respectively. Overall, 4.4% of patients experienced COVID-19-associated hospitalization. For all age groups, the risk of COVID-19-associated hospitalization was greater for patients with any UHC vs. those without (18-39: 2.2% vs. 0.4%; 40-64: 5.6% vs. 0.3%; 65+: 12.2% vs. 2.8%; overall: 5.9% vs. 0.6%). The aRR comparing patients with vs. those without UHCs was notably higher for patients aged 40-64 years (aRR [95% CI] for 18-39: 4.3 [1.8, 10.0]; 40-64: 12.9 [3.2, 52.5]; 65+: 3.1 [1.2, 8.2]; overall: 5.3 [3.0, 9.6]). The aRDs increased across age groups (aRD [95% CI] per 1,000 SARS-CoV-2-positive persons for 18-39: 10 [2, 18]; 40-64: 43 [33, 54]; 65+: 84 [51, 116]; overall: 28 [21, 35]).

**Conclusions:** Individuals with UHCs are at significantly increased risk of COVID-19-associated hospitalization regardless of age. Our findings support the prevention of severe COVID-19 in adults with UHCs in all age groups and in older adults aged 65+ years as ongoing local public health priorities.

## BACKGROUND

Since its recognition in December 2019, coronavirus disease 2019 (COVID-19) – the disease caused by the coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) – has had an unprecedented impact around the world.<sup>1</sup> As of April 2023, the COVID-19 pandemic has led to over 762 million confirmed cases and over 6 million confirmed deaths globally.<sup>1</sup>

While most people with COVID-19 experience mild or moderate illness, some individuals develop severe outcomes (including hypoxia, respiratory failure, and multiorgan system dysfunction) and require hospitalization for management.<sup>106</sup> Adults aged 65 years and older and people with certain underlying health conditions (UHCs), such as cerebrovascular disease, chronic kidney disease, heart conditions, and diabetes mellitus, are at higher risk of developing severe COVID-19.<sup>10–26</sup> However, even healthy young adults may suffer severe or life-threatening COVID-19 symptoms.<sup>9</sup>

In the United States (US), COVID-19 disease patterns have differed by age group.<sup>2,78–81</sup> Young adults under age 40 have represented a substantial proportion of COVID-19 hospitalizations<sup>82</sup> and have had the highest incidence of COVID-19 cases during much of the pandemic.<sup>2</sup> Despite evidence demonstrating young adults are susceptible to severe COVID-19 and the high incidence of COVID-19 cases among young adults, there are relatively few studies exploring the relationship between UHCs and COVID-19 disease severity by age group.<sup>19–25</sup> Improved understanding of these age-stratified relationships – particularly among young adults – may inform public health action including risk communication and prioritization of vaccination and anti-SARS-CoV-2 therapy.

Mirroring national trends, young adults 40 years and under in Washington (WA) State have made up a notable percentage of COVID-19 hospitalizations<sup>89</sup> and have had the highest incidence of COVID-19 cases throughout much of the pandemic.<sup>87</sup> The aim of our study was to

examine the association between any UHC and COVID-19-associated hospitalization, overall and stratified by age group, among patients in a large academic medical system in western WA State.

## **METHODS**

### **Study design, data source, setting, and population**

We conducted a retrospective cohort study using electronic health record (EHR) data from the University of Washington Medicine (UWM) healthcare system – the largest academic medical system in the Central Puget Sound region. The Central Puget Sound region is in the western part of WA State and includes the Seattle metro area; it comprises 56% of the state’s population<sup>88</sup> and, as of April 2023, about 55% of its confirmed and probable COVID-19 cases.<sup>87</sup>

Our study population included living adult patients engaged in care within UWM who tested positive for SARS-CoV-2 within UWM. We defined engagement in care within UWM as presence of at least one encounter (including telephone or telemedicine) in the UWM system from January 1, 2017 to February 28, 2020 (the day before SARS-CoV-2 testing began within UWM on February 29, 2020). We included patients who were aged 18 years or older as of February 28, 2020, who had at least one positive SARS-CoV-2 reverse transcription polymerase chain reaction (RT-PCR) test within UWM from February 29, 2020 to March 13, 2021 (14 days before the date of the data pull, to allow time for COVID-19-associated hospitalization following a positive test), and who were alive at the time of their first positive SARS-CoV-2 RT-PCR test. RT-PCR is the diagnostic standard for SARS-CoV-2 infection used within UWM.

## Data measures

Our cohort, as defined above, contained 7,456 adult UWM patients. Data were collected at the patient level. We defined any UHC (yes/no) as documented diagnosis of at least one UHC identified by the US Centers for Disease Control and Prevention (CDC) as a potential risk factor for severe COVID-19 (Table 1.1).<sup>26</sup> To identify documented UHCs, we evaluated EHR data from January 1, 2017 through the date of the first positive SARS-CoV-2 RT-PCR test. Most UHCs were defined by the presence of at least one relevant international classification of disease, tenth revision, clinical modification (ICD-10-CM) diagnosis code (Table 1.1). In addition to ICD-10-CM data, EHR smoking status data were used to identify patients with the UHC of current or former smoking, and EHR height and weight data were used to calculate BMI ( $\text{kg}/\text{m}^2$ ) to identify patients with the UHCs of overweight and obesity. BMI was based on the most recent encounter from January 1, 2017 through the date of the first positive SARS-CoV-2 RT-PCR test for which height, weight, and the calculated BMI were biologically plausible. Biological plausibility for height was defined as  $\geq 1.2$  m and  $\leq 2.4$  m, for weight as  $\geq 34.0$  kg and  $\leq 272.2$  kg, and for BMI as  $\leq 80.0$   $\text{kg}/\text{m}^2$ .<sup>107</sup> Plausible BMI data were recorded for 5,413 patients (72.6%). The median number of days between height and weight measurement and the first positive SARS-CoV-2 RT-PCR test was 358 (interquartile range = 601 days). Patients who had no indication of any UHCs as defined above were categorized as having no UHCs.

We defined COVID-19-associated hospitalization (yes/no) as an in-patient encounter within UWM that either (1) had an admit date at most three days prior to the date of a positive SARS-CoV-2 test and an indication in the admit note that the hospital encounter was associated with COVID-19, or (2) was within 14 days following a positive SARS-CoV-2 test; this is the standard approach validated and used by the University of Washington Institute of Translational Health Sciences to identify COVID-19-associated hospitalizations.

We also collected EHR data on potential confounders including age (in years) at the time of first positive SARS-CoV-2 RT-PCR test, sex assigned at birth (female/male), race and ethnicity (Hispanic or Latine, non-Hispanic American Indian or Alaska Native, non-Hispanic Asian, non-Hispanic Black, non-Hispanic Native Hawaiian or Pacific Islander, non-Hispanic White, not recorded), and health insurance status (public, private, uninsured, not recorded) as a measure of individual-level socioeconomic position. Four patients (<0.1%) had implausible ages ( $\geq 120$  years) or were missing data on sex assigned at birth and were dropped from the analysis, for a final analytic population of 7,452 patients. Missing race and ethnicity and health insurance data were classified as “not recorded.”

### **Data analyses**

We estimated adjusted risk ratios (aRRs) and risk differences (aRDs) of COVID-19-associated hospitalization (yes/no) by presence of any UHC (yes/no) using multivariable log-binomial and generalized linear regression with a Gaussian distribution and identity link function, respectively, both with Huber-White estimates of the standard error.<sup>108</sup> We adjusted for continuous age, sex assigned at birth, race and ethnicity, and health insurance status. We presented our results overall and stratified by age groups 18-39, 40-64, and 65+ years, which are consistent with the CDC’s reporting of age-stratified COVID-19 data.<sup>2</sup> Model 1 describes the model used to estimate the aRR in the total study population, and Model 2 describes the model used to estimate age-stratified aRRs; these models are comparable in structure to those used to estimate aRDs. Finally, we tested for interaction by age group of the association between any UHC and COVID-19-associated hospitalization using analysis of variance to compare nested models (e.g., in the case of the aRR, we compared Model 1 and Model 2). All analyses were performed in R version 4.1.2 (Vienna, Austria).<sup>109</sup>

$$\log(p_{\text{hospitalization}_i}) \quad \text{Model 1}$$

$$= \beta_0 + \beta_1 X_{\text{any UHC}_i} + \beta_2 X_{\text{age group 40-64}_i} + \beta_3 X_{\text{age group 65+}_i} \\ + \beta_j X_{\text{confounder}_{j_i}} + \dots + \beta_k X_{\text{confounder}_{k_i}}$$

$$\log(p_{\text{hospitalization}_i}) \quad \text{Model 2}$$

$$= \beta_0 + \beta_1 X_{\text{any UHC}_i} + \beta_2 X_{\text{age group 40-64}_i} + \beta_3 X_{\text{age group 65+}_i} \\ + \beta_j X_{\text{confounder}_{j_i}} + \dots + \beta_k X_{\text{confounder}_{k_i}} \\ + \gamma_1 X_{\text{any UHC}_i} X_{\text{age group 40-64}_i} + \gamma_2 X_{\text{any UHC}_i} X_{\text{age group 65+}_i}$$

### Sensitivity analyses

We conducted three sensitivity analyses. First, to account for changes in vaccine availability, we limited the dataset to patients whose first positive SARS-CoV-2 RT-PCR test was before December 11, 2020, when the Food and Drug Administration approved the first COVID-19 vaccine under emergency use authorization.<sup>110</sup> Second, to account for local changes in circulating viral strains<sup>111</sup> and testing practices,<sup>112</sup> we limited the dataset to patients whose first positive SARS-CoV-2 RT-PCR test was between July 1, 2020 and October 31, 2020, when we expect the dominant viral strain<sup>113,114</sup> and testing practices<sup>87,115-118</sup> were relatively stable in the Central Puget Sound region. Finally, since UHCs have different levels of evidence (conclusive, suggestive, and inconclusive) for their association with severe COVID-19 according to the CDC, we repeated the primary regression analyses with a narrower definition of any UHC to include only conditions for which there is a published meta-analysis or systematic review demonstrating a conclusive increase in risk of severe COVID-19 (Table 1.1).<sup>26</sup>

## RESULTS

Among 7,452 individuals, the average age was 45.7 years, 49.8% of patients were assigned female sex at birth, 43.9% were recorded as non-Hispanic White, 36.4% were on public health insurance, and 6.9% were uninsured (Table 1.2). Patients aged 18-39 years comprised the largest group in our study population (N=3,249), followed by 40-64-year-olds (N=2,840), and then those aged 65+ years (N=1,363). The distribution of sex assigned at birth was similar for all age groups. Patients recorded as non-Hispanic White comprised a higher proportion of subjects aged 65+ (59.1%) compared to those aged 18-39 (41.5%) and 40-64 years (39.2%). The proportion of patients on public health insurance increased across age groups, and patients aged 40-64 years were more likely to be uninsured compared to patients aged 18-39 and 65+ years.

Overall, 71.7% of patients had at least one UHC, and this proportion increased across age groups (57.5%, 79.4%, and 89.4%, respectively) (Table 1.2). The distributions of population characteristics stratified by the presence of any UHC are given in Table 1.3. Of note, patients with any UHC (N=5,341) compared to patients with no UHCs (N=2,111) had a higher proportion of individuals assigned male sex at birth (53.1% vs. 42.8%), individuals recorded as non-Hispanic White (45.0% vs. 40.9%), and individuals on public health insurance (41.0% vs. 24.9%). The distributions of specific UHCs overall and stratified by age group are given in Table 1.4. Overall, the most common UHCs were smoking (26.0%), obesity (26.0%), overweight (24.2%), and hypertension (23.2%). For most UHCs, the proportion of patients with a documented diagnosis increased across age groups, though this was not true for some UHCs including obesity, substance use disorders, and human immunodeficiency virus.

## **Risk of COVID-19-associated hospitalization by any underlying health condition and age group**

Overall, 329 (4.4%) of the 7,452 patients with a positive SARS-CoV-2 RT-PCR test experienced COVID-19-associated hospitalization (Table 1.5). Among patients with any UHC, 5.9% experienced COVID-19-associated hospitalization compared to just 0.6% of patients with no UHCs (crude RR [95% CI]=10.4 [5.9, 18.5]). For all age groups, the proportion of patients hospitalized with COVID-19 was higher among those with any UHC compared to those with no UHCs.

After adjustment for confounders, patients with any UHC had a 5.3-fold higher risk of COVID-19-associated hospitalization compared to those with no UHCs (aRR [95% CI]=5.3 [3.0, 9.6]) (Figure 1.1, Table 1.5). Likewise, within each age group and on the relative scale, the risk of COVID-19-associated hospitalization was significantly higher among patients with any UHC compared to those with no UHCs. There was no statistical evidence of interaction by age group for the aRR ( $p=0.2$ ).

Overall, patients with any UHC had 28 additional COVID-19-associated hospitalizations per 1,000 SARS-CoV-2-positive persons during the 13-month study period compared to patients with no UHCs (aRD [95% CI]=28 [21, 35]) (Figure 1.1, Table 1.5). Similarly, within each age group and on the absolute scale, the risk of COVID-19-associated hospitalization was significantly higher among patients with any UHC compared to those with no UHCs. There was statistical evidence of interaction by age group for the aRD ( $p<0.001$ ).

## Sensitivity analyses

The results of all three sensitivity analyses were consistent with those of the primary analyses (Tables 1.6-1.8). Of note, using a narrower definition of any UHC yielded statistical evidence of interaction by age group for the aRR ( $p=0.04$ ) (Table 1.8).

## DISCUSSION

In this retrospective cohort study leveraging EHR data from a large academic medical center, we found that 4.4% of the 7,452 living adult patients engaged in care within UWM who tested positive for SARS-CoV-2 within UWM experienced COVID-19-associated hospitalization.

Overall, patients with documented UHCs had a 5.3-fold higher risk of COVID-19-associated hospitalization compared to those without UHCs, and this positive relative association persisted across age groups. In addition, overall, patients with any UHC had 28 additional COVID-19-associated hospitalizations per 1,000 SARS-CoV-2-positive persons over the 13-month study period compared to those without UHCs, and the magnitude of this absolute association differed significantly across age groups, with older groups experiencing larger absolute differences in risk. Our findings suggest people with UHCs of all ages – including young and middle-aged adults <65 years – are at elevated risk of COVID-19-associated hospitalization on both relative and absolute scales, and that the absolute difference in risk of COVID-19-associated hospitalization between those with and without UHCs increases with age.

Previous studies of the association between UHCs and severe COVID-19 defined severe outcomes in several ways, including clinical symptoms, hospitalization, intensive care unit admission, and mortality.<sup>11-25</sup> Most studies examined individual UHCs, rather than a composite measure of any UHC. *A priori*, we intended to explore age-stratified associations between COVID-19-associated hospitalization and individual UHCs in addition to our composite measure of any UHC, but ultimately did not due to small sample size. In addition, most previous studies

calculated only relative measures of excess risk, rather than both relative and absolute measures as we did here. From an epidemiologic methods standpoint, our findings illustrate the value of presenting both relative and absolute measures of excess risk, which provide different perspectives and together offer a more complete understanding of a risk factor and its potential public health impact.<sup>119</sup> Our estimated overall aRR of 5.3 is consistent with the broad range of other published estimates of relative measures of excess risk.<sup>13–19</sup> For example, estimated hazard ratios for the association between dementia and severe COVID-19 ranged from 1.4 to 7.7 (95% CI range=1.2, 39.6), and odds ratios for the association between liver cirrhosis and severe COVID-19 from 3.2 to 5.9 (95% CI range=0.9, 27.7) in one review.<sup>18</sup> In addition, limited previous studies of the association between UHCs and severe COVID-19 stratified by age group have found the relative risk of severe COVID-19 comparing those with and without UHCs is higher in younger than in older people.<sup>19–25</sup> Although we did not find statistical evidence of effect modification by age group for the aRR in our primary analysis, the magnitudes of the estimated effects and the results of our sensitivity analysis using a narrower definition of any UHC, which did yield statistical evidence of interaction by age group for the aRR, are consistent with these previous findings.

Several of our findings are consistent with clinical expectations based on age as a risk factor for disease.<sup>120</sup> We found that the risk of COVID-19-associated hospitalization among those with and without UHCs increased with age, and that the aRDs describing the association between any UHC and COVID-19-associated hospitalization increased across age groups. A more surprising finding is that – although we did not find statistical evidence of interaction by age group and estimated 95% CIs were wide – qualitatively, the magnitude of the estimated aRR of COVID-19-associated hospitalization was higher among 18-39-year-olds (aRR=4.3) and especially 40-64-year-olds (aRR=12.9) compared to those aged 65+ years (aRR=3.1). In addition, using a narrower definition of any UHC resulted in improved precision and statistical

evidence of interaction by age group for the aRR. These findings suggest the presence of any UHC may be a stronger risk factor for COVID-19-associated hospitalization in younger adults and especially middle-aged adults compared to older adults, which is consistent with previous research of severe COVID-19 outcomes.<sup>19–25</sup> One possible explanation is that individuals in our study aged 65+ years with UHCs were healthy enough to survive to at least 65 years of age; thus, they may have been somewhat resilient against COVID-19, and, on the relative scale, their risk of COVID-19-associated hospitalization compared to their same-age counterparts without UHCs was not as different as it was for the other two age groups. On the other hand, the group of 40-64-year-olds with UHCs in our study likely comprised individuals in poor health who may not have survived to age 65; thus, they were less resilient against COVID-19 and their relative risk of a severe outcome was notably different from other middle-aged adults without UHCs.

Adults of all ages with UHCs and older adults are priority populations for COVID-19 vaccination, including boosters, in WA State,<sup>121,122</sup> and for the use of anti-SARS-CoV-2 therapy among non-hospitalized adults with COVID-19.<sup>123</sup> Our findings support the prevention of COVID-19 through vaccination and the prevention of progression to severe disease through anti-SARS-CoV-2 treatment in adults with UHCs in all age groups – including young and middle-aged adults <65 years of age – and in adults aged 65+ years as ongoing local public health priorities.

We observed differences in our estimated relative and absolute measures of excess risk by age group, suggesting age-group-specific COVID-19 morbidity and mortality prevention activities, including risk communication, may be an appropriate approach for local health departments. Effective risk communication contributes to adequate understanding of personal risk, which has community-level health consequences,<sup>85</sup> and previous studies show age-group-specific risk communication may be advantageous in the context of other health phenomena<sup>124,125</sup> and in the context of COVID-19.<sup>84,126,127</sup> Media reports and government messaging about COVID-19 –

especially early in the pandemic – focused primarily on threats to older individuals, raising concerns that younger people might erroneously assume they were less likely to contract SARS-CoV-2 and/or they were invulnerable to severe COVID-19 outcomes.<sup>84,85</sup> While older adults are at higher risk of severe COVID-19 compared to younger adults,<sup>10</sup> even healthy young adults may develop severe or fatal COVID-19 symptoms.<sup>9</sup> In our study, we found that – while older adults with and without UHCs appeared to be at higher risk of COVID-19-associated hospitalization compared to younger adults – on the relative scale, young adults aged 18-39 years and especially middle-aged adults aged 40-64 years with any UHC were at higher risk than older adults aged 65+ years with any UHC when compared to their same-age counterparts with no UHCs. These results support age-group-specific risk communication in the Central Puget Sound region. As discussed above, our use of a composite measure of any UHC sets our study apart from most previous research, and may be useful for simplified public health messaging.

Our study had several limitations. First, we analyzed EHR data, which are subject to data quality concerns including high levels of missingness for certain variables, specifically race, ethnicity, and health insurance status in our data. Since EHR data often are missing not at random,<sup>128,129</sup> we did not employ multiple imputation methods, which may further increase bias under missing not at random conditions.<sup>130</sup> Instead, we classified individuals missing these data as “not recorded.” Inclusion of these “not recorded” categories, which may be highly heterogenous, may have limited our ability to statistically control confounding and led to bias.<sup>131,132</sup> We also assumed patients who were missing EHR data used for UHC identification (e.g., smoking status) did not have that UHC, which may have resulted in differential exposure misclassification if patients hospitalized with COVID-19 within UWM were more likely to regularly encounter the UWM system (or less likely to receive care at outside institutions, for which records may be missing from the UWM database) and, therefore, had more complete UWM medical records or

more opportunities for UHC diagnosis; this could have falsely exaggerated or falsely minimized estimated associations. In addition, we used presence of at least one relevant ICD-10-CM code to define most UHCs, which also may have resulted in differential exposure misclassification if this definition was too broad (e.g., a single code reflected a diagnostic lab work order, rather than actual diagnosis of the UHC).<sup>133</sup> Second, it was not feasible for us to determine indication for SARS-CoV-2 testing (e.g., SARS-CoV-2 exposure, COVID-19 symptoms, pre-operative testing, etc.), which may be associated with COVID-19-associated hospitalization. While we do not expect the distribution of indication for testing to have impacted our aRR and aRD estimates, it may have impacted the proportion of patients in our study population who were hospitalized with COVID-19. Third, we only captured COVID-19-associated hospitalizations if they occurred within the UWM system, which may have led to differential outcome misclassification if patients without UHCs (who may have been less likely to be regularly engaged in care within UWM), were more likely to be hospitalized with COVID-19 at another facility. Furthermore, differential outcome misclassification may have occurred if patients who tested positive for SARS-CoV-2 within the prior 14 days were hospitalized for other emergent reasons but never experienced severe COVID-19 symptoms, or if patients died from severe COVID-19 without being hospitalized. Fourth, our cohort only included people we identified as being regularly engaged in care within the UWM system and who had a positive SARS-CoV-2 RT-PCT test within UWM, which may have increased the likelihood of selection bias from the oversampling of individuals with UHCs at increased risk of COVID-19-associated hospitalization. Fifth, the number of patients in our study without UHCs was relatively small and those individuals experienced few COVID-19-associated hospitalizations, especially within age group strata, which resulted in statistical limitations including poor precision. Finally, we used data from a single academic medical system, so the generalizability of our findings is unknown.

In conclusion, our findings support the prevention of severe COVID-19 (e.g., via vaccination, including boosters, and anti-SARS-CoV-2 therapy) in adults with UHCs in all age groups – including young and middle-aged adults <65 years of age – and in older adults aged 65+ years as ongoing local public health priorities.<sup>121–123</sup> Moreover, our findings suggest age-group-specific risk communication may be an appropriate approach in the Central Puget Sound region. Although we are in a period of relaxed COVID-19 prevention strategies in the US,<sup>134</sup> we believe our work highlights the importance of age-group-specific research and public health action in our current stage of the SARS-CoV-2 pandemic, potential future waves of this SARS-CoV-2 pandemic, and potential future epidemics and pandemics of other pathogens.

## TABLES AND FIGURES

<b>Table 1.1.</b> UHCs possibly associated with increased risk of severe COVID-19 per the United States Centers for Disease Control and Prevention and identifying ICD-10-CM codes			
<b>UHC*</b>		<b>ICD-10-CM code†</b>	<b>ICD-10-CM description</b>
	Asthma	J45	Asthma
*	Bronchiectasis	J47	Bronchiectasis
	Bronchopulmonary dysplasia	P27.1	Bronchopulmonary dysplasia originating in the perinatal period
*	Cancer	C00-C96	Malignant neoplasms
*	Cerebrovascular disease	I60-I69	Cerebrovascular diseases
*	Chronic kidney disease	N18	Chronic kidney disease (CKD)
*	Chronic obstructive pulmonary disorder	J44	Other chronic obstructive pulmonary disease
*	Corticosteroids or other immunosuppressive medications	D84.821; Z79.52; Z92.25	Immunodeficiency due to drugs; Long term (current) use of systemic steroids; personal history of immunosuppression therapy
*	Cystic fibrosis	E84	Cystic fibrosis
*	Diabetes mellitus, type 1	E10	Type 1 diabetes mellitus
*	Diabetes mellitus, type 2	E11	Type 2 diabetes mellitus
*	Down syndrome	Q90	Down syndrome
*	Heart conditions (e.g., heart failure, coronary artery disease, cardiomyopathies)	I20-I25; I30-I52	Ischemic heart disease; Other forms of heart disease
*	Human immunodeficiency virus	B20; Z21	Human immunodeficiency virus (HIV) disease; Asymptomatic human immunodeficiency virus (HIV) infection status
	Hypertension	I10	Essential (primary) hypertension
*	Immune deficiencies	D80; D81; D82; D83; D84.0; D84.1; D84.81; D84.822; D84.89; D84.9	Immunodeficiency with predominantly antibody defects; Combined immunodeficiencies; Immunodeficiency associated with other major defects; Common variable immunodeficiency; Lymphocyte function antigen-1 [LFA-1] defect; Defects in the complement system; Immunodeficiency due to conditions classified elsewhere; Immunodeficiency due to external causes; Other immunodeficiencies; Immunodeficiency, unspecified
*	Liver disease, chronic (cirrhosis, non-alcoholic fatty liver disease, alcoholic liver disease, autoimmune hepatitis)	K70-K77	Diseases of liver
*	Lung disease, interstitial	J80-J84	Other respiratory diseases principally affecting the interstitium
*	Lung disease, other	I28; J41; J42; J43; J60-J70; J85-J86; J90-J94; Z99.81	Other diseases of pulmonary vessels; Simple and mucopurulent chronic bronchitis; Unspecified chronic bronchitis; Emphysema; Lung diseases due to external agents; Suppurative and necrotic conditions of the lower respiratory tract; Other diseases of the pleura; Dependence on supplemental oxygen
*	Mental health disorders (mood disorders, e.g., depression and schizophrenia spectrum disorders)	F20-F29; F30-F39	Schizophrenia, schizotypal, delusional, and other non-mood psychotic disorders; Mood (affective) disorders

**Table 1.1.** UHCs possibly associated with increased risk of severe COVID-19 per the United States Centers for Disease Control and Prevention and identifying ICD-10-CM codes

UHC*		ICD-10-CM code†	ICD-10-CM description
*	Neurologic conditions	F01; F02; F03; G10-G14; G20; G30-G32; G35; G45; G70; G80-G83	Vascular dementia; Dementia in other diseases classified elsewhere; Unspecified dementia; Systemic atrophies primarily affecting the central nervous system; Parkinson’s disease; Other degenerative diseases of the nervous system; Multiple sclerosis; Transient cerebral ischemic attacks and related syndromes; Myasthenia gravis and other myoneural disorders; Cerebral palsy and other paralytic syndromes
*	Obesity (BMI $\geq 30\text{kg/m}^2$ )‡	E66.0; E66.1; E66.2; E66.8; E66.9	Obesity due to excessive calories; Drug-induced obesity; Morbid (severe) obesity with alveolar hypoventilation; Other obesity; Obesity, unspecified
	Overweight (BMI $25 \geq 29\text{kg/m}^2$ )‡	E66.3	Overweight
*	Pregnancy and recent pregnancy	Z33; Z34; Z36; Z37; Z38; Z39; Z3A	Pregnant state; Encounter for supervision of normal pregnancy; Encounter for antenatal screening of mother; Outcome of delivery; Liveborn infants according to place of birth and type of delivery; Encounter for maternal postpartum care and examination; Weeks of gestation
*	Pulmonary hypertension and pulmonary embolism	I26; I27	Pulmonary embolism; Other pulmonary heart disease
	Sickle cell disease	D57	Sickle-cell disorders
*	Smoking, current and former‡	F17; Z72.0; Z87.891	Nicotine dependence; Tobacco use; Personal history of nicotine dependence
*	Solid organ or blood stem cell transplantation	Z94; T86	Transplanted organ and tissue status; Complications of transplanted organs and tissue
	Substance use disorders	F10-F16; F18; F19	Alcohol related disorders; Opioid related disorders; Cannabis related disorders; Sedative, hypnotic, or anxiolytic related disorders; Cocaine related disorders; Other stimulant related disorders; Hallucinogen related disorders; Inhalant related disorders; Other psychoactive substance related disorders
	Thalassemia	D56	Thalassemia
*	Tuberculosis	A15	Respiratory tuberculosis

UHC=underlying health condition, ICD-10-CM=international classification of disease, tenth revision, clinical modification, COVID-19=coronavirus disease 2019, BMI=body mass index

\*UHCs for which there is a published meta-analysis or systematic review demonstrating a conclusive increase in risk of severe COVID-19 according to the United States Centers for Disease Control and Prevention<sup>26</sup> are marked with an asterisk

†ICD-10-CM codes and other electronic health record (EHR) data for all underlying health conditions were evaluated from 01/01/2017 to the date of the first positive reverse transcription polymerase chain reaction (RT-PCR) test for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), except those for pregnancy and recent pregnancy, which were evaluated for the 60 days prior to the date of the first positive RT-PCR test for SARS-CoV-2

‡In addition to the ICD-10-CM codes indicated, EHR height and weight data were used to calculate BMI to identify patients with overweight and obesity, and EHR smoking data were used to identify patients with a history of smoking. BMI was based on the most recent encounter between 01/01/2017 and the date of the first positive SARS-CoV-2 RT-PCR test for which height, weight, and the calculated BMI were biologically plausible. Biological plausibility for height was defined as  $\geq 1.2\text{m}$  and  $\leq 2.4\text{m}$ , for weight as  $\geq 34.0\text{kg}$  and  $\leq 272.2\text{kg}$ , and for BMI as  $\leq 80.0\text{kg/m}^2$ .<sup>107</sup> Patients who had a smoking status of current or former smoker recorded at any encounter between 01/01/2017 and the date of the first positive SARS-CoV-2 RT-PCR test were classified as current or former smokers in our analyses

<b>Table 1.2.</b> Characteristics of patients with a positive SARS-CoV-2 RT-PCR test, by age group*								
<b>Characteristic</b>	<b>Total N = 7,452</b>		<b>18-39 years<sup>†</sup> N = 3,249</b>		<b>40-64 years<sup>†</sup> N = 2,840</b>		<b>65+ years<sup>†</sup> N = 1,363</b>	
	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>
Age (years) <sup>†</sup> (mean ± SD)	45.7	± 19.1	27.9	± 6.2	51.8	± 7.1	75.5	± 8.3
Sex <sup>‡</sup>								
Female	3,712	49.8	1,694	52.1	1,346	47.4	672	49.3
Male	3,740	50.2	1,555	47.9	1,494	52.6	691	50.7
Race and ethnicity								
Hispanic or Latine	1,301	17.5	608	18.7	589	20.7	104	7.6
NH AIAN	70	0.9	30	0.9	27	1.0	13	1.0
NH Asian	635	8.5	284	8.7	204	7.2	147	10.8
NH Black	1,012	13.6	431	13.3	460	16.2	121	8.9
NH NHPI	147	2.0	64	2.0	69	2.4	14	1.0
NH White	3,268	43.9	1,349	41.5	1,113	39.2	806	59.1
Not recorded	1,019	13.7	483	14.9	378	13.3	158	11.6
Insurance <sup>§</sup>								
Private	3,934	52.8	1,933	59.5	1,375	48.4	626	45.9
Public	2,716	36.4	1,003	30.9	1,042	36.7	671	49.2
Uninsured	517	6.9	165	5.1	319	11.2	33	2.4
Not recorded	285	3.8	148	4.6	104	3.7	33	2.4
Any UHC <sup>  </sup>								
No	2,111	28.3	1,380	42.5	586	20.6	145	10.6
Yes	5,341	71.7	1,869	57.5	2,254	79.4	1,218	89.4

SARS-CoV-2=severe acute respiratory syndrome coronavirus 2, RT-PCR=reverse transcription polymerase chain reaction, SD=standard deviation, NH=non-Hispanic, AIAN=American Indian or Alaska Native, NHPI=Native Hawaiian or Pacific Islander, UHC=underlying health condition  
\*University of Washington Medicine healthcare system, 02/29/2020 to 03/13/2021  
<sup>†</sup>Age at first positive SARS-CoV-2 RT-PCR test within University of Washington Medicine; 2 patients (<0.1%) had implausible ages (≥120 years) and were dropped from the analysis  
<sup>‡</sup>Sex assigned at birth; 2 patients (<0.1%) were missing data on sex assigned at birth and dropped from the analysis  
<sup>§</sup>A measure of individual-level socioeconomic position; to capture information about the pre-pandemic period, health insurance data were based on the most recent encounter from 01/01/2017 to 02/28/2020 for which health insurance data were available; private includes patients with Medicare Advantage (Part C), Medicare Supplement (Medigap), Medicare (Part D), employer-sponsored and individual plans, private military insurance, and other forms of private insurance; public includes patients on Medicaid, Medicare (Part A and/or B only), public military insurance, and other forms of public insurance; uninsured includes patients without health insurance and patients with Indian Health Services insurance<sup>135,136</sup>  
<sup>||</sup>Conditions possibly associated with increased risk of severe coronavirus disease 2019 per the United States Centers for Disease Control and Prevention,<sup>26</sup> (all yes/no) based on electronic health record data; see Table 1.1 for list of conditions

<b>Table 1.3.</b> Characteristics of patients with a positive SARS-CoV-2 RT-PCR test, by any UHC*						
<b>Characteristic</b>	<b>Total N = 7,452</b>		<b>Any UHC<sup>†</sup> N = 5,341</b>		<b>No UHC<sup>†</sup> N = 2,111</b>	
	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>
Age (years) <sup>‡</sup> (mean ± SD)	45.7	± 19.1	49.4	± 18.9	36.3	± 16.0
Age group (years) <sup>‡</sup>						
18-39	3,249	43.6	1,869	35.0	1,380	65.4
40-64	2,840	38.1	2,254	42.2	586	27.8
65+	1,363	18.3	1,218	22.8	145	6.9
Sex <sup>§</sup>						
Female	3,712	49.8	2,504	46.9	1,208	57.2
Male	3,740	50.2	2,837	53.1	903	42.8
Race and ethnicity						
Hispanic or Latine	1,301	17.5	934	17.5	367	17.4
NH AIAN	70	0.9	63	1.2	7	0.3
NH Asian	635	8.5	431	8.1	204	9.7
NH Black	1,012	13.6	763	14.3	249	11.8
NH NHPI	147	2.0	122	2.3	25	1.2
NH White	3,268	43.9	2,405	45.0	863	40.9
Not recorded	1,019	13.7	623	11.7	396	18.8
Insurance <sup>  </sup>						
Private	3,934	52.8	2,667	49.9	1,267	60.0
Public	2,716	36.4	2,190	41.0	526	24.9
Uninsured	517	6.9	383	7.2	134	6.3
Not recorded	285	3.8	101	1.9	184	8.7

SARS-CoV-2=severe acute respiratory syndrome coronavirus 2, RT-PCR=reverse transcription polymerase chain reaction, UHC=underlying health condition, SD=standard deviation, NH=non-Hispanic, AIAN=American Indian or Alaska Native, NHPI=Native Hawaiian or Pacific Islander  
\*University of Washington Medicine healthcare system, 02/29/2020 to 03/13/2021  
<sup>†</sup>Conditions possibly associated with increased risk of severe coronavirus disease 2019 per the United States Centers for Disease Control and Prevention,<sup>26</sup> (all yes/no) based on electronic health record data; see Table 1.1 for list of conditions  
<sup>‡</sup>Age at first positive SARS-CoV-2 RT-PCR test within University of Washington Medicine; 2 patients (<0.1%) had implausible ages (≥120 years) and were dropped from the analysis  
<sup>§</sup>Sex assigned at birth; 2 patients (<0.1%) were missing data on sex assigned at birth and dropped from the analysis  
<sup>||</sup>A measure of individual-level socioeconomic position; to capture information about the pre-pandemic period, health insurance data were based on the most recent encounter from 01/01/2017 to 02/28/2020 for which health insurance data were available; private includes patients with Medicare Advantage (Part C), Medicare Supplement (Medigap), Medicare (Part D), employer-sponsored and individual plans, private military insurance, and other forms of private insurance; public includes patients on Medicaid, Medicare (Part A and/or B only), public military insurance, and other forms of public insurance; uninsured includes patients without health insurance and patients with Indian Health Services insurance<sup>135,136</sup>

**Table 1.4.** Distribution of UHCs among patients with a positive SARS-CoV-2 RT-PCR test, by age group, University of Washington Medicine healthcare system, February 29, 2020-March 13, 2021

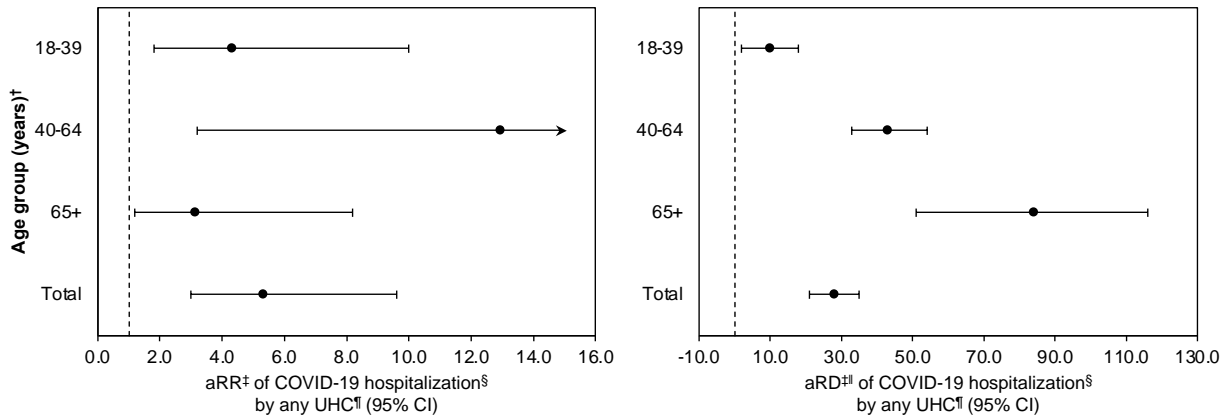
UHC*	Total N = 7,452		18-39 years† N = 3,249		40-64 years† N = 2,840		65+ years† N = 1,363	
	n	%	n	%	n	%	n	%
None	2,111	28.3	1,380	42.5	586	20.6	145	10.6
Asthma	499	6.7	181	5.6	205	7.2	113	8.3
* Bronchiectasis	42	0.6	2	0.1	14	0.5	26	1.9
Bronchopulmonary dysplasia	0	0.0	0	0.0	0	0.0	0	0.0
* Cancer	412	5.5	48	1.5	156	5.5	208	15.3
* Cerebrovascular disease	346	4.6	26	0.8	117	4.1	203	14.9
* Chronic kidney disease	418	5.6	31	1.0	157	5.5	230	16.9
* Chronic obstructive pulmonary disorder	229	3.1	2	0.1	89	3.1	138	10.1
* Corticosteroids or other immunosuppressive medications	106	1.4	19	0.6	53	1.9	34	2.5
* Cystic fibrosis	3	<0.1	2	0.1	1	<0.1	0	0.0
* Diabetes mellitus, type 1	78	1.0	27	0.8	38	1.3	13	1.0
* Diabetes mellitus, type 2	954	12.8	79	2.4	489	17.2	386	28.3
* Down syndrome	12	0.2	3	0.1	9	0.3	0	0.0
* Heart conditions	1,009	13.5	87	2.7	373	13.1	549	40.3
* Human immunodeficiency virus	119	1.6	27	0.8	81	2.9	11	0.8
Hypertension	1,729	23.2	131	4.0	837	29.5	761	55.8
* Immune deficiencies	37	0.5	4	0.1	19	0.7	14	1.0
* Liver disease, chronic	371	5.0	56	1.7	204	7.2	111	8.1
* Lung disease, interstitial	182	2.4	12	0.4	86	3.0	84	8.2
* Lung disease, other	425	5.7	44	1.4	175	6.2	206	15.1
* Mental health disorders	1,217	16.3	389	12.0	514	18.1	314	23.0
* Neurologic conditions	555	7.4	39	1.2	144	5.1	372	27.3
* Obesity (BMI $\geq 30\text{kg/m}^2$ )	1,935	26.0	603	18.6	960	33.8	372	27.3
Overweight (BMI $25 \geq 29\text{kg/m}^2$ )	1,803	24.2	683	21.0	749	26.4	371	27.2
* Pregnancy and recent pregnancy	49	0.7	48	1.5	1	<0.1	0	0.0
* Pulmonary hypertension and pulmonary embolism	174	2.3	20	0.6	75	2.6	79	5.8
Sickle cell disease	10	0.1	7	0.2	3	0.1	0	0.0
* Smoking, current and former	1,937	26.0	564	17.4	859	30.2	514	37.7
* Solid organ or blood stem cell transplantation	108	1.4	18	0.6	49	1.7	41	3.0
Substance use disorders	609	8.2	209	6.4	307	10.8	93	6.8
Thalassemia	10	0.1	5	0.2	5	0.2	0	0.0
* Tuberculosis	16	0.2	5	0.2	7	0.2	4	0.3

UHC=underlying health condition, SARS-CoV-2=severe acute respiratory syndrome coronavirus 2, RT-PCR=reverse transcription polymerase chain reaction, BMI=body mass index

Columns may sum to greater than 100% due to overlapping health conditions

\*Conditions possibly associated with increased risk of severe coronavirus disease 2019 (COVID-19) per the United States Centers for Disease Control and Prevention; [1] UHCs for which there is a published meta-analysis or systematic review demonstrating a conclusive increase in risk of severe COVID-19 are marked with an asterisk

†Age at first positive SARS-CoV-2 RT-PCR test within University of Washington Medicine



**Figure 1.1.** Adjusted risk ratios and differences of COVID-19-associated hospitalization by any UHC, stratified by age group\*

COVID-19=coronavirus disease 2019, UHC=underlying health condition, aRR=adjusted risk ratio, aRD=adjusted risk difference, CI=confidence interval

aRRs estimated by log-binomial regression using Huber-White estimates of the standard error; aRDs estimated using a generalized linear model with a Gaussian distribution and identity link function, and using Huber-White estimates of the standard error

Vertical dashed lines represent the null value of 1.0 in the aRR plot, and the null value of 0.0 in the aRD plot

Analysis of variance used to test for interaction by age group (aRR: p-value=0.2; aRD: p-value<0.001)

\*Among patients with a positive severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) reverse transcription polymerase chain reaction (RT-PCR) test, University of Washington Medicine healthcare system, 02/29/2020 to 03/13/2021

†Age at first positive SARS-CoV-2 RT-PCR test within University of Washington Medicine

‡Adjusted for continuous age (years), sex assigned at birth (female/male), race and ethnicity (Hispanic or Latine, non-Hispanic American Indian or Alaska Native, non-Hispanic Asian, non-Hispanic Black, non-Hispanic Native Hawaiian or Pacific Islander, non-Hispanic White, not recorded), and health insurance status (public, private, uninsured, not recorded); total models also adjusted for age group (18-39, 40-64, 65+ years)

§An indicator variable of COVID-19-associated hospitalization within University of Washington Medicine

¶Difference in cumulative incidence per 1,000 SARS-CoV-2-positive persons over the 13-month study period

¶¶Conditions possibly associated with increased risk of severe COVID-19 per the United States Centers for Disease Control and Prevention,<sup>26</sup> (all yes/no) based on electronic health record data; see Table 1.1 for list of conditions

**Table 1.5.** Risks, risk ratios, and risk differences of COVID-19-associated hospitalization by presence of any UHC among patients with a positive SARS-CoV-2 RT-PCR test, overall and by age group, University of Washington Medicine healthcare system, February 29, 2020-March 13, 2021

Age group (years)*	Any UHC <sup>†</sup>	Risk of COVID-19 hospitalization <sup>‡</sup>		Crude RR		Adjusted RR <sup>§</sup>		Crude RD <sup>  </sup>		Adjusted RD <sup>§  </sup>	
		n/N	%	RR	95% CI	aRR	95% CI	RD	95% CI	aRD	95% CI
18-39	Yes	42 / 1,869	2.2	5.2	2.2, 12.1	4.3	1.8, 10.0	18	11, 26	10	2, 18
	No	6 / 1,380	0.4	Referent		Referent		Referent		Referent	
40-64	Yes	126 / 2,254	5.6	16.4	4.1, 66.1	12.9	3.2, 52.5	52	42, 63	43	33, 54
	No	2 / 586	0.3	Referent		Referent		Referent		Referent	
65+	Yes	149 / 1,218	12.2	4.4	1.7, 11.8	3.1	1.2, 8.2	95	62, 127	84	51, 116
	No	4 / 145	2.8	Referent		Referent		Referent		Referent	
Total	Yes	317 / 5,341	5.9	10.4	5.9, 18.5	5.3	3.0, 9.6	54	47, 61	28	21, 35
	No	12 / 2,111	0.6	Referent		Referent		Referent		Referent	

COVID-19=coronavirus disease 2019, UHC=underlying health condition, SARS-CoV-2=severe acute respiratory syndrome coronavirus 2, RT-PCR=reverse transcription polymerase chain reaction, (a)RR=(adjusted) risk ratio, (a)RD=(adjusted) risk difference, CI=confidence interval  
 RRs estimated by log-binomial regression using Huber-White estimates of the standard error; RDs estimated using a generalized linear model with a Gaussian distribution and identity link function, and using Huber-White estimates of the standard error  
 Analysis of variance used to test for interaction by age group (aRR: p-value=0.2; aRD: p-value<0.001)

\*Age at first positive SARS-CoV-2 RT-PCR test within University of Washington Medicine

<sup>†</sup>Conditions possibly associated with increased risk of severe COVID-19 per the United States Centers for Disease Control and Prevention,[1] (all yes/no) based on electronic health record data; see Table 1.1 for list of conditions

<sup>‡</sup>An indicator variable of COVID-19-associated hospitalization within University of Washington Medicine

<sup>§</sup>Adjusted for continuous age (years), sex assigned at birth (female/male), race and ethnicity (Hispanic or Latine, non-Hispanic American Indian or Alaska Native, non-Hispanic Asian, non-Hispanic Black, non-Hispanic Native Hawaiian or Pacific Islander, non-Hispanic White, not recorded), and health insurance status (public, private, uninsured, not recorded); total models also adjusted for age group (18-39, 40-64, 65+ years)

<sup>||</sup>Difference in cumulative incidence per 1,000 SARS-CoV-2-positive persons over the 13-month study period

**Table 1.6.** Risks, risk ratios, and risk differences of COVID-19-associated hospitalization by presence of any UHC among patients with a positive SARS-CoV-2 RT-PCR test, overall and by age group, University of Washington Medicine healthcare system, February 29, 2020-December 10, 2020 (sensitivity analysis #1)

Age group (years)*	Any UHC†	Risk of COVID-19 hospitalization‡		Crude RR		Adjusted RR§		Crude RD¶		Adjusted RD§¶	
		n/N	%	RR	95% CI	aRR	95% CI	RD	95% CI	aRD	95% CI
18-39	Yes	39 / 1,602	2.4	5.1	2.2, 12.0	4.1	1.7, 9.7	20	11, 28	11	3, 20
	No	6 / 1,257	0.5	Referent		Referent		Referent		Referent	
40-64	Yes	100 / 1,825	5.5	27.1	3.8, 193.7	21.6	3.0, 155.2	53	42, 64	44	33, 56
	No	1 / 494	0.2	Referent		Referent		Referent		Referent	
65+	Yes	111 / 996	11.1	4.5	1.5, 14.1	3.4	1.1, 10.4	87	53, 121	77	43, 111
	No	3 / 122	2.5	Referent		Referent		Referent		Referent	
Total	Yes	250 / 4,423	5.7	10.6	5.6, 19.9	5.7	3.0, 10.7	51	44, 59	28	21, 35
	No	10 / 1,873	0.5	Referent		Referent		Referent		Referent	

COVID-19=coronavirus disease 2019, UHC=underlying health condition, SARS-CoV-2=severe acute respiratory syndrome coronavirus 2, RT-PCR=reverse transcription polymerase chain reaction, (a)RR=(adjusted) risk ratio, (a)RD=(adjusted) risk difference, CI=confidence interval  
 RRs estimated by log-binomial regression using Huber-White estimates of the standard error; RDs estimated using a generalized linear model with a Gaussian distribution and identity link function, and using Huber-White estimates of the standard error  
 Analysis of variance used to test for interaction by age group (aRR: p-value=0.1; aRD: p-value<0.001)

\*Age at first positive SARS-CoV-2 RT-PCR test within University of Washington Medicine

†Conditions possibly associated with increased risk of severe COVID-19 per the United States Centers for Disease Control and Prevention,[1] (all yes/no) based on electronic health record data; see Table 1.1 for list of conditions

‡An indicator variable of COVID-19-associated hospitalization within University of Washington Medicine

§Adjusted for continuous age (years), sex assigned at birth (female/male), race and ethnicity (Hispanic or Latine, non-Hispanic American Indian or Alaska Native, non-Hispanic Asian, non-Hispanic Black, non-Hispanic Native Hawaiian or Pacific Islander, non-Hispanic White, not recorded), and health insurance status (public, private, uninsured, not recorded); total models also adjusted for age group (18-39, 40-64, 65+ years)

¶Difference in cumulative incidence per 1,000 SARS-CoV-2-positive persons over the 13-month study period

**Table 1.7.** Risks, risk ratios, and risk differences of COVID-19-associated hospitalization by presence of any UHC among patients with a positive SARS-CoV-2 RT-PCR test, overall and by age group, University of Washington Medicine healthcare system, July 1, 2020-October 31, 2020 (sensitivity analysis #2)

Age group (years)*	Any UHC†	Risk of COVID-19 hospitalization‡		Crude RR		Adjusted RR§		Crude RD¶		Adjusted RD§¶	
		n/N	%	RR	95% CI	aRR	95% CI	RD	95% CI	aRD	95% CI
18-39	Yes	16 / 640	2.5	6.4	1.5, 27.7	4.9	1.2, 19.9	21	8, 34	13	0, 26
	No	2 / 511	0.4	Referent		Referent		Referent		Referent	
40-64	Yes	28 / 583	4.8	8.5	1.2, 61.9	7.0	0.9, 52.5	42	22, 63	36	15, 57
	No	1 / 176	0.6	Referent		Referent		Referent		Referent	
65+	Yes	21 / 237	8.9	3.2	0.4, 23.1	2.5	0.4, 16.6	61	-4, 126	55	-9, 119
	No	1 / 36	2.8	Referent		Referent		Referent		Referent	
Total	Yes	65 / 1,460	4.5	8.0	2.9, 22.0	4.8	1.8, 13.0	39	27, 51	23	11, 34
	No	4 / 723	0.6	Referent		Referent		Referent		Referent	

COVID-19=coronavirus disease 2019, UHC=underlying health condition, SARS-CoV-2=severe acute respiratory syndrome coronavirus 2, RT-PCR=reverse transcription polymerase chain reaction, (a)RR=(adjusted) risk ratio, (a)RD=(adjusted) risk difference, CI=confidence interval  
 RRs estimated by log-binomial regression using Huber-White estimates of the standard error; RDs estimated using a generalized linear model with a Gaussian distribution and identity link function, and using Huber-White estimates of the standard error  
 Analysis of variance used to test for interaction by age group (aRR: p-value=0.8; aRD: p-value=0.2)

\*Age at first positive SARS-CoV-2 RT-PCR test within University of Washington Medicine

†Conditions possibly associated with increased risk of severe COVID-19 per the United States Centers for Disease Control and Prevention,[1] (all yes/no) based on electronic health record data; see Table 1.1 for list of conditions

‡An indicator variable of COVID-19-associated hospitalization within University of Washington Medicine

§Adjusted for continuous age (years), sex assigned at birth (female/male), race and ethnicity (Hispanic or Latine, non-Hispanic American Indian or Alaska Native, non-Hispanic Asian, non-Hispanic Black, non-Hispanic Native Hawaiian or Pacific Islander, non-Hispanic White, not recorded), and health insurance status (public, private, uninsured, not recorded); total models also adjusted for age group (18-39, 40-64, 65+ years)

¶Difference in cumulative incidence per 1,000 SARS-CoV-2-positive persons over the 13-month study period

**Table 1.8.** Risks, risk ratios, and risk differences of COVID-19-associated hospitalization by presence of any UHC conclusively associated with severe COVID-19, among patients with a positive SARS-CoV-2 RT-PCR test, overall and by age group, University of Washington Medicine healthcare system, February 29, 2020-March 13, 2021 (sensitivity analysis #3)

Age group (years)*	Any UHC <sup>†</sup>	Risk of COVID-19 hospitalization <sup>‡</sup>		Crude RR		Adjusted RR <sup>§</sup>		Crude RD <sup>  </sup>		Adjusted RD <sup>§  </sup>	
		n/N	%	RR	95% CI	aRR	95% CI	RD	95% CI	aRD	95% CI
18-39	Yes	38 / 1,362	2.8	5.3	2.6, 10.5	4.2	2.1, 8.5	23	13, 32	14	4, 24
	No	10 / 1,887	0.5	Referent		Referent		Referent		Referent	
40-64	Yes	122 / 1,923	6.3	9.7	4.3, 21.9	7.8	3.5, 17.7	57	45, 69	48	36, 60
	No	6 / 917	0.7	Referent		Referent		Referent		Referent	
65+	Yes	143 / 1,133	12.6	2.9	1.6, 5.4	2.2	1.2, 4.1	83	50, 115	73	40, 106
	No	10 / 230	4.3	Referent		Referent		Referent		Referent	
Total	Yes	303 / 4,418	6.9	8.0	5.4, 11.9	4.2	2.8, 6.4	60	52, 68	34	26, 42
	No	26 / 3,034	0.9	Referent		Referent		Referent		Referent	

COVID-19=coronavirus disease 2019, UHC=underlying health condition, SARS-CoV-2=severe acute respiratory syndrome coronavirus 2, RT-PCR=reverse transcription polymerase chain reaction, (a)RR=(adjusted) risk ratio, (a)RD=(adjusted) risk difference, CI=confidence interval  
 RRs estimated by log-binomial regression using Huber-White estimates of the standard error; RDs estimated using a generalized linear model with a Gaussian distribution and identity link function, and using Huber-White estimates of the standard error  
 Analysis of variance used to test for interaction by age group (aRR: p-value=0.04; aRD: p-value<0.001)

\*Age at first positive SARS-CoV-2 RT-PCR test within University of Washington Medicine

<sup>†</sup>Conditions conclusively associated with increased risk of severe COVID-19 per the United States Centers for Disease Control and Prevention,[1] (all yes/no) based on electronic health record data; see Table 1.1 for list of conditions

<sup>‡</sup>An indicator variable of COVID-19-associated hospitalization within University of Washington Medicine

<sup>§</sup>Adjusted for continuous age (years), sex assigned at birth (female/male), race and ethnicity (Hispanic or Latine, non-Hispanic American Indian or Alaska Native, non-Hispanic Asian, non-Hispanic Black, non-Hispanic Native Hawaiian or Pacific Islander, non-Hispanic White, not recorded), and health insurance status (public, private, uninsured, not recorded); total models also adjusted for age group (18-39, 40-64, 65+ years)

<sup>||</sup>Difference in cumulative incidence per 1,000 SARS-CoV-2-positive persons over the 13-month study period

### **CHAPTER 3. Associations between insurance, race and ethnicity, and COVID-19-associated hospitalization, beyond underlying health conditions**

#### **ABSTRACT**

**Background:** People of lower socioeconomic position (SEP) and people of color (POC) experience higher risks of severe COVID-19, but understanding of these associations beyond the effect of underlying health conditions (UHCs) is limited. Moreover, few studies have focused on young adults, who have had the highest incidence of COVID-19 during much of the pandemic.

**Methods:** We conducted a retrospective cohort study using electronic health record data from the University of Washington Medicine healthcare system. Our study population included individuals aged 18-39 years who tested positive for SARS-CoV-2 from February 2020 to March 2021. Using regression modeling, we estimated adjusted risk ratios (aRRs) and differences (aRDs) of COVID-19 hospitalization by SEP (using health insurance as a proxy) and race and ethnicity. We adjusted for any UHC to examine these associations beyond the effect of UHCs.

**Results:** Among 3,101 individuals, the uninsured/publicly insured had a 1.9-fold higher risk of hospitalization (aRR [95% CI]=1.9 [1.0, 3.6]) and 9 additional hospitalizations per 1,000 SARS-CoV-2 positive persons (aRD [95% CI]=9 [-1, 20]) compared to the privately insured. Hispanic or Latine, non-Hispanic (NH) Asian, NH Black, and NH Native Hawaiian or Pacific Islander patients had a 1.5-, 2.7-, 1.4-, and 2.1-fold-higher risk of hospitalization (aRR [95% CI]=1.5 [0.7, 3.1]; 2.7 [1.1, 6.5]; 1.4 [0.6, 3.3]; 2.1 [0.5, 9.1]), respectively, compared to NH White patients.

**Conclusions:** Though they should be interpreted with caution given low precision, our findings suggest the increased risk of COVID-19 hospitalization among young adults of lower SEP and young adults of color may be driven by forces other than UHCs, including social determinants of health.

## BACKGROUND

Most people with coronavirus disease 2019 (COVID-19) – caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) – experience mild or moderate illness, but some develop severe outcomes requiring hospitalization.<sup>106</sup> In the United States (US), the disproportionate impact of severe COVID-19 on people of color (POC) is well documented.<sup>27</sup> Compared to non-Hispanic (NH) White individuals, POC have experienced higher rates of COVID-19-associated emergency department visits and hospitalizations and a disproportionate burden of COVID-19 deaths.<sup>28–34</sup> Additionally, COVID-19-associated hospitalizations and mortality have disproportionately impacted people of lower individual-level socioeconomic position (SEP), including people with lower incomes, people without a high school education, uninsured or publicly-insured individuals, and people experiencing homelessness.<sup>39–42</sup>

Frequently, these disparities in COVID-19 severity are attributed to higher rates of underlying health conditions (UHCs) that increase the risk of severe COVID-19<sup>26</sup> among POC<sup>44–47</sup> and people of lower SEP.<sup>47,48</sup> However, an emphasis on UHCs may underplay the importance of social determinants of health (SDOH).<sup>49</sup> SDOH – such as experienced racism, limited healthcare access and utilization, disproportionate representation in essential work settings, living in higher density and multigenerational households, higher rates of unemployment, and inequities in education, income, and wealth – prevent POC and people of lower SEP from having fair opportunities for health, including in the context of the COVID-19 pandemic.<sup>50–53</sup>

Research exploring differences in COVID-19 severity between racial, ethnic, and socioeconomic groups beyond the effect of UHCs is needed to better understand the role of SDOH.

As with POC and people of lower SEP, young adults are more likely to experience lack of health insurance and limited healthcare access and utilization.<sup>83</sup> In the US, adults under age 40 have represented a substantial proportion of COVID-19 hospitalizations<sup>82</sup> and have had the highest

incidence of COVID-19 cases during much of the pandemic.<sup>2</sup> However, there is limited research examining the associations between race and ethnicity, SEP, and COVID-19 severity within young adult populations, which would inform targeted COVID-19 prevention activities.

Mirroring national trends, in Washington (WA) State, POC have experienced higher rates of COVID-19-associated hospitalizations and deaths compared to NH White individuals,<sup>90</sup> and adults under age 40 have made up a notable percentage of COVID-19 hospitalizations<sup>89</sup> and have had the highest incidence of COVID-19 cases throughout much of the pandemic.<sup>87</sup> The aim of our study was to examine the associations between race and ethnicity, SEP, and COVID-19-associated hospitalization, above and beyond the effect of any diagnosed UHC, among young adult patients in a large academic medical system in western WA State.

## **METHODS**

### **Study design, data source, setting, and population**

We conducted a retrospective cohort study using electronic health record (EHR) data from the University of Washington Medicine (UWM) healthcare system, which is the largest academic medical system in the Central Puget Sound region. The Central Puget Sound region is located in western WA State and includes the Seattle metropolitan area; it comprises 56% of the state's population<sup>88</sup> and, as of April 2023, about 55% of WA State's confirmed and probable COVID-19 cases.<sup>87</sup> The University of Washington Institutional Review Board approved this study and waived the informed consent and HIPAA authorization requirements (IRB ID: STUDY00011233). This study was unfunded.

Our study population included living patients engaged in care in the UWM system who tested positive for SARS-CoV-2 within UWM at ages 18-39 years. SARS-CoV-2 testing began within UWM on February 29, 2020. Using EHR data, we identified patients who had at least one

encounter in the UWM system from January 1, 2017 to February 28, 2020, who had at least one positive SARS-CoV-2 reverse transcription polymerase chain reaction (RT-PCR) test within UWM from February 29, 2020 to March 13, 2021 (14 days before the date of the data pull, to allow time for the occurrence of COVID-19-associated hospitalization following a positive test), and who were alive and aged 18-39 years at the time of their first positive SARS-CoV-2 RT-PCR test. Our cohort, as defined above, included 3,251 individuals.

### **Data measures**

We collected data at the patient level on health insurance status, race and ethnicity, any UHC, COVID-19-associated hospitalization, age (in years) at the time of first positive SARS-CoV-2 RT-PCR test, and sex assigned at birth (female/male). Of 3,251 eligible patients, we dropped 148 (4.6%) who were missing health insurance data and two (<0.1%) who had sex assigned at birth recorded as “unknown”, for a final analytic population of 3,101 individuals.

Studies have demonstrated the validity of EHR data for identifying health insurance status,<sup>137</sup> which we used as a measure of individual-level SEP (uninsured or public vs. private). *A priori*, we intended to analyze uninsured and public as separate categories, but ultimately combined them due to the small proportion of uninsured patients in our analytic population (5.3%, n=165); other studies have taken a similar approach.<sup>138</sup> The “uninsured or public” category included patients without health insurance, patients on Medicaid, Medicare (Part A and/or B only), public military insurance, and other forms of public insurance. The “private” category included patients with Medicare Advantage (Part C), Medicare Supplement (Medigap), private military insurance, employer-sponsored and individual plans, and other forms of private insurance.<sup>135,136</sup> We based health insurance status on the most recent encounter between January 1, 2017 and February 28, 2020 for which insurance data were available.

Ethnicity data in the EHR were originally recorded as either “Hispanic or Latino” or “not Hispanic or Latino”, and race data were originally recorded as “American Indian or Alaska Native”, “Asian”, “Black or African American”, “Native Hawaiian or Other Pacific Islander”, or “White”. Consistent with the racial and ethnic categories used by the WA State Department of Health when reporting COVID-19 data,<sup>87</sup> we categorized race and ethnicity in our study as Hispanic or Latine, NH American Indian or Alaska Native (AIAN), NH Asian, NH Black, NH Native Hawaiian or Pacific Islander (NHPI), and NH White. We categorized race and ethnicity data that were missing or recorded as “declined to answer”, “unavailable”, or “unknown” as “not recorded”.

We defined any UHC (yes/no) as documented diagnosis of at least one UHC identified by the US Centers for Disease Control and Prevention (CDC) as conclusively associated with increased risk of severe COVID-19 (Table 2.1).<sup>26</sup> To identify documented UHCs, we evaluated EHR data from January 1, 2017 to the date of the first positive SARS-CoV-2 RT-PCR test. We identified most UHCs exclusively by relevant international classification of disease, tenth revision, clinical modification (ICD-10-CM) diagnosis codes. We categorized patients who had no indication of any UHCs as having no UHCs.

We defined COVID-19-associated hospitalization (yes/no) as an in-patient encounter within UWM that either (1) had an admit date at most three days prior to the date of a positive SARS-CoV-2 test and an indication in the admit note that the patient was hospitalized for COVID-19, or (2) was within 14 days following a positive SARS-CoV-2 test; this is the standard approach validated and used by the University of Washington Institute of Translational Health Sciences to identify COVID-19-associated hospitalizations.

## **Data analyses**

We calculated the unadjusted proportions of patients who experienced COVID-19-associated hospitalization by health insurance status and race and ethnicity, overall and stratified by any

UHC. We estimated 95% confidence intervals (CIs) using the Wilson score interval with Yates' continuity correction. We present these data for all racial and ethnic groups, but do not consider them sufficient to draw conclusions about the risk of COVID-19-associated hospitalization for NH AIAN patients, or for NH Asian or NH NHPI patients without UHCs, due to small sample sizes and/or zero COVID-19-associated hospitalizations in these groups. In addition, we present but do not interpret these data for patients with unrecorded race and ethnicity due to the likely heterogeneity of this group.

In addition, we estimated adjusted risk ratios (aRRs) and risk differences (aRDs) of COVID-19-associated hospitalization by health insurance status and race and ethnicity, adjusted for any UHC, to examine these associations above and beyond the effect of any diagnosed UHC. We also adjusted for potential confounders sex assigned at birth, continuous age, and race and ethnicity in the health insurance models, and sex assigned at birth and continuous age in the race and ethnicity models. We did not adjust for insurance status in the race and ethnicity models as differences in SEP across racial and ethnic groups is an important contributor to racial and ethnicity disparities in health.<sup>139,140</sup> We used patients with private insurance and NH White patients as the referent groups, as we expected these groups to have the lowest risks. In the race and ethnicity regression models, we did not include 29 (0.9%) NH AIAN patients, as insufficient data (small numbers and zero outcomes) would result in an unreliable parameter estimate for this group, nor did we include 447 (14.4%) patients with unrecorded race and ethnicity, as this parameter estimate would be uninterpretable given the probable heterogeneity of this group. We estimated aRRs using multivariable log-binomial regression, and aRDs using generalized linear regression with a Gaussian distribution and identity link function, both with Huber-White estimates of the standard error.<sup>108</sup>

## RESULTS

Among 3,101 SARS-CoV-2-positive 18-39-year-old patients, the average age at the time of first positive SARS-CoV-2 RT-PCR test was 27.9 years (SD=6.2 years), 18.0% of patients were recorded as Hispanic or Latine and 13.5% as NH Black, 52.8% were assigned female sex at birth, and 42.8% had at least one documented UHC (Table 2.2). Overall, 46 patients (1.5%) experienced COVID-19-associated hospitalization (Table 2.3).

Patients who were uninsured or publicly insured (n=1,168, 37.7%) were slightly older and had a higher proportion of individuals with documented diagnosis of at least one UHC compared to the privately insured (n=1,933, 62.3%) (Table 2.2). Patients recorded as Hispanic or Latine, NH AIAN, NH Black, or NH NHPI comprised larger proportions of the uninsured or publicly insured group compared to the privately insured group. Table 2.4 presents patient characteristics by race and ethnicity. Patients recorded as Hispanic or Latine, NH AIAN, NH NHPI, and NH Black had higher proportions of individuals who were uninsured or publicly insured and higher proportions of individuals with at least one UHC compared to NH Asian and NH White patients.

### **Risk of COVID-19-associated hospitalization by health insurance status and race and ethnicity**

Overall, the risk of COVID-19-associated hospitalization was higher among SARS-CoV-2-positive 18-39-year-old patients who were uninsured or publicly insured compared to the privately insured (2.5% [95% CI=1.7%, 3.6%] vs. 0.9% [95% CI=0.5%, 1.4%]) (Figure 2.1; Table 2.3). Among patients without UHCs, the proportion of patients who developed COVID-19-associated hospitalization was higher among the uninsured or publicly insured (1.3%) compared to the privately insured (0.2%), though estimated 95% CIs overlapped. After adjustment for potential confounders and any UHC, patients who were uninsured or publicly insured had a 1.9-fold higher risk of COVID-19-associated hospitalization (aRR [95% CI]=1.9 [1.0, 3.6]) and 9

additional hospitalizations per 1,000 SARS-CoV-2 positive persons during the 13-month study period (aRD [95% CI]=9 [-1, 20]) compared to patients on private health insurance, though 95% CIs were wide and contained the null values (Table 2.5).

Overall, 2.3% of SARS-CoV-2-positive 18-39-year-old patients recorded as Hispanic or Latine, 2.5% of NH Asian patients, 1.9% of NH Black patients, and 3.6% of NH NHPI patients experienced COVID-19-associated hospitalization, compared to 1.1% of NH White patients (Figure 2.1; Table 2.3). Among patients without UHCs, higher proportions of Hispanic or Latine (0.8%) and NH Black patients (1.8%) experienced COVID-19-associated hospitalization compared to NH White patients (0.4%), though estimated 95% CIs were generally wide and overlapping. After adjustment for potential confounders and UHCs, patients who were recorded as Hispanic or Latine, NH Asian, NH Black, or NH NHPI had a 1.5-, 2.7-, 1.4-, and 2.1-fold-higher risk of COVID-19-associated hospitalization (aRR [95% CI]=1.5 [0.7, 3.1]; 2.7 [1.1, 6.5]; 1.4 [0.6, 3.3]; 2.1 [0.5, 9.1]), and 5, 15, 4, and 17 additional hospitalizations per 1,000 SARS-Cov-2-positive persons during the 13-month study period (aRD [95% CI]=5 [-9, 19]; 15 [-5, 34]; 4 [-10, 19]; 17 [-31, 66]), respectively, compared to patients recorded as NH White, though 95% CIs were wide and most contained the null values (Table 2.5).

## **DISCUSSION**

We found that among SARS-CoV-2-positive adults under age 40 without UHCs, a higher proportion of uninsured or publicly-insured patients experienced COVID-19-associated hospitalization compared to the privately insured, and higher proportions of patients recorded as Hispanic or Latine or NH Black experienced COVID-19-associated hospitalization compared to NH White patients. Similarly, though 95% CIs were wide and most spanned the null values, the magnitudes and directions of our adjusted estimated measures of excess risk suggest uninsured or publicly-insured young adults and young adult POC may be at higher relative and

absolute risk of COVID-19-associated hospitalization compared to privately-insured and NH White young adults, above and beyond the effect of any UHC.

Previous studies have demonstrated POC and people of lower SEP are at higher risk of severe COVID-19 compared to NH White individuals<sup>28-34</sup> and people of higher SEP.<sup>39-42</sup> Commentators have largely attributed this excess disease burden to POC and people of lower SEP (1) being more likely to be exposed to SARS-CoV-2 due, in part, to disproportionate representation in essential work settings and living in higher density and multigenerational households,<sup>50-53</sup> and (2) being at increased risk of severe COVID-19 due to higher rates of UHCs.<sup>44-48</sup> Our study builds on this previous work by only including patients who tested positive for SARS-CoV-2, and either stratifying by or statistically adjusting for any UHC. Though they should be interpreted with caution given low precision, our findings suggest the differences in the risk of COVID-19-associated hospitalization between young adults of lower and higher SEP and between young adult POC and NH White young adults may be driven by forces other than UHCs.

Our analyses add to the limited body of research on racial and ethnic disparities in COVID-19 beyond the effect of UHCs, which shows these disparities persist even after controlling for UHCs.<sup>92-96</sup> Similar to our results, an analysis of EHR data from 21 states found racial and ethnic disparities in hospitalizations among COVID-19 cases even after controlling for certain sociodemographic factors and select UHCs, with NH Asian patients exhibiting the highest risk relative to NH White patients, followed by Hispanic patients and NH Black patients.<sup>92</sup> One possible explanation for these findings is that, due to limited healthcare access and utilization,<sup>51</sup> POC and people of lower SEP have higher rates of undiagnosed health conditions,<sup>141-145</sup> creating the potential for disproportionate rates of severe COVID-19 even among those without diagnosed UHCs. Nevertheless, it is critical to also consider the role of SDOH in COVID-19 disparities, including residing in areas of higher deprivation, lower quality of clinical care, racism in healthcare, higher rates of unemployment, chronic stress from racial discrimination, and

inequities in housing, transportation, education, income, and wealth, which previous studies have elucidated.<sup>27,30,146–149</sup>

A novel element of our study is its focus on young adults, who have had the highest incidence of COVID-19 cases throughout much of the pandemic.<sup>2</sup> Our findings highlight the importance of ensuring equitable access to COVID-19 resources, including vaccines and anti-SARS-CoV-2 therapy, for young adult POC and young adults of lower SEP in general, not only for those with UHCs.<sup>121–123</sup> Furthermore, improved understanding of the demographic and clinical features of young adults with COVID-19, and of racial, ethnic, and SEP disparities in COVID-19 outcomes among young adults, allows for targeted local morbidity and mortality prevention initiatives tailored to young adult populations, including culturally- and linguistically-appropriate risk communication and collaboration with community partners.

In addition to the innovative elements highlighted above, strengths of our study include leveraging EHR data from a large academic medical system and estimating both relative and absolute measures of excess risk.<sup>119</sup> Our study also has several important limitations. A primary limitation is low precision, driven by insufficient sample size in the context of relatively low incidence of COVID-19-associated hospitalization among young adults. Even with several thousand patients included in our study, we only identified 56 recorded as NH NHPI and 29 recorded as NH AIAN – the two groups with the highest age-adjusted COVID-19 hospitalization and death rates in WA State as of April 2023.<sup>90</sup> Second, we observed high levels of missingness for race and ethnicity, increasing the likelihood of selection bias in our race and ethnicity regression models. Since EHR data often are missing not at random,<sup>128,129</sup> we did not employ multiple imputation methods, which may further increase bias under missing not at random conditions.<sup>130</sup> Instead, we categorized missing race and ethnicity data as “not recorded”, which may have led to residual confounding and bias in our health insurance regression models.<sup>131,132</sup> Furthermore, race and ethnicity recorded in EHR may not be valid, especially for POC,<sup>150,151</sup>

leading to differential exposure misclassification. Third, health insurance may be an incomplete measure of individual-level SEP, leading to non-differential exposure misclassification. Fourth, since POC and people of lower SEP have higher rates of undiagnosed health conditions,<sup>141–145</sup> we may have disproportionately failed to identify UHCs among POC and uninsured or publicly-insured patients. Fifth, we only captured COVID-19 hospitalizations within the UWM system, which may have led to differential outcome misclassification if the likelihood of COVID-19 hospitalization at an outside facility differed by racial and ethnic or health insurance group. Sixth, our analyses did not account for secular trends, such as changes in vaccine availability, testing practices, and circulating viral strains over time. Finally, we used data from a single academic medical center, which may limit the generalizability of our results. However, the proportion of patients in our study with any UHC was similar to the 2019 national estimate of the prevalence of chronic conditions in adults aged 18-34,<sup>152</sup> which supports the generalizability of our findings.

In conclusion, though they should be interpreted with caution given low precision, our findings suggest an increased risk of COVID-19-associated hospitalization among SARS-CoV-2-positive young adults of lower SEP and young adult POC may be driven by forces other than an increased risk of UHCs, including SDOH. Future research should directly explore the relationships between SDOH and COVID-19 as well as other health outcomes in young adult populations to better understand upstream influences.<sup>153</sup> COVID-19 has exacerbated existing health disparities across the US. Recognizing the roots of these disparities is essential to the development of targeted and effective community- and healthcare system-based public policies and health interventions that emphasize health equity and social justice.<sup>153</sup>

## TABLES AND FIGURES

<b>Table 2.1.</b> UHCs conclusively associated with increased risk of COVID-19-associated hospitalization per the United States Centers for Disease Control and Prevention and identifying ICD-10-CM codes		
<b>UHC<sup>a</sup></b>	<b>ICD-10-CM code<sup>b</sup></b>	<b>ICD-10-CM description</b>
Bronchiectasis	J47	Bronchiectasis
Cancer	C00-C96	Malignant neoplasms
Cerebrovascular disease	I60-I69	Cerebrovascular diseases
Chronic kidney disease	N18	Chronic kidney disease (CKD)
Chronic obstructive pulmonary disorder	J44	Other chronic obstructive pulmonary disease
Corticosteroids or other immunosuppressive medications	D84.821; Z79.52; Z92.25	Immunodeficiency due to drugs; Long term (current) use of systemic steroids; personal history of immunosuppression therapy
Cystic fibrosis	E84	Cystic fibrosis
Diabetes mellitus, type 1	E10	Type 1 diabetes mellitus
Diabetes mellitus, type 2	E11	Type 2 diabetes mellitus
Down syndrome	Q90	Down syndrome
Heart conditions (e.g., heart failure, coronary artery disease, cardiomyopathies)	I20-I25; I30-I52	Ischemic heart disease; Other forms of heart disease
Human immunodeficiency virus	B20; Z21	Human immunodeficiency virus (HIV) disease; Asymptomatic human immunodeficiency virus (HIV) infection status
Immune deficiencies	D80; D81; D82; D83; D84.0; D84.1; D84.81; D84.822; D84.89; D84.9	Immunodeficiency with predominantly antibody defects; Combined immunodeficiencies; Immunodeficiency associated with other major defects; Common variable immunodeficiency; Lymphocyte function antigen-1 [LFA-1] defect; Defects in the complement system; Immunodeficiency due to conditions classified elsewhere; Immunodeficiency due to external causes; Other immunodeficiencies; Immunodeficiency, unspecified
Liver disease, chronic (cirrhosis, non-alcoholic fatty liver disease, alcoholic liver disease, autoimmune hepatitis)	K70-K77	Diseases of liver
Lung disease, interstitial	J80-J84	Other respiratory diseases principally affecting the interstitium
Lung disease, other	I28; J41; J42; J43; J60-J70; J85-J86; J90-J94; Z99.81	Other diseases of pulmonary vessels; Simple and mucopurulent chronic bronchitis; Unspecified chronic bronchitis; Emphysema; Lung diseases due to external agents; Suppurative and necrotic conditions of the lower respiratory tract; Other diseases of the pleura; Dependence on supplemental oxygen
Mental health disorders (mood disorders, e.g., depression and schizophrenia spectrum disorders)	F20-F29; F30-F39	Schizophrenia, schizotypal, delusional, and other non-mood psychotic disorders; Mood (affective) disorders

<b>Table 2.1. UHCs conclusively associated with increased risk of COVID-19-associated hospitalization per the United States Centers for Disease Control and Prevention and identifying ICD-10-CM codes</b>		
<b>UHC<sup>a</sup></b>	<b>ICD-10-CM code<sup>b</sup></b>	<b>ICD-10-CM description</b>
Neurologic conditions	F01; F02; F03; G10-G14; G20; G30-G32; G35; G45; G70; G80-G83	Vascular dementia; Dementia in other diseases classified elsewhere; Unspecified dementia; Systemic atrophies primarily affecting the central nervous system; Parkinson's disease; Other degenerative diseases of the nervous system; Multiple sclerosis; Transient cerebral ischemic attacks and related syndromes; Myasthenia gravis and other myoneural disorders; Cerebral palsy and other paralytic syndromes
Obesity (BMI $\geq 30$ kg/m <sup>2</sup> ) <sup>c</sup>	E66.0; E66.1; E66.2; E66.8; E66.9	Obesity due to excessive calories; Drug-induced obesity; Morbid (severe) obesity with alveolar hypoventilation; Other obesity; Obesity, unspecified
Pregnancy and recent pregnancy	Z33; Z34; Z36; Z37; Z38; Z39; Z3A	Pregnant state; Encounter for supervision of normal pregnancy; Encounter for antenatal screening of mother; Outcome of delivery; Liveborn infants according to place of birth and type of delivery; Encounter for maternal postpartum care and examination; Weeks of gestation
Pulmonary hypertension and pulmonary embolism	I26; I27	Pulmonary embolism; Other pulmonary heart disease
Smoking, current and former <sup>c</sup>	F17; Z72.0; Z87.891	Nicotine dependence; Tobacco use; Personal history of nicotine dependence
Solid organ or blood stem cell transplantation	Z94; T86	Transplanted organ and tissue status; Complications of transplanted organs and tissue
Tuberculosis	A15	Respiratory tuberculosis
<p>BMI, body mass index; COVID-19, coronavirus disease 2019; ICD-10-CM, international classification of disease, tenth revision, clinical modification; UHC, underlying health condition</p> <p><sup>a</sup>UHCs for which there is a published meta-analysis or systematic review demonstrating a conclusive increase in risk of COVID-19-associated hospitalization according to the United States Centers for Disease Control and Prevention<sup>26</sup></p> <p><sup>b</sup>ICD-10-CM codes and other electronic health record (EHR) data for all underlying health conditions were evaluated from 01/01/2017 to the date of the first positive reverse transcription polymerase chain reaction (RT-PCR) test for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), except those for pregnancy and recent pregnancy, which were evaluated for the 60 days prior to the date of the first positive RT-PCR test for SARS-CoV-2</p> <p><sup>c</sup>In addition to the ICD-10-CM codes indicated, EHR height and weight data were used to calculate BMI to identify patients with obesity, and EHR smoking data were used to identify patients with a history of smoking. BMI was based on the most recent encounter between 01/01/2017 and the date of the first positive SARS-CoV-2 RT-PCR test for which height, weight, and the calculated BMI were biologically plausible. Biological plausibility for height was defined as <math>\geq 1.2</math>m and <math>\leq 2.4</math>m, for weight as <math>\geq 34.0</math>kg and <math>\leq 272.2</math>kg, and for BMI as <math>\leq 80.0</math>kg/m<sup>2</sup>.<sup>107</sup> Patients who had a smoking status of current or former smoker recorded at any encounter between 01/01/2017 and the date of the first positive SARS-CoV-2 RT-PCR test were classified as current or former smokers in our analyses</p>		

<b>Table 2.2.</b> Characteristics of SARS-CoV-2-positive 18-39-year-olds, by insurance status, University of Washington Medicine, February 2020-March 2021						
	<b>Total<sup>a</sup> N = 3,101</b>		<b>Uninsured or public health insurance N = 1,168</b>		<b>Private health insurance N = 1,933</b>	
<b>Variable</b>	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>
Age (years) <sup>b</sup> (mean, SD)	27.9	6.2	29.1	6.1	27.1	6.2
Race and ethnicity						
Hispanic or Latine	557	18.0	323	27.7	234	12.1
NH AIAN	29	0.9	16	1.4	13	0.7
NH Asian	277	8.9	66	5.7	211	10.9
NH Black	418	13.5	265	22.7	153	7.9
NH NHPI	56	1.8	26	2.2	30	1.6
NH White	1,317	42.5	332	28.4	985	51.0
Not recorded	447	14.4	140	12.0	307	15.9
Sex <sup>c</sup>						
Female	1,636	52.8	688	58.9	948	49.0
Male	1,465	47.2	480	41.1	985	51.0
Any UHC <sup>d</sup>						
No	1,773	57.2	538	46.1	1,235	63.9
Yes	1,328	42.8	630	53.9	698	36.1
AIAN, American Indian or Alaska Native; NH, non-Hispanic; NHPI, Native Hawaiian or Pacific Islander; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SD, standard deviation; UHC, underlying health condition <sup>a</sup> 148 patients (4.6%) were missing health insurance data and excluded from the final analytic dataset <sup>b</sup> Age at first positive SARS-CoV-2 reverse transcription polymerase chain reaction test within the University of Washington Medicine healthcare system <sup>c</sup> Sex assigned at birth; 2 patients (<0.1%) had sex assigned at birth recorded as “unknown” and were excluded from the final analytic dataset <sup>d</sup> See Table 2.1 for list of UHCs						

**Table 2.3.** Unadjusted proportions of SARS-CoV-2-positive 18-39-year-old patients who experienced COVID-19 hospitalization, by insurance status and race and ethnicity, overall and stratified by any UHC, University of Washington Medicine healthcare system, February 2020-March 2021

Variable		Risk of COVID-19 hospitalization								
		Total (N = 3,101)			No UHC <sup>a</sup> (N = 1,773)			Any UHC <sup>a</sup> (N = 1,328)		
		n/N	%	95% CI	n/N	%	95% CI	n/N	%	95% CI
Insurance	Uninsured or public	29 / 1,168	2.5	1.7, 3.6	7 / 538	1.3	0.6, 2.8	22 / 630	3.5	2.3, 5.3
	Private	17 / 1,933	0.9	0.5, 1.4	2 / 1,235	0.2	0.0, 0.7	15 / 698	2.1	1.3, 3.6
Race and ethnicity	Hispanic or Latine	13 / 557	2.3	1.3, 4.1	2 / 262	0.8	0.1, 3.0	11 / 295	3.7	2.0, 6.8
	NH AIAN	0 / 29	0.0	0.0, 14.6	0 / 11	0.0	0.0, 32.1	0 / 18	0.0	0.0, 21.9
	NH Asian	7 / 277	2.5	1.1, 5.4	0 / 180	0.0	0.0, 2.6	7 / 97	7.2	3.2, 14.8
	NH Black	8 / 418	1.9	0.9, 3.9	4 / 227	1.8	0.6, 4.7	4 / 191	2.1	0.7, 5.6
	NH NHPI	2 / 56	3.6	0.6, 13.4	0 / 20	0.0	0.0, 20.0	2 / 36	5.6	1.0, 20.0
	Not recorded	1 / 447	0.2	0.0, 1.4	0 / 282	0.0	0.0, 1.7	1 / 165	0.6	0.0, 3.8
	NH White	15 / 1,317	1.1	0.7, 1.9	3 / 791	0.4	0.1, 1.2	12 / 526	2.3	1.2, 4.1

AIAN, American Indian or Alaska Native; CI, confidence interval; COVID-19, coronavirus disease 2019; NH, non-Hispanic; NHPI, Native Hawaiian or Pacific Islander; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; UHC, underlying health condition  
95% CIs were calculated using the Wilson score interval with Yates' continuity correction

<sup>a</sup>See Table 2.1 for list of UHCs

**Table 2.4.** Characteristics of SARS-CoV-2-positive 18-39-year-olds, by race and ethnicity, University of Washington Medicine, February 2020-March 2021

Variable	Total N = 3,101		Hispanic or Latine N = 557		NH AIAN N = 29		NH Asian N = 277		NH Black N = 418		NH NHPI N = 56		NH White N = 1,317		Not recorded N = 447	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Age (years) <sup>a</sup> (mean, SD)	27.9	6.2	29.2	5.9	29.5	6.2	27.2	6.0	28.6	6.2	28.8	6.6	27.0	6.3	28.4	6.1
Insurance <sup>b</sup>																
Private	1,933	62.3	234	42.0	13	44.8	211	76.2	153	36.6	30	53.6	985	74.8	307	68.7
Uninsured or public	1,168	37.7	323	58.0	16	55.2	66	23.8	265	63.4	26	46.4	332	25.2	140	31.3
Sex <sup>c</sup>																
Female	1,636	52.8	325	58.3	16	55.2	143	51.6	218	52.2	25	44.6	682	51.8	227	50.8
Male	1,465	47.2	232	41.7	13	44.8	134	48.4	200	47.8	31	55.4	635	48.2	220	49.2
Any UHC <sup>d</sup>																
No	1,773	57.2	262	47.0	11	37.9	180	65.0	227	54.3	20	35.7	791	60.1	282	63.1
Yes	1,328	42.8	295	53.0	18	62.1	97	35.0	191	45.7	36	64.3	526	39.9	165	36.9

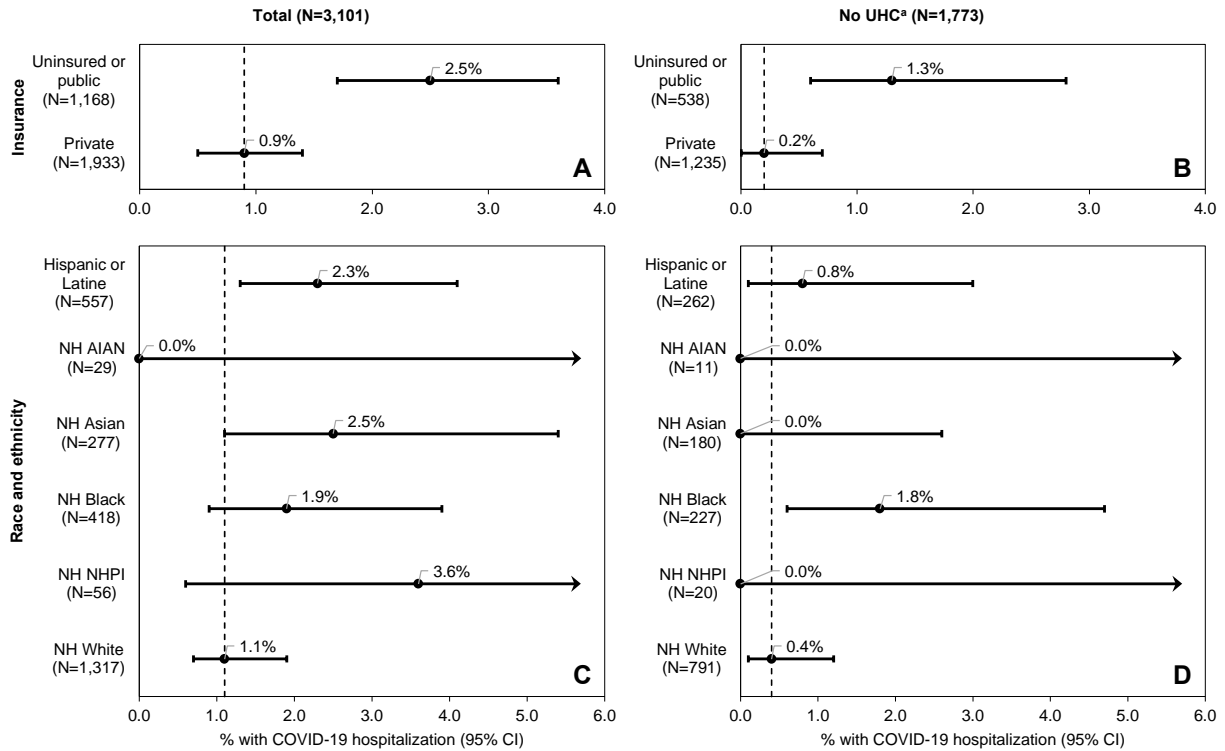
AIAN, American Indian or Alaska Native; NH, non-Hispanic; NHPI, Native Hawaiian or Pacific Islander; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SD, standard deviation; UHC, underlying health condition

<sup>a</sup>Age at first positive SARS-CoV-2 reverse transcription polymerase chain reaction test within the University of Washington Medicine healthcare system

<sup>b</sup>148 patients (4.6%) were missing health insurance data and excluded from the final analytic dataset

<sup>c</sup>Sex assigned at birth; 2 patients (<0.1%) had sex assigned at birth recorded as “unknown” and were excluded from the final analytic dataset

<sup>d</sup>See Table 2.1 for list of UHCs



**Figure 2.1.** Unadjusted proportions of patients who experienced COVID-19 hospitalization, by insurance status, race and ethnicity<sup>b</sup>

Proportions by health insurance status are given for the entire study population in panel A and in the stratum without any UHC in panel B; proportions by race and ethnicity are given for the entire study population in panel C and in the stratum without any UHC in panel D; proportions in the stratum with any UHC and among patients with unrecorded race and ethnicity are given in Table 2.3

AIAN, American Indian or Alaska Native; CI, confidence interval; COVID-19, coronavirus disease 2019; NH, non-Hispanic; NHPI, Native Hawaiian or Pacific Islander; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; UHC, underlying health condition

95% CIs were calculated using the Wilson score interval with Yates' continuity correction

Vertical dashed lines represent the risk of COVID-19-associated hospitalization in patients with private health insurance in the insurance plots, and the risk in NH White patients in the race and ethnicity plots

<sup>a</sup>See Table 2.1 for list of UHCs

<sup>b</sup>Among SARS-CoV-2-positive 18-39-year-old patients within the University of Washington Medicine healthcare system, February 2020-March 2021

Variable <sup>b</sup>		Risk of COVID-19 hospitalization		Crude RR		Adjusted RR <sup>c</sup>		Crude RD <sup>d</sup>		Adjusted RD <sup>cd</sup>	
		n/N	%	RR	95% CI	aRR	95% CI	RD	95% CI	aRD	95% CI
Insurance	Uninsured or public	29 / 1,168	2.5	2.8	1.6, 5.1	1.9	1.0, 3.6	16	6, 26	9	-1, 20
	Private	17 / 1,933	0.9	<i>Referent</i>		<i>Referent</i>		<i>Referent</i>		<i>Referent</i>	
Race and ethnicity	Hispanic or Latine	13 / 557	2.3	2.0	1.0, 4.3	1.5	0.7, 3.1	12	-2, 26	5	-9, 19
	NH Asian	7 / 277	2.5	2.2	0.9, 5.4	2.7	1.1, 6.5	14	-5, 33	15	-5, 34
	NH Black	8 / 418	1.9	1.7	0.7, 3.9	1.4	0.6, 3.3	8	-7, 22	4	-10, 19
	NH NHPI	2 / 56	3.6	3.1	0.7, 13.4	2.1	0.5, 9.1	24	-25, 73	17	-31, 66
	NH White	15 / 1,317	1.1	<i>Referent</i>		<i>Referent</i>		<i>Referent</i>		<i>Referent</i>	

CI, confidence interval; COVID-19, coronavirus disease 2019; NH, non-Hispanic; NHPI, Native Hawaiian or Pacific Islander; (a)RR, (adjusted) risk ratio; (a)RD, (adjusted) risk difference; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2  
RRs estimated by log-binomial regression using Huber-White estimates of the standard error; RDs estimated using a generalized linear model with a Gaussian distribution and identity link function, and using Huber-White estimates of the standard error  
<sup>a</sup>Among SARS-CoV-2-positive 18-39-year-old patients within the University of Washington Medicine healthcare system, February 2020-March 2021  
<sup>b</sup>29 (0.9%) patients recorded as NH American Indian or Alaska Native (AIAN) not included in the race and ethnicity regression models, as insufficient data (small numbers and zero outcomes) would result in an unreliable parameter estimate for this group; 447 (14.4%) patients with unrecorded race and ethnicity also not included in the race and ethnicity regression models, as this parameter estimate would be uninterpretable given the probable heterogeneity of this group  
<sup>c</sup>Insurance aRR and aRD models adjusted for documented diagnosis of any underlying health condition (UHC) (yes/no) (see Table 2.1 for list of UHCs), sex assigned at birth (female/male), continuous age (years), and race and ethnicity (Hispanic or Latine, NH AIAN, NH Asian, NH Black, NH NHPI, NH White, not recorded); race and ethnicity aRR and aRD models adjusted for any UHC, sex, and age  
<sup>d</sup>Difference in cumulative incidence per 1,000 SARS-CoV-2-positive persons over the 13-month study period

## CHAPTER 4. Associations between neighborhood disadvantage and segregation and SARS-CoV-2 testing and infection, adjusted for individual-level factors

### ABSTRACT

**Background:** COVID-19 disparities by race, ethnicity, and socioeconomic position (SEP) are widely documented. Studies also show regions of lower SEP and higher racial residential segregation (RRS) have greater adverse COVID-19 outcomes, but are limited by their geographic coarseness and ecological nature. Multilevel studies at finer geographic scales would inform equitable resource allocation at the local level.

**Methods:** We conducted a multilevel retrospective cohort study using electronic health record data from patients in the University of Washington Medicine healthcare system. We measured RRS using the divergence index and group-level SEP using a previously-developed area deprivation index. We defined "neighborhood" as residential census block group. Using generalized estimating equations to account for clustering by block group and adjusting for individual-level SEP (measured by health insurance status), race and ethnicity, age, and sex, we estimated risk ratios (aRRs) and risk differences (aRDs) of (1) receiving SARS-CoV-2 testing and (2) testing positive from February 2020 to March 2021 by neighborhood-level SEP and RRS (high vs. low disadvantage/segregation).

**Results:** Among 462,106 patients, those living in highly disadvantaged neighborhoods were less likely to receive testing (aRR [95% CI] = 0.84 [0.81, 0.87]; aRD [95% CI] = -329 [-404, -254]) and, among the 117,998 patients tested, more likely to test positive (aRR [95% CI] = 1.26 [1.16, 1.36]; aRD [95% CI] = 149 [95, 203]) compared to patients in low disadvantage neighborhoods. Patients in highly segregated neighborhoods also were less likely to receive testing (aRR [95% CI] = 0.95 [0.93, 0.98]; aRD [95% CI] = -120 [-184, -55]) and, among those tested, more likely to test positive (aRR [95% CI] = 1.06 [0.99, 1.13]; aRD [95% CI] = 30 [-1, 61])

compared to patients in low segregation neighborhoods, although the latter associations were not statistically significant.

**Conclusions:** Our findings suggest the likelihood of receiving SARS-CoV-2 testing is lower and the risk of testing positive is higher for patients living in neighborhoods of lower SEP and higher RRS, after accounting for individual-level SEP, race, and ethnicity. These results support the use of neighborhood measures to inform COVID-19 resource allocation to mitigate disparities.

## BACKGROUND

In the United States (US), the disproportionate impact of COVID-19 on people of color (POC) is extensively documented.<sup>27</sup> Compared to non-Hispanic (NH) White individuals, POC have experienced a higher incidence of SARS-CoV-2 infections<sup>31,35-38</sup> and a disproportionate burden of COVID-19-associated emergency department visits, hospitalizations, and deaths.<sup>28-34</sup> Furthermore, adverse COVID-19 outcomes have disproportionately impacted people of lower socioeconomic position (SEP), including people with lower incomes and lower educational attainment, individuals without health insurance, people experiencing homelessness, and incarcerated individuals.<sup>39-41,43</sup>

Although the mechanisms behind these disparities are not completely understood, social determinants of health (SDOH) shaped by structural racism and other forms of oppression likely play a prominent role.<sup>49,52,53</sup> Residential environment is an important SDOH,<sup>54</sup> and two otherwise identical individuals may have different risks of SARS-CoV-2 exposure,<sup>55</sup> access to timely and accurate COVID-19 information,<sup>56</sup> and access to SARS-CoV-2 testing<sup>57</sup> depending on where they live. Several studies show regions of lower SEP<sup>57-68</sup> and regions of higher racial residential segregation (RRS)<sup>69-74</sup> - the physical separation of racial and ethnic groups in a residential context and a metric of structural racism commonly used in quantitative health research<sup>75-77</sup> - have experienced greater adverse COVID-19 outcomes, but these studies generally are limited by their geographic coarseness and ecological nature. Multilevel studies<sup>42,97-102</sup> at finer geographic scales are needed to strengthen understanding of neighborhood-level characteristics as risk factors for COVID-19 outcomes, which will help public health agencies deliver optimal community-based interventions.

Emulating national trends, in Washington (WA) State, POC have experienced higher rates of COVID-19 cases, hospitalizations, and deaths compared to NH White individuals.<sup>90</sup> A 2020

ecological study of the Seattle, King County, WA State region found SARS-CoV-2 testing rates were lower and test positivity rates were higher in census tracts with higher proportions of POC and lower group-level SEP.<sup>91</sup> We built on this work by incorporating individual-level data and a formal measure of RRS, increasing geographic granularity, and expanding beyond King County.

We examined the associations between census block group-level SEP and RRS and (1) receiving SARS-CoV-2 testing and (2) testing positive, beyond individual-level characteristics including SEP and race and ethnicity, among patients in a large academic medical system in western WA State. We hypothesized that the likelihood of receiving SARS-CoV-2 testing would be lower and the risk of testing positive would be higher for individuals living in block groups of lower SEP and higher RRS, independent of individual-level SEP, race, ethnicity, and other factors.

## **METHODS**

### **Study design, data sources, setting, and population**

We conducted a multilevel retrospective cohort study using electronic health record (EHR) data from the University of Washington Medicine (UWM) healthcare system, the largest academic medical system in the Central Puget Sound region. The Central Puget Sound region is in western WA State and includes the Seattle metropolitan area; it comprises 56% of WA State's population<sup>88</sup> and, as of April 2023, about 55% of its confirmed and probable COVID-19 cases.<sup>87</sup> We also leveraged publicly-available neighborhood-level data from the Neighborhood Atlas<sup>103,104</sup> and from the 2020 decennial census<sup>105</sup> (see below). The University of Washington Institutional Review Board approved this study and waived the informed consent and HIPAA authorization requirements (IRB ID: STUDY00011233). This study was unfunded.

Our study population included living adult residents of the Central Puget Sound region who were engaged in care in the UWM healthcare system as of February 28, 2020. SARS-CoV-2 testing began within UWM on February 29, 2020. Using UWM EHR data, we identified a cohort of 715,228 patients who had at least one encounter in the UWM system from January 1, 2017 to February 28, 2020, who were at least 18 years old on February 28, 2020, and who were alive on February 29, 2020. For each patient, we geocoded the most recent billing address in the UWM system as of February 28, 2020. Geocoding took place within the UWM data warehouse using the PostGIS geocoder with 2021 street centerline TIGER/Line files. Based on prior experience manually inspecting geocoding accuracy within TIGER/Line files in King County, we were concerned that geocoding responses with ratings above 20<sup>154</sup> might indicate the wrong census block group. Accordingly, we considered addresses with ratings above 20 to have failed to geocode. Geocoding was successful for 562,170 patients (78.6%), which conforms to the 78-85% minimum acceptable match rate used by many studies involving geocoding procedures.<sup>155,156</sup> Among the 153,058 patients (21.4%) for whom geocoding was unsuccessful, 0.3% had no billing address recorded, 23.1% had addresses outside WA State, 22.0% had PO boxes listed, and 12.0% had addresses that failed for various other reasons, such as address anomalies. The remaining 42.6% of patient addresses failed to geocode for nonspecific reasons. The dataset was too large for manual inspection, but prior geocoding experience suggests these reasons may include misspelled or abbreviated addresses, incorrect zip codes, and missing regional identifiers. We limited our study population to the 487,731 individuals with a geocoded address in the Central Puget Sound region (King, Kitsap, or Snohomish Counties).

### **Data measures**

Our exposures of interest were neighborhood-level SEP and RRS. We defined "neighborhood" as census block group. Census block groups are statistical divisions of census tracts and generally contain between 600 and 3,000 people.<sup>157</sup> Using ArcGIS Desktop version 10.8.2

(Redlands, CA),<sup>158</sup> residential census block group for each patient was determined by spatially joining geocoded billing address (assumed to represent residential address) as determined above to 2020 census block group shapefiles from the WA State Office of Financial Management.<sup>159</sup>

We approximated neighborhood-level SEP using the 2020 Area Deprivation Index (ADI), which uses factor analysis to combine 17 indicators (including poverty, housing, education, and employment) into an index of disadvantage at the block group level, and is freely available through the Neighborhood Atlas.<sup>103,104,160</sup> The ADI has been proposed as a metric to inform COVID-19 resource allocation<sup>161</sup> and has been used in COVID-19 disparities research.<sup>97</sup> Our analyses used the ADI WA State rank (provided in deciles constructed by ranking the ADI from low to high for WA state alone, without consideration of national ADIs). We dichotomized the ADI as deciles 6-10 vs. deciles 1-5 (high vs. low disadvantage), as previous studies have done.<sup>162</sup>

We approximated neighborhood-level RRS using the divergence index (DI) - a novel measure of segregation comparing the relative proportions of racial and ethnic groups at smaller and larger geographies,<sup>163</sup> and which has been used as a measure of structural racism.<sup>164</sup> We used block group as the smaller geography and core-based statistical area (CBSA) as the larger geography. CBSAs, which are made up of whole counties or county equivalents, are defined by at least one urbanized area (of 10,000 to 49,000 population for micropolitan statistical areas and of 50,000 or more population for metropolitan statistical areas) plus adjacent territory that has a high degree of social and economic integration with the core as measured by commuting ties.<sup>165</sup> RRS is largely a consequence of processes related to housing markets, and the social and economic consequences of RRS are largely related to labor markets.<sup>166</sup> Therefore, CBSAs may be a more appropriate choice of larger geography compared to other options such as cities,

counties, or states. If a block group was not part of a CBSA, we used county as the larger geography instead.

The DI considers the distributions of all racial and ethnic groups simultaneously, and in this way is advantageous over conventional measures of RRS (e.g., the dissimilarity and isolation indices) that generally consider only one or two groups at a time,<sup>166,167</sup> particularly in regions such as the Central Puget Sound that do not have a numerically dominant minoritized racial or ethnic group.<sup>168</sup> Using 2020 decennial census race and ethnicity data (Hispanic or Latino, NH White alone, NH Black or African American alone, NH American Indian and Alaska Native alone, NH Asian alone, NH Native Hawaiian and Other Pacific Islander alone, NH some other race alone, NH two or more races),<sup>165</sup> we calculated DI for all census block groups in WA State as described in Equation 1, where  $D_i$  is the DI for block group  $i$ ,  $\pi_{im}$  is racial and ethnic group  $m$ 's proportion of the population in block group  $i$ , and  $\pi_m$  is racial and ethnic group  $m$ 's proportion of the population in the CBSA containing block group  $i$ .<sup>163</sup> A large difference in the racial and ethnic composition of a block group compared to its CBSA results in a high DI, indicating high segregation. If a block group has the same composition as its CBSA, then  $D_i = 0$ , indicating no segregation. For consistency with the ADI and because there is no established set of DI ranges defining the level of segregation,<sup>164</sup> we ranked block groups by DI decile and dichotomized as deciles 6-10 vs. deciles 1-5 (high vs. low segregation).

$$D_i = \sum_{m=1}^M \pi_{im} \log \frac{\pi_{im}}{\pi_m} \quad \text{Equation 1}$$

We defined ever receiving SARS-CoV-2 testing (yes/no) as record of at least one SARS-CoV-2 reverse transcription polymerase chain reaction (RT-PCR) test within UWM from February 29, 2020 to March 13, 2021 (the time of the data pull). RT-PCR is the diagnostic standard for

SARS-CoV-2 infection used within UWM. We defined ever testing positive (yes/no) as record of at least one positive SARS-CoV-2 RT-PCR test within UWM during this time frame.

We used health insurance status based on UWM EHR data as a measure of individual-level SEP (private, public, uninsured). Studies have demonstrated the validity of EHR data for identifying health insurance status,<sup>137</sup> and health insurance status is a valid measure of individual-level SEP commonly used in EHR-based research given the lack of SEP data (e.g., income) recorded in EHR systems.<sup>169</sup> To capture information about the pre-pandemic period, health insurance status was based on the most recent encounter from January 1, 2017 to February 28, 2020 for which health insurance data were available. The “private” category included patients with Medicare Advantage (Part C), Medicare Supplement (Medigap), private military insurance, employer-sponsored and individual plans, and other forms of private insurance; the “public” category included patients on Medicaid, Medicare (Part A and/or B only), public military insurance, and other forms of public insurance; and the “uninsured” category included self-pay patients and those with Indian Health Services insurance.<sup>135,136</sup>

We also collected UWM EHR data on race and ethnicity (Hispanic or Latine, NH American Indian or Alaska Native [AIAN], NH Asian, NH Black, NH Native Hawaiian or Pacific Islander [NHPI], NH White, not recorded), age (in years) on February 28, 2020, and sex assigned at birth (female/male). Of 487,731 eligible patients, 11,507 (2.4%) were missing ADI state rank, 6 (<0.1%) DI state rank, 14,593 (3.0%) health insurance data, 10 (<0.1%) had implausible ages (>111 years), and 82 (<0.1%) had sex assigned at birth recorded as “unknown” and were excluded for a final analytic population of 462,106 individuals. We categorized missing race and ethnicity data as “not recorded.” In addition, 2 patients (<0.1%) were recorded as NH multiple races and categorized as “not recorded” in our analyses.

Among the 487,731 eligible patients described above, 2,267 block groups were represented, 25 (1.1%) of which were missing ADI and/or DI, generally as a consequence of data suppression due to small population size (<100 people).<sup>104</sup> Among the 462,106 patients in the final analytic population, 2,241 block groups were represented, or 97.0% of the 2,310 block groups in the three study counties. The average number of patients per block group in the final analytic dataset was 206 (SD = 158).

### **Data analyses**

We used generalized estimating equations (GEE)<sup>170</sup> to estimate adjusted risk ratios (aRRs) and risk differences (aRDs) of (1) receiving SARS-CoV-2 testing and (2) testing positive by neighborhood disadvantage and segregation, accounting for clustering by residential census block group and adjusting for individual-level health insurance status, race and ethnicity, continuous age, and sex assigned at birth. GEE with a binomial distribution and log link function were used to estimate aRRs, and with a Gaussian distribution and identity link function to estimate aRDs.<sup>108,171</sup> *A priori*, we specified a binomial or Poisson GEE model with identity link to estimate aRDs, but these models failed to converge. All models used an exchangeable correlation structure and robust standard errors. For the outcome of testing positive, we limited the analytic population to patients who had received SARS-CoV-2 RT-PCR testing. All analyses were performed in R version 4.1.2 (Vienna, Austria),<sup>109</sup> and GEE models were fit using the *geepack* package.<sup>172</sup>

### **Sensitivity analyses**

We conducted three sensitivity analyses. We repeated the primary analyses (1) restricting the time frame to July 1, 2020 to October 31, 2020, when we expect the dominant SARS-CoV-2 viral strain<sup>113,114</sup> and testing practices<sup>87,115–118</sup> were relatively stable in the Central Puget Sound region, and before the Food and Drug Administration approved the first SARS-CoV-2 vaccine

under emergency use authorization on December 11, 2020,<sup>110</sup> (2) separating highly segregated block groups into those with a proportion of NH White residents greater than that of the surrounding CBSA/county (high segregation, high % NH White) and less than or equal to that of the surrounding CBSA/county (high segregation, high % POC), and (3) analyzing ADI and DI as WA State rank quintiles rather than as binary (high/low) variables.

## RESULTS

Maps of census block group ADI and DI in the study area are presented in Figure 3.1. In general, neighborhoods of low disadvantage were concentrated in and around the Seattle metropolitan area and central and southeastern King County. Highly segregated neighborhoods were distributed throughout the study region, with the least segregated neighborhoods generally concentrated in western King County, southwestern Snohomish County, and Kitsap County.

Among the 462,106 adult UWM patients living in the Central Puget Sound region included in our analyses, the average age was 47.3 years (SD = 18.1 years), 54.7% were assigned female sex at birth, 12.6% were recorded as NH Asian and 53.0% as NH White, 26.1% were on public health insurance, and 81.7% were King County residents (Tables 3.1 and 3.2). Among the 2,241 block groups represented in our final analytic population, 444 (19.8%) were categorized as highly disadvantaged and 1,404 (62.7%) were categorized as highly segregated. Among patients living in highly disadvantaged neighborhoods (n = 59,371, 12.8%), a higher proportion were recorded as Hispanic or Latine, NH AIAN, NH Black, and NH NHPI, were publicly insured or uninsured, lived in highly segregated neighborhoods, and lived in Kitsap or Snohomish Counties compared to patients living in neighborhoods of low disadvantage (n = 402,735, 87.2%) (Table 3.1). Among patients living in highly segregated neighborhoods (n = 276,586, 59.9%), a higher proportion were recorded as NH Asian and NH Black and a lower proportion as NH White, and a higher proportion lived in highly disadvantaged neighborhoods and in King

County compared to patients living in neighborhoods of low segregation (n = 185,520, 40.1%) (Table 3.2).

The distributions of patient characteristics by neighborhood disadvantage and segregation among the 117,998 patients (25.5%) who received at least one SARS-CoV-2 RT-PCR test within UWM from February 29, 2020 to March 13, 2021 are presented in Tables 3.3 and 3.4.

The distributions of characteristics in the sample of patients who received testing, including across neighborhood disadvantage and segregation groups, are similar to those in the overall analytic population. Among patients who received RT-PCR testing, 5,334 (4.5%) tested positive for SARS-CoV-2 at least once (Table 3.5).

### **Risks of SARS-CoV-2 testing and infection by neighborhood disadvantage and segregation**

Neighborhoods in which higher proportions of UWM patients received SARS-CoV-2 testing (Figure 3.2) were generally concentrated in regions of lower disadvantage and/or segregation (Figure 3.1), including the Seattle metropolitan area, southeastern King County, and central Kitsap County. Neighborhoods in which a high proportion of patients tested positive were distributed throughout the western part of the study area (Figure 3.2), but generally fell into regions of higher disadvantage and/or segregation and lower SARS-CoV-2 testing in southern and central King County and western Snohomish County.

Among patients living in highly disadvantaged neighborhoods, 21.9% received SARS-CoV-2 testing, compared to 26.1% of patients living in neighborhoods of low disadvantage (Table 3.5). Of those tested, 7.3% of patients living in highly disadvantaged neighborhoods tested positive, compared to 4.2% of patients living in neighborhoods of low disadvantage.

After accounting for clustering by residential block group and adjustment for individual-level characteristics, patients living in highly disadvantaged neighborhoods were 16% less likely to receive SARS-CoV-2 testing and had 329 fewer patients tested per 10,000 persons during the 13-month study period compared to those living in neighborhoods of low disadvantage (aRR [95% CI] = 0.84 [0.81, 0.87]; aRD [95% CI] = -329 [-404, -254]) (Table 3.5). Among those tested, patients in highly disadvantaged neighborhoods were 26% more likely to test positive and had 149 more patients test positive per 10,000 persons tested compared to those living in neighborhoods of low disadvantage (aRR [95% CI] = 1.26 [1.16, 1.36]; aRD [95% CI] = 149 [95, 203]).

Among patients living in highly segregated neighborhoods, 24.8% received SARS-CoV-2 testing, compared to 26.6% of patients living in neighborhoods of low segregation (Table 3.5). Of those tested, 4.7% of patients living in highly segregated neighborhoods tested positive, compared to 4.3% of patients living in neighborhoods of low segregation.

After accounting for clustering by residential block group and adjustment for individual-level characteristics, patients living in highly segregated neighborhoods were 5% less likely to receive SARS-CoV-2 testing and had 120 fewer patients tested per 10,000 persons during the 13-month study period compared to those living in neighborhoods of low segregation (aRR [95% CI] = 0.95 [0.93, 0.98]; aRD [95% CI] = -120 [-184, -55]) (Table 3.5). Among those tested, patients in highly segregated neighborhoods were 6% more likely to test positive and had 30 more patients test positive per 10,000 persons tested compared to those living in neighborhoods of low segregation (aRR [95% CI] = 1.06 [0.99, 1.13]; aRD [95% CI] = 30 [-1, 61]), although these associations were not statistically significant.

## Sensitivity analyses

The results of the temporal sensitivity analysis restricting the time frame to July 1, 2020 to October 31, 2020 to account for changes in circulating viral strains, testing practices, and vaccine availability were consistent with those of our primary analysis (Table 3.6).

Among patients who received SARS-CoV-2 testing, those living in highly segregated neighborhoods with a high percentage of people of color (POC) were 23% more likely to test positive and had 122 more patients test positive per 10,000 persons tested compared to those living in neighborhoods of low segregation (aRR [95% CI] = 1.23 [1.14, 1.32]; aRD [95% CI] = 122 [81, 162]) (Table 3.7). Patients living in highly segregated and highly NH White neighborhoods were 19% less likely to test positive and had 66 fewer patients test positive per 10,000 persons tested compared to patients living in neighborhoods of low segregation (aRR [95% CI] = 0.81 [0.74, 0.88]; aRD [95% CI] = -66 [-98, -35]). There was no statistically significant difference in the likelihood of receiving testing for patients living in highly segregated and highly NH White neighborhoods compared to those living in neighborhoods of low segregation, and estimates for patients in highly segregated and highly POC neighborhoods were similar to those for patients in highly segregated neighborhoods in the primary analysis.

When ADI and DI were analyzed as quintiles, patients at every level of neighborhood disadvantage were less likely to receive testing and, among those tested, more likely to test positive compared to patients living in the least disadvantaged neighborhoods (Tables 3.8 and 3.9). However, only patients living in the most segregated neighborhoods were less likely to receive testing and, among those tested, more likely to test positive compared to patients living in the least segregated neighborhoods (for testing: aRR [95% CI] = 0.86 [0.82, 0.90]; aRD [95% CI] = -342 [-448, -237]; for testing positive: aRR [95% CI] = 1.19 [1.07, 1.33]; aRD [95% CI] = 96

[42, 151]); results for all other levels of neighborhood segregation were not statistically significantly different from the null.

## **DISCUSSION**

In this multilevel retrospective cohort study leveraging publicly-available neighborhood-level data and EHR data from a large academic medical system in western WA State, we found that 25.5% of 462,106 adult UWM patients received SARS-CoV-2 RT-PCR testing from February 29, 2020 to March 13, 2021. Among the 117,998 patients who received testing, 4.5% tested positive at least once. On both relative and absolute scales, the likelihood of receiving SARS-CoV-2 testing was lower and, among those tested, the risk of testing positive was higher for patients living in highly disadvantaged or highly segregated neighborhoods compared to patients living in neighborhoods of low disadvantage or segregation, independent of individual-level characteristics including health insurance status and race and ethnicity.

Although our estimated aRR and aRD for testing positive by neighborhood segregation were not statistically significant in our primary analyses, when we separated highly segregated neighborhoods into those with a high percentage of POC and those with a high percentage of NH White residents, we found that, among patients who received SARS-CoV-2 testing, those living in highly segregated and highly POC neighborhoods were more likely to test positive and those living in highly segregated and highly NH White neighborhoods were less likely to test positive compared to patients living in neighborhoods of low segregation. Mathematically, the  $DI^{163}$  (our measure of RRS) indicates a high level of segregation when the racial and ethnic composition of a neighborhood differs substantially from that of the broader geographic area, including when a neighborhood contains a substantially higher proportion of NH White residents compared to the broader region. However, we would not expect people living in highly segregated and highly NH White neighborhoods to experience the same manifestations of

structural racism as people living in highly segregated and highly POC neighborhoods.<sup>75,76</sup> Therefore, our sensitivity analysis incorporating neighborhood racial and ethnic composition may be more relevant to the lay understanding of segregation as a process by which residential clustering by racial and ethnic group manifests as disadvantage for POC living in highly POC neighborhoods. The results of our sensitivity analysis illustrate the potential importance of accounting for racial and ethnic composition when investigating the associations between DI as a measure of RRS and COVID-19 outcomes. Other quantitative health researchers have advocated for adjustment for racial and ethnic composition when employing conventional RRS measures like the dissimilarity index.<sup>173</sup>

Furthermore, when we analyzed DI as quintiles, only patients living in the most segregated neighborhoods were less likely to receive testing and, among those tested, more likely to test positive compared to patients living in the least segregated neighborhoods. Therefore, in addition to considering racial and ethnic composition, when assessing DI as a measure of RRS, it may be valuable to use granular segregation categories to identify people experiencing the greatest differences in COVID-19 outcomes.

Several ecological studies in the US have shown that regions of lower SEP<sup>58-68</sup> (such as those with higher percent crowding, lower median household income, or higher proportions of uninsured residents, residents without a high school degree, or people experiencing poverty) and regions of higher RRS<sup>69-73</sup> (especially areas in which POC are more residentially segregated from NH White residents) have experienced greater COVID-19 morbidity and mortality. Ecological studies cannot distinguish between individual-level and contextual-level effects, as inference is limited to the group-level unit of analysis (e.g., county).<sup>174</sup> Multilevel studies, which examine individual-level and group-level exposures and individual-level outcomes, allow for the simultaneous assessment of factors defined at multiple levels, and inform both individual-level and group-level health interventions. Since place has been a

principal actor in SARS-CoV-2 transmission and in public health mitigation strategies, understanding COVID-19 risk requires consideration both of people and of the places they live.<sup>100</sup> Our findings are consistent with limited previous multilevel studies of residential environment and COVID-19, which show increased adverse COVID-19 outcomes among people living in areas of lower SEP, ethnic enclaves, and neighborhoods with a higher proportion of racialized populations.<sup>42,97-102</sup> For example, a 2022 multilevel study by Hu et al. that employed the ADI<sup>103,104</sup> as a measure of neighborhood disadvantage found that the odds of COVID-19 in-hospital mortality were 74% higher (95% CI = 1.13, 2.67) for patients living in the most disadvantaged neighborhood quintile, independent of individual-level race.<sup>97</sup>

Relatively few analyses of residential environment have focused on SARS-CoV-2 testing - an important outcome as studies show an inverse relationship between testing and COVID-19 mortality.<sup>175</sup> Limited previous research has found lower testing in neighborhoods with higher proportions of POC.<sup>57,74</sup> A 2020 ecological study of the Seattle, King County, WA State region by Seto et al. found testing rates were lower and test positivity rates were higher in census tracts with higher proportions of POC and lower group-level SEP.<sup>91</sup> Our study builds on the work of Seto et al. by incorporating individual-level data and a formal measure of RRS, and including other counties in the Central Puget Sound region. Ours is one of the first multilevel studies examining the association between a formal measure of RRS and COVID-19 outcomes, including SARS-CoV-2 testing. Moreover, most COVID-19 neighborhood effects research has been conducted at larger geographic scales (e.g., counties, ZIP Codes, or ZCTAs). Studies of more granular geographic units - such as our analysis at the census block group level - may lead to health interventions that are better adapted to local contexts, which may enhance effectiveness.<sup>176,177</sup> The provision of testing services, for example, is neighborhood focused, so analyses of small area-level features may inform ongoing disease control needs.<sup>91,178</sup>

As awareness of the structural factors likely driving racial, ethnic, and socioeconomic COVID-19 disparities in the US<sup>49,52,53</sup> has increased during the pandemic, so too have calls to use neighborhood measures to inform public health action, including the equitable allocation of COVID-19 resources.<sup>97,100,161</sup> Readily available, granular, geographic metrics of disadvantage, like the ADI,<sup>103,104</sup> are a foundational component of many global health systems.<sup>97</sup> Our findings support the use of neighborhood metrics representative of structural inequalities - such as the ADI<sup>103,104</sup> and the DI<sup>163,164</sup> as a measure of RRS and structural racism<sup>75-77</sup> - by local public health departments in the US to strengthen COVID-19 community risk assessment, surveillance systems, community partner engagement, and the equitable allocation of resources including culturally- and linguistically-appropriate informational materials, testing, vaccination, and anti-SARS-CoV-2 therapy.

In addition to the innovative elements discussed above, strengths of our study include leveraging EHR data from a large academic medical system and estimating both relative and absolute measures of association.<sup>119</sup> Furthermore, measures such as area deprivation and RRS are commonly used in studies of chronic diseases, birth outcomes, life expectancy, and mental health, but historically have not been widely used in infectious disease epidemiology. Ours is also one of the first studies to use the DI<sup>163,164</sup> as a measure of RRS in quantitative health research.

Our study also has several important limitations. First, we used EHR data, which are subject to data quality concerns.<sup>179</sup> We observed high levels of missingness for race and ethnicity in our UWM EHR data. Since EHR data often are missing not at random,<sup>128,129</sup> we did not employ multiple imputation methods, which may further increase bias under missing not at random conditions.<sup>130</sup> Instead, we classified individuals missing these data as “not recorded;” the probable heterogeneity of this category may have limited our ability to statistically control confounding and led to bias.<sup>131,132</sup> Our analyses controlled for health insurance status, which

may be an incomplete measure of individual-level SEP, resulting in residual confounding. Future multilevel studies using EHR data could consider including additional measures of individual-level SEP based on geocoded addresses, such as property value.<sup>98,180</sup> We did not adjust for preferred language, which is associated with SARS-CoV-2 testing and infection<sup>181</sup> and which previous studies show modifies the association between neighborhood-level characteristics and SARS-CoV-2 infection.<sup>100</sup> Future related research should consider incorporating language data, which often are available in EHR systems. It was not feasible for us to determine indication for SARS-CoV-2 testing (e.g., SARS-CoV-2 exposure, COVID-19 symptoms, pre-operative testing, etc.) from UWM EHR data. While we do not expect the distribution of indication for testing to have impacted our aRR and aRD estimates, it may have impacted the proportion of patients in our study population who tested positive. In addition, we were unable to identify patients who received SARS-CoV-2 testing outside UWM, which may have led to differential outcome misclassification if the likelihood of receiving testing outside UWM (e.g., at drive-through testing sites) differed by neighborhood SEP and/or RRS. Similarly, patients who live farther away from UWM testing sites may have been more likely to receive testing elsewhere, which may have resulted in uncontrolled spatial confounding in our analyses. Patients whose addresses failed to geocode may have been different from patients whose addresses geocoded successfully, resulting in selection bias. For example, a higher proportion of EHR billing addresses failed to geocode for NH AIAN patients compared to the other racial and ethnic groups, with close to 40% of those failed addresses being PO boxes; this is consistent with previous research and could represent American Indian reservation residence,<sup>182</sup> which may have biased our findings towards the null from the exclusion of patients living in highly disadvantaged and highly segregated regions and who have been disproportionately impacted by adverse COVID-19 outcomes,<sup>90,183</sup> although the number of failed geocodes among NH AIAN patients was relatively small (n = 2,235) and unlikely to impact overall findings.

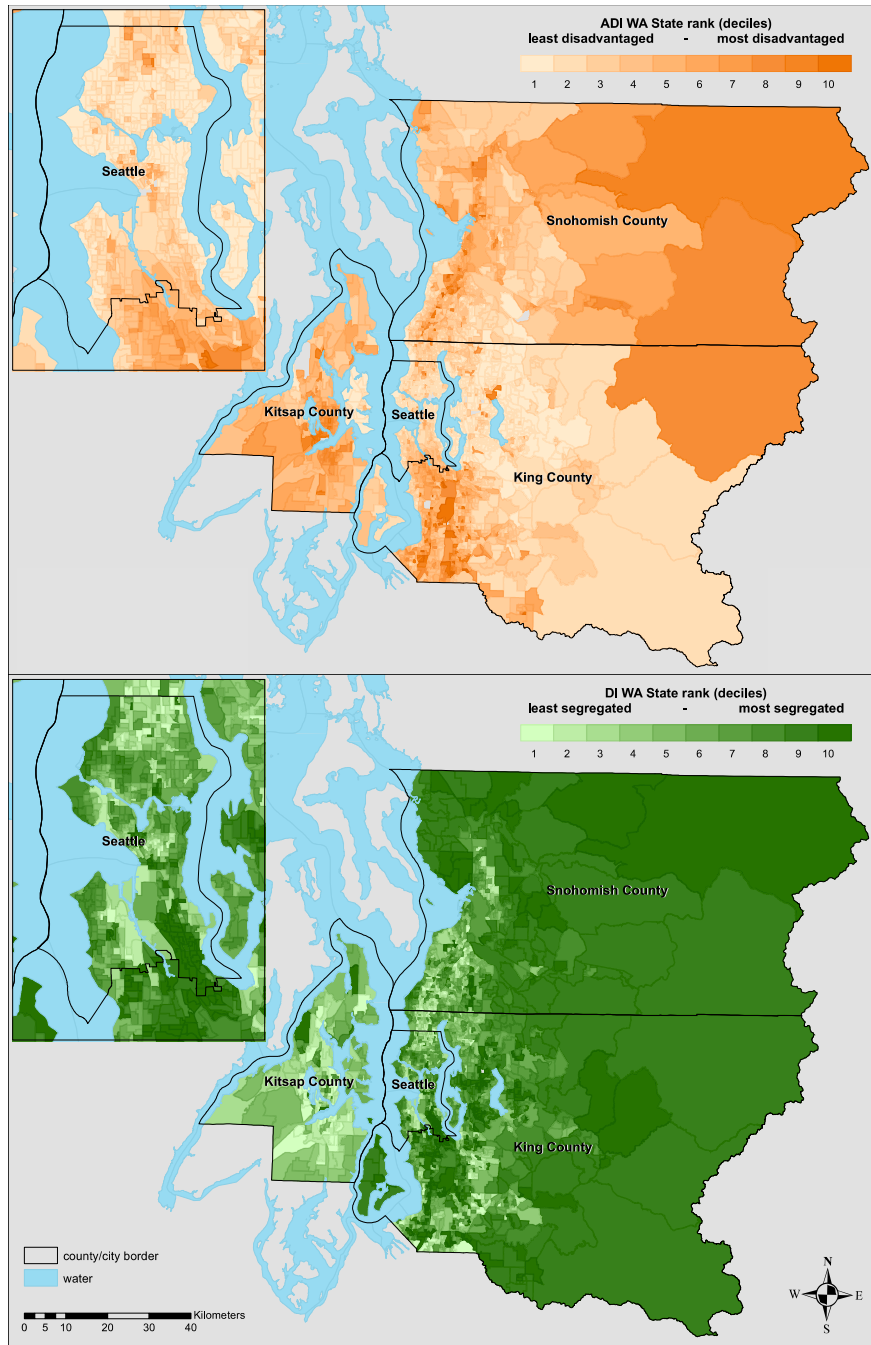
Second, neighborhood effects research is subject to biases - including the modifiable areal unit problem,<sup>184</sup> the uncertain geographic context problem,<sup>185</sup> and the "residential" effect fallacy<sup>186</sup> - that may arise from the geographic scale at which contextual exposures are measured and from the complexity of temporal and spatial individual-level behaviors inside and outside the defined neighborhood unit. In the same vein, we used the aspatial DI as our measure of RRS, which assumes block groups are spatially independent units. Future researchers may wish to consider a spatial version of the DI that accounts for local spatial autocorrelation.<sup>163,187,188</sup> Third, we did not investigate the joint effects of neighborhood ADI and RRS,<sup>70</sup> nor the joint effects of neighborhood-level and individual-level factors,<sup>100</sup> which may help hone COVID-19 interventions.

Fourth, we used data from a single academic medical system, so the generalizability of our findings to populations served by other medical systems is unknown. Overall, our analytic population was highly advantaged within the context of WA State, with over 80% of patients living in census block groups at or below the median state rank ADI. This is not surprising, as most of the wealth in WA State is concentrated in the Seattle, King County region.<sup>189</sup> Future research should incorporate data from other medical centers in WA State to improve generalizability to the population of the state as a whole. Finally, we intended to include residents of Pierce County in our analyses but, due to a technical challenge, these residents' addresses failed to geocode and it was not feasible to repeat geocoding at the time of analysis. Of the 2,928 block groups in the Central Puget Sound region (King, Kitsap, Pierce, and Snohomish Counties), 618 (21.1%) are in Pierce County. We do not expect our associations of interest to differ between Pierce County and other counties in the Central Puget Sound region; therefore, we expect minimal scientific loss from the exclusion of Pierce County residents.

In conclusion, our results suggest the likelihood of receiving SARS-CoV-2 testing is lower and the risk of testing positive is higher for Central Puget Sound UWM patients living in

neighborhoods of lower SEP and higher RRS, independent of individual-level characteristics including SEP and race and ethnicity. When assessing DI as a measure of RRS, it may be important to account for racial and ethnic composition and/or use granular segregation categories to identify people experiencing the greatest differences in COVID-19 outcomes. Our findings support the use of neighborhood measures, such as the ADI<sup>103,104</sup> and the DI,<sup>163,164</sup> to inform equitable resource allocation and other local public health action to mitigate racial, ethnic, and socioeconomic disparities.

**TABLES & FIGURES**



**Figure 3.1.** Census block group disadvantage (top) and segregation (bottom) in the Central Puget Sound region, 2020. The Area Deprivation Index (ADI) is a validated measure of census block group neighborhood socioeconomic disadvantage.<sup>103</sup> Analyses used the ADI Washington (WA) State rank (provided in deciles). The Divergence Index (DI) is a measure of racial residential segregation comparing the relative proportions of racial and ethnic groups at smaller and larger geographies.<sup>163</sup> Using 2020 decennial census race and ethnicity data,<sup>105</sup> DI was calculated for all census block groups in Washington (WA) State using the core-based statistical area or county as the larger geography, then ranked by decile.

**Table 3.1.** Patient characteristics by census block group disadvantage, University of Washington Medicine, 2020

Variable	Total (N = 462,106)		ADI WA State rank <sup>a</sup>			
			High disadvantage (N = 59,371)		Low disadvantage (N = 402,735)	
	n	%	n	%	n	%
Age (years) (mean ± SD)	47.3 ± 18.1		47.6 ± 17.6		47.2 ± 18.1	
Sex assigned at birth						
Female	252,752	54.7	32,914	55.4	219,838	54.6
Male	209,354	45.3	26,457	44.6	182,897	45.4
Race and ethnicity						
Hispanic or Latine	28,710	6.2	6,608	11.1	22,102	5.5
NH AIAN	3,180	0.7	595	1.0	2,585	0.6
NH Asian	58,296	12.6	5,388	9.1	52,908	13.1
NH Black	31,674	6.9	7,278	12.3	24,396	6.1
NH NHPI	3,137	0.7	812	1.4	2,325	0.6
NH White	244,755	53.0	28,184	47.5	216,571	53.8
Not recorded	92,354	20.0	10,506	17.7	81,848	20.3
Insurance						
Private	331,128	71.7	32,483	54.7	298,645	74.2
Public	120,756	26.1	23,835	40.1	96,921	24.1
Uninsured	10,222	2.2	3,053	5.1	7,169	1.8
DI WA State rank <sup>b</sup>						
High segregation	276,586	59.9	39,755	67.0	236,831	58.8
Low segregation	185,520	40.1	19,616	33.0	165,904	41.2
County of residence						
King	377,717	81.7	39,404	66.4	338,313	84.0
Kitsap	6,850	1.5	2,644	4.5	4,206	1.0
Snohomish	77,539	16.8	17,323	29.2	60,216	15.0

AIAN, American Indian or Alaska Native; ADI, Area Deprivation Index; DI, Divergence Index; NH, non-Hispanic; NHPI, Native Hawaiian or Pacific Islander; SD, standard deviation; WA, Washington  
 10 patients (<0.1%) had implausible ages (>111 years), 82 patients (<0.1%) had sex assigned at birth recorded as "unknown", 14,593 (3.0%) were missing health insurance data, 11,507 (2.4%) were missing ADI data, and 6 (<0.1%) were missing DI data and excluded from the final analytic dataset; 2 patients (<0.1%) were recorded as NH multiple races and categorized as "not recorded" for race and ethnicity

<sup>a</sup>A validated measure of census block group neighborhood socioeconomic disadvantage.<sup>103</sup> Analyses used the ADI WA State rank (provided in deciles) dichotomized as deciles 6-10 vs. deciles 1-5 (high vs. low disadvantage)

<sup>c</sup>A measure of racial residential segregation comparing the relative proportions of racial and ethnic groups at smaller and larger geographies.<sup>163</sup> Using 2020 decennial census race and ethnicity data,<sup>105</sup> DI was calculated for all census block groups in WA State using the core-based statistical area or county as the larger geography, then ranked by decile and dichotomized as deciles 6-10 vs. deciles 1-5 (high vs. low segregation)6/9/2023 6:23:00 PM

<b>Table 3.2. Patient characteristics by census block group segregation, University of Washington Medicine, 2020</b>						
Variable	Total (N = 462,106)		DI WA State rank <sup>a</sup>			
	n	%	High segregation (N = 276,586)		Low segregation (N = 185,520)	
			n	%	n	%
Age (years) (mean ± SD)	47.3 ± 18.1		47.6 ± 18.1		46.8 ± 18.0	
Sex assigned at birth						
Female	252,752	54.7	151,457	54.8	101,295	54.6
Male	209,354	45.3	125,129	45.2	84,225	45.4
Race and ethnicity						
Hispanic or Latine	28,710	6.2	17,527	6.3	11,183	6.0
NH AIAN	3,180	0.7	1,768	0.6	1,412	0.8
NH Asian	58,296	12.6	37,545	13.6	20,751	11.2
NH Black	31,674	6.9	20,614	7.5	11,060	6.0
NH NHPI	3,137	0.7	1,963	0.7	1,174	0.6
NH White	244,755	53.0	141,073	51.0	103,682	55.9
Not recorded	92,354	20.0	56,095	20.3	36,258	19.5
Insurance						
Private	331,128	71.7	197,276	71.3	133,852	72.1
Public	120,756	26.1	72,317	26.1	48,439	26.1
Uninsured	10,222	2.2	6,993	2.5	3,229	1.7
ADI WA State rank <sup>b</sup>						
High disadvantage	59,371	12.8	39,755	14.4	19,616	10.6
Low disadvantage	402,735	87.2	236,831	85.6	165,904	89.4
County of residence						
King	377,717	81.7	229,946	83.1	147,771	79.7
Kitsap	6,850	1.5	1,815	0.7	5,035	2.7
Snohomish	77,539	16.8	44,825	16.2	32,714	17.6

AIAN, American Indian or Alaska Native; ADI, Area Deprivation Index; DI, Divergence Index; NH, non-Hispanic; NHPI, Native Hawaiian or Pacific Islander; SD, standard deviation; WA, Washington

10 patients (<0.1%) had implausible ages (>111 years), 82 patients (<0.1%) had sex assigned at birth recorded as "unknown", 14,593 (3.0%) were missing health insurance data, 11,507 (2.4%) were missing ADI data, and 6 (<0.1%) were missing DI data and excluded from the final analytic dataset; 2 patients (<0.1%) were recorded as NH multiple races and categorized as "not recorded" for race and ethnicity

<sup>a</sup>A measure of racial residential segregation comparing the relative proportions of racial and ethnic groups at smaller and larger geographies.<sup>163</sup> Using 2020 decennial census race and ethnicity data,<sup>105</sup> DI was calculated for all census block groups in WA State using the core-based statistical area or county as the larger geography, then ranked by decile and dichotomized as deciles 6-10 vs. deciles 1-5 (high vs. low segregation)

<sup>b</sup>A validated measure of census block group neighborhood socioeconomic disadvantage.<sup>103</sup> Analyses used the ADI WA State rank (provided in deciles) dichotomized as deciles 6-10 vs. deciles 1-5 (high vs. low disadvantage)

<b>Table 3.3.</b> Characteristics of patients who received SARS-CoV-2 RT-PCR testing, by census block group disadvantage, University of Washington Medicine, 2020						
Variable	Total (N = 117,998)		ADI WA State rank <sup>a</sup>			
			High disadvantage (N = 12,976)		Low disadvantage (N = 105,022)	
	n	%	n	%	n	%
Age (years) (mean ± SD)	45.6 ± 17.9		47.3 ± 17.6		45.4 ± 17.9	
Sex assigned at birth						
Female	66,416	56.3	7,439	57.3	58,977	56.2
Male	51,582	43.7	5,537	42.7	46,045	43.8
Race and ethnicity						
Hispanic or Latine	7,795	6.6	1,566	12.1	6,229	5.9
NH AIAN	904	0.8	145	1.1	759	0.7
NH Asian	12,960	11.0	1,124	8.7	11,836	11.3
NH Black	9,099	7.7	1,922	14.8	7,177	6.8
NH NHPI	865	0.7	220	1.7	645	0.6
NH White	68,266	57.9	6,272	48.3	61,994	59.0
Not recorded	18,109	15.3	1,727	13.3	16,382	15.6
Insurance						
Private	85,746	72.7	6,918	53.3	78,828	75.1
Public	29,955	25.4	5,404	41.6	24,551	23.4
Uninsured	2,297	1.9	654	5.0	1,643	1.6
DI WA State rank <sup>b</sup>						
High segregation	68,560	58.1	8,598	66.3	59,962	57.1
Low segregation	49,438	41.9	4,378	33.7	45,060	42.9
County of residence						
King	103,073	87.4	9,807	75.6	93,266	88.8
Kitsap	1,179	1.0	478	3.7	701	0.7
Snohomish	13,746	11.6	2,691	20.7	11,055	10.5

AIAN, American Indian or Alaska Native; ADI, Area Deprivation Index; DI, Divergence Index; NH, non-Hispanic; NHPI, Native Hawaiian or Pacific Islander; RT-PCR, reverse transcription polymerase chain reaction; SD, standard deviation; WA, Washington

1 patient (<0.1%) was recorded as NH multiple races and categorized as "not recorded" for race and ethnicity

<sup>a</sup>A validated measure of census block group neighborhood socioeconomic disadvantage.<sup>103</sup> Analyses used the ADI WA State rank (provided in deciles) dichotomized as deciles 6-10 vs. deciles 1-5 (high vs. low disadvantage)

<sup>c</sup>A measure of racial residential segregation comparing the relative proportions of racial and ethnic groups at smaller and larger geographies.<sup>163</sup> Using 2020 decennial census race and ethnicity data,<sup>105</sup> DI was calculated for all census block groups in WA State using the core-based statistical area or county as the larger geography, then ranked by decile and dichotomized as deciles 6-10 vs. deciles 1-5 (high vs. low segregation)

**Table 3.4.** Characteristics of patients who received SARS-CoV-2 RT-PCR testing, by census block group segregation, University of Washington Medicine, 2020

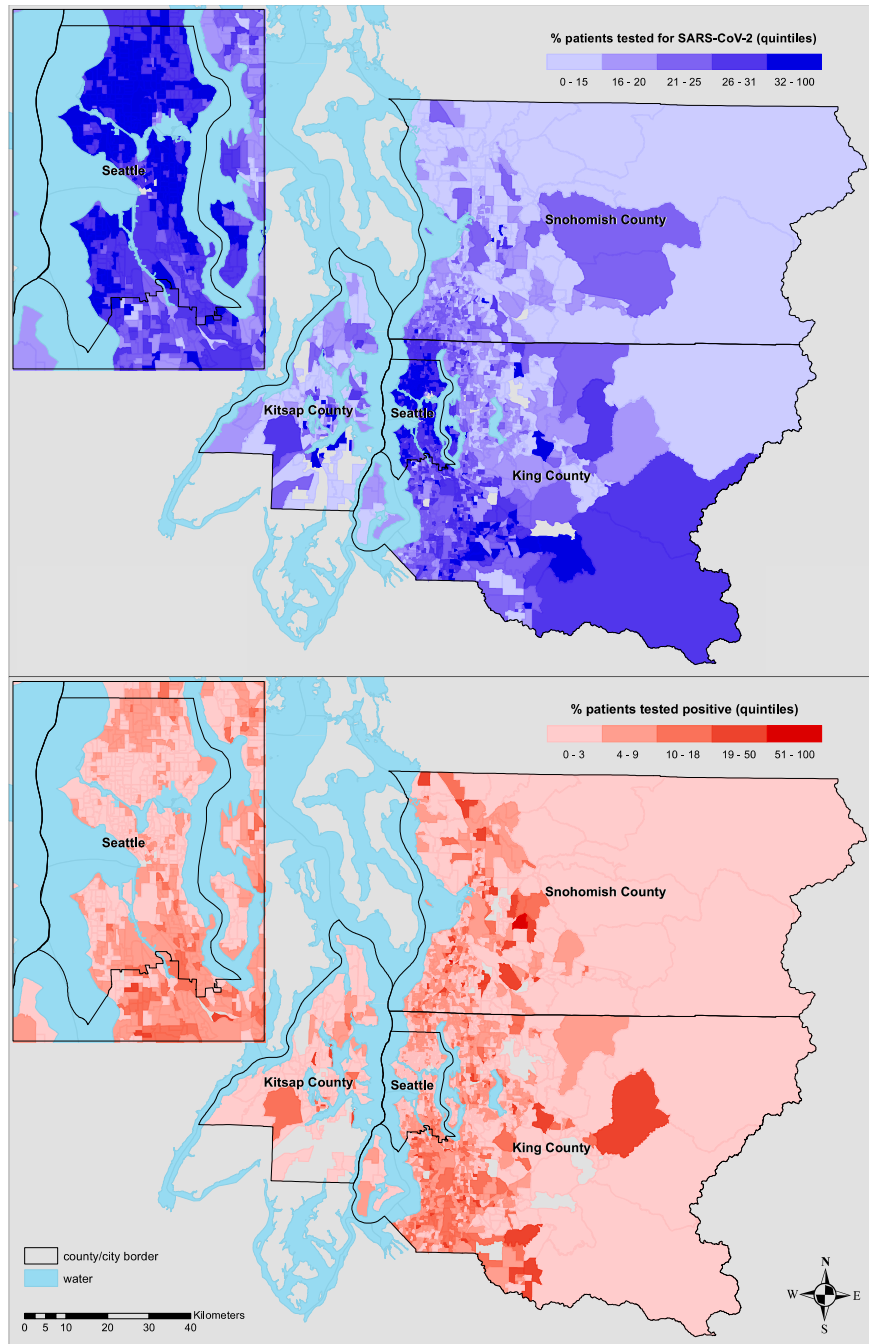
Variable	Total (N = 117,998)		DI WA State rank <sup>a</sup>			
			High segregation (N = 68,560)		Low segregation (N = 49,438)	
	n	%	n	%	n	%
Age (years) (mean ± SD)	45.6 ± 17.9		46.1 ± 18.0		45.0 ± 17.7	
Sex assigned at birth						
Female	66,416	56.3	38,575	56.3	27,841	56.3
Male	51,582	43.7	29,985	43.7	21,597	43.7
Race and ethnicity						
Hispanic or Latine	7,795	6.6	4,517	6.6	3,278	6.6
NH AIAN	904	0.8	468	0.7	436	0.9
NH Asian	12,960	11.0	7,796	11.4	5,164	10.4
NH Black	9,099	7.7	5,769	8.4	3,330	6.7
NH NHPI	865	0.7	524	0.8	341	0.7
NH White	68,266	57.9	38,718	56.5	29,548	59.8
Not recorded	18,109	15.3	10,768	15.7	7,341	14.8
Insurance						
Private	85,746	72.7	49,641	72.4	36,105	73.0
Public	29,955	25.4	17,408	25.4	12,547	25.4
Uninsured	2,297	1.9	1,511	2.2	786	1.6
ADI WA State rank <sup>b</sup>						
High disadvantage	12,976	11.0	8,598	12.5	4,378	8.9
Low disadvantage	105,022	89.0	59,962	87.5	45,060	91.1
County of residence						
King	103,073	87.4	60,601	88.4	42,472	85.9
Kitsap	1,179	1.0	321	0.5	858	1.7
Snohomish	13,746	11.6	7,638	11.1	6,108	12.4

AIAN, American Indian or Alaska Native; ADI, Area Deprivation Index; DI, Divergence Index; NH, non-Hispanic; NHPI, Native Hawaiian or Pacific Islander; RT-PCR, reverse transcription polymerase chain reaction; SD, standard deviation; WA, Washington

1 patient (<0.1%) was recorded as NH multiple races and categorized as "not recorded" for race and ethnicity

<sup>a</sup>A measure of racial residential segregation comparing the relative proportions of racial and ethnic groups at smaller and larger geographies.<sup>163</sup> Using 2020 decennial census race and ethnicity data,<sup>105</sup> DI was calculated for all census block groups in WA State using the core-based statistical area or county as the larger geography, then ranked by decile and dichotomized as deciles 6-10 vs. deciles 1-5 (high vs. low segregation)

<sup>b</sup>A validated measure of census block group neighborhood socioeconomic disadvantage.<sup>103</sup> Analyses used the ADI WA State rank (provided in deciles) dichotomized as deciles 6-10 vs. deciles 1-5 (high vs. low disadvantage)



**Figure 3.2.** Percentage of patients who received SARS-CoV-2 RT-PCR testing (top) and, among those tested, percentage who tested positive (bottom), by residential census block group, University of Washington Medicine, 2020-2021. RT-PCR = reverse transcription polymerase chain reaction, SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

**Table 3.5.** Risk ratios and differences of ever receiving SARS-CoV-2 RT-PCR testing and ever testing positive, by census block group disadvantage and segregation, University of Washington Medicine, 2020-2021

Variable		Proportion ever tested		Crude RR		Adjusted RR <sup>a</sup>		Crude RD <sup>b</sup>		Adjusted RD <sup>a,b</sup>	
		n/N	%	RR	95% CI	aRR	95% CI	RD	95% CI	aRD	95% CI
ADI WA State rank	High disadvantage	12,976 / 59,371	21.9	0.87	0.84, 0.90	0.84	0.81, 0.87	-302	-377, -226	-329	-404, -254
	Low disadvantage	105,022 / 402,735	26.1	Referent		Referent		Referent		Referent	
DI WA State rank	High segregation	68,560 / 276,586	24.8	0.94	0.91, 0.97	0.95	0.93, 0.98	-144	-210, -77	-120	-184, -55
	Low segregation	49,438 / 185,520	26.6	Referent		Referent		Referent		Referent	
Variable		Proportion ever tested positive <sup>c</sup>		Crude RR		Adjusted RR <sup>a</sup>		Crude RD <sup>b</sup>		Adjusted RD <sup>a,b</sup>	
		n/N	%	RR	95% CI	aRR	95% CI	RD	95% CI	aRD	95% CI
ADI WA State rank	High disadvantage	946 / 12,976	7.3	1.67	1.53, 1.82	1.26	1.16, 1.36	294	235, 353	149	95, 203
	Low disadvantage	4,388 / 105,022	4.2	Referent		Referent		Referent		Referent	
DI WA State rank	High segregation	3,200 / 68,560	4.7	1.13	1.04, 1.21	1.06	0.99, 1.13	56	21, 92	30	-1, 61
	Low segregation	2,134 / 49,438	4.3	Referent		Referent		Referent		Referent	

ADI, Area Deprivation Index; (a)RD, (adjusted) risk difference; (a)RR, (adjusted) risk ratio; CI, confidence interval; DI, Divergence Index; RT-PCR, reverse transcription polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; WA, Washington RRs estimated by generalized estimating equations (GEE) with a binomial distribution and log link function; RDs estimated by GEE with a Gaussian distribution and identity link function; all models used an exchangeable correlation structure, robust standard errors, and accounted for clustering by residential census block group

<sup>a</sup>All models adjusted for continuous age (years), sex assigned at birth (female, male), race and ethnicity (Hispanic or Latine, NH AIAN, NH Asian, NH Black, NH NHPI, NH White, not recorded), and health insurance status (private, public, uninsured)

<sup>b</sup>Difference in cumulative incidence per 10,000 persons over the 13-month study period

<sup>c</sup>Among patients who received SARS-CoV-2 RT-PCR testing

**Table 3.6.** Risk ratios and differences of ever receiving SARS-CoV-2 RT-PCR testing and ever testing positive, by census block group disadvantage and segregation, University of Washington Medicine, July 1, 2020 - October 31, 2020 (sensitivity analysis #1)

Variable		Proportion ever tested		Crude RR		Adjusted RR <sup>a</sup>		Crude RD <sup>b</sup>		Adjusted RD <sup>a,b</sup>	
		n/N	%	RR	95% CI	aRR	95% CI	RD	95% CI	aRD	95% CI
ADI WA State rank	High disadvantage	6,718 / 59,371	11.3	0.76	0.73, 0.80	0.73	0.70, 0.77	-328	-380, -275	-317	-369, -265
	Low disadvantage	62,883 / 402,735	15.6	Referent		Referent		Referent		Referent	
DI WA State rank	High segregation	40,404 / 276,586	14.6	0.93	0.90, 0.97	0.96	0.92, 0.99	-92	-142, -42	-69	-116, -21
	Low segregation	29,197 / 185,520	15.7	Referent		Referent		Referent		Referent	
Variable		Proportion ever tested positive <sup>c</sup>		Crude RR		Adjusted RR <sup>a</sup>		Crude RD <sup>b</sup>		Adjusted RD <sup>a,b</sup>	
		n/N	%	RR	95% CI	aRR	95% CI	RD	95% CI	aRD	95% CI
ADI WA State rank	High disadvantage	285 / 6,718	4.2	2.07	1.77, 2.42	1.50	1.28, 1.75	226	163, 289	138	78, 199
	Low disadvantage	1,249 / 62,883	2.0	Referent		Referent		Referent		Referent	
DI WA State rank	High segregation	935 / 40,404	2.3	1.19	1.05, 1.35	1.11	0.99, 1.25	41	12, 70	29	2, 56
	Low segregation	599 / 29,197	2.1	Referent		Referent		Referent		Referent	

ADI, Area Deprivation Index; (a)RD, (adjusted) risk difference; (a)RR, (adjusted) risk ratio; CI, confidence interval; DI, Divergence Index; RT-PCR, reverse transcription polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; WA, Washington RRs estimated by generalized estimating equations (GEE) with a binomial distribution and log link function; RDs estimated by GEE with a Gaussian distribution and identity link function; all models used an exchangeable correlation structure, robust standard errors, and accounted for clustering by residential census block group

<sup>a</sup>All models adjusted for continuous age (years), sex assigned at birth (female, male), race and ethnicity (Hispanic or Latine, NH AIAN, NH Asian, NH Black, NH NHPI, NH White, not recorded), and health insurance status (private, public, uninsured)

<sup>b</sup>Difference in cumulative incidence per 10,000 persons over the 13-month study period

<sup>c</sup>Among patients who received SARS-CoV-2 RT-PCR testing

**Table 3.7.** Risk ratios and differences of ever receiving SARS-CoV-2 RT-PCR testing and ever testing positive, by census block group segregation and racial and ethnic composition, University of Washington Medicine, 2020-2021 (sensitivity analysis #2)

Variable		Proportion ever tested		Crude RR		Adjusted RR <sup>a</sup>		Crude RD <sup>b</sup>		Adjusted RD <sup>a,b</sup>	
		n/N	%	RR	95% CI	aRR	95% CI	RD	95% CI	aRD	95% CI
DI WA State rank <sup>c</sup>	High segregation, high % POC	32,499 / 142,153	22.9	0.91	0.89, 0.94	0.93	0.90, 0.95	-205	-274, -135	-171	-238, -104
	High segregation, high % NH White	36,061 / 134,433	26.8	0.97	0.93, 1.01	0.98	0.95, 1.02	-74	-162, 14	-61	-147, 25
	Low segregation	49,438 / 185,520	26.6	<i>Referent</i>		<i>Referent</i>		<i>Referent</i>		<i>Referent</i>	
Variable		Proportion ever tested positive <sup>d</sup>		Crude RR		Adjusted RR <sup>a</sup>		Crude RD <sup>b</sup>		Adjusted RD <sup>a,b</sup>	
		n/N	%	RR	95% CI	aRR	95% CI	RD	95% CI	aRD	95% CI
DI WA State rank <sup>c</sup>	High segregation, high % POC	2,156 / 32,499	6.6	1.50	1.39, 1.62	1.23	1.14, 1.32	223	178, 267	122	81, 162
	High segregation, high % NH White	1,044 / 36,061	2.9	0.71	0.65, 0.77	0.81	0.74, 0.88	-130	-163, -96	-66	-98, -35
	Low segregation	2,134 / 49,438	4.3	<i>Referent</i>		<i>Referent</i>		<i>Referent</i>		<i>Referent</i>	

ADI, Area Deprivation Index; (a)RD, (adjusted) risk difference; (a)RR, (adjusted) risk ratio; CI, confidence interval; DI, Divergence Index; NH, non-Hispanic; POC, people of color; RT-PCR, reverse transcription polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; WA, Washington

RRs estimated by generalized estimating equations (GEE) with a binomial distribution and log link function; RDs estimated by GEE with a Gaussian distribution and identity link function; all models used an exchangeable correlation structure, robust standard errors, and accounted for clustering by residential census block group

<sup>a</sup>All models adjusted for continuous age (years), sex assigned at birth (female, male), race and ethnicity (Hispanic or Latine, NH AIAN, NH Asian, NH Black, NH NHPI, NH White, not recorded), and health insurance status (private, public, uninsured)

<sup>b</sup>Difference in cumulative incidence per 10,000 persons over the 13-month study period

<sup>c</sup>Highly segregated census block groups were divided into those with a proportion of NH White residents greater than that of the surrounding core-based statistical area (high segregation, high % NH White) and less than or equal to that of the surrounding core-based statistical area (high segregation, high % POC)

<sup>d</sup>Among patients who received SARS-CoV-2 RT-PCR testing

**Table 3.8.** Risk ratios and differences of ever receiving SARS-CoV-2 RT-PCR testing, by census block group disadvantage and segregation (quintiles), University of Washington Medicine, 2020-2021 (sensitivity analysis #3)

Variable		Proportion ever tested		Crude RR		Adjusted RR <sup>a</sup>		Crude RD <sup>b</sup>		Adjusted RD <sup>a,b</sup>	
		n/N	%	RR	95% CI	aRR	95% CI	RD	95% CI	aRD	95% CI
ADI WA State rank: quintile	5th: most disadvantaged	2,653 / 11,893	22.3	0.86	0.80, 0.93	0.82	0.76, 0.87	-342	-497, -188	-391	-544, -237
	4th	5,484 / 24,984	22.0	0.82	0.77, 0.86	0.79	0.75, 0.83	-458	-573, -343	-487	-600, -373
	3rd	13,102 / 57,445	22.8	0.85	0.82, 0.88	0.82	0.79, 0.85	-379	-467, -291	-400	-486, -314
	2nd	28,345 / 117,759	24.1	0.89	0.86, 0.92	0.88	0.85, 0.91	-281	-358, -205	-291	-364, -217
	1st: least disadvantaged	68,414 / 250,025	27.4	<i>Referent</i>		<i>Referent</i>		<i>Referent</i>		<i>Referent</i>	
DI WA State rank: quintile	5th: most segregated	21,282 / 96,547	22.0	0.84	0.81, 0.88	0.86	0.82, 0.90	-384	-493, -275	-342	-448, -237
	4th	32,784 / 124,975	26.2	0.97	0.92, 1.02	0.99	0.94, 1.03	-77	-192, 37	-48	-159, 62
	3rd	26,582 / 102,329	26.0	0.95	0.91, 1.00	0.97	0.92, 1.01	-119	-235, -4	-97	-208, 13
	2nd	21,901 / 81,524	26.9	0.99	0.94, 1.04	0.99	0.94, 1.04	-36	-159, 86	-28	-145, 89
	1st: least segregated	15,449 / 56,731	27.2	<i>Referent</i>		<i>Referent</i>		<i>Referent</i>		<i>Referent</i>	

ADI, Area Deprivation Index; (a)RD, (adjusted) risk difference; (a)RR, (adjusted) risk ratio; CI, confidence interval; DI, Divergence Index; RT-PCR, reverse transcription polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; WA, Washington RRs estimated by generalized estimating equations (GEE) with a binomial distribution and log link function; RDs estimated by GEE with a Gaussian distribution and identity link function; all models used an exchangeable correlation structure, robust standard errors, and accounted for clustering by residential census block group

<sup>a</sup>All models adjusted for continuous age (years), sex assigned at birth (female, male), race and ethnicity (Hispanic or Latine, NH AIAN, NH Asian, NH Black, NH NHPI, NH White, not recorded), and health insurance status (private, public, uninsured)

<sup>b</sup>Difference in cumulative incidence per 10,000 persons over the 13-month study period

**Table 3.9.** Risk ratios and differences of ever testing positive for SARS-CoV-2, among patients who received RT-PCR testing, by census block group disadvantage and segregation (quintiles), University of Washington Medicine, 2020-2021 (sensitivity analysis #3)

Variable		Proportion ever tested positive		Crude RR		Adjusted RR <sup>a</sup>		Crude RD <sup>b</sup>		Adjusted RD <sup>a,b</sup>	
		n/N	%	RR	95% CI	aRR	95% CI	RD	95% CI	aRD	95% CI
ADI WA State rank: quintile	5th: most disadvantaged	212 / 2,653	8.0	2.23	1.90, 2.62	1.47	1.28, 1.70	435	315, 556	215	110, 320
	4th	421 / 5,484	7.7	2.19	1.92, 2.50	1.54	1.36, 1.74	421	326, 516	248	160, 335
	3rd	828 / 13,102	6.3	1.84	1.67, 2.02	1.37	1.26, 1.50	297	243, 351	154	104, 203
	2nd	1,539 / 28,345	5.4	1.54	1.42, 1.69	1.32	1.21, 1.43	193	150, 235	119	80, 158
	1st: least disadvantaged	2,334 / 68,414	3.4	<i>Referent</i>		<i>Referent</i>		<i>Referent</i>		<i>Referent</i>	
DI WA State rank: quintile	5th: most segregated	1,305 / 21,282	6.1	1.41	1.26, 1.59	1.19	1.07, 1.33	183	122, 245	96	42, 151
	4th	1,350 / 32,784	4.1	0.99	0.87, 1.11	1.02	0.91, 1.14	-6	-60, 47	6	-43, 56
	3rd	1,032 / 26,582	3.9	0.95	0.83, 1.07	0.98	0.87, 1.11	-25	-79, 30	-7	-58, 43
	2nd	961 / 21,901	4.4	1.04	0.92, 1.18	1.05	0.93, 1.18	17	-40, 74	15	-38, 69
	1st: least segregated	686 / 15,449	4.4	<i>Referent</i>		<i>Referent</i>		<i>Referent</i>		<i>Referent</i>	

ADI, Area Deprivation Index; (a)RD, (adjusted) risk difference; (a)RR, (adjusted) risk ratio; CI, confidence interval; DI, Divergence Index; RT-PCR, reverse transcription polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; WA, Washington RRs estimated by generalized estimating equations (GEE) with a binomial distribution and log link function; RDs estimated by GEE with a Gaussian distribution and identity link function; all models used an exchangeable correlation structure, robust standard errors, and accounted for clustering by residential census block group

<sup>a</sup>All models adjusted for continuous age (years), sex assigned at birth (female, male), race and ethnicity (Hispanic or Latine, NH AIAN, NH Asian, NH Black, NH NHPI, NH White, not recorded), and health insurance status (private, public, uninsured)

<sup>b</sup>Difference in cumulative incidence per 10,000 persons who received SARS-CoV-2 RT-PCR testing over the 13-month study period

## CHAPTER 5. Conclusions

In this dissertation, we leveraged electronic health record (EHR) data from the University of Washington Medicine (UWM) healthcare system and publicly-available neighborhood-level data from the Neighborhood Atlas<sup>103,104</sup> and the 2020 decennial census<sup>105</sup> to address limitations in sociodemographic and socioeconomic coronavirus disease 2019 (COVID-19) disparities research in three retrospective cohort studies of UWM patients. In our first study, we examined the association between any underlying health condition (UHC) and COVID-19-associated hospitalization, stratified by age group (Chapter 2). We found that patients of all ages with UHCs were at elevated risk of COVID-19-associated hospitalization. In addition, we found that the relative difference in risk of hospitalization between those with and without UHCs was higher in younger adults and especially middle-aged adults compared to older adults. In our second study, we examined the associations between health insurance status, race and ethnicity, and COVID-19-associated hospitalization, adjusting for any UHC, among patients aged 18-39 (Chapter 3). Though our results should be interpreted with caution given low precision, we found that uninsured or publicly-insured young adults and young adult people of color (POC) may be at higher risk of COVID-19-associated hospitalization compared to privately-insured and non-Hispanic (NH) White young adults, above and beyond the effect of any UHC, suggesting these differences in risk may be driven by forces other than UHCs, including social determinants of health (SDOH). In our third study, we examined the associations between census block group-level socioeconomic position (SEP) and racial residential segregation (RRS) and receiving severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) testing and testing positive, adjusting for individual-level characteristics (Chapter 4). We found that the likelihood of receiving SARS-CoV-2 testing was lower and the risk of testing positive was higher for patients living in neighborhoods of lower SEP and higher RRS, independent of individual-level characteristics including SEP and race and ethnicity.

Findings from these studies have several important implications for local public health action. First, our findings support the prevention of COVID-19 through vaccination (including boosters) and the prevention of progression to severe disease through anti-SARS-CoV-2 treatment in adults with UHCs in all age groups – including young and middle-aged adults under age 65 – as ongoing local public health priorities.<sup>121–123</sup> Furthermore, our findings underscore the importance of equitable access to vaccines and anti-SARS-CoV-2 therapy for young adults of color and young adults of lower SEP in general, not only for those with UHCs. As discussed above, COVID-19 messaging has focused largely on threats to older individuals, raising concerns that younger people might wrongly assume they are unlikely to contract SARS-CoV-2 and/or they are invulnerable to severe disease.<sup>84,85</sup> Our research strengthens knowledge of the demographic and clinical features of local young adults with COVID-19, and of racial, ethnic, and SEP disparities in COVID-19 outcomes among young adults, which supports targeted local morbidity and mortality prevention initiatives tailored to young adult populations, including culturally- and linguistically-appropriate risk communication. Finally, our findings support the use of neighborhood metrics representative of structural inequalities - such as the Area Deprivation Index (ADI)<sup>103,104</sup> and the divergence index (DI)<sup>163,164</sup> as a measure of RRS and structural racism<sup>75–77</sup> - by local public health departments to improve COVID-19 community risk assessment, surveillance systems, community partner engagement, and the equitable allocation of resources including testing and vaccines.

Our studies also highlight several considerations for future COVID-19 disparities research, and health disparities research in general. First, future studies should consider presenting both relative and absolute measures of excess risk, which - as our findings demonstrate - provide different perspectives and together offer a more complete understanding of a health determinant and the potential public health impact of related interventions.<sup>119</sup> Second, future EHR-based research might consider alternative approaches to operationalizing variables used in our

analyses. For example, future studies should consider stricter criteria for identifying UHC diagnoses,<sup>133</sup> as the use of a single relevant diagnosis code may be too broad. Our analyses used health insurance status as a measure of individual-level SEP, which is a valid approach commonly used in EHR-based research given the lack of SEP data recorded in EHR systems.<sup>169</sup> However, health insurance status may be an incomplete measure of individual-level SEP, and future studies using EHR data could consider including additional measures, such as property value based on geocoded billing address.<sup>98,180</sup> In addition, future EHR-based research of disparities in COVID-19 testing and infection should consider incorporating preferred language data,<sup>100,181</sup> which often are available in EHR systems. Third, additional research directly exploring the relationships between SDOH and COVID-19 outcomes would improve understanding of the upstream influences driving COVID-19 disparities.<sup>153</sup> Neighborhood disadvantage and segregation are two important upstream factors, for which small area-level metrics are readily available or calculated, including the ADI<sup>103,104</sup> and the DI.<sup>163,164</sup> Future studies using the DI as a measure of RRS should consider accounting for racial and ethnic composition and/or using granular segregation categories to identify people experiencing the greatest differences in COVID-19 outcomes, and may wish to consider a spatial version of the DI that accounts for local spatial autocorrelation.<sup>163,187,188</sup> Fourth, additional research investigating the joint effects of neighborhood-level factors<sup>70</sup> and the joint effects of neighborhood-level and individual-level characteristics<sup>100</sup> is needed to help hone COVID-19 interventions. Finally, future research should incorporate data from other medical centers in Washington State to improve generalizability to the population of the state as a whole.

In conclusion, COVID-19 has exacerbated existing health disparities across the US, including in Washington State. Although we are in a period of relaxed COVID-19 prevention strategies in the US,<sup>134</sup> it is imperative that we continue striving to understand sociodemographic and socioeconomic disparities in adverse COVID-19 outcomes at both the individual and

neighborhood level, so that we may develop targeted and effective community- and healthcare system-based policies and interventions, especially those that emphasize health equity and social justice.<sup>153</sup>

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